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**Examination of the Ginseng Utility
from the Perspective of the Nutrition Professional**

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THESIS ABSTRACT

Title: Examination of the Ginseng Utility from the Perspective of the Nutrition Professional

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Background: Many Natural Health Products (NHPs), such as ginseng, have been used to help with type 2 diabetes mellitus (T2DM) management. Although numerous studies have investigated the effect of ginseng on glycemic control in people living with T2DM, research exploring the direct relationship between ginseng consumption and satiety among T2DM population was almost non-existent. Also, research studies in the field of health professionals' knowledge and perception of NHPs in the past have mainly focused on Pharmacists' views, and a few studies investigated Dietitians' perspectives. There is limited published information available, however, on nutrition student's knowledge and perception of as well as interest in NHPs

Methods: The research completed for this thesis includes two studies. Study 1 examined the effect of Korean white ginseng (KWG) on satiety in people living with T2DM. It was a secondary data analysis study based on a double-blind, randomize-controlled, cross-over trial completed at St Michael's Hospital, Toronto, ON. The relationship between satiety and KWG was identified as a knowledge gap in terms of ginseng's clinical utility, intending to supplement "knowledge inquiry and knowledge synthesis" and its connection to "knowledge application" of Knowledge-to-Action cycle (KTA). Study 2 was to facilitate the investigation of nutrition students' knowledge, perception of and interest in NHPs by developing a face and content validated Natural Health Products Questionnaire (NHP-Q). Study 2 focused on knowledge dissemination ("knowledge application" of KTA).

Results / Conclusions: Twenty-five participants (n=25) completed Study 1. Study 1 did not show significant dose-dependent effect of KWG on either blood glucose concentration (p=0.8) or incremental appetite score (p=0.64), and correlation between blood glucose concentration and incremental appetite score was not observed (p=0.19). Future studies with increased dosage and/or treatment exposure time are needed. NHP-Q in Study 2 was revised twice based on the feedback from a sample composed of ten health professionals (n=10) and twenty-two nutrition students (n=22). Based on the feedback data from health professionals sample, 28 out of 32 total questions in NHP-Q were revised. Based on the feedback data from nutrition students sample, 18 out of 28 total questions in NHP-Q were revised. The revised NHP-Q has improved overall structure, specificity and objectivity.

(Note: Abstract for each individual study is provided before each study's chapter.)

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SHORT-HAND DEFINITIONS

DM: Diabetes Mellitus
T1DM: Type 1 Diabetes Mellitus
T2DM: Type 2 Diabetes Mellitus
GDM: Gestational Diabetes Mellitus
BMI: Body Mass Index
KWG: Korean White Ginseng
FPG: Fasting plasma glucose
2hPG: Two Hours Post-Prandial Plasma Glucose
1hPG: One Hour Post-Prandial Plasma Glucose
HbA1C: Hemoglobin A1C (percentage of glycated hemoglobin)
IR: Insulin Resistance
OGTT: Oral Glucose Tolerance Test
VAS: Visual Analog Scale
ROS: Reactive Oxygen Species
FFAs: Free Fatty Acids
NO: Nitric Oxide
UCP-2: Uncoupling-Protein-2
CCK: Cholecystokinin
GLP-1: Glucagon-like-peptides-1
PYY: Peptide YY
GI: Glycemic Index
NHPs: Natural Health Products
NHP-Q: Natural Health Products Questionnaire
CAMs: Complementary and Alternative Medications
TCL: Thin Layer Chromatography
GC: Gas Chromatography
HPLC: High-performance Liquid Chromatography
KG: Korean Ginseng
AG: American Ginseng
KWG: Korean White Ginseng
KRG: Korean Red Ginseng
GLUT4: Glucose Transport 4
KT: Knowledge Translation
SBP: Systolic Blood Pressure
DBP: Diastolic Blood Pressure
iAUC: Incremental Area Under the Curve
CPG: Clinical Practice Guideline
MSVU: Mount Saint Vincent University
St.FX: Saint Francis Xavier University

INTRODUCTION

During the past several decades, numerous research studies have been conducted by Scientists and healthcare professionals to explore the underlying etiology of type 2 diabetes mellitus (T2DM), seek effective interventions to help people prevent developing T2DM, as well as help people living with T2DM manage their symptoms and complications. Among them, seeking effective dietary interventions to help people living with T2DM improve their quality of life has become one focus of Dietitians and nutrition professionals.

At the same time, the functions of Natural Health Products (NHPs) in disease management have become an interesting topic for many health professionals. Some NHPs have been used to help with T2DM management. Dietitians might particularly be interested in how NHPs affect food consumption and energy intake among people living with T2DM. Currently, NHPs related courses are not offered in every university, although some nutrition programs, such as Applied Human Nutrition program (AHN) at Mount Saint Vincent University (MSVU), offer the course as an elective. Nutrition students might benefit from taking education in the field of NHPs while they are still in school completing Foundational Knowledge Specifications for Dietetics Education.

The following five questions, therefore, have become the center of this thesis:

- (1) What have been known regarding ginseng's (an example of NHPs) therapeutic effects in T2DM management?
- (2) What is the knowledge gap regarding ginseng's therapeutic effects that still needs to be explored, especially from nutritional perspective?
- (3) What do nutrition students know about NHPs and ginseng?
- (4) Do nutrition students perceive NHPs differently from other health professionals?
- (5) Are nutrition students interested in learning NHPs/ginseng related knowledge?

These five questions are addressed in the following three main chapters:

- (1) Literature Review: overview of T2DM, ginseng's therapeutic effect on T2DM management, and health professionals' perception of and attitude toward NHPs;
- (2) Study 1: exploring the knowledge gap between ginseng and T2DM from dietetic perspective;
- (3) Study 2: exploring effective ways of disseminating NHPs knowledge to target audience.

1. LITERATURE REVIEW

1.1 An Overview of Diabetes Mellitus

1.1.1 Diabetes Mellitus

Diabetes mellitus (DM) is a metabolic disorder often first characterized by the diagnosis of hyperglycemia. Hyperglycemia of DM maybe caused by insufficient insulin production (by beta-cells of the pancreas) or deficient target cell insulin response (i.e. insulin resistance) (1,2). Insulin is a hormone that is needed for glucose transport from the bloodstream into cells. Glucose is a source of energy for the body (1,2). DM can be categorized into three main types: Type 1, Type 2 and Gestational (1). In addition to the three main types, DM includes other “specific types”. Theses specific types are most commonly associated with other diseases (such as pancreatitis, cystic fibrosis, pancreatic trauma) or use of some medications (such as glucocorticoids) (1,3).

According to Diabetes Canada—Clinical Practice Guideline (CPG), the diagnosis of DM is based on several laboratory blood sample tests, as indicated in the following list:

- Fasting plasma glucose (FPG) ≥ 7.0 mmol/L (fasting: no calorie intake for at least 8 hours);
- Two hours post-prandial plasma glucose (2hPG) in a 75g oral glucose tolerance test (OGTT) ≥ 11.1 mmol/L;
- Random plasma glucose ≥ 11.1 mmol/L;
- Hemoglobin A1C (HbA1C) $\geq 6.5\%$ (in adults) or ≥ 11.1 mmol/L (HbA1C measures the amount of glycated hemoglobin when glucose is attached to hemoglobin). (1)

If results of any two or more different laboratory tests from the list above are above the diagnostic thresholds, the diagnosis of DM is confirmed (1). If only a single laboratory test result is in the DM range, a confirmatory laboratory test (preferable the same test) needs to be repeated on another day (1).

Type 1 diabetes mellitus (T1DM) results from cellular-mediated autoimmune destruction of beta-cells of the pancreas, which causes the pancreas unable to produce insulin, rendering absolute insulin deficiency (1-3). T1DM, therefore, is a result of insufficient insulin production by pancreatic beta-cells. Although it is commonly proposed that autoimmune destruction of beta-cells of the pancreas is caused by the combination of

multiple genetic predispositions and exposure to some environmental factors (such as Coxsackie virus and rubella), the exact etiology is still poorly understood due to the lapse between exposure to environmental factors and the development of T1DM (2). People living with T1DM have to rely on daily administration of exogenous insulin (usually through subcutaneous injection or infusion using either an insulin syringe, insulin pen, or insulin pump) combined with nutrition therapy and physical activity in order to maintain blood glucose concentrations within standardized range (FPG between 4.7-7.0 mmol/L and 2hPG 5.0-10.0mmol/L) and HbA1C values not above 7% (2,4).

Type 2 diabetes mellitus (T2DM) is a result of one or combination of both of the following issues: (1.) Insulin resistance (IR), in which cells fail to respond normally to insulin produced by the pancreas; (2.) pancreatic (insulin) secretory insufficiency (1-3). When cells of peripheral tissues develop IR and cannot respond to insulin, glucose cannot be taken up by cells, resulting in hyperglycemia. Acute/ chronic hyperglycemia increases insulin production to compensate (2). Chronically, pancreatic beta-cell failure may occur, resulting in insufficient or no insulin production (2). IR and diminishing pancreatic insulin production can develop over the course of many years (2). A cornerstone of T2DM management is medical nutrition therapy and physical activity; considered “first line” interventions (5,6). A goal T2DM management is to help the body increase insulin sensitivity and decrease insulin resistance through engaging in healthy lifestyle (5,6). As Dr. Grant often says,

“T2DM treatment is often thought of as using a three-pronged approach, with lifestyle interventions acting as the first line of defense” (7).

Oral antihyperglycemic medications (such as Acarbose, Metformin, Thiazolidinedione Linagliptin, etc.) and exogenous insulin administration can be added into the treatment if glycemic control cannot be achieved (2,8). The target ranges for glycemic control in people living with T2DM is the same as those living with T1DM (FPG between 4.7-7.0 mmol/L, 2hPG 5.0-10.0 mmol/L and HbA1C values not above 7% (2,4). T2DM accounts for 90% of the total DM prevalence (2).

Gestational diabetes mellitus (GDM) is a condition which results from glucose intolerance with onset or first recognition during pregnancy, especially during the second or third trimester (1,9). During the second or third trimesters of pregnancy, maternal and fetal demands for energy are significantly increased, which may in some cases cause inability of pancreatic beta-cells to meet the increased insulin needs, resulting in higher level of blood glucose concentration (2). GDM affects approximately 7% of pregnant women (2). Although most pregnant women with GDM will revert to normal glucose tolerance postpartum, the likelihood of developing GDM in subsequent pregnancy and T2DM later in life is increased after diagnosis of GDM, compared to women without pre-existing GDM (2). Diabetes Canada has recommended that all pregnant women between 24 and 28 weeks of gestation should be screened for GDM (9). For GDM, the treatment target ranges for glycemic control are FPG < 5.3 mmol/L, 1hPG < 7.8 mmol/L and 2hPG < 6.7 mmol/L (9). Nutrition interventions are commonly used to treat women with GDM, and insulin therapy is often added if nutrition interventions are unsuccessful at obtaining glycemic control within two weeks (9).

1.1.2 Symptoms and Complications of Untreated Hyperglycemia

Chronic hyperglycemia has been associated with secondary symptoms and complications, if untreated. Untreated acute / chronic hyperglycemia has been associated with blurred vision, polyuria (frequent urination), urinary tract infections (UTIs), polydipsia (frequent feeling of thirst due to excessive urinary loss of water and dehydration of organs), weight loss, polyphagia (excessive feeling of hunger), frequent or recurring infection, numbness or tingling in the hands and feet, and feeling of fatigue or lack of energy (10).

Specifically, polyuria and polydipsia are directly related to hyperosmolar status in blood, induced by high blood glucose concentration. This hyperosmolar status in blood will cause water to move from organs into the bloodstream and to be excreted along with glucose by the kidneys, which will render excessive urinary loss of water, followed by dehydration of organs and cell shrinking (11). As a result, glycosuria (glucose in urine) and polyuria occur, the body respond to this loss of water by promoting thirst as a compensation mechanism—polydipsia (11). Cell shrinking induced by this hyperosmolar

status in the blood can also affect nerve system and induce nervous system malfunction (2). At the same time, when glucose in the blood is not available for cells which are dependent on glucose for energy (such as brain cells), the body respond to it by promoting the feeling of hunger (polyphagia) as a compensation mechanism (2).

Untreated chronic hyperglycemia can also cause overproduction of reactive oxygen species (ROS) in the mitochondria at cellular level, a form of oxidative stress to the body (12). Chronic hyperglycemia can also increase the free fatty acids (FFAs) flux from adipocytes into endothelial cells of arteries (a thin layer of epithelial cells that lines the interior surface of arteries) (12). The overproduction of ROS leads to oxidation of LDL accumulated in arteries, which will eventually lead to a series of vascular consequences, such as blood flow abnormality, capillary occlusion, vascular occlusion and inflammation (12).

If these complications induced by chronic hyperglycemia are not treated properly, a series of related conditions can develop, such as retinopathy (which can potentially lead to blindness), nephropathy (which may lead to renal failure), neuropathy (which may lead to foot ulcer), as well as increased risk for developing cardiovascular, peripheral vascular, and cerebrovascular diseases (10).

1.1.3 Risk Factors for Developing Type 2 Diabetes Mellitus:

A list of risk factors for developing DM, especially T2DM, has been provided by Diabetes Canada. These risk factors include but are not limited to:

- being a member of high-risk populations (such as African, Aboriginal, Asian, South Asian descent, or Hispanic);
- ≥ 40 years of age;
- having a first-degree relative living with T2DM;
- having history of prediabetes;
- having history of GDM;
- use of specific drugs (such as glucocorticoids, atypical antipsychotics, anti-rejection drugs) that are associated with diabetes;

- vascular risk factors are present (such as high blood triglycerides, hypertension, overweight and obesity). (13)

These risk factors above suggest that DM, especially T2DM, is related to a combination of environmental, behavioral and genetic factors (14). Overweight and obesity, as highlighted in the list, are one of many risk factors for developing T2DM. According to the Health Canada BMI Nonogram, Body Mass Index (BMI) is commonly used to categorize underweight, normal weight, overweight and obesity (15). BMI is calculated by dividing body weight in kilograms by the square of the body weight in metres (kg/m^2). According to the nomogram, for adults aged over 18 years,

- Underweight: $\text{BMI} < 18.5 \text{ kg}/\text{m}^2$;
- Normal weight: $18.5 \leq \text{BMI} < 25.0 \text{ kg}/\text{m}^2$;
- Overweight: $25.0 \leq \text{BMI} < 30.0 \text{ kg}/\text{m}^2$;
- Obesity: $\text{BMI} \geq 30.0 \text{ kg}/\text{m}^2$. (15)

The prevalence of T2DM is 2.6 times higher among overweight and obese individuals than among those with normal weight (14). In fact, more than 75% of Canadian with T2DM have BMI above $29 \text{ kg}/\text{m}^2$, classified as overweight or obese (14).

According to World Health Organization (WHO), more than half a billion adults worldwide living with a BMI in the overweight/ obese category (16). Approximately 52% (18 million/ 35 million) of the total Canadian population lives with a BMI falling within the overweight/ obese category (highlighted above) (15,17). Obesity is listed as one of the risk factors for developing T2DM as mentioned above, many studies have explored the physiological mechanisms behind the contribution of obesity to the development of T2DM.

Adipose tissue and skeletal muscle are the two major sites for insulin-mediated energy metabolism. In people with normal weight and without T2DM, blood glucose concentration rises after meal consumption with corresponding insulin production by the pancreatic beta-cells to help the body enter the anabolic status. Insulin has eight main functions, including:

- (1) Promoting glucose uptake by cells;
- (2) Promoting glycogenesis (glycogen synthesis from glucose in the liver and muscles);

- (3) Inhibiting glycogenolysis (breaking down glycogen stored in liver and muscle into glucose);
- (4) Promoting triglycerides synthesis (stored in adipose tissues);
- (5) Inhibiting gluconeogenesis (the production of new glucose from amino acids and other non-carbohydrate precursors);
- (6) Inhibiting lipolysis (breaking down fat stored in the adipose tissues into free fatty acids);
- (7) Promoting amino acids uptake from the blood stream and muscle protein synthesis from amino acids;
- (8) Inhibiting muscle protein degradation into amino acids. (2)

As outlined in the list above, for people with no T2DM, excessive amounts of glucose absorbed from foods after meal will be converted to glycogen (stored in the liver and skeletal muscle) and triglyceride (stored in adipose tissue) as energy reserve (18). After meals, increased plasma insulin concentration will also suppress lipolysis to prevent an excessive amount of FFAs from being released from adipose tissue as an energy source (18). On the other hand, during fasted state when blood glucose concentration is low, insulin production by pancreas is inhibited while glucagon production by pancreatic alpha-cells is increased (2). Glucagon increases blood glucose concentration by stimulating the glycogenolysis (breakdown of stored glycogen) and gluconeogenesis (2). Glucagon also stimulates lipolysis, resulting in FFAs release from adipocytes as an additional energy source (2,18,19). Both glucagon and insulin, therefore, support energy metabolism (but in the opposing directions). They are complementary to each other in regulating hormonal/energy homeostasis.

When people develop obesity, however, they tend to have decreased insulin-mediated suppression of lipolysis (in other words, an increase in lipolysis) (18,20,21). This enhanced lipolysis results in increased circulating FFAs (18,20,21). Elevated circulating FFAs further lead to an accumulation of lipids in muscle cells. This accumulation of intramyocellular lipids can not only inhibit glucose uptake from bloodstream by blocking glucose transport/phosphorylation at cellular level but also suppress glycogen synthesis in the muscle (18,22-24). These inhibitory effects of plasma FFAs on glucose utilization lead to further enhanced IR, followed by a further decrease in insulin-mediated suppression of

lipolysis in adipose tissue, and more FFAs enter the circulation as a result (18). Since insulin serves to inhibit gluconeogenesis as mentioned above, this elevated plasma FFA concentration in circulation and the following development of IR can promote gluconeogenesis in the liver. This change can result in more endogenous glucose production and further increases in blood glucose concentration (18,25). Indeed, in poorly controlled T2DM, there is a 60% increase in the rate of gluconeogenesis (18,25). As a result of the increased rate, endogenous glucose production is 25% higher in patients with poorly controlled T2DM than in healthy individuals (18,25).

It has been suggested that in obesity, elevated plasma FFAs in circulation can also have “lipotoxic” effect on the pancreas and contribute to beta-cell dysfunction, rendering decreased insulin production and secretion from the pancreas (26-28). One proposed mechanism, based on *in vitro* studies, is elevated FFAs in the circulation might render triglyceride accumulation in the islet cells of the pancreas, and chronic triglyceride accumulation in the islet cells will increase the formation of nitric oxide (NO) (28,29). Excessive NO can induce pancreatic beta-cell apoptosis (cell death) (28,29). Elevated FFAs in the pancreas can also diminish insulin secretion from beta-cells by opening potassium channels and enhancing the expression of uncoupling-protein-2 (UCP-2) (29,30). This UCP-2 can inhibit adenosine triphosphate production necessary for insulin production (29,30).

Adipose tissue and adipocytes not only serve as energy reserve but also produce a wide range of hormones and cytokines (called adipocytokines), which are involved in glucose metabolism, lipid metabolism, coagulation, blood pressure, inflammation and feeding behavior (29). In people living with obesity, increased adipose tissue and adipocyte volume lead to significantly elevated cytokine production. Some adipocytokines (such as adiponectin, resistin, visfatin, omentin and vaspin) are involved in glucose metabolism. Excessive amounts of adipocytokine production in obesity are believed to be involved in the development of IR in T2DM, although the exact metabolic properties of them are not clear yet and are under current investigations (29). For example, some Scientists believe that one specific type of adipocytokines, called tumor necrosis factor-alpha (TNF- α), can inhibit the phosphorylation of insulin receptor, thus inhibiting insulin signaling (29). In people living with obesity, excessive TNF- α produced from adipocytes may also promote

apoptosis in pancreatic beta-cells by enhancing NO synthesis, as well as cause damage to insulin DNA (deoxyribonucleic acid) strand (31,32).

Obesity, therefore, can bring a series of metabolic abnormalities at cellular level, which can potentially lead to the development of T2DM.

1.1.4 The Prevalence, Incidence and Economic Cost of Diabetes Mellitus

In 2015, people diagnosed with DM worldwide had reached 415 million (33), and will continue to rise to above 450 million by 2030 (34). In Canada, currently 9.3% of the total population (approximately 3.4 million Canadians) are diagnosed with diabetes, which is an increase of over 200%, compared to two decades ago (17,33). Furthermore, there are more than 60,000 newly diagnosed T2DM each year in Canada (35). The prevalence of DM in Canada is projected to reach 5 million (12% of the total population) by 2025—a 44% of increase comparing to 2015 (33). Diabetes-related health expenditure in Canada reached \$6.3 billion in 2000 and continued to rise to \$17 billion in 2015 (33,36).

The prevalence of undiagnosed T2DM, however, is estimated to range from 2.8% to 10% of the general population, depending on the effectiveness of different health-care service systems in different countries and regions (37-39). On a global scale, among all diabetes cases in adults, approximately 45% of them are still undiagnosed (40). According to Diabetes Canada CPG, screening for T2DM using fasting plasma glucose (FPG) and/or glycated hemoglobin (A1C) should be performed at least once every three years in individuals who are above 40 years of age or in individuals who are at high risk of developing T2DM, as listed above (13). The purpose of this recommendation is to increase early stage detection of T2DM, and to use subsequent interventions to reduce morbidity and mortality (13).

1.2 Hunger and Satiety

As highlighted above, obesity is a risk factor for developing T2DM. Many Scientists have been interested in investigating the causes for energy over-consumption, especially among people with obesity. The cause of obesity is heterogeneous and can be very complex. An *Obesity System Influence Diagram* (commonly called obesity “loop-map”) has been used to explain the complexity of developing obesity (41). According to this loop-map,

factors that contribute to obesity can be categorized into 10 domains: (1.) media influence, (2.) social influence, (3.) psychology, (4.) economic situation, (5.) food production and consumption, (6.) physical activity, (7.) infrastructure, (8.) medical conditions, (9.) biological factors and, (10.) developmental factors (41). These 10 domains are inter-woven with one another, and each domain contains various sub-factors that are also inter-related (41). Many factors in this loop-map are linked to dysregulated perception of hunger and satiety cues as well as dysregulated appetite, thus inducing energy over-consumption (41). Some healthcare Scientists, therefore, are particularly interested in the perception and regulation of hunger and satiety by the body, and its contribution to obesity. At the same time, one symptom seen in many T2DM patients is called hyperphagia or polyphagia (constant feeling of hunger), as mentioned earlier. The relationship between obesity and T2DM has made Scientists wonder if there is any common etiology or mechanism related to hunger and satiety, which might be shared between obesity and T2DM. If this is true, perhaps Scientists and health professionals can target this common mechanism and find effective interventions to help people with higher weights and/or T2DM to control their energy intake and decrease chronic disease risk.

1.2.1 Satiety

Satiety refers to inhibition of further eating after an eating occasion has terminated (42,43). Satiation refers to a feeling of fullness during a meal that leads to termination or reduction of further food intake (43). Hunger is the opposite of satiation. Satiety (or satiation) and hunger can be impacted by various physiological and environmental factors (which will be discussed in *Section 1.2.2*).

Satiety is a subjective perception, and it is commonly quantified using one of the following two approaches: (1.) pictures or (2.) visual analog scales (VAS) (42,44). When satiety is measured by pictures in research studies, pictures of foods shown in standardized portion sizes are often used to obtain participants' perception of satiety. Participants usually need to indicate how many portions they want to eat if the foods in the pictures are served to them (44). Satiety scores are calculated based on the portions that participants indicate they want to eat (44). The advantage of using pictures to measure satiety is that it presents to participants more visually direct appetite-related signals, and it

might represent a better predictor of actual food intake during a subsequent meal (44). The disadvantage of this approach is that it takes more time and effort to select representative foods in the pictures and can be influenced by participants' cultural and religious background. For example, if the food in a picture is not considered as edible or considered as a taboo to a specific culture, it will not elicit an accurate response regarding hunger perception from a participant with this cultural background. Also, there might be some difficulties to optimize portion size in each picture to increase the accuracy, when using it as a measuring tool (44).

The second way of measuring satiety is VAS, recommended by Health Canada (43). The most commonly used VAS is a series of unstructured line (usually 100 to 150mm horizontal lines) on a page, with each line represented by a different question, such as "How hungry are you?", "How full are you?", "How strong is your desire to eat?" and "How much do you think you could eat?" (43). One end of the line is termed "None", "Not full at all" or "Not hungry at all", and the other end is termed "Extremely full," "As full as I ever feel," or "As hungry as I ever felt" or "A large amount" (42,43,45). By marking on the line (usually a dot, a cross or a circle), a subject divides the line into two portions, indicating his/her current level of hunger or satiety (43). The distance from the left end of the line to the mark is measured and VAS score is calculated based on proportion of the measured distance out of the length of the full line (43,46). VAS questions and response options are shown in figure 1.

How strong is your desire to eat?	
Very weak _____ Very strong	
How hungry do you feel?	
Not hungry at all _____ As hungry as I have ever felt	
How full do you feel?	
Not full at all _____ As full as I have ever felt	
How much do you think you could eat now?	
Nothing at all _____ A large amount	

Figure 1. Visual Analog Scale Sample Questions

Advantages to using a VAS to measure satiety include:

(1) Easy to use

VAS can be easily applied and interpreted by investigators and subjects. It does not require the participants to use their own descriptive terms, which can potentially be affected by their language and cultural background;

(2) Suitable for mathematical and statistical handling

Because VAS is presented in a standardized line format, they can undergo further mathematical conversion and statistical manipulations to compare with each other across different experimental conditions;

(3) High test-retest reliability (reproducibility)

Because studies on hunger and satiety often involve repeated measures over time on the same group of participants, high test-retest reliability means that most of the variance in VAS scores of a group of participants is inner-subject variation in response

to time or experimental conditions. This also means VAS is an ideal tool to be used in within-subject comparisons;

(4) High validity and predictability on feeding behavior

VAS score is an indicator of subjectively-rated hunger. Subjectively-rated hunger is a valid predictor of subsequent feeding behavior in terms of meal size and frequency, although not necessarily an predictor of actual energy intake. VAS score, therefore, is a valid reflection of a participant's motivation to eat;

(5) High sensitivity

It is highly sensitive to a number of experimental manipulations, including changes in physiological variables and alterations of diet composition (such the composition of carbohydrate, protein and fat in a meal). (42,43,47)

Limitations of VAS include that perceptual distances between the scales do not necessarily reflect the mathematical properties of true ratio scales (42). For example, on a VAS line of "How hungry are you?" with 100mm length in total, if a participant places a marking dot on the line which is 75mm from the left end for the first time and 25mm from the left end for the second time, it does not necessarily mean that the participant feels 50% more hungry in the first time than in the second time. The reason is that the abstract nature of a VAS score sometimes might prevent participants from associating their feeling of hunger and satiety with a straight line (44). Also, the score on VAS varies from person to person and from situation to situation, depending on each individual's physiological signal, psychological status, environmental factors and past experiences (47). Another concern regarding using VAS to measure hunger and satiety is that a score on VAS is subjectively expressed—it reflects an individual's motivation to eat and predicts approximate meal size and frequency, but does not necessarily reflect the actual energy intake (such as amount eaten) during the following meal (47). Several studies showed that degree of hunger rated by participants did not reliably predict their actual feeding behavior (measured by calories consumed) (48-51). It has been suggested that subjectively rated motivation to eat (such as VAS score) should not be treated as inevitable outcome of underlying physiological process (47). Scientists should not always expect high correlation between subjectively expressed hunger and satiety score and actual feeding behavior (47).

Despite these disadvantages and concerns above, VAS is still a commonly used research tools for measuring hunger and satiety due to the advantages mentioned above and it has been recommended by Health Canada as a main tool to measure satiety (43).

1.2.2 The Satiety Cascade Model: Factors Influencing Satiety

As mentioned earlier, satiety can be influenced by many factors. The *Satiety Cascade Model* provides a conceptual framework for understanding the multi-factor impact of satiety on food intake (52). According to this model, hunger and satiety can be influenced by the interaction of factors categorized into five fields, including:

- (1) Sensory factors (such as texture, smell, taste as well as the visual presentation of foods);
- (2) Cognitive factors (such as knowledge or awareness of how much food has been consumed as well as how much is supposed to be consumed based on pre-meal expectation);
- (3) Psychological factors (such as conditioning of certain favorite or un-favorite foods based on past rewards or reinforcements and anticipated pleasure);
- (4) Social and environmental factors (such as time of day, environmental cues or triggers, social situations, peer and family influences, and cultural and religious background);
- (5) Physiological and metabolic factors (such as blood glucose and insulin levels, and gastrointestinal peptides and hormones). (52)

According to this model, sensory factors such as texture, flavor and palatability of foods can have significant impact on the feeling of hunger and satiety. Some Scientists tried to manipulate the sensory cues in order to perceive their impact on satiety. A study showed that participants reported a higher degree of hunger two hours after consuming a meal with highly preferred flavor than after a meal with less preferred flavor (53). Indeed, people tend to feel hungrier and eat more when foods with their preferred flavor are provided. Also, people tend to judge energy density of food based on texture and flavor cues. In a more recent study, 12 participants were assigned to one of four food conditions: a 150g or 300g serving portion with or without flavor cues indicating high or low energy density (by altering sweetness and creaminess without altering actual total calories) (54).

After consuming the food, the participants were asked to rate their hunger on a VAS scale. The results showed that their ratings on hunger increased significantly even after consuming the larger portion (300g) but with flavor cues indicating low energy density (with low sweetness and creaminess) (54). These results have indicated that perception of hunger and satiety can be learned based on texture and flavor cues.

Visual cues, such as perceived volume or portion size of food, can also affect hunger and satiety ratings. In a study conducted by Rolls et al. (1998), 20 participants were given a 300, 450, or 600 ml milk drink as a preload 30 minutes before a lunch meal (55). The three milk drink choices had the same total energy content but different energy density via adding water and thickeners to modify the volume while maintaining the same sensory characteristics (55). The results showed that the visual perception of the volume of the food played an important role. The participants who had a 600ml milk drink preload reported a significantly lower degree of hunger during the following lunch time than the participants who had a 300ml milk drink preload (55). The participants who had a 600ml milk drink preload might have believed that they already had a large portion of food intake and were “supposed” to feel less hungry during the following lunch, compared to participants who had a 300ml milk drink preload (55). Visual cues of food, in this case, might have influenced participants’ cognitive status, thus their subsequent eating behavior. These results have indicated that perception of hunger and satiety can be induced by foods’ visual cues (such as volume) even though they can be deceiving sometime.

Cognitive factors along with other psychological factors, therefore, can play an important role in human eating behavior. People’s anticipation of food availability and accessibility, for example, can also significantly influence their feeling of hunger. In a study conducted by de Graaf et al. (1999), the participants were first presented with tomato soup as preload before the test meal, but with different time schedules (56). Results showed that the participants consumed 20% more soup when they knew that they had to wait 90 minutes for the following test meal, compared to the participants who only had to wait 15 minutes for the test meal (56). People’s knowledge of future food accessibility and availability, therefore, can influence their subsequent eating behavior.

Social influence (such as peer influence), as one aspect of psychological factors, can also have significant impact on satiety. In a study investigating the modeling effect of food

intake in young women, the participants consumed more foods when they were exposed to peers (confederates) with high intake of foods, compared to the participants exposed to peers with low intake of foods (57). A focus group study was conducted in 2008 based on 31 participants, investigating possible factors that could potentially affect hunger and fullness based on the participants' experiences and opinions (58). Besides physical and metabolic symptoms indicating hunger, other psychological factors that affected the feeling of hunger or fullness were also listed by the participants, which included "boredom," "thoughts towards foods," "desire to chew something," "happiness or joy," "feeling of satisfaction," "regret or feeling of guilty for eating certain foods," "planning to skip the next meal in order to lose weight" (58).

Physiological factors, also have significant impact on hunger and satiety, and extensive research studies in this field have been conducted. Various theories, models and hypotheses have been proposed to explain how hunger and satiety are perceived and regulated by the body, either from the perspective of the digestive system, the brain reward circuitry system, or from blood glucose and hormonal feedback system.

The Satiety Cascade Model models the complexity of human eating behaviors. Although these aforementioned fields can all contribute to the perception of hunger and satiety, it is difficult to separate any one single factor without considering the influences from other factors. In the following sections, the focus will be on the discussion of physiological factors that can affect hunger and satiety, the association of these factors with T2DM, as well as their indications on nutritional interventions.

1.2.3 Glucostatic Theory

When talking about hunger and satiety, one of the well-recognized theories is the classic Glucostatic Theory—a theory commonly used to explain hunger and satiety, proposed by Jean Mayer in 1953 (59). According to this theory, blood glucose concentration is the main signal for satiety and hunger, with low blood glucose levels (usually during fasting) triggering the feeling of hunger and the onset of feeding behavior, and high postprandial blood glucose levels (usually after a meal) triggering satiety (59).

This theory was supported by several clinical trials. In a randomized controlled trial, children aged two to five years (n=24) were given a 90kcal sucrose (a disaccharide

composed of glucose and fructose) drink as preload, and then randomly assigned to one of the three conditions—they were provided with a subsequent meal with different time schedules (0, 30, or 60 minutes after the sucrose preload). Their calorie intake during the subsequent meal was measured (60). The results of this study showed that compared to the other two conditions, calorie intake during the subsequent meal scheduled 30 minutes after the sucrose preload was significantly suppressed, with 100% calorie compensation (60). This study demonstrated that raising blood glucose concentration before meal time can suppress people's appetite during the subsequent meal, rendering less food consumption. Some other Scientists suggested that blood glucose concentration can actually act as an inter-cue for meal initiation. When 18 healthy subjects were put in a condition of absence of time-cue and their blood glucose concentrations were continuously monitored, transient decline in blood glucose concentration was significantly related to an increase in hunger rating and following requests for a meal (61).

According to Mayer's proposed theory, when peripheral arterio-venous difference in blood glucose becomes negligible, the body will enter "metabolic hypoglycemia" status because glucose can no longer enter "metabolizing cells", which can further lead to decreased glucose utilization in critical brain regions and subsequent perception of hunger (62). According to Glucostatic Theory, this "metabolic hypoglycemia" status, therefore, is the fundamental reason for the perception of hunger and subsequent feeding behavior (62). Some Scientists also believe that blood glucose concentration can have effect on long-term energy balance and weight control, especially for people with obesity (62). In a randomized controlled placebo clinical trial, 44 participants with obesity participated in a 15-week weight-loss program and they were assigned to either a drug therapy group or a placebo group combined with energy intake restriction. At the end of the 15 weeks, participants were given an Oral Glucose Tolerance Test (OGTT) along with weight measurement (63). The study results showed that weight loss was significantly correlated with the drop of postprandial blood glucose concentration below fasting values at the end of the OGTT (at 120 minutes of the OGTT)—participants who had significant weight loss at the end of 15-week period showed significant drop of postprandial blood glucose concentration below the fasting values at the end of the OGTT, compared to participants who did not have significant weight loss (63). More interestingly, during the follow-up visit

81 weeks after the intervention, participants who had lower postprandial blood glucose concentrations at the end of the OGTT also showed significantly higher amount of weight regain 81 weeks later (63). It was speculated that low blood glucose concentration in this study triggered enhanced hunger perception and subsequent increased energy intake, which led the subsequent weight regain over the period of 81 weeks (63).

This speculation was further confirmed by another prospective study conducted in Quebec, in which 259 participants between age of 20 and 65 years were recruited (63). An OGTT was performed on each participant and postprandial blood glucose concentration were recorded at 120 minutes of the OGTT. These participants were followed prospectively for six years and their body weights were monitored throughout the six-year period (63). The results showed that there was significant inverse correlation between blood glucose concentrations at 120 minutes of OGTT and weight gain over time ($r=-0.42$ $P<0.01$), which means the lower the blood glucose concentration at 120 minutes of OGTT, the more weight gain throughout the six-year follow-up period (63).

Some Scientists believe that rapid weight loss in obese individuals beyond a certain point (approximately 10% of the initial weight) can disturb the plasma glucose stability and induce a metabolic hypoglycemia status (63). This will trigger a counter-regulatory hormonal response of the body to protect against hypoglycemia (63). Indeed, hyperglucagonemia has been observed in obese individuals who are in the status of weight-reduction (64). As discussed in *Section 1.1.3*, increased glucagon in the blood reflects the need of the body for increased BG level to prevent further hypoglycemia. This disrupted glucose homeostasis induced by rapid weight loss will trigger the brain to send signals (such as hunger perception) favoring weight regain, which can help the body restore the original glucose homeostasis (62).

Glucostatic Theory has been challenged because of inconsistent research results. For example, although some research studies did show the correlations between arterio-venous differences in blood glucose concentration and hunger ratings and subsequent energy intake, some other studies failed to observe such correlations (65-67). Furthermore, if low blood glucose concentration is associated with hunger and meal initiation, and if high blood glucose concentration is associated with satiety and meal termination, exogenous infusion of glucose should induce satiety and suppress hunger

according to the theory. Several studies using exogenous infusion of glucose, however, failed to report such correlations (66,68,69). Some Scientists, therefore, have proposed that intracellular glucose concentration (or cellular glucose utilization) rather than absolute blood glucose concentration plays a key role in hunger perception and meal initiation (62). Many Scientists have been exploring various other theories, models or hypothesis that can help explain the mechanisms behind the perception of hunger and satiety, as being discussed in the following sections.

1.2.4 The Brain, Hormones, and Satiety

Research has shown us that a number of hormones regulate energy metabolism, not just insulin and glucagon. Some of them can trigger hunger and satiety in the short term and regulate immediate energy intake, some others are involved in hunger and satiety perception in the long-term and play an important role in weight control. This section will explore some of these hormones under two headings: (1.) Short-Term Satiety and Hunger Hormones and (2.) Long-Term Satiety Hormones.

1.2.4.1 Short-Term Satiety and Hunger Hormones

The presence of food/nutrients in the stomach and small intestine (especially macronutrients such as carbohydrates, fats and proteins) triggers release of several peptide hormones, which are responsible for or partially involved in satiety perception within a period of hours (70). Three of them are frequently highlighted in literature:

- (1) Cholecystokinin (CCK)
- (2) Glucagon-like-peptides-1 (GLP-1)
- (3) Peptide YY (PYY)

CCK is a peptide hormone mainly released from enteroendocrine cells in the duodenum (71). It helps the body digest fat and protein content in the foods by stimulating pancreatic secretion and gallbladder contraction, as well as by inhibiting gastric emptying (71). Fat and protein consumption can, therefore, produce potent satiety through stimulating the release of CCK from the gastrointestinal track (72). Peripheral administration of CCK has been noted to inhibit food intake in most mammalian species, including monkeys and humans (71). CCK receptors are widely distributed in the brain and

afferent vagal nerves, and in the stomach (particularly in the pyloric area) (71). When food intake triggers the release of CCK from the duodenum, CCK will activate the CCK receptors on the duodenal afferent vagal nerves as well as in the stomach. The duodenal afferent vagal nerves will further pass the neural signal to the brain to induce the satiety signal. At the same time, CCK can inhibit gastric emptying by stimulating the contraction of the pyloric sphincter, thus suppressing further food intake (71,73,74).

Food consumption, especially carbohydrates and protein, can also stimulate the release of another gastrointestinal peptide hormone: GLP-1. GLP-1 is produced by the L-cells of the small intestine (75-77). GLP-1 is believed to play an important role in inhibiting gastric mobility and secretion in the presence of macro-nutrients (such as carbohydrates and proteins) in the ileal lumen, which is called “ileal break mechanism” (78,79). Inhibition of gastric emptying, therefore, might be one mechanism that GLP-1 promotes satiety and limits further food intake. Furthermore, GLP-1 neural receptors also exist in the hypothalamic and extrahypothalamic areas of the brain, which implies that elevated circulating GLP-1 after meal can induce satiety signal from the brain through neural-receptor pathway (80). The satiety inducing effect of GLP-1 has been demonstrated in a placebo-controlled, randomized, blinded, crossover clinical trial, in which 20 young, healthy, normal-weight men were given GLP-1 infusion after an energy-fixed breakfast. A visual analogue scale (VAS) was used to assess their appetite sensations throughout the experiment. The results of the study showed that GLP-1 administration enhanced participants' satiety, as evidenced by significantly reduced appetite VAS scores along with reduced energy intake during the lunch, compared to the placebo-control group (78).

The exact effect of GLP-1 on satiety is still under investigation because it is usually released along with other gastrointestinal hormones in response to meal consumption, making it difficult to isolate its influence on food intake (78). PYY, for example, is another peripheral hormone released synchronously with GLP-1 from the L-cells of the distal small intestine in response to meal ingestion. It is believed to have additive inhibitory effects on gastric acid secretion and mobility (81). When healthy participants were intravenously infused with normal postprandial concentration of PYY, their appetite ratings significantly reduced by 33% over the next 24 hours (82). A similar effect was observed in another

human trial, in which intravenous infusion of a single dose of PYY reduced participants' subsequent calorie intake by more than 30% (83).

Exogenous CCK, GLP-1 or PYY administration used in the clinical trials above, however, might not have the same effect of postprandial endogenous CCK, GLP-1 or PYY. Hormones released from the gastrointestinal track in response to meal consumption can interact with each other to achieve synergistic or antagonistic effect (81). CCK and GLP-1, for example, both have receptors in the stomach and small intestine, and endogenous CCK, GLP-1 can directly act upon on these receptors after release, affecting gastric-intestinal mobility (71,78,79). Whereas, intravenous administration of exogenous CCK, GLP-1 or PYY bypasses this process in the digestive track and might only have partial effect of what endogenous CCK, GLP-1 or PYY can achieve. Nevertheless, CCK, GLP-1 or PYY have been indicated by literature as the hormones that can help the body regulate appetite and energy intake in the short term (during and after meal).

In contrast to the satiety-inducing hormones CCK, GLP-1 and PYY, ghrelin (a 28-amino acid peptide-hormone) is released from the oxyntic gland of the stomach and can promote appetite and suppress satiety, especially when the stomach is empty (84,85). Ghrelin, released during fasting or period of low dietary intake, is sometimes called the "hunger hormone". Interestingly, the receptors for ghrelin (ghrelin/growth hormone secretagogue receptor [GHSR]) are also located in the hypothalamus of the brain (84,85). Intracerebral-ventricular injection of ghrelin on rodents significantly increased subsequent food intake in a dose-dependent manner (84). This "hunger stimulating" effect of ghrelin is also demonstrated in a randomized double-blind cross-over human trial, in which intravenous infusion of ghrelin significantly increased subjects' energy consumption during a subsequent buffet meal, compared to the placebo-control group with only saline infusion (86). Human trials have shown that there are indeed pre-meal increases of and post-meal decreases of circulating ghrelin levels (87,88).

Based on the discussion above, meal consumption can induce gastric distention, and gastric distention can suppress ghrelin produced and released from the stomach (85). On the other hand, ghrelin production is stimulated when the stomach is empty during fasting (85). Based on this logic, if gastric distention induced by food consumption can suppress ghrelin production, then it might be possible that satiety can be regulated by food texture

modification such as increasing bulk volume of food without adding extra calories. This might be an effective way of helping people with obesity and/or T2DM control their energy intake. In fact, modifying the Glycemic Index (GI) of food by adjusting fiber content can actually have an impact on satiety, which will be discussed in later sections.

1.2.4.2 Long-Term Satiety Hormones

Leptin and insulin are often highlighted due to their significant effect on energy-intake regulation over the long-term and roles in energy homeostasis. Leptin and insulin are produced by adipose tissue and pancreatic beta-cell (as discussed in the earlier sections) respectively. These hormones also have neural receptors in the brain (e.g. hypothalamus). Together, they participate in the regulation of energy consumption through neuro-hormonal feedback system (89,90).

Leptin is produced by adipocytes and currently believed to be one of the main circulating factors that help the brain assess satiety and prevent excessive energy intake (89,90). It is, therefore, sometimes called the “satiety hormone”. After leptin is produced from adipocytes, it enters blood circulation and reaches the hypothalamus in the brain where the leptin receptors are located. Once leptin enters the hypothalamus of the brain, it activates catabolic neural circuits that increase energy expenditure and suppress food intake, and it inhibits the anabolic circuits that decrease energy expenditure and stimulate eating (90). Leptin production from adipocytes and the correspondent concentration in the blood are in proportion to body fat content. This means that the more adipose tissue an individual has (such as during weight gain), the more leptin the adipocytes will produce and release, which gives stronger signal to the brain to reduce food intake (90). This negative feedback system helps the body regulate body weight and maintain homeostasis.

The satiety effect of leptin can also be enhanced by the presence of CCK. Studies based on animal models demonstrated that administrating leptin and CCK combination produced a greater feeding inhibitory effect over the long term and resulted in greater body weight loss than did CCK or leptin alone (71,91,92). Co-injection of leptin and CCK also resulted in 60% more expression of c-Fos positive cells (a type of hypothalamic cell involved in energy metabolism) in the hypothalamus than injection of leptin or CCK alone

(71,91). These results suggest that leptin and CCK work in a synergistic way to help the body regulate energy intake and metabolism.

Interestingly, people with obesity tend to have elevated circulating leptin in the blood, but this does not seem to help them suppress their appetite or control food intake (89,90). Some Scientists have suggested that as people become more obese, they start to develop leptin resistance, and the neural circuits in the brain start to lose sensitivity towards leptin, hence losing the ability to induce satiety perception (89,90). One proposed possibility is that the resistance of the leptin receptors on endothelial cells of the brain prevents circulating leptin from transporting across endothelial cells of the blood-brain barrier and entering the interstitial fluid of the brain (93). As a result, the adipocytes start to produce more leptin into circulation in order to compensate for leptin resistance (89,90). As obesity further develops, this elevated circulating leptin eventually becomes insufficient to compensate leptin resistance. The result is hyperphagia (constant feeling of hunger) (89,90).

Parallel to leptin, insulin also has a similar effect on the hypothalamic area of the brain (90). The earlier sections have discussed the role of insulin in helping the body with energy metabolism, especially after meal consumption. In addition, insulin is also a hormone which can trigger the brain to signal satiety. After meal, insulin is produced and released from the pancreas into the blood stream and circulated to the brain, where it can interact with certain neuron receptors and further signal satiety (94-96). For example, when insulin reaches the brain through blood circulation, it can reduce fusiform gyrus (located in hypothalamus) activity, which is a brain area that displays reduced activity during satiation but increased activity when experiencing hunger or craving for foods (97-99). Also, insulin receptors in the brain exist in dopaminergic neurons in the ventral tegmental area and substantia nigra (also located in the hypothalamus), and insulin can potentially decrease the rewarding quality from eating by suppressing dopaminergic signaling (100-103). Insulin and leptin, therefore, might function in a synergistic way to help the body maintain energy homeostasis (90).

Similar to leptin resistance in obesity as mentioned above, in the case of insulin resistance (IR) in people living with obesity and/or T2DM, the phosphorylation of insulin-receptor substrate (IRS) in brain neurons cannot be activated. These neurons, therefore,

are unable to respond to the signal transduction from insulin (90). When increased insulin delivery to the hypothalamus fails to stimulate signal transduction via insulin receptors, impaired satiety perception follows (90).

These hormonal mechanisms related to the perception of hunger and satiety cues has raised an implication: if leptin/insulin resistance in the brain impairs satiety perception and induce hyperphagia, it might be possible that people with obesity and/or T2DM can benefit from interventions that target increasing leptin or insulin sensitivity, hence improving their satiety perception. Furthermore, if research studies can prove that a specific nutritional supplement or herbal product (such as ginseng to be discussed in later sections) can help improve insulin sensitivity in people with obesity and/or T2DM, it is beneficial to know if it will also help them regulate energy intake by enhancing satiety perception. Future research studies are needed in this field.

Based on the discussions above, satiety-regulating hormones released either from adipose tissue, the pancreas, or the gastrointestinal tract interacts with one other (either synergistically or antagonistically) and participate in food intake regulation and energy metabolism. The brain has various types of receptors for these hormones, receives biochemical signals from multiple sources, and functions as a “master commander” to combine bio-information and send out feedback to the body. As mentioned in the *Section 1.2.1*, however, subjectively rated motivation to eat (such as VAS score) should not be treated as inevitable outcome of underlying physiological process (47). These hormonal effects might only represent one of many underlying physiological process that can potentially but not necessarily bring out subjective feeling of hunger and satiation. Nevertheless, Glucostatic Theory and the neuro-hormonal aspect of hunger and satiety have raised some implications from dietetic perspective, such as the effect of macronutrients on satiety.

1.2.5 Macronutrients and Satiety

A balanced meal usually contains a combination of carbohydrates, proteins and fats. Carbohydrates consumption during a meal can raise blood glucose concentration. Carbohydrates (including polysaccharides, oligosaccharide and disaccharides in the form of starch and sugar) in foods are broken down in the gastrointestinal track into the smallest and absorbable units—monosaccharides (such as glucose, fructose and galactose) and

enter the blood stream (104). Fructose and galactose are further metabolized by the liver, and glucose is the main circulating unit. Ingesting carbohydrates, therefore, will raise blood glucose concentration. Protein consumption can also indirectly contribute to elevated blood glucose concentration under specific situations. In the small intestine, proteins undergo a bio-process called hydrolysis and are broken down into the smallest and absorbable units—amino acids by proteolytic enzymes (called proteases) produced by the pancreas. Amino acids are then absorbed into circulation undergo further metabolism (such as being used as building blocks for growth, replacement and repair) (105). When ingesting excessive amount of protein, however, the excessive amount of amino acids in the circulation can be used as metabolic fuel or be converted to glucose and further glycogen storage by the process of gluconeogenesis in the liver (106). In healthy individuals, this gluconeogenesis process is very slow and has minimal effect on blood glucose concentration. In people living with T2DM, however, due to enhanced gluconeogenesis by the liver as mentioned in the earlier section, protein can be converted to glucose over a period of hours and contribute to elevated blood glucose concentration eventually (106).

Carbohydrates consumption results in a postprandial increase in blood glucose concentration. Much of what is known on the mechanisms/ metabolism of related to carbohydrate metabolism can be, in part, attributed to the Glycemic Index (GI). This concept, and associated methodology were proposed as a method to categorize carbohydrate foods according to postprandial glycaemic effect (107-112). Food and drink with higher GI produce a quicker and higher rise and fall in postprandial blood glucose concentration, compared to foods with lower GI, producing a more gradual and flattened rise and fall in postprandial blood glucose concentration (112,113). According to Glucostatic Theory, if satiety is inversely correlated to blood glucose concentration, it can be predicted that quick and sharp fluctuation of post-prandial glycemic response brought by consuming high GI foods should bring quick suppression of appetite when blood glucose concentration surges to the peak, followed by quick return of hunger once the blood glucose concentration falls to the bottom again. On the other hand, foods with lower GI, which produce more gradual and flattened postprandial glycemic response, should induce delayed and more sustained satiety over a prolonged period, comparing to foods with high GI.

In a crossover study, when 12 obese teenage boys were randomly assigned to three conditions: consuming breakfast followed by lunch with either (1.) low GI, (2.) medium GI or (3.) high GI (the breakfast provided was identical to the lunch on that day) (114). All meals provided had equal total calories across different conditions. A hunger VAS rating and blood sample were obtained every 30 minutes for 5 hours from the start of breakfast. *Ad libitum* food intake was recorded within the 5-hour period after lunch (114). The results showed that ratings of hunger were greater after the high-GI breakfast at all time points in the morning, compared to the low-GI and medium-GI breakfast. Also, voluntary post-lunch energy intake in the high-GI lunch condition was 53% higher than the medium-GI lunch condition, and 84% higher than the low-GI lunch condition (114). Furthermore, the mean blood glucose concentration nadir before lunch time in the high-GI meal condition was significantly lower than in the medium- and low-GI meal conditions, despite the fact that the mean glycemic area under the curve (AUC) for the high-GI meal condition was greater than that of the medium- and low-GI meal conditions (114). Another randomized crossover study tried to minimize the confounding factor by matching test meals with participants' habitual meals in a more natural setting. In this study, 37 children aged 9 to 12 years were randomly assigned to one of the three types of experimental breakfast condition (with identical total energy) for three days (high-GI, low-GI, low-GI with 10% added sucrose) (115). Lunch was a buffet style meal served in the school hall where the participants could eat with other schoolchildren together. Participants' food intake and plate waste during lunch time were unobtrusively observed and recorded (115). The results showed that participants who had high-GI breakfast had greater hunger ratings before lunch time, compared to other two conditions. Furthermore, there was a significant inverse correlation between pre-lunch satiety scores and subsequent food intake (115). These results from both studies above have suggested that GI of foods can not only have impact on postprandial glycemic response, but also influence appetite and energy intake during the next few hours, supporting Glucostatic Theory.

Some other mechanisms are also used to explain the impact of GI of foods on satiety. One proposed mechanism is that low GI foods can promote satiety by delaying gastric emptying. In a cross-over study conducted on six healthy male participants, when pectin supplementation was added to each meal (rendering decreased GI), a significant

prolongation of gastric emptying was observed (by using radioisotope), compared to either solid meal or liquid meal on the previous days (116). As discussed in *Section 1.2.4.1*, ghrelin (a “hunger hormone” produced from oxyntic gland of the stomach) is released into the circulation when the stomach is empty and inhibited when food is present in the stomach (84,85). Prolonged gastric emptying, therefore, can lead to sustained inhibition of ghrelin production, thus contributing to delayed hunger perception.

Furthermore, *Section 1.2.4* has discussed that carbohydrates and protein consumption can induce the production of GLP-1 and PYY, and fat and protein consumption can stimulate the release of CCK from the gastrointestinal tract, all of which can induce satiation by acting on neural-hormonal receptors in the hypothalamic area of the brain, along with inhibiting gastric mobility. Also based on the discussions in *Section 1.2.4*, we have already known that increased blood glucose due to carbohydrates ingestion will trigger insulin release from the pancreas, and insulin is a hormone which not only helps to lower postprandial blood glucose level but also has neural-receptors in the hypothalamus and can induce satiety through the neural-hormonal feedback from the brain. Although it is true that a high blood glucose concentration is usually observed after meal consumption (which is typically accompanied by satiety perception and inhibition of further eating), it can be argued that high postprandial blood glucose concentration might simply be a physiological status of energy absorption from foods consumed but not the actual cause for satiety. GLP-1, PYY, CCK and insulin production related to micronutrients ingestion during meal time might be the true cause behind it.

Based on the above discussions, since a balanced meal usually contains a combination of carbohydrates, proteins and fats, carbohydrates components of the meal and the related GI can be related to satiety by using Glucostatic Theory, and protein and fat components can also be related to satiety by using the neuro-hormonal feedback mechanisms. Glucostatic Theory, therefore, should be combined with neuro-hormonal feedback mechanisms to give us a better overall picture of the factors that can have impact on satiety. Future research studies, therefore, might help Scientists unveil more underlying mechanisms that can better explain hunger and satiety related to food consumption.

1.3 Natural Health Products and Satiety

1.3.1 An Overview of Natural Health Products in Canada

According to the definition provided by Food and Drug Act—Natural Health Products (NHPs) Regulation in Canada, NHPs are defined as:

“One or a combination of substances that is manufactured, sold or represented for use in:

(a) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state or its symptoms in humans;

(b) restoring or correcting organic functions in humans;

(c) modifying organic functions in humans, such as modifying those functions in a manner that maintains or promotes health” (117).

NHPs include vitamin and mineral supplements, herbal medicines, homeopathic medicines, traditional medicines, probiotics, and other products such as essential fatty acids and amino acids supplements (118). NHPs can be products that are ground, powdered or pressed from plant materials, or components that are extracted or purified from plants, animals, or micro-organisms (119). They come in a variety of forms such as capsules, solutions, tablets, drops, powder, creams, ointments and tinctures (119). Different countries might use different nomenclature. In the United States of America (USA), for example, nutrition supplements, herbal medicines, homeopathic medicines and traditional medicines are categorized as Complementary and Alternatives Therapies or Complementary and Alternative Medications (CAMs), instead of NHPs (120). CAMs, therefore, is the common name used in American research studies in this field. Falling under the umbrella of NHPs, there is a subclass called nutraceuticals. These refer to products isolated, purified or concentrated from foods that are usually sold in medicinal form (in pill, capsule, or liquid form) and can potentially provide physiological benefits or protection against chronic disease (121).

Another close relative to NHPs is functional food. Functional foods are similar in appearance to conventional foods and can be consumed as part of a usual diet, but they have additional physiological benefits beyond basic nutritional functions and/or can help reduce the risk of developing chronic disease (119,121). Functional foods can include foods

fortified with vitamins and minerals, foods with an addition of bioactive ingredients, and foods that are enhanced with bioactive components through genetic modification, plant breeding, special processing, or special livestock feeding techniques (119). In other words, NHPs can be added into foods (such as fortification) to convert them into functional foods.

NHPs and functional foods are regulated under different regulation bodies in Canada. The licensing provision and commercial sale of NHPs is regulated by *Natural Health Products Regulations*, whereas functional foods are regulated like other foods and are subject to health claim on foods (122). The administration of *Natural Health Products Regulations* is conducted by Health Canada's *Natural Health Products Program* (122). One important function of *Natural Health Products Program* is to make sure that health claims associated with NHPs are evidenced-based and products are safe and effective (122). The evidence used to support the health claims should come from clinical trial data, academic journals, published studies and pharmacopoeias (122,123). Health claims associated with NHPs must be assessed and approved by Health Canada (122,123). Also, companies who produce NHPs must list “medicinal ingredients, source material, dosage, potency, non-medicinal ingredients, and recommended use(s)” on the product label (122,123).

According to a NHPs tracking survey conducted by Health Canada (2010) based on 2001 participants across Canada, approximately 73% (1461/2001) of respondents reported using NHPs at least once within the past year, and 32% (640/2001) of them reported using NHPs daily (124). Furthermore, 53% (1061/2001) of the respondents reported using vitamins and minerals, 18% (360/2001) reported using essential fatty acids, and 11% (220/2001) reported using herbal tea (124). When respondents were asked about the reasons or purposes of using NHPs: 85% (1701/2001) of them agreed with the statement that NHPs can be used to maintain and promote health, and 76% (1521/2001) of them agreed with the statement that NHPs can strengthen the immune system and prevent illness (124). In addition, 71% (1421/2001) of respondents believed that NHPs were better for them than drugs, despite the fact that 15% (300/2001) of them reported experiencing side effects from using NHPs (124).

Given the apparent interest Canadian have in NHPs, health professionals and Scientists have become interested in the effectiveness and safety of NHPs. A focus-group study based on a total 16 focus groups composed of 50 NHPs consumers and 47

Pharmacists (recruited from Toronto, Halifax, Edmonton and Vancouver) was conducted in 2008 (125). Analysis and interpretation of the transcripts showed that consumers tended to use various information resources as the guidance to make informed choices regarding which products they should consume (125). These information recourses included internet, family, friends, magazines, newspapers, books, health food stores, or health care professionals (such as Naturopathic Doctors, Physicians, Pharmacists, Registered Dietitians) (125). Also, based on the analysis and interpretation of the transcripts, both the consumers and Pharmacists agreed that health professionals (especially Pharmacists) need to be knowledgeable and able to provide consumers with up-to-date and accurate information regarding the effectiveness and safety of NHPs (125). Responses highlighted the key role that health professionals can play in supporting respondents' / consumers' informed choice (125).

1.3.2 Ginseng

Ginseng belongs to a family of slow-growing fleshy-rooted deciduous perennial plants (126). It typically grows in cool and shady ground environments, such as hardwood forests (126). In China, the ginseng plant, especially the root, has been used as an herbal medicine for thousands of years due to its potential pharmacological properties (127,128). In ancient China, ginseng was used to treat “Xiao Ke” symptoms, which included constant feelings of thirst and emaciation. “Xiao Ke” symptoms equate to diabetes symptoms, when using modern medical explanation in place of traditional words (128). In the most famous ancient compendium of *Materia Medica*—“*Ben Cao Gang Mu*”, written by Shi-Zhen Li during the Ming Dynasty of China, ginseng was recorded as having been used to treat diabetes symptoms, such as polydipsia, polyphagia and polyuria (127). Many Chinese herb products and traditional Chinese medicine formulas contain ginseng, especially those effective in treating DM (129). Ginseng is one of the top 10 most frequently prescribed anti-hyperglycemic herbs in China (129). Ginseng falls under the umbrella of NHPs, based on the definition provided by Food and Drug Act—Natural Health Products Regulation in Canada and Agriculture and Food in Canada (117-119).

Two main ginseng species are Asian or Korean ginseng (KG) (also called *Panax ginseng* C.A. Meyer), which is native to Korea and the northeastern part of China, and

American ginseng (AG) (*Panax quinquefolius*), which is native to the eastern part of North America. (130,131). Canadian ginseng belongs to the category of AG and is mainly cultivated in British Columbia and Ontario (130). Commercial ginseng products on the Canadian NHPs market take many forms, including dried ginseng root, powdered root (loose or capsulated), extracts (pills or capsules) and tea, based on different process and extraction technologies (132).

1.3.3 Active Components of Ginseng

The nutrient components in ginseng include carbohydrates, protein, fat, minerals, along with a series of ginsenosides, but ginseng is most commonly recognized for its “active” or “therapeutic” components (133). Ginsenosides are believed to be the main active components of ginseng. Different species and different parts of the ginseng plant (such as its roots, stems, leaves, flowers buds and berries) have different ginsenoside profiles (127,134). More than 60 different ginsenosides have been identified or isolated so far from ginseng roots, leaves, stems, flowers and berries (135,136). All ginsenosides share a dammarane-type triterpenoid saponin backbone structure with several side chains, including arabinose, glucose, xylose and rhamnose, and they belong to a family of steroids with a four trans-ring rigid steroid skeleton (135,137,138). Different side chains have different polarity, inducing different physiological effects in the body (137,138).

In the lab, ginsenosides are usually separated and identified by using thin layer chromatography (TLC), gas chromatography (GC) or high-performance liquid chromatography (HPLC) technologies (139). TLC is the most commonly used technology in the lab due to its ease of use and low cost (139). It is a two-dimensional thin layer sprayed with certain solid adsorbent material (139,140). Compounds are usually dissolved in certain solvent and are drawn up and travel along the thin layer through capillary action, interacting with the adsorbent on the layer (140). Different compounds have different retention-factor values on TLC based on their different polarities (140).

HPLC is also commonly used in the lab to detect and quantify non-volatile and polar compounds, which makes it ideal for the analysis of ginsenosides (139). During HPLC analysis, compounds in a sample are first dissolved in a solvent such as methanol or ethanol. This sample liquid then passes through a column filled with certain adsorbent

material (usually tiny sorbent particles with the size of 0.2-5 μm in diameter, such as non-porous silica) using a pressure pump that delivers a desired flow rate of the sample (141). The column filled with adsorbent material is called the stationary phase, and the sample liquid passing through the column is called the mobile phase (141). When the sample liquid passes through the column, each component in the sample interacts with the adsorbent material differently based on its own polarity. The different polarities of components in the sample result in different retention-factors, which cause different flow rates in the column. The different flow rates for different components eventually lead to the separation of the components in the column (139). As the sample liquid eventually flows out the column, different components in the sample liquid can then be collected separately at the outlet of the column at different times.

Ginsenosides are differentiated and named based on their retention-factor values (136,139), and they are commonly written in Rx form (x=0, a, b, c, d, e, f, g, h) (137). Ginsenosides are generally classified into two groups: protopanaxadiol—PPD (Rb1, Rb2, Rb3, Rc, Rd and Compound K) and propanaxatriol—PPT (Re, Rf, Rg1, Rg2, Rg3, Rh1) (127,128,134,136), based on the differences in their side chains. Ginsenosides in the group PPD usually contain two side chains on the backbone. Ginsenosides in the group of PPT contain one more side chain than ginsenosides in the group of PPD (133).

Although AG has a higher amount of ginsenosides concentration than KG, the number of ginsenoside types in KG (38 types) is greater than in AG (19 types) (135,142). Furthermore, KG is high in ginsenoside Rf and Rg2, which are usually not contained in the ginsenosides profile of AG (139,143). Also, Rg1 content in KG is 10 times higher than in AG (143). AG, however, contains twice the level of ginsenoside Re, compared to KG (144). The comparison of the active components—ginsenosides between AG and KG is shown in the following table 1.

Table 1. Active Components Comparison between American Ginseng and Korean (Asian) Ginseng

Ginsenoside Profile	American Ginseng	Korean Ginseng
Total ginsenosides	40-60 g/kg	20-40g/kg
Main ginsenosides	Rb1, Re, Rd	Rb1, Rg1, Rb2
Rf	0	1.0-2.0/kg
Rb1: Rg1 ratio	>5.0	<5.0
Rg1: Re ratio	<1.0	>1.0
Rb1:Rc2 ratio	<0.4	>0.4
PPD:PPT ratio	>2.0	<2.0

*Rx (x=0, a, b, c, d, e, f, g, h): ginsenosides with different retention-factor values on thin layer chromatography (TLC)

*PPD: protopanaxadiol—ginsenosides (Rb1, Rb2, Rb3, Rc, Rd), containing 2 side chains on the backbone

*PPT: propanaxatriol—ginsenosides (Re, Rf, Rg1, Rg2, Rg3, Rh1), containing 1 side chains on the backbone

(135,139,145)

Panax ginseng C.A. Meyer is sometimes steamed and dried to produce red ginseng. During the steaming process, ginseng starch is gelatinized (146). This gelatinization gives ginseng its red colour (146). During the steaming process, the polarity of ginsenosides also changes, which can induce different pharmacological effects (135,147). For example, after the heating process, the ginsenosides (Rb1 and Rb2) components will change into Rg3, Rk1 and Rg5 through the elimination of glycosyl and the epimerization of carbon-20 (148,149). This reaction will render 30% loss of the weight of ginsenosides due to the elimination of glycosyl (150). Also, the resulting Rg3 and Rg5 components after the heating process are less polar than the original structures (148,149). Although the total ginsenosides content is reduced by the heating process, the less-polar ginsenosides have stronger radical-scavenging and anti-inflammatory capabilities than the original structures (151,152). The steaming process can also improve the bioavailability of ginsenosides by decreasing their molecular weight and reducing their polarity, thus enhancing their absorption in the intestinal track (137,153-155).

1.3.4 Ginseng and Type 2 Diabetes Mellitus

Both AG and KG have been shown to have a wide range of pharmacological effects on different systems of the body, including the central nervous system, endocrine system, cardiovascular system and immune system (135,156-158). Given the prevalence and incidence of T2DM highlighted in *Section 1.1.4*, it is not surprising that anti-hyperglycemic properties of ginseng have captured the interest of many health professionals and Scientists.

Animals studies have supported a significant anti-hyperglycemic effect of ginseng. When diabetic mice were treated with either dried Korean white ginseng (KWG) root or Korean red ginseng (KRG) root at 100mg/kg body weight/day for 20 days, they showed significant improvement in blood glucose control and reduction in urine protein, compared to the control group (159). Another animal study using American ginseng (AG) demonstrated similar results. After obese diabetic *db/ob* mice were treated with dried AG root or heat-processed AG root at 100mg / kg body weight / day for 20 days, mice in both conditions showed significant improvement in blood glucose control, along with significant reduction in serum glycosylated protein and urine protein (147). In addition, when mice were treated with fermented steam-dried ginseng berries at 0.1g / kg body weight / day, they showed increased expression of GLUT1 mRNA expression in the skeletal muscle cells, which indicated improved glucose uptake by the muscle (155).

Human clinical trials have also demonstrated similar results of the efficacy of ginseng in treating hyperglycemia. Fifteen participants (11 males and 8 females, 64±2 years, BMI 28.9±1.4 kg/m²) with well-controlled T2DM were randomly assigned to either dried KRG root treatment condition (at dose of 2g KRG/meal) or placebo control condition for 12 weeks. The KRG treatment group showed significant improvement in oral glucose tolerance test along with 33% net increase of insulin sensitivity indices, compared to the control group (160). Similar results were also demonstrated in a short-term study. Participants (63±2 years, BMI 27.7±1.5 kg/m²) with T2DM were randomly assigned to AG treatment condition or placebo control condition. Participants in the treatment group were given AG root powder capsules with dose of 3g, 6g or 9g at 0, 40, 80, or 120 minutes before a 25g oral glucose challenge. Blood glucose levels were tested at 0, 15, 30, 45, 60 and 90 minutes after the oral glucose challenge (161). Participants in the treatment group showed

significant reduction in blood glucose levels at all three doses across the test time line, compared to the placebo control group (161). A systematic review based on a number of randomized-controlled clinical trials from the past concluded that ginseng did show an anti-hyperglycemic effect in treating T2DM by promoting insulin secretion, stimulating glucose uptake, protecting pancreatic islets, and enhancing insulin sensitivity (162).

The anti-hyperglycemic effect of ginseng also applies to people with no T2DM. In a randomized-controlled crossover clinical trial, 10 participants without T2DM and 9 participants with T2DM were treated with 3g AG either 0 or 40 minutes before a 25g oral glucose tolerance challenge. The results showed that compared to the placebo control condition, AG treatment condition had significant reduction in blood glucose level after the glucose challenge across all the participants with or without T2DM, but the anti-hyperglycemic effect was slightly stronger in the participants with T2DM than in the participants without T2DM (163).

Numerous animal studies and clinical trials have indicated that the active components (ginsenosides) in both KG and AG can potentially reduce fasting as well as postprandial blood glucose, increase insulin sensitivity, and improve other symptoms related to DM (such as the presence of protein in urine and polydipsia) (147,155,159-161,163-168). Higher ginsenosides concentration, however, does not necessarily mean higher efficacy in lowering postprandial blood glucose, and it depends on the bio-availability and ratio of different active components (169). Across the four AG clinical studies conducted by Vuksan et al. (2000-2001), doses from 1 to 9 g of American ginseng did not make a significant difference in reducing postprandial blood glucose concentration, and they were equally efficacious (133,161,163,165,166). These results were confirmed by another study conducted by Sieveniper et al. (2006), in which a higher dose of ginseng (4-6 g) did not differ significantly from a lower dose (2g) in changing postprandial blood glucose concentration, and the lower dose achieved the same therapeutic effect as the higher dose (170). The results from these studies have indicated the possible saturation effect of ginsenosides in reducing postprandial blood glucose concentration—escalation of dose of ginsenosides beyond a certain threshold offers no additional anti-hyperglycemic benefits in people with T2DM.

1.3.5 Mechanisms of the Anti-Hyperglycemic Effect of Ginseng

Two mechanisms have been proposed to explain ginseng's anti-hyperglycemic effects: (1.) Enhanced pancreatic beta-cell function (enhanced insulin production and secretion) and (2.) Reduced IR and increased insulin sensitivity at the cellular level.

1.3.5.1 Ginseng and Pancreatic Beta-cell Function

Insulin deficiency is related to a lack of ATP production in the mitochondria of pancreatic beta-cells (171-173). Ginseng can potentially increase pancreatic beta-cell insulin production by enhancing its ATP production and reducing its apoptosis (programmed cell death) (171). Also, uncoupling protein-2 (UCP-2) in the cell can suppress ATP production (171). Therefore, even a modest increase in UCP-2 in pancreatic beta-cells can suppress insulin production and reduce cell survival rate (171,173-176). Ginseng treatment, however, can possibly reduce mitochondrial UCP-2 via suppressing IL-1beta protein, hence increasing ATP production in the pancreas (171). Furthermore, apoptosis is one of the common causes of cell death in pancreatic beta-cells (171). Some Scientists have suggested that ginseng can potentially reduce apoptosis in the pancreas by increasing the levels of specific proteins and enzymes in the pancreas, such as caspase-3/9 and Bcl-2 protein, which are the major proteins that protect the pancreas against apoptosis (171).

In an in vitro study, beta-cells cultured with ginseng extracts displayed significantly lower levels of UCP-2 expression and higher levels of ATP production (171). In an animal study, rats were injected with high dose of Streptozotocin (STZ), which severely damaged pancreatic beta-cells and induced type 1 diabetes (177). However, after 3 weeks of ginsenosides treatment, the blood insulin level showed a small but significant increase, suggesting that ginsenosides could possibly help the pancreas regenerate beta-cells or recover beta-cell function to a certain extent (177).

1.3.5.2 Ginseng and Insulin Sensitivity

Muscles are the primary tissue for glucose uptake and play an important role in the regulation of energy balance (178,179). The insulin-independent AMP-activated protein kinase (AMPK) pathway in muscle cells is important for maintaining energy homeostasis. Once the AMPK pathway is activated, it will accelerate ATP generating catabolic pathways,

which involve fatty acids beta-oxidation and glucose uptake (134,180). The downstream target of the AMPK-mediated pathway is the Glucose Transport 4 (GLUT4), especially during muscle contraction (134,181). Enhancing the expression of GLUT4 in skeletal muscle represents increased sensitivity to insulin, decreased insulin resistance, and improved efficiency in transporting glucose from the blood stream into muscle cells (136). Data from past in vitro and animal research studies showed that certain ginsenosides, such as Rg1, Rg3, Rh2 and Rc, could significantly activate the AMPK signaling pathway and enhance the expression of GLUT4 in insulin-resistant cells (134,136,138,182,183). When diabetic rats in the experimental group were treated with KRG at a dose of 200mg / kg of body weight / day for 50 days, the KRG treatment group had significantly improved insulin sensitivity and preserved glucose tolerance, compared to the controlled group (184). Also, KRG treatment resulted in higher fatty acids oxidation and increased expression of GLUT4 in mitochondria compared to the control group (184). In a recent animal study conducted in 2012, rats were randomly assigned to one of three conditions: high-fat diet with KRG treatment, high-fat diet without KRG treatment, or standard diet without KRG treatment (185). At the end of the study, the KRG treated group showed significant improvement in fatty acids oxidation as evidenced by the reduction in body fat, as well as increased GLUT4 expression in muscle cells, compared to the other two conditions (185).

1.4 Translating Ginseng Knowledge to Action

Knowledge translation (KT) includes effectively disseminating novel research findings to end users; often referred to as “bringing knowledge to action” (186). According to the definition provided by Canadian Institute of Health Research, KT is defined as:

“A dynamic and iterative process that includes synthesis, dissemination, exchange and ethically sound application of knowledge to improve the health of Canadians, provide more effective health services and products, and strengthen the health care system” (187).

Without effective KT, the evidence-to-practice gap widens and patients/clients fail to benefit from new research findings and might receive unnecessary or even potentially

harmful treatment (186,188). Many health professionals may perceive NHPs knowledge (and skill) as outside their scope or might approach NHPs research studies from different angles related to their professions. Their different perceptions of NHPs, therefore, might have different impact on KT.

1.4.1 Health Professionals' Knowledge of and Attitude towards Natural Health Products.

1.4.1.1 Pharmacists', Physicians' and Nurses'

In Canada, NHPs are readily available in many drug stores, health food stores, and even in many big supermarket stores. Pharmacists are in a position to educate and support the public while they make an informed choice of whether or not to use NHPs. Apart from prescribed drugs, it is beneficial to know whether Pharmacists are also knowledgeable in the field of NHPs and willing to give consultations to customers regarding how to choose appropriate NHPs. In a study conducted in the USA, a survey was distributed to 164 Pharmacists, assessing their knowledge in herbal medications' use, side effects and cautions, as well as their attitudes toward herbal medications. The participants answered each question by selecting "yes", "no" or "I don't know" or by indicating their answers on a five-item attitudinal response scale ("1" being "strongly agree" and "5" being "strongly disagree") (189). The results showed that Pharmacists were more knowledgeable about the popularity of different herbal products based on their daily sales experiences than about potential adverse effects, drug interactions and precautions of certain herbal products (189).

The variance of opinions toward NHPs does exist across different healthcare disciplines. In a Canadian study investigating three different health care providers' (Nurses, Pharmacists and Physicians) attitudes toward alternative products and therapies (such as over-the-counter products, herbs and old-time-remedies), a questionnaire using a Likert attitude scale ("1" being the most positive attitude and "5" being the most negative attitude toward alternative products and therapies) was distributed to 153 participants (52 Physicians, 49 Pharmacists and 52 Nurses) (190). The results showed that approximately 50% (26 of 52) of Physicians, but only 33% (16 of 49) of Pharmacists and 25% (13 of 52) of Nurses, asked their patients about their alternative products and therapy use. In

addition, Nurses tended to show more positive attitudes toward alternative therapies, compared to Physicians and Pharmacists (190). Pharmacists, on the other hand, among all the health care professionals, expressed the most concerns and alarm about the current NHP market without standards, regulation or proper labelling (190). These results have suggested that different healthcare expertise and practice experiences might render different attitudes toward the application of NHPs in a clinical setting.

Another Canadian survey study using an online questionnaire to investigate Pharmacists' familiarity with NHPs and NHPs-related adverse events showed similar results in terms of Pharmacists' concerns of the current NHP market. Among the 132 Pharmacists in this study, 90% (118/132) of them expressed moderate to extreme concern about the quality of NHPs due to lack of standardization and the potential NHP-drug interaction and adverse effects (191). The same study also revealed that although 89% (117/132) of the Pharmacists reported that they spent approximately 30 minutes per day counseling patients about NHPs, and only 5% of the patients who purchased NHPs inquired about potential NHP-drug interactions and adverse effects in particular (191). Furthermore, over 90% (118/132) of the Pharmacists indicated that they wished to have continuing education or training to improve their knowledge in the field of NHPs (191).

Interestingly, health professionals' attitudes toward recommending NHPs to patients can be imparted by their personal use and knowledge of these products. An American survey investigated Pharmacists' use and attitude toward CAM (192). In this study, among the 423 participants, 37% of them reported using CAMs regularly, including ginseng. The results also showed that Pharmacists who received professional training in the field of CAM and who reported personal use of CAMs were more like to regularly ask patients about their use of CAMs, compared to Pharmacists without personal experience or professional training in this field (192).

These results are consistent with the results from another study involving 70 Pharmacists. More than half of the respondents to this survey (53%, 37/70) reported taking supplements, and slightly fewer than half of them indicated that they had recommended supplements to their patients (193). Pharmacists also indicated that their primary information sources were published clinical trials, alternative medicine practitioners, and allopathic health providers, as well as the internet and word of mouth

(193). The results of this study have suggested that personal use of supplements by a Pharmacist would increase the likelihood by twofold that he/she would recommend a supplement to a patient (193). These study results have raised concerns that personal use of NHPs among these healthcare professionals might have the potential to induce biased attitudes toward NHPs and the possibility of recommending NHPs to their patients purely based on their personal experiences with and preferences of these products.

In addition, the difference of knowledge and attitude towards NHPs also exists between different generations in the same profession. A cross-sectional survey investigated the different interest in and attitude toward complementary and alternative therapies between practicing Pharmacists and pharmacy students. The results showed significant differences between the two groups (194). Compared to the pharmacy students, the Pharmacists were more likely to believe that complementary and alternative therapies were not based on scientific research evidence and were “quackery” (a term referring to being fraudulent and pretending to have professional medical skills) (194). The pharmacy students, however, held a significantly more positive attitude toward alternative therapies and believed that there was sufficient research evidence supporting incorporating alternative therapies into practice. They were also more willing to refer patients to a Naturopath Practitioner as well as stock natural health products in their pharmacy (194). These results imply that if the difference of attitudes toward NHPs exists between practicing Pharmacists and pharmacy students, it is possible that the same inter-generational difference might also exist in other healthcare professions, such as between practicing Registered Dietitians and nutrition students / interns. Investigating nutrition students’ knowledge of and attitudes toward NHPs, therefore, might be beneficial for researchers to translate new knowledge and research findings in the field of NHPs to a wider audience and help them use these findings in their future clinical practice.

In summary, despite the variance among healthcare professionals, many of them do believe that alternative therapies (such as using NHPs) have become increasingly important in patients’ daily lives, and at the same time have expressed concerns about the current NHPs market as well as the willingness of becoming the information resource for patients through continuing education and training to help patients make informed decisions.

1.4.1.2 Dietitians'

Dietitians conduct nutrition screening, assessment and intervention in clinical settings. Information on NHPs has been identified as a key part of assessment and evaluation (e.g. in the context of NHP-drug-diet interaction). According to a study involving 681 dietetic interns and 68 internship program directors in the USA, over 650 participants indicated that they had been asked or consulted by clients about vitamin/mineral supplements, and over 500 of them reported being asked about herbal/botanical remedies or products within the past five years (195). Furthermore, over 440 of them reported using over-the-counter vitamin/mineral supplements or herbal remedies themselves, either occasionally or on a daily basis (195). Similar data was collected in Canada. Based on a recent survey administrated in Ontario, which involved 558 Registered Dietitians, 98% (547/558), 94% (524/558) and 91% (508/558) of the participants reported that they had been asked about nutrition supplements (including vitamin/mineral supplements, amino acids and fatty acids supplements), functional foods and herbal products by their clients, respectively. The same Ontario study also revealed that 89% (497/558), 82% (457/558) and 57% (318/558) of the Dietitians reported having ingested nutrition supplements, functional foods and herbal products, respectively (196). Based on the estimation, more than half of the Canadian population uses herbal or nutritional supplements and the consumption rate continues to rise (124). It is not surprising that more and more clients and patients start to consult Dietitians about consuming NHPs.

In Canada, dietetic scope of practice includes

“Conducting research, product development, product marketing, and consumer education to develop, promote and market food and nutritional products and pharmaceuticals related to nutrition disorders or nutritional health” (197).

According to this definition, Dietitians should be knowledgeable in the field of NHPs and capable of engaging in NHP-related counselling activities if they are related to nutrition disorders or nutritional health. Although Dietitians are knowledgeable in nutritional values of different food groups and their relationship with health promotion and disease

prevention, NHP related courses are not currently mandatory for dietetic programs, even though some universities (such as Mount Saint Vincent University in Halifax, Nova Scotia) do offer NHP-related courses as electives. Dietitians, therefore, might not have sufficient knowledge to engage in counselling activities in the field of NHPs due to lack of systematic education and training.

In order to improve Dietitians' capability of engaging in NHPs-related counselling activities, investigating Canadian Dietitians' as well as nutrition students' knowledge of and interest in NHPs has become a first important step to approach this goal. Although several Canadian research studies were conducted in this field, the majority of the published literature so far is based on studies conducted in the USA. One reason might be that there are a larger population and larger CAM market in the USA, compared to Canada. Institutions and universities there might be able to get more research funding either from sponsors or the government. These USA-based studies, however, can still provide us with some insights about current Dietitians' perspectives on NHPs.

In Canada, although more studies in the field of Dietitians' knowledge of and interest in NHPs are needed, insight on this topic can still be implied based on studies in other closely related fields, such as Dietitians' attitudes toward functional foods. A telephone survey was conducted in 2008 to investigate Canadian Registered Dietitians' views on functional foods and nutraceuticals (198). Based on the answers from 151 respondents, over 120 of them (79%) believed that Dietitians were the most appropriate healthcare professionals to make recommendations on functional foods. When asked to rank on a rating scale of 1 to 10 ("1" as being not important at all, "10" as being extremely important), they also believed that being knowledgeable about functional foods and nutraceuticals was extremely important for Dietitians (198). Furthermore, most of the Dietitians believed that engaging in unbiased scientific research studies and establishing partnership with other healthcare professionals, especially Pharmacists, are important for gaining further knowledge in this field (198). Although NHPs and functional foods fall under different regulations in Canada, Dietitians' positive attitudes toward functional foods imply that further Canadian research studies are needed to investigate whether they hold similar attitudes toward NHPs as well.

Dietitians' attitudes towards NHPs may differ from other health professionals, such as Pharmacists, Nurses and Physicians. In a survey conducted in Oregon, USA, questionnaires were mailed to a sample of 202 registered Dietitians. Unlike the Pharmacists' concerns about NHPs highlighted above, more than 89% (180/202) of the Dietitians in this study believed that nutrition supplements were safe to use, and 75% (151/202) of them considered herbs to be safe (199). At the same time, 80% (162/202) of them were confident of the effectiveness of nutrition supplements for preventing or treating chronic diseases, but only 50% (101/202) of them were confident of the effectiveness of herbs (199). Interestingly, despite their confidence in the effectiveness and safety of nutrition supplements and herbs, only 10% of the Dietitians considered themselves as being knowledgeable in this field, especially about herbal products (199). These results were further confirmed by another cross-sectional survey study conducted in Massachusetts, which investigated the knowledge, personal use and recommendation of herbal supplements among 158 Registered Dietitians (200). Approximately 73% (115/158) of the participants in the study perceived themselves as having little or no knowledge in the field of herbal supplements (200). On the other hand, 89% (140/158) of the participants strongly agreed that education in the field of herbal supplements should be incorporated into the dietetic curriculum, indicating their willingness to increase their knowledge in this field (200). One implication from these results is that the attitude that Dietitians hold toward NHPs, either positive or negative, might be biased due to their lack of knowledge in this field, and future education or training programs might be beneficial to help them develop a more objective and comprehensive view of NHPs.

Similar to Pharmacists, Dietitians' knowledge of and interest in NHPs might also be influenced by their personal ingestion of these products. According to the results from the same Massachusetts study, the Dietitians' knowledge scores in herbal products were positively related to the frequency of their personal use of these products, and Dietitians who reported having consumed herbal products personally were more likely to recommend them to clients, compared to those who did not have personal use experiences with herbal supplements (200). Furthermore, based on the Ontario study (2013) mentioned earlier, the Registered Dietitians who reported having consumed nutrition supplements or herbal products were significantly more likely to hold the belief that

recommending NHPs to clients should be included within the dietetic scope of practice than those who had not personally consumed NHPs (196). These results indicate that Dietitians who consume NHPs personally might be interested in acquiring knowledge in this field and might therefore spend more time reading related information and literatures from different sources to improve their knowledge, resulting in higher knowledge scores in this field. Their opinions or attitudes toward NHPs in general, however, might be subject to their personal use of these products. This is an interesting item, as (Canadian) Dietitians are encouraged to approach intervention evaluation from an evidence-based medicine perspective.

Dietitians' interest in NHPs might also differ based on categories of products as well as on the specific type of dietetic job activities these professionals engage in. According to the same Ontario study (2013), while over 90% (502/558) of the Dietitians believed that recommending nutrition supplements to clients should be included within their current scope of practice, only 47% (262/558) of them believed that recommending herbal products should be included (196). Furthermore, the Dietitians who provided group-level counselling/workshops or one-on-one counseling services were less likely to hold the belief that recommending herbal products to clients should be included within the dietetic scope of practice. This indicates an inverse relationship between views about herbal products and dietetic counselling activities (196). This result has some critical implications. Dietitians who frequently engage in counselling activities are more likely to be asked or consulted by their clients about taking nutrition or herbal supplements. As a result, they might be more likely to read different research studies related to NHPs in order to answer their clients' questions, hence developing a more comprehensive view of NHPs. Dietitians who frequently engage in counselling activities might hear more feedback from their clients about the adverse effects of herbal products they use. No matter what the reasons are, improving Dietitians' and nutrition students' knowledge in the field of NHPs through systematic education and training is beneficial for them to develop comprehensive and objective views of NHPs and to apply the knowledge in a clinical setting. In order to achieve this, the first step is to investigate the current attitude toward NHPs and the interest in gaining knowledge in this field through conducting research studies.

Based on the discussions above, it is not surprising that there has been some consensus among healthcare professionals regarding knowledge, personal attitude and interest in the field of NHPs, such as demanding more government regulation, feeling a lack of knowledge, and being willing to continue education or training in this field. Most research results have also indicated that different educational backgrounds, job activities and personal use experiences can bring different attitudes toward NHPs.

1.4.2 Nutrition Students' Perspectives and Research Knowledge Dissemination

Research studies in the field of health professionals' knowledge and perception of NHPs in the past have mainly focused on Pharmacists' views, and a few studies investigated Dietitians' perspectives. More studies, especially Canadian studies, focusing on nutrition students' knowledge of and attitude toward NHPs are needed. Nutrition students' perspectives regarding NHPs might be different from practicing Dietitians' and other health professionals'. If nutrition students are interested in learning NHPs, it might be beneficial to disseminate research findings to this specific audience when they are still in school absorbing a wide variety of information. The question here is how to effectively translate and disseminate evidence / knowledge in the field of NHPs to this specific group, since many nutrition students do not have dietetic working experience yet and completing Foundational Knowledge Specifications for Dietetics Education.

According to the Knowledge-to-Action Cycle (figure 2), KT includes eight phases:

- (1) "Identifying a problem that needs to be addressed";
- (2) "Identifying, reviewing and selecting knowledge or research findings relevant to the problem or knowledge gap";
- (3) "Adapting the new research findings or knowledges to the local context";
- (4) "Assessing barriers to knowledge use";
- (5) "Selecting, tailoring and implementing interventions that promote the dissemination of knowledge to the target audience";
- (6) "Monitoring the process of knowledge dissemination";
- (7) "Evaluating the outcomes of KT";
- (8) "Sustaining the ongoing use of knowledge" (186).

The final phase leads back to the first phase—“*Identifying a problem that needs to be addressed*”, and forms a cycle as shown in figure 2.

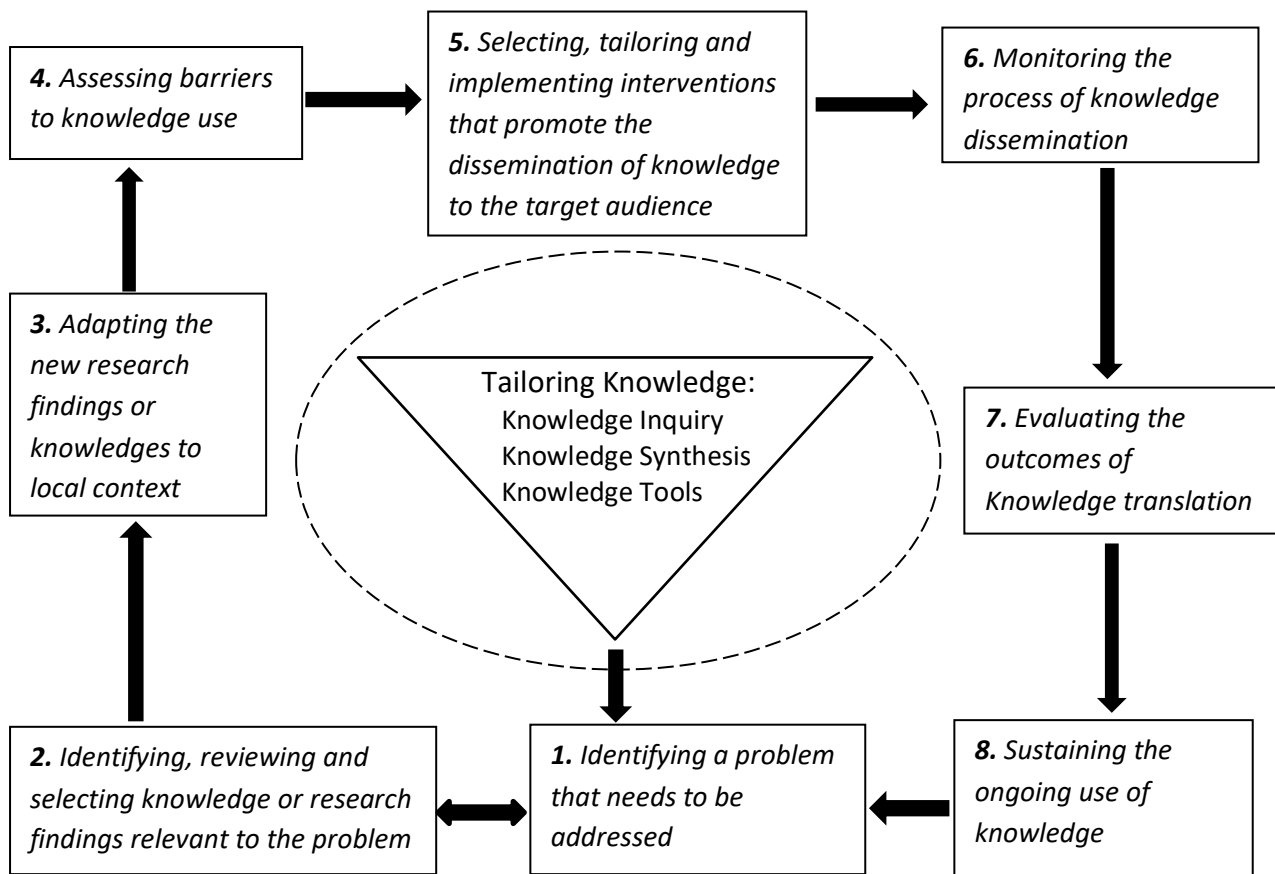


Figure 2. Knowledge-to-Action Cycle (186)

Shown in figure 2 above, all the eight phases in the Knowledge-to-Action cycle are centered around the core—“Tailoring Knowledge” to facilitate effective KT. “Tailoring Knowledge” has three components—“Knowledge Inquiry”, “Knowledge Synthesis” and “Knowledge Tool”, which represent knowledge creation through finding research gaps, conducting new research studies and presenting new research findings in a clear, concise and user friendly format (186). The out circle is the eight phases highlighted above, which represent the knowledge application that translate the knowledge created (from the core) to potential users to help them utilize the knowledge and apply it in practice (186).

This thesis project was divided into two sub-studies (Study 1 and Study 2) to address the five questions below:

- (1) What have been known regarding ginseng's therapeutic effects in T2DM management (based on literature reviews as highlighted in the previous sections)?
- (2) What is the knowledge gap regarding ginseng's therapeutic effects that still needs to be explored (such as ginseng's effect on satiety), especially from nutritional perspective?
- (3) What do nutrition students know about NHPs and ginseng (as an example of NHPs)?
- (4) Are nutrition students' perceptions of NHPs different from those of other health professionals (based on literature reviews)?
- (5) Are nutrition students interested in learning NHPs/ginseng related knowledge and what aspects of NHPs/ginseng knowledge are they interested in learning?

Study 1 addressed the first two questions above, and Study 2 addressed the rest three questions. Study 1 is the knowledge creation, representing the inner core (triangle) of the Knowledge-to-Action cycle. Study 2 is the knowledge application, representing the out-circle of the Knowledge-to-Action cycle.

In Study 1, based on the literature reviews highlighted in the previous sections, it is well known that ginseng has been used to help with T2DM management due to its anti-hyperglycemic effect. Also, various literatures have highlighted the correlation between blood glucose concentration and satiety, as discussed in the previous sections. The "knowledge inquiry" in Study 1 was to explore whether ginseng can have any effect on satiety in people living with T2DM through conducting new research studies. The "knowledge synthesis" was to integrate new research findings into existing literatures to draw conclusions regarding ginseng's therapeutic effect in T2DM management from nutritional perspective. The "knowledge tool" here was to format the research findings and conclusions based on the characteristics of the target audience (nutrition students), so that the knowledge can be presented to them clearly and concisely.

In study 2, to effectively disseminate knowledge and new research findings in the field of NHPs and ginseng to nutrition students, the first step was to formulate questions through a face-content validated survey questionnaire. The development of the questionnaire aimed for a nutritional science study body rather than for Pharmacists or other health professions. Through administrating the questionnaire, the results can help health educators identify whether there is any problem that needs to be addressed regarding integrating NHPs related knowledge into nutrition education. They then can

select, tailor or adapt NHPs related knowledge and new research findings based on the requirements of nutrition science and nutrition education (adapting to local context). Through administering the questionnaire, it can also help health educators assess the barriers to disseminating NHPs related knowledge to nutrition students. In return, it will further help them select and tailor knowledge before disseminating it to them. Study 2, therefore, involves the first four phases of the Knowledge-to-Action cycle.

The fifth phase of the Knowledge-to-Action cycle involves finding effective strategies and educational tools of translating and disseminating NHPs/ginseng knowledge to nutrition students based on the results from administering the questionnaire. The sixth phase of the cycle involves constantly assessing how effectively the knowledge are disseminated to nutrition students, and its subsequent impact on their understanding of and attitudes toward NHPs. The seventh phase involves evaluating knowledge application in their future career, such as their health care practice, their future research engagement in the field of NHPs, and whether the knowledge they have learned makes a difference in terms of health outcomes. The eighth phase of the cycle involves establishing a long-term feedback loop from nutrition students and practicing Dietitians assessing new emerging problems and knowledge gaps to promote sustained knowledge use, which leads back to the first phase, forming a cycle.

STUDY 1:

Acute Dose Response Effects of Korean White Ginseng (*Panax ginseng* C.A. Meyer) on Blood Glucose Concentration and Satiety in Individuals Living with Type 2 Diabetes Mellitus.

ABSTRACT

Title: Acute Dose-Response Effects of Korean White Ginseng (*Panax ginseng* C.A. Meyer) on Blood Glucose Concentration and Satiety in Individuals Living with Type 2 Diabetes Mellitus

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Background: Approximately 6% of all Canadian are diagnosed with diabetes mellitus (DM), with 90% being diagnosed with type 2 diabetes mellitus (T2DM). People living with a body mass index (BMI) ≥ 30 are at increased risk for developing T2DM. Dysfunctional satiety cues have been observed in both T2DM and obesity. Investigating interventions that impact satiety is warranted.

Objectives: To measure: (1.) the dose-response effect of Korean white ginseng (KWG) on blood glucose concentration in people living with T2DM, (2.) the dose-response effect of Korean white ginseng (KWG) on satiety in people living with T2DM and (3.) the correlation between BG and satiety.

Methods: This study represents a secondary data analysis of a double-blind, randomized-controlled, cross-over trial completed at St Michael's Hospital. Participants with T2DM (n=30) were recruited. Participants were asked to visit the research clinic for a total of 5 times, with each visit being 4 days apart. During each visit, participants were randomly assigned to one of the five conditions (0, 1g, 3g and 6g of dried KWG root, and 0.5g of dried Korean red ginseng root). Satiety was measured using four Visual Analog Scale (VAS) questions at baseline, 1, 2, 3 and 4 hours post KWG treatment. Blood glucose concentration was measured by taking blood sample through finger prick at baseline, 15, 30, 45, 60, 90, 120 and 180 minutes post KWG treatment. Incremental appetite score was calculated based on the four VAS scores.

Results: Twenty-five participants (n=25) completed the procedures (five withdrew before baseline visit). Time had significant impact on both blood glucose concentration and incremental appetite score ($p < 0.01$). Different KWG treatment conditions did not have significant impact on either BG ($p = 0.8$) or incremental appetite score ($p = 0.64$). Correlation between BG and incremental appetite score was not observed ($p = 0.19$).

Conclusion: The doses of KWG used in this study did not have significant impact on either blood glucose concentration or satiety, counter to our hypothesis. Although useful data/analysis, future studies with increased dosage and/or treatment exposure time is needed to further investigate the effect of KGW on BG and satiety.

Funded by: Department of Herbal Crop Research; National Institute of Horticultural and Herbal Science, RDA, Korea.

Clinicaltrials.gov Identifier: NCT01699074

2 METHODOLOGY AND RESULTS FOR STUDY 1

2.1 Rationale, Hypothesis and Objectives

Rationale:

The literature review highlighted two key relationships: (1.) The relationship between blood glucose/insulin and satiety, and (2.) the relationship between ginseng and blood glucose/insulin. These two relationships have inspired the following question: If blood glucose and insulin level is truly related to satiety, and if ginseng consumption can truly lower blood glucose and improve insulin sensitivity, does it mean that ginseng consumption is related to hunger and satiety, or ginseng consumption can increase appetite and food intake? In simple language, as shown in figure 3, if we know that A is related to B, and B is related to C, it is interesting to know with confidence if A is related to C.

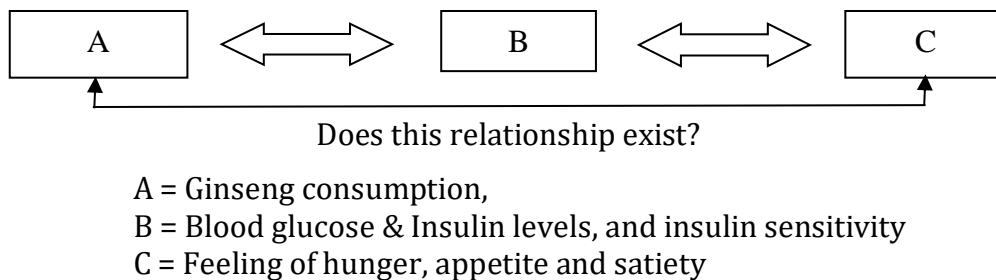


Figure 3. The relationship between ginseng, satiety and blood glucose/insulin

The above question involves two sub-questions:

- (1) If ginseng consumption decreases blood glucose concentration, and if low blood glucose concentration is associated with increased hunger perception according to Glucostatic Theory, does this mean that ginseng consumption can induce hunger perception and stimulate appetite?
- (2) Based on the discussions in *Section 1.2.4.2*, if ginseng consumption can increase insulin sensitivity among people with T2DM and/or obesity, and improved insulin sensitivity can lead to improved satiety perception (90,94-96), does this mean that ginseng

consumption in the long-term can improve satiety perception and help with energy intake control in people with T2DM and/or obesity?

The first question focuses on the short-term, and the second question focuses on the long-term. Although numerous studies have investigated the effect of ginseng on glycemic control in people living with T2DM, research exploring the direct relationship between ginseng consumption and satiety among T2DM population was almost non-existent. It cannot be assumed that ginseng consumption is related to satiety and hunger simply because of the two separated facts that ginseng consumption can lower postprandial blood glucose and improve insulin sensitivity, and that blood glucose/insulin level is related to satiety.

This research study aims to address this gap by exploring the relationship between ginseng intake and satiety. The results of this study can provide evidence to help health professionals, such as Dietitians, find effective interventions to improve diabetes patients' daily energy intake and to further improve their quality of life.

Hypothesis: Korean white ginseng (KWG) consumption will increase the subjective appetite measured by VAS score.

Objectives:

- (1) To investigate the dose-response effect of KWG on hunger and satiety (measured by VAS) within a sample of participants living with T2DM.
- (2) To investigate the dose-response effect of KWG on blood glucose concentration in participants living with T2DM.
- (3) To investigate the correlation between blood glucose concentration and satiety in participants living with T2DM.

2.2 Methods

2.2.1 Participants / Sample

The participants inclusion criteria included individuals who had been living with T2DM for minimal one year (with A1c between 6.5% and 8.5%), and had been treated with unchanged diet alone or diet and oral hypoglycemic medications for at least 3 months prior to this study. In addition, the inclusion criteria included age range between 18-75 years, Body Mass Index (BMI) between 25-35 kg/m², systolic blood pressure (SBP) < 160 mmHg and diastolic blood pressure (DBP) < 100 mmHg, normal hepatic and renal functions, no other major illness, non-pregnant, not taking supplements or other herbs, no excessive use of cigarette (>10 cigarettes/day) or alcohol (> 3 drinks/day), as well as no history of allergy or sensitivity to the research interventions (KWG) or gelatin used in the capsules. All participants provided informed written consent. The main study was reviewed and approved by St. Michael's Hospital's Research Ethics Board. Secondary analysis approval was obtained from both St. Michael's Hospital's and Mount Saint Vincent University's Research Ethics Boards.

2.2.2 Study design, interventions and protocol

This secondary data analysis is based on a randomized, double-blind, placebo-controlled, cross-over trial conducted at St Michael's Hospital in Toronto. The aim of this study was to investigate the effect of Korean white ginseng (KWG) on cardiovascular disease risk factors in individuals with metabolic syndrome or T2DM.

Each participant visited the clinic on five separate occasions, with each visit being four days apart. During each visit, the participants were randomly assigned to one of the five treatment conditions: 0g (placebo negative control), 1g, 3g or 6g encapsulated KWG dried root powder, or 500mg encapsulated KRG root powder (positive control). The placebo negative control capsules contained wheat bran. Treatment condition randomization was based on a computer-generated random table. Four-year old dried KWG whole root powder samples were provided by the Department of Herbal Crop Research and National Institute of Horticulture & Herbal Science, RDA, Korea. All samples

(including the control samples) were capsulated in white gelatin capsules. Each treatment condition was administered in a set of 12 gelatin capsules.

The analysis of ginsenoside profile was conducted by the Department of Herbal Crop Research; National Institute of Horticultural & Herbal Science; RDA; Korea, using TLC technique. The ginsenoside profile of the KWG sample is summarized in the table 2 below.

Table 2. KWG Sample Components Test Report

Test Item	Unit	Test Result
Ginsenoside Rg1	mg/g	2.836
Ginsenoside Re	mg/g	4.713
Ginsenoside Rf	mg/g	0.953
Ginsenoside Rg2	mg/g	0.391
Ginsenoside Rh1	mg/g	0.910
Ginsenoside Rb1	mg/g	2.670
Ginsenoside Rc	mg/g	1.722
Ginsenoside Rb2	mg/g	1.973
Ginsenoside Rb3	mg/g	0.622
Ginsenoside Rd	mg/g	0.616
Ginsenoside Rg3	mg/g	0.087
Ginsenoside Rh2	mg/g	0.000

*Rx (x=0, a, b, c, d, e, f, g, h): ginsenosides with different retention-factor values on thin layer chromatography (TLC)

During each visit, the participants arrived Clinical Nutrition and Risk Modification Center at St Michael’s Hospital (Toronto, ON, Canada) in the morning after an approximate 10-12 hours of fasting. Each participant was instructed to maintain the same dietary and exercise pattern the night before the test day. A preclinical information questionnaire was used to assess the compliance with these conditions. In addition, in the morning of each visit, the participants were asked to refrain from their diabetes medications. Between any two visits, there was a minimal 4-day wash-out period in order to prevent the carry-over effects. At the beginning of each study visit, anthropometric measurements such as weight and height were taken, followed by orally consuming 12 capsules containing KWG interventions or wheat bran (negative control) or KRG (positive control), along with 50g oral glucose challenge. Blood samples through finger prick were taken at baseline, 15, 30,

45, 60, 90, 120 and 180 minutes post-treatment for analyzing the blood glucose concentration.

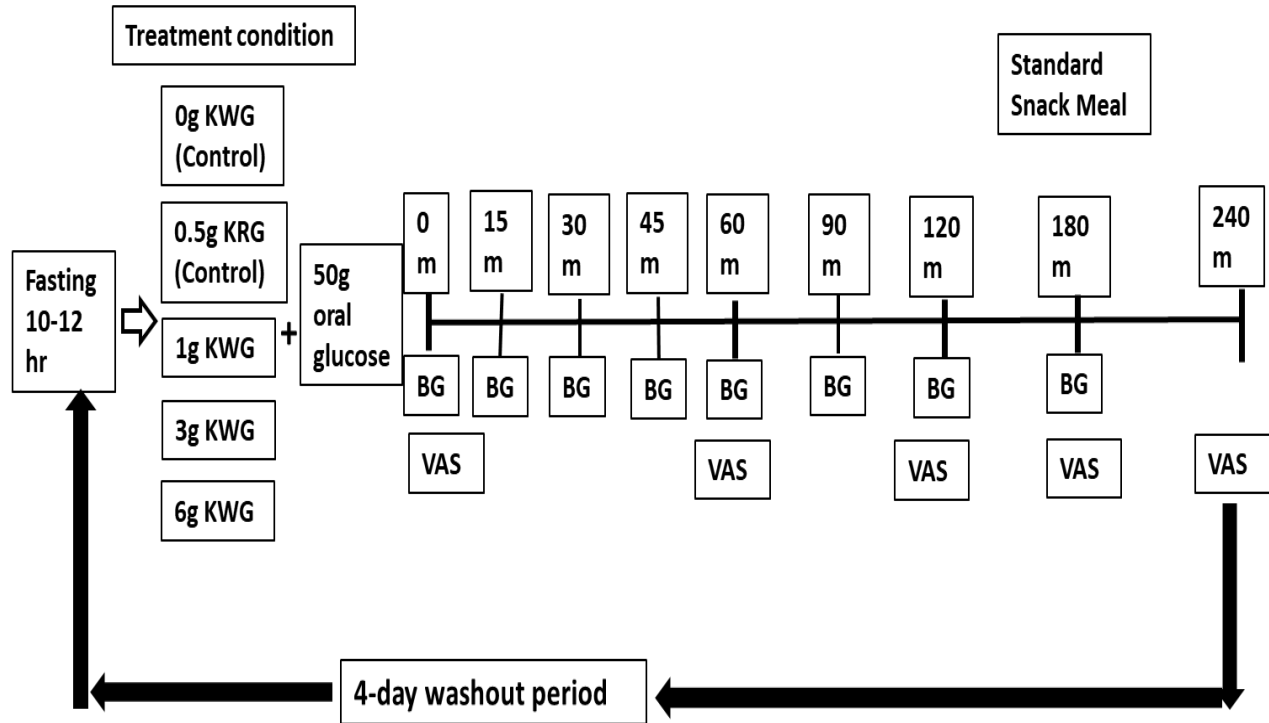
VAS scores via a questionnaire (Appendix 1) were measured at baseline, 60, 120, 180, and 240 minutes post-treatment for analyzing satiety levels. The VAS questionnaire contained four questions: “how strong is your desire to eat?”, “how hungry do you feel?”, “how full do you feel?” and “how much do you think you could eat now?” Each question was followed by a 100mm unstructured horizontal line scale anchored from one end of the line (termed “very weak,” “not hungry at all,” “not full at all,” “not full at all” and “nothing at all”) to the other end (termed “very strong,” “as hungry as I have ever felt”, “as full as I have ever felt” and “a large amount”).

At 180 minutes post-treatment, the participants were provided with a standardized snack, which included one slice of toast (Dempster’s 100% whole wheat bread), 15 g (1 tbsp) low fat cream cheese (Philadelphia, Kraft Canada Inc., North York, ON, Canada) and 200 ml water. Based on the calculation from Canadian Nutrient File (201), the total energy and macro-nutrient content is summarized in table 3 below.

Table 3. Macro-Nutrients of the Snack Provided

Macro-nutrition Content	Energy Content
Carbohydrates: 12.22g	49 kCal
Protein: 4.38g	17.5 kCal
Fat: 2.78g	25 kCal
Fiber: 1.3g	
Added sugar: 1.18g	5 kCal
Total	96.5 kCal

At the end of each visit, the participants were given a 24-hour symptom form (Appendix 2) and instructed to bring the completed form back to the clinic during the next scheduled visit. The entire process is shown in figure 4.



- * KWG: dried Korean white ginseng root powder
- * KRG: dried Korean red ginseng root powder
- * BG: blood glucose concentration testing
- * VAS: Visual Analog Scale measurement
- * m: minutes
- * hr: hours

Figure 4. Flow-Chart of the KWG Study Design

2.2.3 Data Collection

For each question on the VAS questionnaire, the participants had to place a vertical line across the horizontal line scale at a point which best indicated their feelings. The VAS scores were calculated by using the following formula:

$$\text{VAS score} = (\text{length from the left end to the marking point}) / (\text{full length of the scale})$$

Since the scale is 100mm in length, the above formula can be converted into the following formula:

$$\text{VAS score} = (\text{length from the left end to the marking point}) \text{ mm} / 100\text{mm}$$

A composite score for the four VAS questions on each questionnaire was calculated based on the content of the questions. Question 1, 2 and 4 on the VAS questionnaire measure the degree of desire to eat, hunger and prospective consumption, but Question 3 measures the degree of fullness. A composite appetite score, therefore, was calculated by using the following formula:

$$\text{Appetite score} = [\text{desire to eat score} + \text{hunger score} + (100 - \text{fullness score}) + \text{prospective consumption score}] / 4$$

(202,203)

Because different people have different appetite baseline, all appetite scores at 60, 120, 180 and 240 minutes subtracted their corresponding baseline appetite scores (at 0 minutes). The formula above, therefore, was further mathematically converted to the following formula:

Incremental Appetite Score

$$= [\text{desire to eat score change upon baseline} + \text{hunger score change upon baseline} - \text{fullness score change upon baseline} + \text{prospective consumption score change upon baseline}] / 4$$

(202,203)

2.2.4 Statistical Analysis

All the quantifiable data (including heights, weights, ages, blood glucose concentration, VAS scores and the composite appetite scores) were entered and analyzed using SPSS (Version 22, IBM) to calculate the means \pm SEM and statistical power. Based on the objectives of Study 1 highlighted in *Section 2.1*, the statistical analysis was divided into three main parts:

- (1) The dose-response effect of KWG on incremental appetite score;
- (2) The dose-response effect of KWG on post-prandial blood glucose concentration;
- (3) The correlation between post-prandial blood glucose concentration and incremental appetite score.

Due to the fact that each participant was exposed to each of the five different interventions (including the control condition) on five visits, and each intervention involved repeated measures of VAS score and blood glucose concentration over the course of 240 minutes, *ANOVA repeated measure general linear model* was used to analyze “effect of KWG on post-prandial VAS score” and “effect of KWG on post-prandial blood glucose concentration”. All VAS scores were represented by the mathematically calculated “Incremental Appetite Score” (corrected for baseline value) as mentioned above.

Due to the fact that both blood glucose concentration and appetite score were measured at baseline, 60 minutes, 120 minutes and 180 minutes, correlation analysis between blood glucose concentration and appetite score was conducted at these four time-points. Furthermore, “Incremental Area Under the Curve” (iAUC) between 0 and 180 minutes for both incremental blood glucose concentration and incremental appetite score were also used to analyze the correlation.

For the covariates, height and weight were combined and represented by BMI. The potential effects of age, BMI and sex on the main interested outcome (VAS score represented by incremental appetite score) were analyzed individually. The analysis of the difference in VAS score between male and female participants across the 240 minutes’ study period was based on the repeated measure general linear model. The analysis of the correlation between age and VAS score and between BMI and VAS score were based on correlational analysis.

2.3 Results

2.3.1 Participant Characteristics

A total of 30 participants living with T2DM were recruited through available research database as well as newspaper. Among them, five participants dropped out the project before the procedures were initiated due to time conflict (unrelated to interventions). The remaining 25 participants finished the project. The remaining 25 participants started and completed the study (12 males, 13 females). Completing participants had a mean age of 63.0 ± 8.5 years, mean BMI of 29.0 ± 4.2 kg/m², mean fasting blood glucose concentration of 7.4 ± 0.1 mmol/L at study baseline. The mean period since T2DM diagnosis among the participants was 9.0 ± 7.0 years, with 15 participants taking anti-hyperglycemic and antihypertensive medications. Medications were not taken during the period of each visit and medication type was not available. During the ginseng administration days and wash out period, there were no differences in reported symptoms between KWG treatment groups.

2.3.2 Effect of Korean White Ginseng on Post-Prandial Blood Glucose Concentration

As shown in figure 5 below, blood glucose concentration (mmol/L, mean \pm SEM) was not impacted by ginseng dosage (11.6 ± 1.0 mmol/L, $p=0.80$). A significant effect of time (minutes) on mean post-prandial blood glucose concentration (across the five treatment conditions at each time point), however, was detected ($p<0.01$). Time point analysis showed a significant difference in mean post-prandial blood glucose concentration (mmol/L, mean difference \pm SEM) between 0 and 15 minutes (2.6 ± 0.2 mmol/L, $p<0.01$), between 15 and 30 minutes (2.3 ± 0.2 mmol/L, $p<0.01$), between 30 and 45 minutes (2.0 ± 0.4 mmol/L, $p<0.01$), between 60 and 90 minutes, (-1.1 ± 0.2 mmol/L, $p<0.01$), between 90 and 120 minutes (-1.9 ± 0.1 mmol/L, $p<0.01$), and between 120 and 180 minutes, (-3.4 ± 0.2 mmol/L, $p<0.01$).

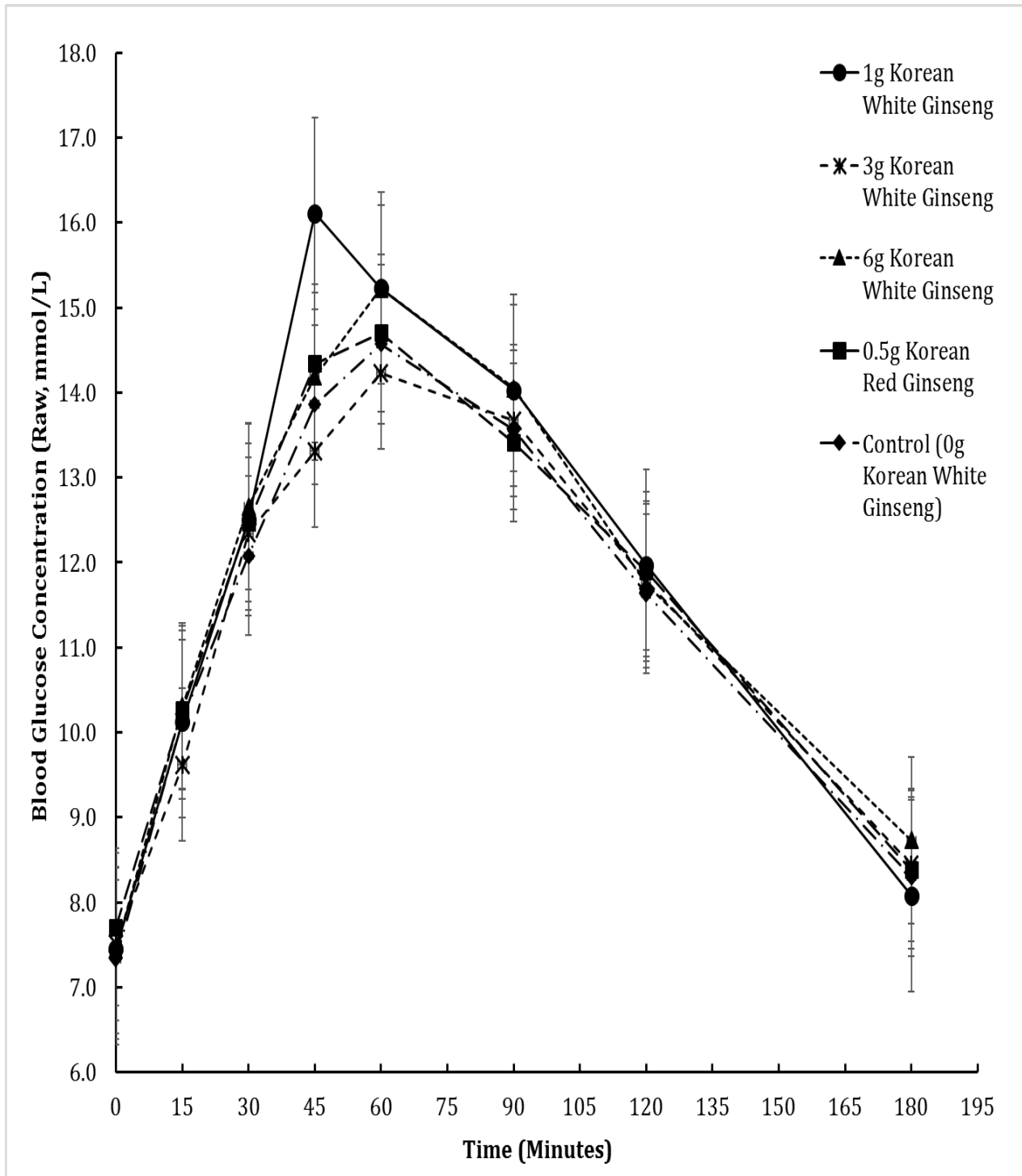


Figure 5. Blood Glucose Concentration Cross-Time and Doses

Effects of treatment doses 0g (control), 1g, 3g, 6g Korean white ginseng or 0.5g Korean red ginseng on post-prandial blood glucose concentration after 75g oral glucose tolerance test (OGTT). Values are presented as mean post-prandial blood glucose concentration (mmol/L) over three hours (180 minutes) post-intervention (n=25). Control represents placebo with 0g of Korean white ginseng. Values are mean \pm SEM. Repeated Measure ANOVA: Cross-dose (p=0.80), Cross-time (p<0.01).

2.3.3 *Effect of Korean White Ginseng on Post-Prandial Visual Analog Score*

2.3.3.1 *Incremental Appetite Score*

Shown in figure 6, analysis indicated that incremental appetite score (mean \pm SEM) was not impacted by ginseng dosage (7.9 ± 2.7 , $p=0.64$). The mean value of incremental appetite score for each dose is: 1g KWG (9.9 ± 2.8), 3g KWG (8.5 ± 2.8), 6g KWG (4.4 ± 2.4), 0.5g KRG (9.1 ± 3.3), Control (0g KWG) (7.6 ± 2.5). A significant effect of time (minutes) on mean incremental appetite score (across the five treatment conditions at each time point), however, was detected after 60 minutes from the baseline ($p<0.01$). Time point analysis showed a significant difference in mean incremental appetite score (mean difference \pm SEM) between 60 and 120 minutes (7.0 ± 0.8 , $p<0.01$), between 120 and 180 minutes (5.8 ± 1.0 , $p<0.01$), and between 180 and 240 minutes (-4.2 ± 1.3 , $p=0.01$), but no significant difference in mean incremental appetite score between 0 and 60 minutes (0.8 ± 1.1 , $p=1.00$).

There was no significant impact of participants' sex on incremental appetite score ($p=0.32$). There was no significant correlation between participants' age and mean incremental appetite score at either 60 minutes ($p=0.60$) or 240 minutes ($p=0.36$) but significant inverse correlations at 120 minutes ($p<0.01$) and 180 minutes ($p=0.04$). There was no significant correlation between participants' BMI and mean incremental appetite score at either 120 minutes ($p=0.20$) or 180 minutes ($p=0.83$) but significant inverse correlations at 60 and 240 minutes ($p<0.01$).

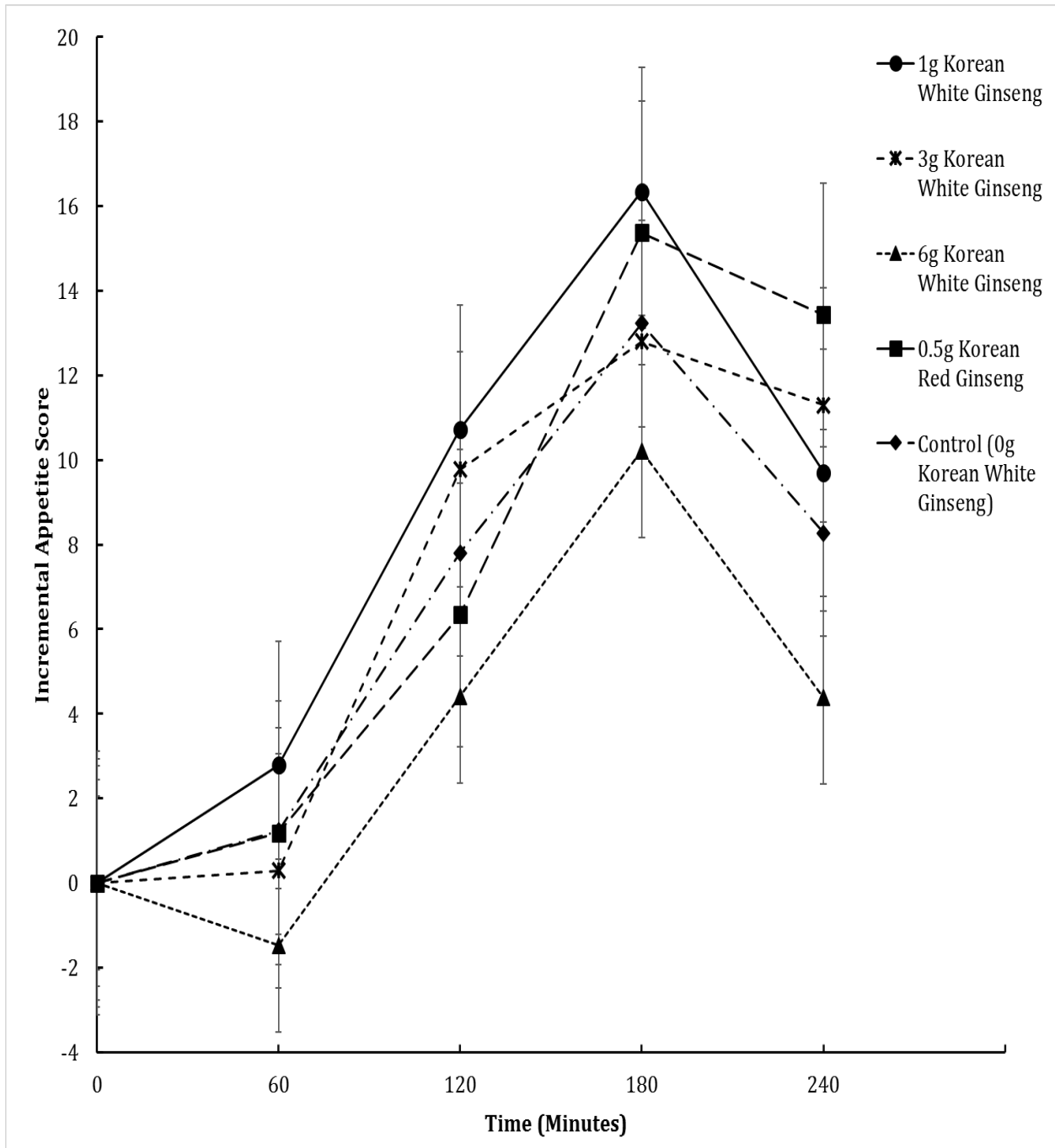


Figure 6. Incremental Appetite Score Cross-Time and Doses

Effects of treatment doses 0g (control), 1g, 3g, 6g Korean white ginseng or 0.5g Korean red ginseng on incremental appetite score after 75g oral glucose tolerance test (OGTT). Values are presented as mean incremental appetite score over four hours (240 minutes) post-intervention (n=25). Control represents placebo with 0g of Korean white ginseng. Values are mean \pm SEM. Repeated Measure ANOVA: Cross-dose (p=0.64), Cross-time (before 60 mins, p=1.00; after 60 mins, p \leq 0.01).

2.3.3.2 Incremental Composite Visual Analog Score

Shown in Figure 7, analysis indicated that incremental composite VAS score (Question 1, 2 and 4 on the VAS questionnaire) (mean \pm SEM) was not impacted by ginseng dosage (10.7 ± 1.4 , $p=0.54$). A significant effect of time (minutes) on mean incremental composite score concentration (across the five treatment conditions at each time point), however, was detected. Time point analysis showed a significant difference in mean incremental composite score (mean difference \pm SEM) between 60 and 120 minutes (8.1 ± 0.9 , $p<0.01$) and between 120 and 180 minutes (7.3 ± 1.0 , $p<0.01$), but no significant difference between 0 and 60 minutes (1.9 ± 1.1 , $p=0.82$) and between 180 and 240 minutes (-3.2 ± 1.3 , $p=0.15$).

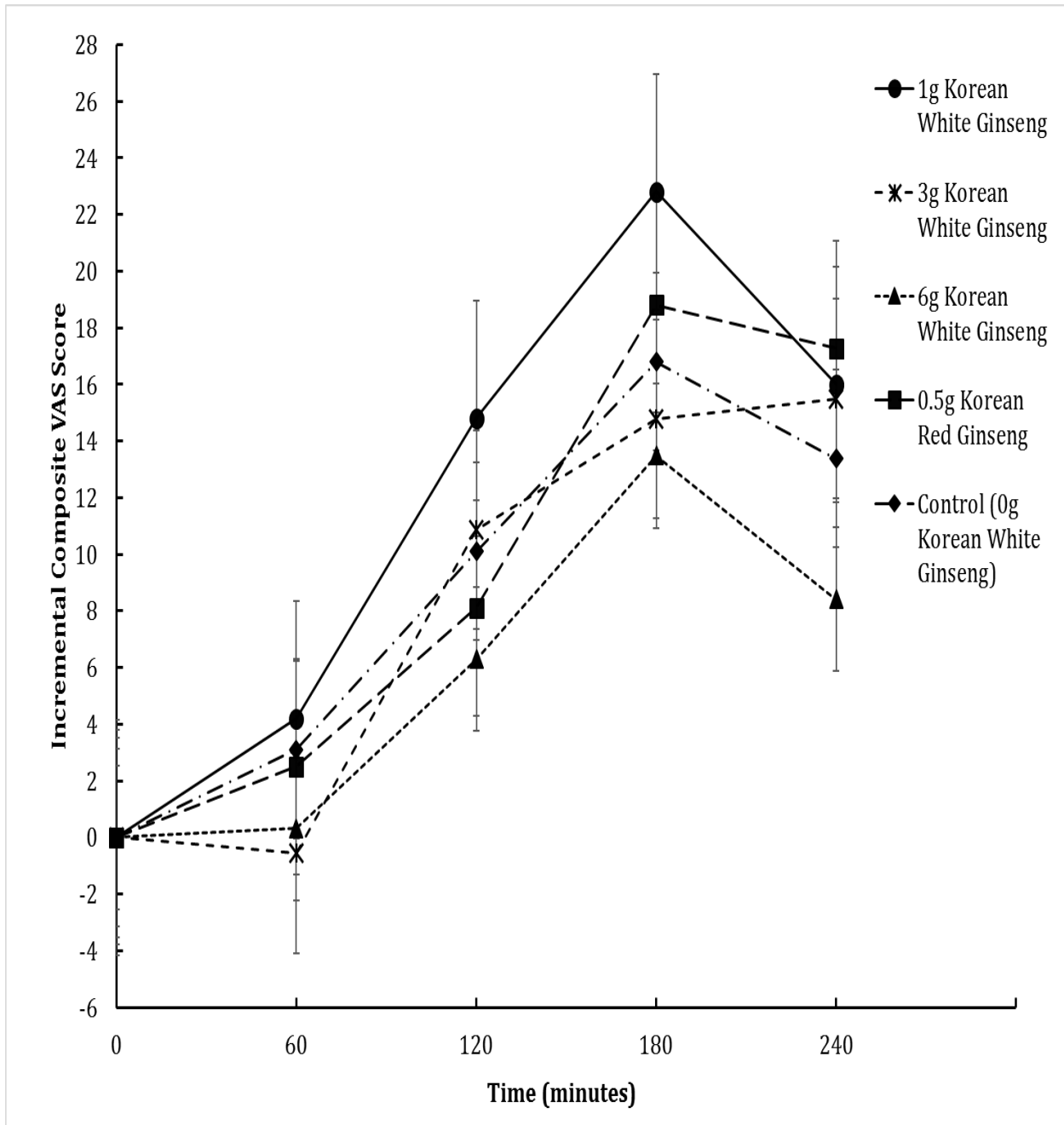


Figure 7. Incremental Composite VAS Score Cross-Time and Doses

Effects of treatment doses 0g (control), 1g, 3g, 6g Korean white ginseng or 0.5g Korean red ginseng on incremental composite VAS score (Question 1,2 and 4 on the VAS questionnaire) after 75g oral glucose tolerance test (OGTT). Values are presented as mean incremental composite VAS score over four hours (240 minutes) post-intervention (n=25). Control represents placebo with 0g of Korean white ginseng. Values are mean \pm SEM. Repeated Measure ANOVA: Cross-dose (p=0.54), Cross-time (0-60 min, p=0.82; 60-120 mins, p<0.01; 120-180 mins, p<0.01; 180-240 mins, p=0.15)

2.3.4 Correlation Between Blood Glucose Concentration and Visual Analog Score

Table 4 below shows the mean blood glucose concentrations and appetite scores (Mean \pm SEM) at 0, 60, 120 and 180 minutes.

Table 4. Blood Glucose Concentration and Appetite Score at 0, 60, 120 and 180 Minutes

	Mean	SEM
Blood Glucose Concentration at 0 min (mmol/L)	7.5	0.1
Blood Glucose Concentration at 60 min (mmol/L)	14.8	0.2
Blood Glucose Concentration at 120 min (mmol/L)	11.8	0.2
Blood Glucose Concentration at 180 min (mmol/L)	8.4	0.2
Appetite Score from 0min to 0 min	48.8	1.5
Appetite Score from 0min to 60 min	49.5	1.5
Appetite Score from 0min to 120 min	56.7	1.5
Appetite Score from 0min to 180 min	62.0	1.2

*SEM = standard error of mean

Table 5 below shows the correlations between blood glucose concentration and appetite score at 0, 60, 120 and 180 minutes. Due to the fact that appetite score was not normally distributed (Shapiro-Wilk normality $p < 0.05$), Spearman correlational analysis was conducted. Blood glucose concentration was not correlated to appetite score at both 0 minutes ($p = 0.81$) and 60 minutes ($p = 0.19$), but a positive correlation between the two variables was observed at 120 minutes ($p < 0.01$) and 180 minutes ($p = 0.01$).

Table 5. Correlation between Blood Glucose Concentration and Appetite Score at 0, 60, 120 and 180 Minutes

	Correlation at 0 minute	Correlation at 60 minutes	Correlation at 120 minutes	Correlation at 180 minutes
Spearman's Correlation Coefficient	0.02	0.11	0.34	0.21
p Value	0.81	0.19	<0.01	0.01

Table 6 below shows the incremental area under the curve (iAUC) values of both postprandial BG concentration (188.9 ± 31.0) and appetite score (919.0 ± 150.5) between 0 and 180 minutes.

Table 6. iAUC of Blood Glucose Concentration and Appetite Score between 0 and 180 Minutes

	Mean	SEM
Blood Glucose Concentration iAUC from 0min to 180min	788.9	31.0
Appetite Score iAUC from 0min to 180min	919.0	150.5

*SEM = standard error of mean;

*iAUC = incremental area under the curve

Table 7 below shows no significant correlation between incremental blood glucose concentration and incremental appetite score ($p=0.19$). In other words, blood glucose concentration could not predict appetite score. Note: due to the fact that the iAUC of both postprandial blood glucose concentration and appetite score (between 0 and 180 minutes) were not normally distributed (Shapiro-Wilk normality $p<0.05$), Spearman correlational analysis was conducted.

Table 7. Correlation between Blood Glucose Concentration iAUC and Appetite Score iAUC

Blood Glucose iAUC from 0min to 180min (n=150)	Appetite Score iAUC from 0min to 180min (n=149)
Spearman's Correlation Coefficient	0.1
p Value	0.19

* iAUC = incremental area under the curve

2.4 Discussion

2.4.1 Blood Glucose Concentration and Visual Analog Score

The participants of this study had been diagnosed with T2DM for approximately 10 years before study enrolment. According to Diabetes Canada CPG, glycemic targets for people living with T2DM are: between 4.0 and 7.0 mmol/L when fasting, and between 5.0 and 10.0 mmol/L 2-hour postprandial (204). As shown in figure 3, the participants' mean blood glucose concentration at baseline was above 7.5 ± 0.1 mmol/L, and rose to 14.8 ± 0.2 mmol/L at 60 minutes. After 60 minutes, the mean blood glucose concentration started to fall back and reached 11.6 ± 0.1 mmol/L at 120 minutes. Since the participants did not take any anti-hyperglycemic medication before and during each visit, these results were expected to occur (blood glucose concentration fell outside of target range). This fluctuation of blood glucose concentration provides a good setting for assessing the impact of blood glucose concentration on satiety.

Shown in table 7, the overall correlation between blood glucose concentration and satiety between 0 and 180 minutes (calculated by iAUC) was not observed ($r=0.1$, $p=0.19$). Despite the overall insignificance in correlation between the two variables, it is interesting to take a close look of each individual time-point. If looking closely at each time-point (shown in table 5), at 0 and 60 minutes, blood glucose concentration was not correlated to appetite score ($p=0.81$ and 0.19), but a positive correlation between the two variables was observed at 120 and 180 minutes ($p<0.01$). These results were not consistent with what Glucostatic Theory has predicted. According to Glucostatic Theory, blood glucose concentration is inversely related to appetite, with high level of blood glucose concentration predicting low level of appetite (high level of satiety), and low level of blood glucose concentration predicting high level of appetite (low level of satiety) (59). Apart from the insignificant correlation between the two variables at 0 and 60 minutes, the results at 120 and 180 minutes, however, have shown that higher blood glucose concentration was correlated to higher level of appetite score. One possible reason for these contradictory results (especially at 120 and 180 minutes) is that the participants did not take anti-hyperglycemic medications before and during each visit. The elevated blood glucose concentration (from the 50g OGTT), therefore, could not be effectively taken up by

cells as energy source, which would continue to signal the body of energy depletion (10). This is a typical symptom of T2DM—polyphagia (constant feeling of hunger despite high blood glucose concentration), as mentioned in *Section 1.1.2* (10). The positive correlation between blood glucose concentration and appetite score at 120 and 180 minutes can indicate that without taking anti-hyperglycemic medications, patients with higher blood glucose concentrations were the ones who were less efficient to utilize ingested glucose as energy source, which further led to enhanced hunger perception indicated by higher appetite scores.

If further looking at the trend of change of blood glucose concentration and appetite score over the course of 180 minutes, the results were still not consistent with Glucostatic theory. Blood glucose concentration significantly increased from 7.5 ± 0.1 mmol/L at baseline to 14.8 ± 0.2 mmol/L at 60 minutes ($p < 0.01$) due to the 50g OGTT, as expected. Their mean incremental appetite score, however, did not show significantly decrease from baseline to 60 minutes (mean difference 1.6 ± 0.7 , $p = 0.60$). The result from the first 60 minutes, therefore, was not in line with what Glucostatic Theory has predicted (increased blood glucose concentration predicts hunger suppression). Significant increase of incremental appetite score, however, was observed from 60 to 180 minutes (mean difference 12.8 ± 0.9 , $p < 0.05$), accompanied by significant decrease of blood glucose concentration from 60 to 180 minutes (mean difference 6.4 ± 0.1 mmol/L, $p < 0.01$). One possible reason for these inconsistent results could be that the participants went through fasting for 10-12 hours before the baseline measurements were collected. As mentioned in the earlier section, hunger and satiety are also influenced by many other factors, such as hormones. Ghrelin (also called “hunger hormone”), for example, as mentioned in *Section 1.2.4.1*, is produced from the oxyntic gland of the stomach and can promote appetite and suppress satiety, especially when the stomach is empty (84,85). Ghrelin is released during fasting or period of low dietary intake (84,85). Although the main study did not measure the participants’ blood ghrelin level, the correlation between blood glucose concentration and appetite score might potentially have been confounded by increased blood ghrelin level caused by the prolonged fasting process. In other words, high amount of blood ghrelin concentration related to prolonged fasting could “overpower” the satiety induced by high blood glucose concentration, and still induce hunger perception as a result.

At 180 minutes, a standardized snack was provided to each participant. Based on the results shown in figure 5, incremental appetite scores significantly decreased from 180 minutes (13.6 ± 1.1) to 240 minutes (9.4 ± 1.5) ($p < 0.05$). These results indicate that the snack provided at 180 minutes did have significant impact on satiety afterwards. The reason behind this impact could be due to the macro-nutrient content of the snack. As calculated in *Section 2.2.2*, based on the calculation from Canadian Nutrient File, the macro-nutrients in the snack include: Total energy (96.5kCal), carbohydrates (12.22g), protein (4.38g), fat (2.78g), fiber (1.3g), added sugar (1.18g) (201). As discussed in *Section 1.2.4*, presence of foods (especially macronutrients such as carbohydrates, fats and proteins) in the stomach and small intestine can trigger the release of several gastro-intestinal peptide hormones (such as CCK, GLP-1 and PYY), which are involved in regulating hunger and satiety through the hormonal-neural feedback system (70). Fat and protein consumption can trigger satiety through stimulating the release of CCK from the duodenum (72). CCK has its receptors distributed in the brain and can signal the brain to promote satiety (71). At the same time, CCK can inhibit gastric emptying by stimulating the contraction of the pyloric sphincter, thus suppressing further food intake (71,73,74). Carbohydrates and protein consumption can also trigger the release of GLP-1, which is produced by the L-cells of the small intestine (75-77). GLP-1 facilitates satiety by inhibiting gastric mobility (78,79). PYY is also released synchronously with GLP-1 from the L-cells of the distal small intestine in response to meal ingestion, and it has additive inhibitory effects on gastric acid secretion and mobility (81). In addition, presence of food in the stomach can lead to inhibition of ghrelin production as mentioned earlier, thus suppressing hunger perception (84,85). Ingesting carbohydrates can also raise blood glucose concentration, and elevated blood glucose concentration can suppress hunger and promote satiety, according to the prediction of Glucostatic Theory. The snack contained 12.22g of carbohydrates from the bread (1 serving) and 1.18g of added sugar. Although the blood glucose concentration was not measured after 180 minutes, it can be assumed that the participants had elevated blood glucose concentrations at 240 minutes, rendering decreased VAS values at 240 minutes, compared to 180 minutes, as shown in figure 5.

In summary, although Glucostatic Theory is relevant to satiety and can be used to explain some results of this study, it should not be used as the only mechanism to explain

hunger and satiety. Many other factors, such as hormonal factors, are involved in hunger and satiety regulation and can be used to explain why the correlation between blood glucose concentration and satiety was not observed during the first 60 minutes. Future research studies, therefore, can be improved by measuring blood hormone level (such as blood CCK, GLP-1, PYY and ghrelin level) along with blood glucose concentration in order to create a better picture of the factors that can have impact on hunger and satiety.

2.4.2 Impact of Korean White Ginseng on Satiety

KWG did not have a statistically significant impact on blood glucose concentration or VAS Score. Potential explanations on why KWG did not have significant impact on these outcomes can be explored from three perspectives: (1.) treatment duration, (2.) ginsenoside composition and (3.) ginseng dosage administered.

2.4.2.1 Treatment Duration

As discussed in *Section 1.3.5*, two mechanisms have been proposed to explain ginseng's anti-hyperglycemic effects at cellular level: (1.) Enhanced pancreatic beta-cell function and enhanced insulin production and secretion; (2.) Reduced IR and increased insulin sensitivity at the cellular level (136). Changing cellular function and sensitivity through treatment, however, depends on the duration of the treatment. As mentioned in *Section 1.3.5*, increased UCP-2 expression in pancreatic beta-cells can suppress insulin production and reduce cell survival rate (171,173-176). Suppressed UCP-2 expression can therefore increase insulin production. An *in vitro* study showed that pancreatic beta-cells had to be cultured with ginseng extracts for at least 24 hours to exhibit enhanced ATP production, suppressed uncoupling protein-2 (UCP-2) expression and increased insulin production (171). In this study, the participants' total exposure time to ginseng treatment from baseline to the end of each visit was only 240 minutes (4 hours), far less than 24 hours. In other words, after the participants took the assigned KWG doses at the baseline, the 4-hour window for BG concentration and VAS measurement might have been too short to allow the consumed KWG to show its potential effect on glycemic control and related

hunger and satiety. After four-day washout period, when the participants returned to the next visit, the KWG consumed during the last visit had lost its intended effect.

Although *in vitro* study is based on studying cell functioning outside of its normal biological context (such as in a tube or on a plate), many clinical trials did try to provide participants with sufficient exposure time to ginseng treatment in order to achieve the intended therapeutic outcomes. A meta-analysis study systematically reviewed ginseng's therapeutic effects based on 65 randomized-controlled human trials worldwide administrated in the past (162). The results showed that out of the 65 ginseng clinical trials, 54 of them used continuous treatment method by asking participants to take assigned ginseng doses every day for 2-12 weeks (commonly 8-12 weeks) in order to observe the therapeutic effect of ginseng over time (162). In this main study, however, the participants were only asked to take assigned ginseng doses on the day of visit, followed by a 4-day washout period (during which they did not take ginseng supplements). Each participant in this study had 5 visits with a total of 5 treatments, which did not satisfy the sustained or continuous exposure to ginseng treatment condition over weeks or months commonly used in other ginseng studies. If the research method in this study could be modified by using continuous treatment method (such as by asking participants to take KWG supplements every day for 8-12 weeks), it would allow cells to be exposed to KWG treatment long enough to show its intended effect and the results could potentially be different from current results.

2.4.2.2 Ginsenoside Composition

As discussed in *Section 1.3.3*, ginsenosides are the main active components of ginseng, and ginsenoside compositions are different between AG and KG (127,134). In short, KG is high in ginsenoside Rf and Rg2 (which are usually not contained in the ginsenoside profile of AG) and Rg1 content in KG is 10 times higher than in AG (139,143). AG, however, contains twice the level of ginsenoside Re, compared to KG (144). The ratio between PPD (Rb1, Rb2, Rb3, Rc, Rd and Compound K) and PPT (Re, Rf, Rg1, Rg2, Rg3, Rh1) is also different from AG to KG. The PPD:PPT ratio is > 2.0 in AG, but < 2.0 in KG (135,139,145). Different ginsenoside compositions might potentially render different research outcomes.

In this main study, four-year old dried KWG whole root powder product was provided by the Department of Herbal Crop Research and National Institute of Horticulture & Herbal Science, RDA, Korea. The analysis of ginsenoside profile of the KWG sample revealed that the total ginsenoside concentration was only 1.8%, which was almost half of the ginsenoside concentration found in the AG sample (3.2%) used in another study by Vuksan et al. (2000) (163). Also, based on the calculations from table 2 in *Section 2.2.2*, the PPD/PPT ratio in the KWG sample was only 0.35. This value which was lower by 6-folds, comparing to the typical PPD/PPT ratio in AG (>2.0) (135,139,145). In the study conducted by Vuksan et al. (2000), administering 3g AG showed significant postprandial glycaemic-lowering effect in both diabetic and non-diabetic groups (163).

In addition, literature has revealed that the ginsenosides Rg1/Re ratio in KWG is usually found to be greater than 1.0, and the Rb1/Rc ratio is usually found to be approximately 0.8 (205). Based on the calculations from table 2 in *Section 2.2.2*, the Rg1/Re and Rb1/Rc ratios of KWG used in this study, however, were 0.6 and 1.6, respectively. This means that the Rg1/Re ratio was almost half of the typical value 1.0, and the Rb1/Rc ratio doubled the typical value 0.8. It is unclear why the ginsenoside components of the KWG sample used in this study did not satisfy the typical KWG ginsenoside profile.

The KWG used in this study did not show significant impact on blood glucose concentration and on satiety. The lab results of ginsenoside profile have indicated that perhaps the low ginsenosides concentration and low PPD components (Rb1, Rb2, Rb3, Rc, Rd and Compound K) of KWG sample used in this study, as well as the significant deviation of ginsenoside profile from typical values in KWG might have potentially influenced the effect of KWG on lowering postprandial blood glucose concentration as well as on satiety. The test-results of KWG components in this study have implied that standardization of the components of products used in any NHPs related research studies is important and can potentially have significant impact on study results. Component-profiles of NHPs used in research studies, therefore, should be carefully analyzed and closely monitored.

2.4.2.3 Ginseng Dosage Administrated to Participants

In the main study, 1g, 3g and 6g of KWG were used as the doses for treatment during each visit. The doses used in this study are comparable to doses used in previous clinical trials conducted by the Vuksan Laboratory (160,161,163,165,166,170,206). Despite the fact that incremental appetite score was not significantly different between dose administrations, figure 5 still shows that incremental appetite score of 1g KWG treatment is the highest (9.9 ± 2.8), and incremental appetite score of 6g KWG treatment is the lowest (4.4 ± 2.4). Based on the ginseng clinical trials systematic review by Shergis et. al (2013), ginseng doses used in other studies in the past (although for different purposes) usually ranged from 1g/day up to 9g /day (162). If the highest dose of KWG in this study could be adjusted from 6g to 9g, it might potentially increase the mean difference of incremental appetite score between 1g and 9g KWG, or between control (0g) and 9g KWG administration, thus potentially changing the study results.

2.4.3 Limitations

This study (and the secondary data analysis conducted for the purposes of this thesis) has several limitations. First, despite the fact that the inclusion criteria for age was 18-75 years, the actual age range of participants enrolled in this study was 46-75 years. Energy intake tends to decrease with aging, appetite and hunger perception might be different in a younger sample in comparison to an older sample (207). The impact of KWG treatment on blood glucose concentration as well as on hunger and satiety might also be different among different age groups. In other words, results from this study cannot be applied to younger population (≤ 45 years). Also, as mentioned earlier, the KWG treatment in this study was not continuous (administrated only on the day of visit), the study results cannot be applied to the potential impact of KWG on satiety if consumed over the period of weeks (such as 8-12 weeks) or months. In addition, the participants were taking anti-hyperglycemic medications and antihypertensive medications. Although they did not take these medications during the visits, they took the medications 12-24 hours prior to the visits and there might have been some residual effects on blood glucose concentration from the medications during the visits. The metabolites of these medications might have been

present in the blood during the period of visits, which might have potentially affected glycemic response as well as hunger perception. Metformin (an insulin sensitizer), for example, as a commonly prescribed anti-hyperglycemic medication, is sometimes associated with gastrointestinal side effects (such as diarrhea, nausea and vomiting) (208). If any participants experienced these side effects associated with their medications, it might potentially have impacted their appetite scores during the visit. Since the list of medications that the participants took was not available, it has created a limitation for further analyzing the potential confounding effect of medications on hunger perception and VAS scores.

2.5 Conclusion

This study was the first to explore the direct relationship between KWG consumption and satiety in participants with T2DM. The hypothesis was that KWG consumption would decrease the subjective satiety rating measured by VAS score. The results of this study showed that 1g, 3g and 6g KWG did not have significant impact on either postprandial blood glucose concentration or appetite scores. Also, despite the fact that time had significant impact on both blood glucose concentration and appetite score, the significant correlation between blood glucose concentration and appetite score was not observed. At this stage, therefore, there is insufficient evidence to claim that KWG consumption has a significant impact on hunger satiety in people living with T2DM. There is also insufficient evidence to claims that it does not due to the study limitations highlighted above. Future studies should focus on the effect of long term KWG consumption (over weeks and months) on hunger and satiety, as well as explore the effect of different ginsenoside compositions on glycemic control. It will also be beneficial for future studies to measure satiety-related blood hormone level (such as blood CCK, GLP-1, PYY and ghrelin level) along with blood glucose concentration in order to create a better picture of the factors influencing hunger and satiety.

STUDY 2

Investigating Nutrition Students' Knowledge and Perception of and Interest in NHPs —Questionnaire Development Phase One.

ABSTRACT

Title: Investigating Nutrition Students' Knowledge and Perception of and Interest in NHPs: Questionnaire Development Phase One.

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Background: Current research environment encourages integrative knowledge translation (iKT) with the aim of effectively delivering research findings to end users in a timely manner. In the medical model, end users are often patients who are educated/ counseled by healthcare providers making healthcare providers (and trainees) and key player in knowledge transfer. Canadian Dietitians have expressed interest in learning more about Natural Health Products and how to integrate this knowledge into practice and training.

Goal: To develop a questionnaire that can be used to investigate nutrition students' knowledge and interest in and perception of Natural Health Products (NHP).

Methods: A Natural Health Products-Questionnaire (NHP-Q) was created using published peer-reviewed literature and questionnaires. A standardized feedback form (composed of open-end and closed-end questions) and the NHP-Q were provided to participants (health professionals and nutrition students). Data provided were organized by themes; theme-code development and data interpretation were conducted by a pair of scientists trained in qualitative methods. Decisions regarding revising the NHPs were made when two or more participants per participant group highlighted difficulty for a specific question in NHP-Q and provided actionable supporting qualitative feedback.

Results: Health professionals (n=10) and undergraduate nutrition students (n=22) provided feedback. NHP-Q was carefully revised twice based on the feedback data from both health professional participants and nutrition student participants. Based on the feedback data from health professionals sample, 28 out 32 total questions in NHP-Q were revised. Based on the feedback data from nutrition students sample, 18 out 28 total questions in NHP-Q were revised.

Conclusion: This data collection tool has taken standardized/ published questions from other allied health care professions, adapting them to the nutrition profession, and has been face and content validated. The revised NHP-Q has improved overall structure and content flow, has become more inclusive and specific in content and avoided leading questions. It is now ready for pre-testing during the next phase.

3 METHODOLOGY AND RESULTS FOR STUDY 2

3.1 Rationale and Objectives

Rationale:

Research examining health professionals' knowledge and interest in and perception of NHPs have mainly focused on Pharmacists', with a few studies including the nutrition professional perspective. There is limited published information available on (Canadian) nutrition trainees'/students' knowledge and perception of and interest in NHPs and inconsistent attention to this topic across Canada in *Partnership for Dietetic Education and Practice* accredited Universities.

This study is divided into three phases: (1.) *Phase One*: questionnaire development, (2.) *Phase Two*: Pre-testing the questionnaire at Mount Saint Vincent University (MSVU) and Saint Francis Xavier University (St.FX), (3.) *Phase Three*: Administration of the questionnaire. *Phase One* has been completed and is included in this thesis.

Objectives of Phase One:

- (1) To develop a questionnaire to collect the following information:
 - a) Undergraduate nutrition students' knowledge and perception of NHPs and ginseng.
 - b) Undergraduate nutrition students' interest in NHPs and ginseng.
- (2) Face-content-validation of questionnaire.
 - a) Face validation involves selecting appropriate font and size as well as space-arrangement of the questionnaire.
 - b) Content validation involves the readability and appropriateness of the content of the questionnaire.
- (3) To develop a questionnaire that can be completed by undergraduate nutrition students within approximately 10 minutes.

3.2 Methods

3.2.1. Sample Recruitment

The study sample was divided into two sub-samples: (1.) health professionals and (2.) nutrition students. The target sample size for face-content validating a questionnaire can vary from five to thirty (209). Evidence suggests that a sample size more than 30 typically does not bring incremental diagnostic information and is not cost-effective (209). Thirty was the total target sample size in this study.

Note: These two sub-samples were recruited sequentially: first health professionals' sample, then nutrition students' sample. The feedback from health professionals was integrated in the questionnaire before the nutrition students reviewed the questionnaire.

The inclusion criteria for health professionals sample were: healthcare providers, educators or researchers, aged between 18-70 years. A letter of invitation letter (Appendix 3) was sent via email to selected health professionals. If they agreed to participate, a pre-designed NHP-Q draft and a *NPH-Q-Feedback Form* (Appendix 4) would be emailed to them. After completion, they would be asked to send the completed feedback form back to the research investigator via email.

The inclusion criteria for nutrition students sample were: undergraduate students enrolled in AHN program at MSVU, above 18 years of age, and can read and write English at a grade seven reading level or higher. A letter of invitation (Appendix 5) was posted to the Moodle page of several undergraduate nutrition courses at MSVU, with the permission of faculty. Students who showed interest in participation contacted the Study Coordinator (H.H.) via email. A meeting between a potential participant and the Study Coordinator (or Research Assistant) was then set up in Room EV422 at MSVU, where the study coordinator reviewed the consent form (Appendix 12) with the potential participant. After the informed consent form was signed by both the student participant and Study Coordinator, he/she then received a package via email containing two attachments: the NPH-Q (the second version) and an updated *NHP-Q-Feedback Form* (Appendix 6), along with the instructions about how to complete the feedback form. After completion, student

participants were asked to submit a hard copy of the *NHP-Q-Feedback Form* to the physical dropbox located in EV422 at a prearranged date and time.

3.2.2 Data Collection

Two administration tools were used in this study:

- (1) A Natural Health Products-Questionnaire (NHP-Q)—designed to investigate nutrition students' knowledge and perception of and interest in NHPs.
- (2) A *NHP-Q-Feedback Form*—designed to ask for feedback from participants regarding the content, format and readability of NHP-Q.

The *NHP-Q-Feedback Form* was the main tool in this study (*Phase One*) to collect data from the participants.

3.2.2.1 Natural Health Products-Questionnaire

NHP-Q draft was first created based on literature review. It was adapted and modified from questionnaires used in other survey studies conducted in the past, which investigated healthcare workers' (such as medical students, Pharmacists and Registered Dietitians) knowledge and attitude towards NHPs (210-212). Questions in the NHP-Q draft involve two fields: participants' demographic data (age, educational background, cultural background, and working experience, etc.), and their knowledge and perception of and interest in NHPs.

As for the format of NHP-Q, anonymous closed-end multiple-choice questions mixed with some open-ended questions was the chosen format. There are two benefits of using close-ended questions in this study. First, it is easier for study participants to answer, and takes less time and effort for them to complete the questionnaire (213). Second, by using multiple-choice questions, it is easy for the researchers in the future Phase Two to categorize different answers and to conduct a descriptive statistical analysis by using mean, frequency and percentage, and to further compare the differences between categories. Some multiple-choice questions were also followed by open-ended sub-questions to allow the participants to justify or explain their choices.

3.2.2.2 NHP-Q-Feedback Form

NHP- Q and the *NHP-Q-Feedback* Form were presented to the participants to ask feedback from them. This *NHP-Q-Feedback* facilitated data provision from participants with the aim of ensuring that the NHP-Q was:

- (1) Specific: Questions in NHP-Q should provide clear and detail information for participants to understand;
- (2) Brief: Questions in NHP-Q should ideally consist no more than 20 words or 3 commas, and avoid redundancy;
- (3) Unambiguous: Questions in NHP-Q should avoid words that have multiple meanings and can potentially be confusing to participants;
- (4) Free of highly technical words, jargons and slang words (if some technical words were necessary, explanations needed to be provided below the words);
- (5) Relevant: Questions not relevant to the goal of the research study should not be included in NHP-Q;
- (6) Objective and unbiased: Questions in NHP-Q should avoid suggesting an answer or leading the answer toward a desired direction (214).

Based on these standards above, the *NHP-Q-Feedback Form* used nine questions designed to illicit feedback regarding the content, format and readability of NHP-Q. The first six questions in *NHP-Q-Feedback* addressed the six outcome standards listed above, and the last three questions addressed font size and white space arrangement of NHP-Q, as well asked participants to provide additional feedback (if any). Each of the nine feedback questions, therefore, focused on a different theme, including:

- (1) Feedback Question 1: whether any questions in NHP-Q were easy to understand.
It reflects the first, second and fourth standard above (being brief but still providing clear and detail information for participants to understand, and avoiding highly technical words, jargons and slang words) (214).
- (2) Feedback Question 2: whether any questions in NHP-Q contained words that might be interpreted differently by different people.

It reflects the third standard above (avoiding words that have multiple meanings and can potentially be confusing to participants) (214).

(3) Feedback Question 3: whether any questions in NHP-Q contained offensive words.

It reflects the fourth standard above (avoiding words, such as some slang words, which might be offensive to some people) (214).

(4) Feedback Question 4: whether any questions in the questionnaire were constructed in a way that a particular answer was favored over others.

It reflects the sixth standard above (avoiding suggesting an answer or leading the answer toward a desired direction) (214).

(5) Feedback Question 5: whether any questions in the questionnaire did not provide sufficient response options.

It also reflects the first standard above (providing clear and detail information for participants to understand) (214).

(6) Feedback Question 6: whether general content flow from question to question in the questionnaire was easy to follow.

It reflects the fifth standard above (logical flow being highly relevant to the goal of the study) (214).

(7) Feedback Question 7: whether the font size of the questionnaire was appropriate.

(8) Feedback Question 8: whether the questionnaire provided enough white space.

(9) Feedback Question 9: additional feedback (if any) based on participants personal thoughts and experiences.

For the first five questions on *NHP-Q-Feedback Form* (understandability, ambiguity, offensiveness, leading question, sufficient response options), each response option represents a specific question on NHP-Q. If participants felt any questions in NHP-Q had content issues that needed to be fixed or revised (such as low understandability, high ambiguity, etc.), they could choose the corresponding response options provided under each feedback question. For Question 6, 7 and 8 on *NHP-Q-Feedback Form* (content logic flow, font size and white space), the participants were asked to choose “Yes” or “No” as the response option. All these choices were collected as quantitative data.

Each feedback question also had an open-ended sub-question, and participants were asked to provide written explanations to justify their choices. These written comments were collected as qualitative data.

The nutrition student participants were also asked to complete NPH-Q (a simulation process) and report the amount of time it took them to complete NHP-Q. The professional sample was not asked to complete NHP-Q.

3.2.3 Data

3.2.3.1 Quantitative data

For the nutrition students sample, they were asked to complete NHP-Q (a simulation process) first and record the time they spent in completing NHP-Q on the first page of the feedback form. All the values of NHP-Q completion time were inputted into Microsoft® (MS) EXCEL 2013 to calculate the mean value (mean \pm SD).

For each question on *NHP-Q-Feedback Form*, participants were provided with different response options in the format of multiple-choice, the total number of participants who chose a specific response option gave a specific numeric value. Different response options on *NHP-Q-Feedback Form*, therefore, will have different numeric values. These numeric values were inputted into Microsoft® (MS) EXCEL 2013 to compare the values. A higher numeric value for a response option indicates greater number of the participants who agreed upon this response option.

3.2.3.2 Qualitative data

For each question on *NHP-Q-Feedback Form*, participants were also invited to provide written explanations (feedback comments) to justify their choices. The content of each feedback comment was analyzed and broken down based on identification of the underlying themes. The study coordinator and research assistant conducted the theme interpretation independently to prevent bias. They then came together to compare themes in order to reach a consensus. A theme codebook was then created to summarize all the themes identified from the feedback comments. A theme-code was also assigned to each theme. Each feedback comment was then attached with the identified theme-codes.

3.2.3.3 Questionnaire Revision

Decisions regarding revising the NHPs were made when two or more participants per participant group highlighted difficulty for a specific question in NHP-Q and provided actionable supporting qualitative feedback. For example, for a specific feedback question from *NHP-Q-Feedback Form*, if the numeric value for a specific response option (number of participants who chose this response option) was above 2, the theme-codes for the feedback comments (written by the participants) for this response option were analyzed to verify if the content of the feedback comments supported the response option chosen by the participants. Revision decision regarding the question from NHP-Q was then made based on the consensus between the study coordinator and research assistant. How to revise the question was based on the theme-codes and content of the feedback comments.

After taking feedback from the healthcare professionals sample, NPH-Q draft was revised to the second version. This second version of NHP-Q was then presented to the nutrition students sample. The same process repeated. After taking feedback from the nutrition students sample, NPH-Q was revised again to the third version—the final version.

3.2.4 General Flow Sequence

The following figure 7 summarizes the general flow sequence of the study, including sample recruitment, data collection, data analysis, as well as questionnaire revision process.

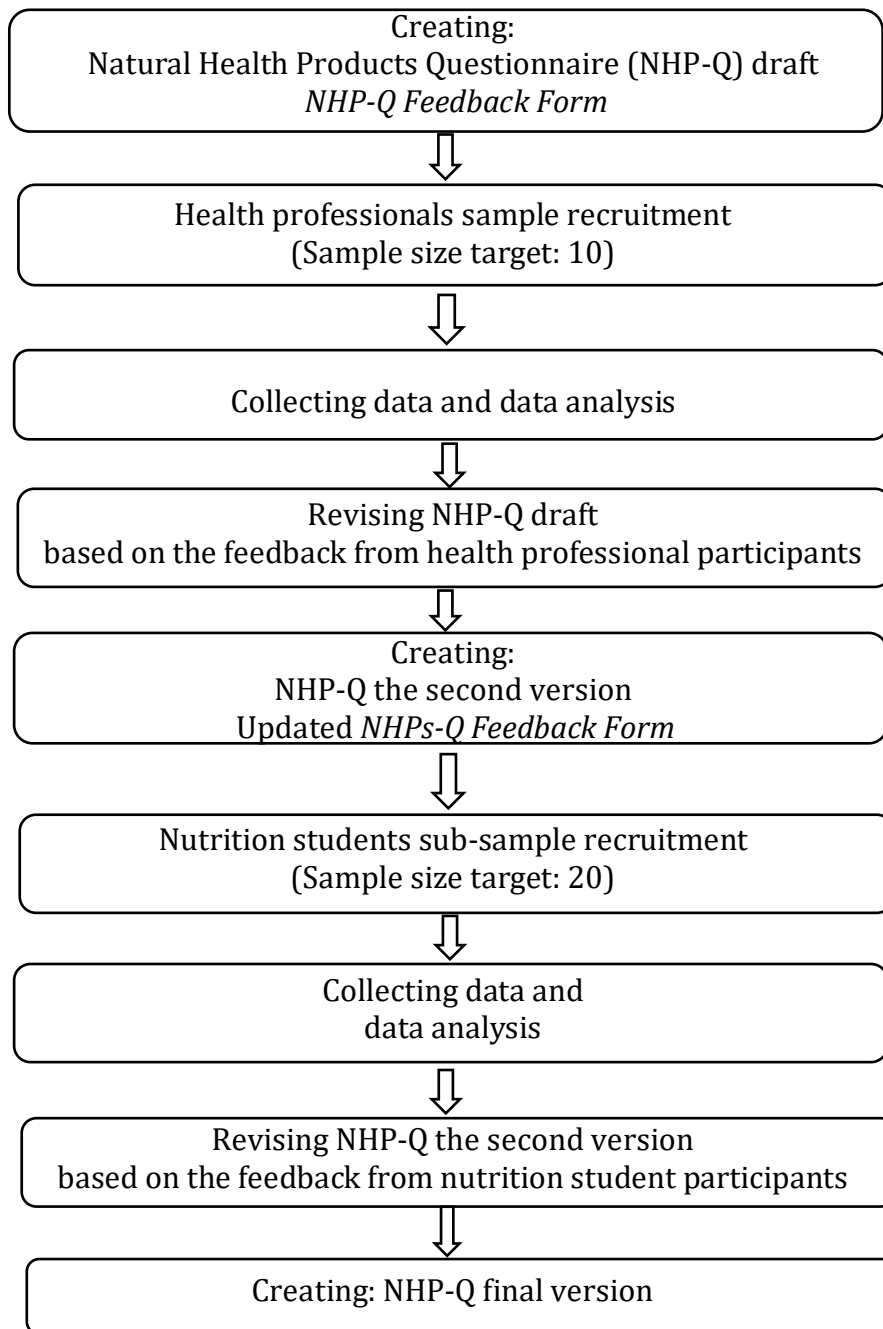


Figure 8: Flow sequence of NHP-Q development: sample recruitment, data collection and analysis, and questionnaire revision

3.3 Results

3.3.1. Participants

A total of ten healthcare professionals (n=10) were recruited and completed the *NHP-Q Feedback Form*. Participants' demographic information was not collected.

A total of twenty-two undergraduate AHN students at MSVU (n=22) were recruited and completed the study. Participants' demographic information was not collected.

As mentioned earlier, the total target sample size was 30. The actual total sample size (n=32) (10 healthcare professionals and 22 nutrition students) was above the target sample size by two participants. This is because during the sample recruitment, considering the possibility that some participants might withdraw from the study, two more participants were recruited. Interestingly, no participant (n=0) withdrew from the study.

3.3.2 Feedback Data from Health Professionals Sample

The NHP-Q draft was divided into 2 sections: Section A contained 22 questions, Section B contained 10 questions. This NHP-Q draft along with *NHP-Q-Feedback Form* (Appendix 4) were presented to health professionals sample for collecting feedback data. Nine participants (n=9) provided both quantitative and qualitative feedback, one of them (n=1) only provided qualitative feedback data but did not provide quantitative feedback data.

3.3.2.1 Quantitative data

Shown in table 8 below, the first two columns represent the question number in NHP-Q. For examples, Q2 (Section A) in this table represents Question 2 (Section A) in NHP-Q; Q5 (Section B) represents Question 5 (Section B) in NHP-Q; so on and so forth.

Also in table 8 and table 9, the first two rows represent the feedback question number in *NHP-Q-Feedback Form*. For example, FQ1 in this table represents Feedback Question 1 in *NHP-Q-Feedback Form*; FQ2 represents Feedback Question 2 in *NHP-Q-*

Feedback Form; so on and so forth. The meaning of each question in NHP-Q and each feedback question in *NHP-Q Feedback Form* in table 8 and table 9 are included in Appendix 7.

For example, in table 8, at the cross of FQ5 and Q2 (Section A), the value 1/9 (11%) means that one out of nine health professional participant (11% of the total health professional participants) indicated that Question 2 of Section A in NHP-Q did not provide sufficient response options. For another example, at cross of FQ2 and Q15 (section A), the value 3/9 (33%) means that three out of nine health professional participants (33% of the total health professional participants) indicated that Question 15 of Section A in NHP-Q might be interpreted differently by differently people; at cross of FQ1 and Q9 (Section B), the value 2/9 (22%) means that two out of nine health professional participants (22% of the total health professional participants) indicated that Question 9 of Section B in NHP-Q was difficult to understand; so on and so forth. The blank cells in table 8 indicate that no health professional participant (n=0, 0%) selected the corresponding questions from NHP-Q.

Table 8. Summary of Feedback Question 1-5 Quantitative Data from Health Professional Participants

NHP-Q Question Number		Feedback Form: Feedback Question Number				
		FQ1 n/x (%)	FQ2 n/x (%)	FQ3 n/x (%)	FQ4 n/x (%)	FQ5 n/x (%)
Section A	Q2					1/9(11%)
	Q4		2/9(22%)	2/9(22%)		1/9(11%)
	Q6		1/9(11%)			
	Q7					1/9(11%)
	Q13		1/9(11%)			
	Q14	1/9(11%)				
	Q15	1/9(11%)	3/9(33%)			
	Q16	1/9(11%)	2/9(22%)			
	Q17	3/9(33%)	2/9(22%)			
	Q18		1/9(11%)			
	Q19	2/9(22%)	3/9(33%)			
	Q20		1/9(11%)			
	Q22		1/9(11%)			
Section B	Q1				1/9(11%)	
	Q2		1/9(11%)		1/9(11%)	
	Q3		1/9(11%)			
	Q5		1/9(11%)			1/9(11%)
	Q7					1/9(11%)
	Q8	1/9(11%)	1/9(11%)			
	Q9	2/9(22%)	1/9(11%)			
	Q10					1/9(11%)

* Q: Question in NHP-Q draft

* FQ: Feedback Question in *NHP-Q-Feedback Form*

* n/x: participant number out of total participant number

* %: percentage of total participant number

Table 8 above indicates that Question 17 (Section A) in NHP-Q had the highest number of participants (n=3/9, 33%) indicating that this question was difficult to understand. Also, for Question 15 (Section A) and Question 19 (Section A) on NHP-Q, both had the highest number participants (n=3/9, 33%) indicating that the questions contained words that could be interpreted differently by different people.

Shown in table 9 below, the value 9/9 (100%) under FQ6 means that nine health professional participants (100% of the total health professional participants) thought the

content logic flow of NHP-Q was easy to follow; the value 7/9 (78%) under FQ7 means that seven out of nine health professional participants (78% of the total health professional participants) thought the font size of NHP-Q was appropriate, one out of nine health professional participants (11% of the total health professional participants) thought it was not, and one participant did not answer this question; the value 9/9 (100%) under FQ8 means that nine health professional participants (100% of the total health professional participants) thought NHP-Q provided enough “white space”.

Table 9. Summary of Feedback Question 6-8 Quantitative Data from Health Professional Participants

	Feedback Question Number		
	FQ6 n/x (%)	FQ7 n/x (%)	FQ8 n/x (%)
Yes	9/9(100%)	7/9(78%)	9/9(100%)
No	0	1(11%)	0

* FQ: Feedback Question in *NHP-Q-Feedback Form*

* n/x: participant number out of total participant number

* %: percentage of total participant number

Table 9 above indicates that all health professional participants (n=9/9, 100%) agreed that NHP-Q had good content logic flow and appropriate “white space”, and majority of the health professional participants (7/9, 78%) agreed that NHP-Q had appropriate font size.

3.3.2.2 Qualitative Data

All quantitative data above were carefully matched with qualitative data (written feedback comments) to verify if the comments supported the quantitative data. Underlying theme for each comment was identified. A color-coded Theme Codebook (Appendix 13) was created to summarize all the identified themes from comments. The following subsections discuss the general feedback comments from the health professional participants regarding the structure, content flow, font size and white space of the NHP-Q draft, as well as the feedback comments specific to each individual question in NHP-Q, including the total number of participants who commented on this question.

General Comments

A total of eight participants (n=8) provided general comments on NHP-Q: five comments on overall content flow (code 301), two comments on readjusting questions order (code 301.1), four comments on choosing precise words (code 201.1 and 202.4), one comment on providing broader response options (code 202.1). Some examples of the comments in table 10 below:

Table 10. General Feedback Comments on NHP-Q

Theme-Code	Example of Quote Comment
301.1	“Can you reorganize it to be more logical – what level of education have they completed, what program are they in, and what year of that program and then internship or something like that?”
301	“Easy to follow, questions progressed in a logical manner.” “Concise, easy to understand.”
201.1	“Replace all answer ‘I do not know the answer to this question’ with ‘I have no opinion’ – there isn’t really a right answer or a wrong answer but they may have an opinion, or no opinion.”
202.1	“Each of these questions should have a ‘Prefer not to answer’ response option.”

These comments support the quantitative data from Feedback Question 6. Nine participants (n=9, 100%) selected “Yes” on Feedback Question 6—meaning majority of the participants agreed that the general content flow of NHP-Q was easy to follow, although one participant did not provide quantitative data.

Also, a total of two participants (n=2) also commented the font size of NHP-Q. Some examples of the comments are provided in table 11 below:

Table 11. General Feedback Comments on the Font Size of NHP-Q

Theme-Code	Example of Quote Comment
401	“I don’t know if the questionnaire will be provided electronically or via paper-based survey. Consider increasing the font size to 14 pt.” “As the target audience is university students, the font size used is one they would be familiar with through their courses.” “Found it easy to read.”

These comments support the quantitative data from the feedback form, with seven participants (n=7, 78%) indicating that the font size was appropriate, and only one participant (n=1, 11%) indicating that the font size was inappropriate.

Furthermore, a total of three participants (n=3) commented the white space of NHP-Q. Some examples of the comments are provided in table 12 below:

Table 12. General Feedback Comments on the White Space of NHP-Q

Theme-Code	Example of Quote Comment
402.1	"The lines should be closer together."
402.2	"It is visual appealing." "The pages are not crowded"

These comments support the quantitative data from the feedback form, with all participants (n=9, 100%) indicating that the white space was enough.

Section A of NHP-Q

Question 1: Which response option includes your current age in years?

A total of one participant (n=1) commented on this question: choosing precise/appropriate words in the question (code 201.1). Since no participant (n=0) selected this question on the feedback form, it means that this question did not have readability/ understandability issue in general, but the wording can be more precise.

Question 2: Which response option best represents your marital status?

A total of two participants (n=2) commented on this question: one comment on providing broader response options (code 202.1), and one comment on unnecessary / redundant question (code 201.2). Example of the comments are provided in table 13.

Table 13. Feedback Comments on NHP-Q Section A-Question 2

Theme-Code	Example of Quote Comment
202.1	"single / married / common-law / living with partner / divorced / separated / widowed / living alone / living with support person)"
202.2	"Is this a requires question?"

The first comment supports the quantitative data from Feedback Question 5, with one participant (n=1, 11%) indicating that the question did not provide sufficient response options. The second comment regarding the necessity of the question, however, was not reflected by the quantitative data.

Question 3: Do you currently have dependents (under the age of 18 years of age) living in your household?

A total of one participant (n=1) commented on this question: one comment on choosing precise/appropriate words in the question (code 201.1), one comment on unnecessary / redundant question (code 201.2). Examples of the comments are proved in table 14 below:

Table 14. Feedback Comments on NHP-Q Section A-Question 3

Theme-Code	Example of Quote Comment
201.1	“What if they have dependents over the age of 18 living with them? How do they answer?”
201.2	“Does it matter for the purposes of this survey?”

These comments, however, were not reflected in the quantitative data from the feedback form, since no participant (n=0) chose this question in the feedback form.

Question 4: Which ethnic group(s) do you identify with?

A total of five participants (n=5) commented on this question: All comments focus on the controversy on ethnic identity topic (code 202.3)—by giving suggestions on providing broader / appropriate response options (code 202.1), and choosing precise / appropriate words in the question (code 201.1) as well as in the response options (code 202.4). Some examples are proved in table 15 below:

Table 15. Feedback Comments on NHP-Q Section A-Question 4

Theme-Code	Example of Quote Comment
202.1	“Answer choices should include: Arab/West Asian (eg. Armenian, Iranian, Lebanese, Moroccan); Black (eg. African, Haitian, Jamaican, Somali); Chinese; Filipino; Japanese; Korean; First Nation: Metis; Inuit; Latin American; Caucasian/European; South Asian (eg. East Indian, Pakistani, Sri Lankan); south Asian (eg. Indonesian, Laotian, Thai, Vietnamese).” “What if someone was from Pakistan (not India), South Asia is not an option. Scottish should be with English; Caribbean and West India should be together.”
201.3	“Are you asking for a list of ethnic backgrounds that they have in their family background or are you asking something different?”
202.3	“Are you determining demographic based on race/region?” “You appear to have confused racial origins with ethnicity (ethnicity has a strong cultural component)”
202.4	“Indigenous is the preferred word in Canada.”

These comments support the quantitative data from the feedback form, with two participants (n=2, 22%) indicating that this question contained words that might be interpreted differently by different people, two participants (n=2, 22%) indicating that this

question contained offensive words, and one participant (n=1, 11%) indicating that this question did not provide sufficient response options.

Question 5: What is the highest level of education you have finished?

A total of three participants (n=3) commented on this question: two comments on grammar mistake (code 201.4) in the response option, one comment on providing broader / appropriate response options (code 202.1), such as “*expand ‘Graduate degree’ to ‘Graduate or Professional degree’*”.

Despite these comments, no participant (n=0) chose this question in any feedback question.

Question 6: Which of the following options best represents your current program at Mount Saint Vincent University?

A total of two participant (n=2) commented on this question: both comments focus on grammar mistake in the response options (code 202.5). This result supports the quantitative data from the feedback form, with one participant (n=1, 11%) indicating that this question contained words that might be interpreted differently by different people. It shows that the original wording of the question and response options had negative impact on people’s understanding of the question and might have caused confusion.

Question 7: Do you plan to become a Registered Dietitian in the future?

A total of one participant (n=1) commented on this question: one comment on providing broader / appropriate response options (code 202.1)—“*Add ‘Not sure/I don’t know yet’ as one answer option*”.

This comment supports the quantitative data from the feedback form, with one participant (n=0, 11%) indicating this question did not provide sufficient response option.

Question 8: Are you currently enrolled in the Department of Applied Human Nutrition Internship Education Program?

A total of two participants (n=2) commented on this question: one comment on being less intrusive when asking students (code 201.5), one comments on choosing precise

/ appropriate terminology in the question (code 201.1). Examples of the comments are provided in table 16 below:

Table 16. Feedback Comments on NHP-Q Section A-Question 8

Theme-Code	Example of Quote Comment
201.5	“Asking people about their internship might be a sensitive topic, is it necessary to include it? This can be a sensitive topic for some and may add bias to answer or discourage the participant from answering fully/truthfully.”
201.1	“Is it called ‘internship’? We seem to have been moving away from that language in other programs – to ‘practicum program’ or ‘post-graduate practicum program’.”

Despite these comments, no participant (n=0) chose this question in any feedback question. The comments for this question did not support the quantitative data from the feedback form.

Question 10: Are you currently a full-time student?

A total of two participants (n=2) commented on this question: two comments on making question easier for audience to answer (code 201.9), one comment on defining / explaining terms clearly in the question (code 201.6). A typical example of the comments is *“What does ‘full-time’ mean – you may have to define”*.

Despite these comments, no participant (n=0) chose this question in any feedback question. The comments for this question, therefore, did not support the quantitative data from the feedback form.

Question 11: Are you a transfer student?

A total of one participant (n=1) commented on this question: one comment suggesting that it is an unnecessary question (code 201.2), one comment on defining / explaining terms clearly in the question (code 201.6)—*“Are you asking about transferring in from another program or from another university?”*

Despite these comments, no participant (n=0) chose this question in any feedback question. The comments for this question, therefore, did not support the quantitative data from the feedback form.

Question 12: Are you an international student?

A total of one participant (n=1) commented on this question: two comments on defining / explaining terms clearly in the question (code 201.6)—*“what do you mean when you say international?”*

Despite these comments, no participant (n=0) chose this question in any feedback question. The comments for this question, therefore, did not support the quantitative data from the feedback form.

Question 13: Do you have professional experience in any of the following fields?

A total of five participants (n=5) commented on this question: three comments suggesting that it is a redundant question with Question 14 (code 201.4), one comment on choosing precise / appropriate words in the question (code 201.1), two comments on defining / explaining terms clearly in the response options (code 202.6). Some examples of the comments are proved in table 17 below:

Table 17. Feedback Comments on NHP-Q Section A-Question 13

Theme-Code	Example of Quote Comment
201.2	“Could you combine Q13 + Q14? It seems redundant to separate them.”
201.1	“Change ‘professional experience’ to ‘work experience’ in the question.”
202.6	“‘Clinical’ is very broad”

These comments support the quantitative data from the feedback form, with one participant (n=1, 11%) indicating that this question contained words that might be interpreted differently by different people. The comment regarding redundancy of this question with Question 14, however, is not reflected in the feedback form.

Question 14: Do you have professional experience in the following fields?

A total of five participants (n=5) commented on this question: three comments suggesting that it is a redundant question with Question 13 (code 201.2), one comment on choosing precise / appropriate words in the question (code 201.1), one comment on redundant response options (code 202.8), one comment on adding extra section heading after this question—to make content flow better (code 301.2). Some examples of the comments are provided in table 18 below:

Table 18. Feedback Comments on NHP-Q Section A-Question 14

Theme-Code	Example of Quote Comment
301.2	“Do you need to put a new section heading in here? You move from demographics to use of supplements without transition. It’s a bit confusing.”
201.1	“What do you mean by ‘professional experience’ – I was a skilled server in a high-end restaurant? What counts as ‘professional experience’ in a food – I am a chef?”

These comments support the quantitative data from the feedback form, with one participant (n=1, 11%) indicating that this question was hard to understand. Some wording (such as “professional experience”) in the question might have caused some confusion to the participants.

Question 15: Have you taken nutritional supplements within past year?

A total of five participants (n=5) commented on this question: four comments on grammar and spelling mistake in the question (code 201.4), two comments on being more inclusive in the Note brackets in the question (code 201.10). One comment on choosing precise / appropriate words in the question (code 201.1). Some examples of the comments are provided in table 19 below:

Table 19. Feedback Comments on NHP-Q Section A-Question 15

Theme-Code	Example of Quote Comment
201.10	“What about protein powders or performance enhancers they may have taken through a gym? They may not be extracts but they are supplements. What if they are combos of these things?”
201.1	“Wondering if you are using the term ‘nutritional supplements’ because it is better understood by consumers as referring to vitamins & minerals, etc.?”

These comments support the quantitative data from the feedback form, with one participant (n=1, 11%) indicating that this question was hard to understand, three participants (n=3, 33%) indicating that this question contained words that might be interpreted differently by different people. The unclear explanation about examples of NHPs and some inappropriate wording in the question and response options might have caused some confusion to the participants.

Question 16: Have you taken herbal products within past year?

A total of four participants (n=4) commented on this question: two comments on grammar mistake in the question (code 201.4), one comment on defining / explaining

terms clearly in the question (code 201.6), one comment on choosing precise / appropriate words in the question (code 201.1). Some examples of the comments are provided in table 20 below:

Table 20. Feedback Comments on NHP-Q Section A-Question 16

Theme-Code	Example of Quote Comment
201.6	“Is this the correct current definition of herbal supplements? I think there is more to that...”
201.1	“Avoid high literacy word, need to simplify it.”

These comments support the quantitative data from the feedback form, with one participant (n=1, 11%) indicating that this question was hard to understand, two participants (n=2, 22%) indicating that this question contained words that might be interpreted differently by different people. The unclear explanation about examples of herbal products and some inappropriate wording in the question and response options might have caused some confusion among the participants.

Question 17: Have you taken ginseng root within past year?

A total of six participants (n=6) commented on this question: two comments on defining / explaining terms clearly in the question (code 201.6), two comments on grammar mistake in the question (code 201.4), one comments on choosing precise / appropriate words in the question (code 201.1), one comment on improving the content flow of the instruction in the Note brackets (code 301), one comment suggesting that it is a redundant question with Question 18 (code 201.2). Some examples of the comments are provided in table 21 below:

Table 21. Feedback Comments on NHP-Q Section A-Question 17

Theme-Code	Example of Quote Comment
201.6	“Respondents usually don’t know the difference between ginseng root and ginseng products. It might be worthwhile to add more information or explanation prior to the questions.”
201.1	“Consider rewording: consumed ginseng or taken ginseng root as a supplement.”
201.2	“This is repetitive with Q18- only one of them is necessary.”

These comments support the quantitative data from the feedback form, with three participants (n=3, 33%) indicating that this question was hard to understand, two participants (n=2, 22%) indicating that this question contained words that might be interpreted differently by different people. The unclear explanation about the difference

between ginseng root and ginseng products and the redundancy with Question 18 might have caused some confusion among the participants.

Question 18: What form of ginseng do you use?

A total of one participant (n=1) commented on this question: one comment on redundant question (suggesting combining this question with Question 17) (code 201.2).

These comments support the quantitative data from the feedback form, with one participant (n=1, 11%) indicating that this question contained words that might be interpreted differently by different people. The redundancy with Question 17 might be the reason behind the quantitative data result.

Question 19: Have you taken ginseng products within past year?

A total of six participants (n=6) commented on this question: one comment on grammar mistake in the question (code 201.4), two comments on defining / explaining terms clearly in the question (code 201.6), two comments on choosing precise / appropriate words in the question (code 201.1), one comment on redundant question (suggesting combining this question with Question 20) (code 201.2). Some examples of the comments are provided in table 22 below:

Table 22. Feedback Comments on NHP-Q Section A-Question 19

Theme-Code	Example of Quote Comment
201.6	“If you only want to focus on NHPs and not foods that contain added vitamins, minerals, amino acids, herbal or bioactive ingredients that have these ingredients, it may be helpful to clarify this in your survey.”
201.1	“Change the question into ‘Excluding ginseng root, have you taken any other ginseng products within the past year?’”
201.2	“This is repetitive with Q20 – only one of these is necessary”.

These comments support the quantitative data from the feedback form, with two participants (n=2, 22%) indicating that this question was hard to understand, three participants (n=3, 33%) indicating that this question contained words that might be interpreted differently by different people. The unclear explanation about the difference between ginseng root and ginseng products, the redundancy with Question 20 and some unprecise wording might have caused some confusion among the participants.

Question 20: What form of ginseng products do you use?

A total of three participants (n=3) commented on this question: three comments on grammar mistakes in the response options (code 202.5), one comment on redundant question (suggesting combining this question with Question 19) (code 201.2), one comment on defining / explaining terms clearly in the response options (code 202.6)—*“Liquid extract’, ‘tablet’ and ‘capsule’ may be difficult for some audiences to understand.”* (code 202.6)

These comments support the quantitative data from the feedback form, with one participant (n=1, 11%) indicating that this question contained words that might be interpreted differently by different people. The unclear explanation about the forms of ginseng products as well as the redundancy with Question 19 might be the reason behind the quantitative data result.

Question 21: Have you recommended ginseng root to other people (such as friends, family members, clients, customers, etc.)?

A total of one participant (n=1) commented on this question: one comment on choosing precise / appropriate words in the question (code 201.1)—*“Do you recommend’ sounds like a prescription.”*

Despite the comments, no participant (n=0) chose this question in any feedback question. The comments for this question, therefore, did not support the quantitative data from the feedback form.

Question 22: Have you recommended ginseng products to other people (such as friends, family members, clients, customers, etc.)?

A total of two participants (n=2) commented on this question: two comments on choosing precise / appropriate words in the question (code 201.1). Examples of the comments are provided in table 23 below:

Table 23. Feedback Comments on NHP-Q Section A-Question 22

Theme-Code	Example of Quote Comment
201.1	“Replace ‘ginseng products’ with ‘ginseng products other than ginseng root’” “By what authority do these respondents ‘recommend’?”

These comments support the quantitative data from the feedback form, with one participant (n=1, 11%) indicating that this question contained words that might be interpreted differently by different people. The unclear / inappropriate wording in the question might have caused some confusion among the participants.

Section B of NHP-Q

Question 1: Do you think that clients should tell their Dietitians if they are using Natural Health Products?

A total of four participants (n=4) commented on this question: three comments on using consistent term in the question (code 201.7), one comment on being more inclusive in the question (code 201.10)—*"Should not only mention 'Dietitian', but also other healthcare practitioners, because not everyone has access to RDs."*

The comments, however, do not match with the quantitative data from the feedback form. The data from the feedback form indicates that one participant (n=1, 11%) believed that this question was constructed in a way that a particular answer is favored over others (leading question). The comments, however, just focused on using consistent / appropriate terms and did not involve this aspect.

Question 2: Do you think Dietitians should recommend Natural Health Products to their clients based on nutritional assessment?

A total of two participants (n=2) commented on this question: one comment on using consistent term in the question (code 201.7), one comment on choosing precise / appropriate words in the question (code 201.1)—*"Replace the 'should' in the question with 'maybe' or other words, because 'some people may think recommending NHPs are dependent on each individual case and therefore, may not be feeling RDs should or shouldn't as they are of the middle ground."*

The comments, however, do not completely match with the quantitative data from the feedback form. The data from the feedback form indicates that one participant (n=1, 11%) believed that this question was constructed in a way that a particular answer is favored over others (leading question). The comments, however, just focused on using consistent / appropriate terms and did not involve this aspect. Another participant (n=1,

11%) believed that this question contained words that might be interpreted differently by different people. This result is consistent with the comments regarding unprecise / inappropriate use words.

Question 3: Do you think that Dietitians have a role to play in ensuring clients use Natural Health Products correctly (such as time and dose)?

A total of two participants (n=2) commented on this question: one comment on defining / explaining term clearly in the question (code 201.6), one comment on choosing precise / appropriate words in the question (code 201.1). Examples of the comments are provided in table 24 below:

Table 24. Feedback Comments on NHP-Q Section B-Question 3

Theme-Code	Example of Quote Comment
201.1	"You can't ensure anyone does anything you say but one can advise."
201.6	"I am not sure what you mean by 'time' (maybe clarify)."

These comments support the quantitative data from the feedback form, with one participant (n=1, 11%) indicating that this question contained words that might be interpreted differently by different people.

Question 4: Do you think that nutrition students should learn about Natural Health Products as part of their undergraduate training/ education?

A total of one participant (n=1) commented on this question: one comment on being more specific when asking a question (code 201.8)—"*What would you learn? Are you thinking students should learn specifics about specific products or learn about where to look for current, evidence-based analysis of NHPs? And regulation of NHPs? And packaging/ labelling of NHPs?*"

Despite the comment, no participant (n=0) chose this question in any feedback question. The comments for this question, therefore, did not support the quantitative data from the feedback form.

Question 5: Which of the following options are your main source of information on Natural Health Products?

A total of three participants (n=3) commented on this question: two comments on providing broader / appropriate response options (code 202.1), one comment on being

more specific in response options (code 202.7). Some examples of the comments are provided in table 25 below:

Table 25. Feedback Comments on NHP-Q Section B-Question 5

Theme-Code	Example of Quote Comment
202.1	“Perhaps add in an option for online courses or reference databases. Don’t know how many people use textbooks to source this info”
202.7	“University is a very broad term – from courses there, on campus resources, be more specific.”

These comments support the quantitative data from the feedback form, with one participant (n=1, 11%) indicating that this question contained words that might be interpreted differently by different people, and one participant (n=1, 11%) indicating that this question did not provide sufficient response options.

Question 6: Is ginseng a Natural Health Product?

A total of one participant (n=1) commented on this question: one comment on unnecessary question (suggesting removing this question) (code 201.2)—“*Why are you asking this? Especially at this point in the survey? You are implying here it is but it seems like a test question at this point.*”

Despite the comments, no participant (n=0) chose this question in any feedback question. The comments for this question, therefore, did not support the quantitative data from the feedback form.

Question 7: Do you think that ginseng has a role to play in chronic disease management?

A total of two participants (n=2) commented on this question: one comment on switching the question’s order to make content flow better (code 301.1), one comment on defining / explaining terms clearly in the question (code 201.6). Some examples of the comments are provided in table 26 below:

Table 26. Feedback Comments on NHP-Q Section B-Question 7

Theme-Code	Example of Quote Comment
301.1	“If you are planning to ask these, would you not put up higher, before you ask whether a client should be telling their RD or get counselling/ support in appropriate use of this product?”
201.6	“Some students don’t know what conditions would be considered as ‘chronic.’”

The comments, however, do not match with the quantitative data from the feedback form. The data from the feedback form indicates that one participant (n=1, 11%) believed that this question did not provide sufficient response options. The comments, however, just focused on adjusting the question order to make the content flow better, as well as defining / explaining term (the word “chronic”) clearly.

Question 8: Do you think that consuming ginseng can have side effects?

A total of four participants (n=4) commented on this question: one comment on switching the question’s order to make content flow better (code 301.1), two comments on grammar mistake in the question (code 201.4), one comment on making question more realistic or easier for participants to answer (201.9), one comment on being more inclusive in the question (201.10). Some examples of the comments are provided in table 27 below:

Table 27. Feedback Comments on NHP-Q Section B-Question 8

Theme-Code	Example of Quote Comment
301.1	“The order of these questions is odd – why are you asking this, especially so late in the survey?”
201.9	“What does it matter what they think on this question – is this a test? Would anyone be able to come up with potential side effects, especially if they have never used it or studied it?”
201.10	“Should also mention drug interactions”

These comments support the quantitative data from the feedback form, with one participant (n=1, 11%) indicating that this question was hard to understand, one participant (n=1, 11%) indicating that this question contained words that might be interpreted differently by different people. The comments regarding the difficulty of answering question related to side effects of consuming ginseng could be the reason behind these quantitative data results.

Question 9: From which course at Mount Saint Vincent University you learned ginseng?

A total of five participants (n=5) commented on this question: three comments on grammar mistake in the question (code 201.4), one comment on grammar mistake in the response option (code 202.5), two comments suggest revising the question to make it more realistic or easier for audience to answer (201.9). Some examples of the comments are provided in table 28 below:

Table 28. Feedback Comments on NHP-Q Section B-Question 9

Theme-Code	Example of Quote Comment
201.9	“Why this question? Is it not clear from the curriculum or source files for the courses?” “Would they expect to come across a discussion of ginseng in all of these classes?”

These comments support the quantitative data from the feedback form, with two participants (n=2, 22%) indicating that this question was hard to understand, one participant (n=1, 11%) indicating that this question contained words that might be interpreted differently by different people. The inappropriate wording of this question could be the reason behind the quantitative data results.

Question 10: Are you interested in taking a course that teaches you about Natural Health Products?

A total of two participants (n=2) commented on this question: one comment on providing broader / appropriate response options (code 202.1), one comment on making question more realistic or easier for audience to answer (code 201.9). Examples of the comments are provided in table 29 below:

Table 29. Feedback Comments on NHP-Q Section B-Question 10

Theme-Code	Example of Quote Comment
201.9	“Professional courses on this already exist and could be integrated into any of the classes mentioned above as a learning package for students.”
202.1	“Add ‘I have taken a course on NHPs’ as one answer choice.”

These comments support the quantitative data from the feedback form, with one participant (n=1, 11%) indicating this question did not provide sufficient response options.

3.3.2.3 NHP-Q Revision

After discussing the feedback data from the healthcare professionals sample between the research coordinator and the research assistant, a consensus was reached regarding how to revise the questions in the NHP-Q draft. All the revisions made on the questions in the NHP-Q draft have been summarized in Appendix 8.

NHP-Q was then revised to the second version based on the feedback data from health professional participants. This second version of NHP-Q divided the questionnaire into three sections (Section A, B and C). Section A (demographic questions) contained 13 questions, Section B (participants' personal experience with NHPs) contained six questions and Section C (participants' knowledge and perception of as well as interest in NHPs) contained nine questions.

3.3.3 Feedback Data from Nutrition Students Sample

The second version of NHP-Q along with the updated NHP-Q Feedback Form (Appendix 6) were presented to nutrition student participants for collecting feedback data. All of them provided both quantitative feedback data and qualitative feedback data.

3.3.3.1 Quantitative Data

3.3.3.1.1 NHP-Q Completion Time

A total of twenty-two student-participants' (n=22) self-recorded completion time of NHP-Q. The mean \pm SD completion time was 6 mins 48 secs \pm 2 mins 58 secs. The highest completion time was 15 mins 20 secs, the lowest completion time was 4 mins 6 secs.

Only three participants (n=3) spent more than 10 minutes in completing NHP-G-Q Version 2. The rest nineteen participants (n=19) spent less than 10 minutes. Among them, six participants (n=6) spent less than 5 minutes.

3.3.3.1.2 *Feedback Questions*

In table 30 below, the first two columns represent the question number in the new revised version of NHP-Q. For examples, Q2 (Section A) in this table represents Question 2 (Section A) in NHP-Q; Q5 (Section B) represents Question 5 (Section B) in NHP-Q; Q7 (Section C) represents Question 7 (Section C) in NHP-Q; so on and so forth.

Also in table 30 and table 31, the first two rows represent the feedback question number in *NHP-Q-Feedback Form*. For example, FQ1 in this table represents Feedback Question 1 in *NHP-Q-Feedback Form*; FQ2 represents Feedback Question 2 in *NHP-Q-Feedback Form*; so on and so forth. The meaning of each question in NHP-Q and each feedback question in *NHP-Q Feedback Form* in table 30 and table 31 are included in Appendix 9.

Shown in table 30 below, for example, at the cross of FQ1 and Q4 (Section A), the value 4/22(18%) means that four out of 22 nutrition student participants (18% of the total nutrition student participants) indicated that Question 4 of Section A in NHP-Q was hard to understand. For another example, at cross of FQ2 and Q3 (section B), the value 2/22(9%) means that two out of 22 nutrition student participants (9% of the total nutrition student participants) indicated that Question 3 of Section B in NHP-Q can be interpreted differently by differently people; at cross of FQ5 and Q7 (Section C), the value 1(5%) means that one out of 22 nutrition student participant (5% of the total nutrition student participants) indicated that Question 7 of Section C in NHP-Q did not provide sufficient response options. The blank cells in table 26 indicate that no nutrition student participant (n=0, 0%) selected the corresponding questions from NHP-Q.

Table 30. Summary of Feedback Question 1-5 Quantitative Data from Nutrition Student Participants

NHP-G Question Number		Feedback Form: Feedback Question Number				
		FQ1 n/x(%)	FQ2 n/x(%)	FQ3 n/x(%)	FQ4 n/x(%)	FQ5 n/x(%)
Section A	Q1					1/22(5%)
	Q2	2/22(9%)	1/22(5%)			1/22(5%)
	Q3		1/22(5%)			
	Q4	4/22(18%)				
	Q5	2/22(9%)				3/22(14%)
	Q6	1/22(5%)	1/22(5%)			1/22(5%)
	Q7					2/22(9%)
	Q9	1/22(5%)				1/22(5%)
	Q10	1/22(5%)				
	Q12	3/22(14%)				
	Q13		1/22(5%)			
Section B	Q1	1/22(5%)	2/22(9%)			2/22(9%)
	Q2	1/22(5%)	2/22(9%)			
	Q3	3/22(14%)	2/22(9%)			1/22(5%)
	Q5	2/22(9%)	1/22(5%)			2/22(9%)
	Q6	1/22(5%)				
Section C	Q1		2/22(9%)		1/22(5%)	4/22(18%)
	Q2					2/22(9%)
	Q3				1/22(5%)	
	Q4	1/22(5%)			1/22(5%)	1/22(5%)
	Q5	2/22(9%)	1/22(5%)		2/22(9%)	1/22(5%)
	Q6	1/22(5%)				4/22(18%)
	Q7					1/22(5%)
	Q8				1/22(5%)	
	Q9		1/22(5%)		1/22(5%)	1/22(5%)

* Q: Question in NHP-Q the second version

* FQ: Feedback Question in *NHP-Q-Feedback Form*

* n/x: participant number out of total participant number

* %: percentage of total participant number

Table 30 above indicates that Question 4 (Section A) in NHP-Q had the highest number of nutrition student participants (n=4/22, 18%) indicating that this question was difficulty to understand, followed by Question 12 (Section A) and Question 3 (Section B) each with three nutrition student participants (n=3/22, 14%) indicating that the question

was difficulty to understand. Also, Question 1 (Section C) and Question 6 (Section C) in NHP-Q had the highest number of nutrition student participants (n=4/22, 18%) indicating that these two questions did not provide sufficient response options, followed by Question 5 (Section A) with three nutrition student participants (n=3/22, 14%) indicating that this question did not provide sufficient response options. Further, no nutrition student participant (n=0, 0%) indicated that any question in NHP-Q contained offensive words.

Shown in table 31 below, the value 22/22(100%) under FQ6 means that all 22 nutrition student participants thought the content logic flow of NHP-Q was easy to follow; the value 21(95%) under FQ7 means that 21 out of 22 nutrition student participants (95% of the total nutrition student participants) thought the font size of NHP-Q was appropriate and one out of 22 nutrition student participants (5% of the total nutrition student participants) thought it was not; the value 22/22 (100%) under FQ8 means that all 22 nutrition student participants thought NHP-Q provided enough “white space”.

Table 31. Summary of Feedback Question 6-8 Quantitative Data from Nutrition Student Participants

	Feedback Question Number		
	FQ6 n/x(%)	FQ7 n/x(%)	FQ8 n/x(%)
Yes	22/22 (100%)	21/22(95%)	22/22(100%)
No	0	1(5%)	0

* FQ: Feedback Question in *NHP-Q-Feedback Form*

* n/x: participant number out of total participant number

* %: percentage of total participant number

Table 31 above indicates that all nutrition student participants (n=22/22, 100%) agreed that NHP-Q had good content logic flow and appropriate “white space”, and majority of the nutrition student participants (21/22, 95%) agreed that NHP-Q had appropriate font size.

3.3.3.2 Qualitative Data

All quantitative data above were carefully matched with qualitative data (written feedback comments) to verify if the comments supported the quantitative data. The following sub-sections discuss the general feedback comments from the nutrition student participants regarding the structure, content flow, font size and white space of the second version of NHP-Q, as well as the feedback comments to each individual question on NHP-Q.

General Comments

A total of 20 participants (n=20) provided general comments on Section A, B & C: seventeen comments on the overall content flow of the second version of NHP-Q (code 301), one comment on switching specific question order (code 301.1), three comments on inserting extra questions to help with the content flow (code 301.3), three comments on selecting proper format (code 403), five comments on grammar mistake on the section title (code 201.4), one comment on choosing appropriate words for the section title (code 201.1), one comment on explaining terms in some questions more clearly (code 201.6), one comment on choosing appropriate words in the response options for some questions (code 202.4), one comment on the easiness of answering this questionnaire (code 201.9).

Apart from some minor suggestions regarding some grammatical issues, some examples of the comments are provided in table 32 below:

Table 32. General Feedback Comments on NHP-Q

Theme-Code	Example of Quote Comment
301	"I feel that is was good transition from general demographic questions to specific ginseng-knowledge questions. Each individual question transitioned nicely as well. No confusion." "It has a logical flow, easy to understand. Everything was clear." "The questions make sense and are easy to follow. They follow a theme."

These comments support the quantitative data from the feedback form, with all participants (n=22, 100%) choosing "Yes" in Feedback Question 6. It indicates that the second version of NHP-Q was well structured and very easy to follow from question to question.

A total of fifteen participants (n=15) also provided general comments on the font size of NHP-Q. Some examples of the comments are provided in table 33 below:

Table 33. General Feedback Comments on the Font Size of NHP-Q

Theme-Code	Example of Quote Comment
401	<p>“Font size is certainly suitable—readable but not too large.”</p> <p>“Not too large that it looks clumsy, but accessible for those with vision difficulties.”</p> <p>“It appeared to be standard sized font, common to most documents/questionnaire.”</p> <p>“I think the questionnaire would seem less long if the font was a little smaller. It is really large.”</p>

These comments support the quantitative data from the feedback form, with twenty-one participants (n=21, 95%) indicating that the font size of the questionnaire was suitable, and one participant (n=1, 5%) indicating that the font size was not suitable (too large).

Furthermore, a total of 6 participants (n=6) provided general comments on the white space of NHP-Q: five comments on page space density (code 402.2), two comments on space between lines (code 402.1). Most of them are positive comments. Some examples of the comments are provided in table 34 below:

Table 34. General Feedback Comments on the White Space of NHP-Q

Theme-Code	Example of Quote Comment
402.1	<p>“Gave clear distinction between questions.”</p> <p>“Each question and answer has plenty of space, so as not to be cluttered to confusing.”</p>
402.2	<p>“Enough white space doesn’t make it look too empty, enough content on each page without making look too messing.”</p> <p>“Good amount of white space. Any more would create too many pages.”</p> <p>“There can be more questions added to each page (maybe the margin can be widened).”</p> <p>“It was well spaced, did not feel clustered.”</p>

These comments support the quantitative data from the feedback form, with all participants (n=22, 100%) indicating that the white space of the questionnaire was enough and visually appealing.

Section A of NHP-Q

Question 1: What is your current age?

A total of two participants (n=2) provided comments on this question: one comment of choosing appropriate words for the question (code 201.1), one comment on

providing appropriate response options (code 202.1)—“*It may be beneficial to just ask for age instead of grouping the ages. That way you know the exact age group of participants— Group them in Phase 2.*” (code 202.1)

These comments support the quantitative data from the feedback form, with one participant (n=1, 5%) indicating that this question did not provide sufficient response options. The personal preference for how to answer this question might be the reason behind the quantitative data result.

Question 2: What is your current marital/living status?

A total of four participants (n=4) provided comments on this question: two comments on providing broader / appropriate response options (code 202.1), one comment on suggesting dividing the question into two sub-questions to help with the content flow (code 301.4), one comment on defining the term clearly in the response option (code 202.6), one comment indicating too many response options (code 202.9). Some examples of the comments are provided in table 35 below:

Table 35. Feedback Comments on NHP-Q Section A-Question 2

Theme-Code	Example of Quote Comment
301.4	“Not hard to understand, but should maybe separate marital and living status in separate questions.”
202.1	Living status should include more option, such as with immediate family, extended family, residence, with friends/roommates, etc.”
202.6	“What is ‘support person’? Does this imply friend or someone with special needs?”
202.9	“Almost too many options for this question.”

These comments support the quantitative data from the feedback form, with two participants (n=2, 9%) indicating this question was hard to understand, one participant (n=1, 5%) indicating that this question contained words that might be interpreted differently by different people, and one participant (n=1, 5%) indicating that this question did not provide sufficient response options.

Question 3: Do you currently have dependents living in your household?

A total of one participant (n=1) provided comment on this question: one comment on defining/ explaining term in the question clearly (code 201.6)—“*Should maybe define ‘dependents’.*”

This comment supports the quantitative data from the feedback form, with one participant (n=1, 5%) indicating that this question contained words that might be interpreted differently by different people. In this case, different people might understand the word “dependents” in the question in different ways.

Question 4: Which ethnic group(s) do you identify with?

A total of five participants (n=5) provided comments on this question: five comments on typo / spelling mistake in the question (code 201.4), one comment on choosing appropriate words in the response option (code 202.4)—“*Perhaps the term ‘white’ can also be presented in the answer along with ‘Caucasian’, just in case someone does not know meaning of the word ‘Caucasian’.*”

The comments support the quantitative data from the feedback form, with four participants (n=4, 18%) indicating that this question was hard to understand. The typo / spelling mistake in the question confused the participants”.

Question 5: What is the highest level of education you have received?

A total of five participants (n=5) provided comments on this question: two comments on being more specific when asking this question (code 201.8), one comment on choosing appropriate words in the question (code 201.1), two comments on providing broader / appropriate response options (code 202.1). Some examples of the comments are provided in table 36 below:

Table 36. Feedback Comments on NHP-Q Section A-Question 5

Theme-Code	Example of Quote Comment
201.8	“Does it include my undergraduate degree if I am in the last year?”
201.1	“I think it should say ‘completed’, not ‘received’.”
202.1	“A good addition would be ‘some college/university education’, because this is higher than a high school education, but the person may not have yet received a degree.”

The comments support the quantitative data from the feedback form, with two participants (n=2, 9%) indicating that this question was hard to understand, and three participants (n=3, 14%) indicating that this question did not provide sufficient response options.

Question 6: Which of the following options best represents your current program at Mount Saint Vincent University?

A total of two participants (n=2) provided comments on this question: one comment on choosing appropriate words for the question (code 201.1), one comment on providing appropriate response options (code 202.1). Examples of the comments are provided in table 37 below:

Table 37. Feedback Comments on NHP-Q Section A-Question 6

Theme-Code	Example of Quote Comment
201.1	"Maybe ask 'What program are you enrolled in?'"
202.1	"I think student identify as dietetics, nutrition or nutrition minor students, not just major vs minor."

The comments support the quantitative data from the feedback form, with one participant (n=1, 5%) indicating that this question was hard to understand, one participant (n=1, 5%) indicating that question contained words that might be interpreted differently by different people, and one participant (n=1, 5%) indicating that this question did not provide sufficient response options. Students' different understanding of their own program status might have induced them to interpret this question in different ways.

Question 7: Which academic year of your program are you currently in?

A total of two participants (n=2) provided comments on this question: one comment on switching specific questions' order (between Question 8 and Question 9) to make the content flow better (code 301.1), one comment on providing broader / appropriate response options (code 202.1)—"*As a transfer student, I am between 3rd and 4th year.*"

The comments support the quantitative data from the feedback form, with two participants (n=2, 9%) indicating that this question did not provide sufficient response options. Transfer students' program status might have created some barriers from them to choose appropriate response options from this question.

Question 9: Are you a transfer student?

A total of two participants (n=2) provided comments on this question: one comment on switching specific questions' order to make the content flow better (code 301.1), one

comment on grammar mistake in the question (code 201.4). Example of the comments provided in table 38 below:

Table 38. Feedback Comments on NHP-Q Section A-Question 9

Theme-Code	Example of Quote Comment
301.1	“Q7 and Q9 should maybe be combined into the same question, or Q9 should be Q8 instead, so they follow each other.”

The comments, however, do not support the quantitative data from the feedback form, with one participant (n=1, 5%) indicating that this question was hard to understand, and one participant (n=1, 5%) indicating that this question did not provide sufficient response options. The comments regarding content flow and the minor grammatical error, however, do not necessarily relate to the difficulty of understanding the question as well as whether the question provided enough response options.

Question 10: Are you an international student?

A total of one participant (n=1) provided comment on this question: one comment on grammar mistake in the question (code 201.4)

The comments, however, do not support the quantitative data from the feedback form, with one participant (n=1, 5%) indicating that this question was hard to understand. The comment regarding the minor grammatical mistake, however, does not necessarily relate to the difficulty of understanding the question.

Question 12: Are you currently enrolled in the Department of Applied Human Nutrition—Internship Education Program?

A total of three participants (n=3) provided comments on this question: two comments on explaining term clearly in the question (code 201.6), one comment on providing broader response options (code 202.1). Some examples of the comments are provided in table 39 below:

Table 39. Feedback Comments on NHP-Q Section A-Question 12

Theme-Code	Example of Quote Comment
201.6	“Does the question ask if you are accepted into IEP or that you are planning on taking it?” “Does this mean people who have selected the internship option, or people who are already doing their internship?”
202.1	“Should have (N/A) option—I am a visiting student.”

These comments support the quantitative data from the feedback form, with one participants (n=3, 14%) indicating that this question was hard to understand. The clarity of the meaning of the word “enrolled” in the question might have confused the participants.

Question 13: Do you have work experience in any of the following fields?

A total of one participant (n=1) provided comment on this question: one comment on defining / explaining terms clearly in the question (code 201.6)—“*Does it include volunteer / not paid experience?*”

This comment supports the quantitative data from the feedback form, with one participant (n=1, 5%) indicating that this question contained words that might be interpreted differently by different people. The clarity of the meaning of “work experience” in the question might have confused the participants, since different people might think of “work experience” in different ways.

Section B of NHP-Q

Question 1: Have you taken any of the listed nutritional supplements below within the past year?

A total of 4 participants (n=4) provided comments on this question: two comments on being more specific in response options (code 202.7), two comments on providing broader response options (code 202.1), one comment on choosing precise / appropriate words in the response option (code 202.4). Some examples of the comments are provided in table 40 below:

Table 40. Feedback Comments on NHP-Q Section B-Question 1

Theme-Code	Example of Quote Comment
202.7	“Should be less confusing with an example for each one (response option).” “Maybe some more descriptions besides the nutritional supplements would help.”
202.4	“Maybe change ‘Protein powder supplement’ (in the response option) to ‘protein supplement’, because I had seen protein tablets.”
202.1	“I was surprised that there wasn’t a response option specifically for multivitamins, as they contain vitamins, minerals and sometimes fatty acids. This could be confusing if people are unsure what to check—check nothing or check all the response options?”

The comments support the quantitative data from the feedback form, with one participant (n=1, 5%) indicating that this question was hard to understand, two participants (n=2, 9%) indicating that this question contained words that might be interpreted differently by different people, and two participants (n=2, 9%) indicating that this question did not provide sufficient response options.

Question 2: Have you taken herbal products within the past year?

A total of three participants (n=3) provided comments on this question: two comments on defining / explaining term clearly in the question (code 201.6), one comment on choosing appropriate word in the question (code 201.1). Some examples of the comments are provided in table 41 below:

Table 41. Feedback Comments on NHP-Q Section B-Question 2

Theme-Code	Example of Quote Comment
201.6	“Does this include herbal teas? e.g. Green teas with ginseng.” “Examples will be helpful.”

The comments support the quantitative data from the feedback form, with one participant (n=1, 5%) indicating that this question was hard to understand, two participants (n=2, 9%) indicating that this question contained words that might be interpreted differently by different people. Most comments demanded examples of herbal products to help them understand the question.

Question 3: Have you consumed ginseng root within the past year?

A total of four participants (n=4) provided comments on this question: two comments on grammar mistakes in the question (code 201.4), two comments on being more specific when asking this question (code 201.8), one comment on improving content flow (code 301). Some examples of the comments are provided in table 42 below:

Table 42. Feedback Comments on NHP-Q Section B-Question 3

Theme-Code	Example of Quote Comment
201.8	“Herbal teas? Not sure if it includes the root or if it’s an extract.” “It was unclear that this question was asking specifically about ginseng in pure ‘root’ form, not in alternative products.”

The comments support the quantitative data from the feedback form, with three participants (n=3, 14%) indicating that this question was hard to understand, two participants (n=2, 9%) indicating that this question contained words that might be interpreted differently by different people, and one participant (n=1, 5%) indicating that this question did not provide sufficient response options. The diversity of ginseng root and their related products on the market might have confused the participants.

Question 4: Have you encouraged other people to consume ginseng root? (Such as your friends, family members, clients, customers, etc.)

A total of one participant (n=1) provided comment on this question: one comment on defining / explaining the term clearly in the question (code 201.6)—*"If someone never heard about 'ginseng', how would they distinguish between ginseng products/roots?"*

Despite this comment, it does not support the quantitative data from the feedback form, since no participant (n=0, 0%) chose this question in any feedback question.

Question 5: Excluding ginseng root, have you taken any of the listed ginseng products below as a supplement within the past year?

A total of four participants provided comments on this question: two comments on providing broader / appropriate response options (code 202.1), one comment on being more specific in response options (code 202.7), one comment on defining terms clearly in the question (code 201.6). Some examples of the comments are provided in table 43 below:

Table 43. Feedback Comments on NHP-Q Section B-Question 5

Theme-Code	Example of Quote Comment
202.1	"What about ginseng tea?"
202.7	"It was hard to understand, because it was hard to think of specific products that contain ginseng products. Maybe listing examples of food products that commonly contain ginseng products would help the recall process."
201.6	"This question tricked me. I am not sure if ginseng is one ingredient of any vitamin supplement or protein powder I have ever used."

The comments support the quantitative data from the feedback form, with two participants (n=2, 9%) indicating that this question was hard to understand, one participant (n=1, 5%) indicating that this question contained words that might be interpreted differently by different people, and two participants (n=2, 9%) indicating that

this question did not provide sufficient response options. Based on these comments, the difficulty for the participants to recall if they had consumed ginseng products might have prevented them from choosing appropriate response options.

Section C of NHP-Q

Question 1: Do you think that ginseng has a role to play in disease management?

A total of six participants (n=6) provided comments on this question: four comments on providing broader / appropriate response options (code 202.1), one comment on choosing precise / appropriate words in the question (code 201.1), one comment on avoiding leading-question (code 201.11), one comment on define the term “disease management” clearly (code 201.6). Some examples of the comments are provided in table 44 below:

Table 44. Feedback Comments on NHP-Q Section C-Question 1

Theme-Code	Example of Quote Comment
202.1	“Just want to confirm that ‘I have no opinion’ also includes a response of ‘I don’t know’.” “Should have a response option that includes ‘not enough knowledge/research to provide a response’.”
201.1	“Very vague question, not really sure what it meant by ‘play a role’.”
201.11	“The question sounds like people would say ‘Yes’, including if people did not believe so.”
201.6	“People might be confused by this question about ‘disease management’.”

The comments support the quantitative data from the feedback form, with two participants (n=2, 9%) indicating that this question contained words that might be interpreted differently by different people, one participant (n=1, 5%) indicating that this question was constructed in a way that a particular answer was favored over others (leading question), and four participants (n=4, 18%) indicating that this question did not provide sufficient response options. Based on these comments, some participants had difficulty in understanding the term “disease management” and felt confused and not sure how to answer. Some felt pressed to choose “Yes” response option due to that the question was leading them to choose “Yes”.

Question 2: Do you think ginseng is safe to consume?

A total of two participants (n=2) provided comments on this question: one comment of providing broader / appropriate response options (code 202.1), one comment on being more specific when asking the question (code 201.8). Some examples of the comments are provided in table 45 below:

Table 45. Feedback Comments on NHP-Q Section C-Question 2

Theme-Code	Example of Quote Comment
202.1	"Just want to confirm that 'I have no opinion' also includes a response of 'I don't know'."
201.8	"Recommend more direct question such as 'do you think ginseng is safe for the general public who have no counter indicating drug/health risks?'"

One comment (regarding the response options) supports the quantitative data from the feedback form, with two participants (n=2, 9%) indicating that this question did not provide sufficient response options. But the other comment (regarding being more specific when asking the question) does not have quantitative data from the feedback form to support.

Question 3: Do you think that clients should tell their Registered Dietitian if they are using Natural Health Products?

A total of one participant (n=1) provided comment on this question: one comment on avoiding leading-question (code 201.11)—"*The question sounds like people would say 'Yes', including if people did not believe so.*"

The comment supports the quantitative data from the feedback form, with one participant (n=1, 5%) indicating that this question was constructed in a way that a particular answer is favored over others (leading question)—the question was leading the participants to choose "Yes".

Question 4: Do you think Registered Dietitian has a role to play in recommending Natural Health Products to their clients based on nutritional assessment?

A total of five participants (n=5) provided comments on this question: two comments on grammar mistake in the question (code 201.4), one comment on using consistent term (code 201.7), one comment on providing broader response options (code

202.1)—*"Should include 'unsure' option"*, one comment on avoiding leading-question (code 201.11)—*"The question sounds like people would say 'Yes', including if people did not believe so."*

The comments support the quantitative data from the feedback form, with one participant (n=1, 5%) indicating that this question was hard to understand, one participant (n=1, 5%) indicating that this question did not provide sufficient response options, and one participant (n=1, 5%) indicating that this question was constructed in a way that a particular answer is favored over others (leading question)—the question was leading the participants to choose "Yes".

Question 5: Do you think that Registered Dietitian has a role to play in advising clients to use Natural Health Products correctly (such as taking them at correct time during the day and at correct dose)?

A total of seven participants (n=7) provided comments on this question: one comment on using consistent term (code 201.7), three comments on grammar mistake in the question (code 201.4), one comment on providing broader response options (code 202.1), one comment on being more specific when asking a question (code 201.8), one comment on avoiding leading-question (code 201.11), one comment on choosing appropriate words in the question (code 201.1). Some examples of the comments are provided in table 46 below:

Table 46. Feedback Comments on NHP-Q Section C-Question 5

Theme-Code	Example of Quote Comment
201.8	"Is this question asking if they do currently have a role at advising clients about natural medicine or they should? I feel like they don't currently have that responsibility but it would be nice if they did."
201.1	"It's a stretch, but some people may think this implies that clients don't know how to take NHPs correctly on their own."
201.11	"The question sounds like people would say 'Yes', including if people did not believe so."
202.1	"Should include 'unsure' option."

The comments support the quantitative data from the feedback form, with two participants (n=2, 9%) indicating that this question was hard to understand, one participant (n=1, 5%) indicating that this question contained words that might be

interpreted differently by different people (such as the word “should” in the question), two participants (n=2, 9%) indicating that this question was constructed in a way that a particular answer is favored over others (the question was leading the participants to choose “Yes”), and one participant (n=1, 5%) indicating that this question did not provide sufficient response options (such as “unsure” option).

Question 6: What is your main source of information on Natural Health Products?

A total of four participants (n=4) provided comments on this question: Five comments on providing broader response options (code 202.1). Some examples of the comments are provided in table 47 below:

Table 47. Feedback Comments on NHP-Q Section C-Question 6

Theme-Code	Example of Quote Comment
202.1	“This response list must have ‘friends, family, grandmother’ option.” “Other response options should be ‘doctors’, ‘naturopaths’, ‘dietitian’, ‘television doctor shows’, etc.” “Naturopath doctors are the only doctors that have the education to specialize in natural medicine, and they should really be a response option.” “There could a response option of ‘friends/family’ or ‘word of mouth’ perhaps”

These comments support the quantitative data from the feedback form, with four participants (n=4, 18%) indicating that this question did not provide sufficient response options. One participant (n=1, 5%) also indicated that this question was hard to understand. There is no comment, however, to support this data.

Question 7: Have you learned about ginseng from any courses you took at Mount Saint Vincent University?

A total of one participant (n=1) provided comment on this question: one comment on making the question more inclusive (code 201.10)—“*Does not consider if the individual has learned about ginseng from other university or education programs?*”

The comment supports the quantitative data from the feedback form, with one participant (n=1, 5%) indicating that this question did not provide sufficient response options. It implies that the question should be revised to include a response option of “learned ginseng from other universities or education programs”.

Question 8: Do you think that nutrition students should learn about Natural Health Products as part of their training/education?

A total of one participant (n=1) provided comment on this question: one comment on avoiding leading-question (code 201.11)—*"The question sounds like people would say 'Yes', including if people did not believe so."*

The comment supports the quantitative data from the feedback form, with one participant (n=1, 5%) indicating that this question was constructed in a way that a particular answer is favored over others (leading question)—the question was leading the participants to choose "Yes".

Question 9: Do you think knowledge and information in the field of Natural Health Products should be integrated into undergraduate nutrition courses offered at Mount Saint Vincent University?

A total of 4 participants provided comments on this question: two comments on choosing appropriate words in the question (code 201.1), one comment on being more specific when asking the question (code 201.8), one comment on avoiding leading-question (code 201.11). Some examples of the comments are provided in table 48 below:

Table 48. Feedback Comments on NHP-Q Section C-Question 9

Theme-Code	Example of Quote Comment
201.1	"'Integrated' might be hard to understand."
201.8	"Does not mention if these courses should be mandatory or optional?"
201.11	"The question sounds like people would say 'Yes', even if they did not believe so."

These comments support the quantitative data from the feedback form, with one participant (n=1, 5%) indicating that this question contained words that might be interpreted differently by different people (such as the word "integrated" in the question), one participant (n=1, 5%) indicating that this question was constructed in a way that a particular answer is favored over others (the question was leading the participants to choose "Yes"), and one participant (n=1, 5%) indicating that this question did not provide sufficient response options (such as providing "mandatory" or "optional" as response options).

3.3.3.3 NHP-Q Revision

To ensure the revision of NHP-Q was objective, the feedback data from the nutrition students sample were discussed between the research coordinator and the research assistant, a consensus was reached regarding how to revise the questions again in the second version of NHP-Q. All the revisions made on the questions in the second version of NHP-Q have been summarized Appendix 10.

NHP-Q was then revised to the third version based on the feedback data from nutrition student participants. This third version of NHP-Q was still divided into three sections (Section A, B and C). Section A contained 13 questions, Section B contained six questions and Section C contained 10 questions. This third version of NHP-Q was the final version (Appendix 11) to be used as the reach tool in Phase Two.

3.4 Discussion

The revision of NHP-Q was based on the objectives in *Section 3.1* and guided by the six standards listed in *Section 3.2.2.2*.

3.4.1 Content Density

One objective of Phase One of this study is to develop a questionnaire that can be completed by nutrition students within approximately 10 minutes. Based on the completion time self-recorded by the twenty-two nutrition student participants' (n=22), the mean \pm SD completion time was 6 mins 48 secs \pm 2 mins 58 secs. This result has shown that the content density of NHP-Q was within the target range and will not demand too much of students' time. This supported by feedback provided, such as:

"It was a fun easy survey to fill out. Not too time consuming, and overall very clear", "The questions cover enough material that I don't think more needs to be covered".

3.4.2 Structure and Content Flow

The NHP-Q draft was originally divided into two main sections. Two health professional participants (n=2) suggested that dividing the questionnaire into three sections can help improve the content flow of the questionnaire and help them understand the questionnaire better. Based on the feedback comments, questionnaire was then divided into three main sections to facilitate the content flow: Section A (demographic questions), Section B (participants' personal experience with NHPs), and Section C (participants' knowledge and perception of as well as interest in NHPs). By dividing the questionnaire into three main sections, each section now focuses on a more specific field. The revised version was then presented to nutrition student participants. All nutrition student participants (n=22) agreed that the revised structure very clear and easy to follow, based on their comments.

Also, the order of several questions in NHP-Q were adjusted based on the feedback comments to facilitate the content flow—all questions related to a similar field (such as questions regarding job experience and future career plan) were grouped together. For example, in the draft of NHP-Q, two questions in Section A asking participants' intention or plan for becoming a Registered Dietitian in the future, and whether they are currently enrolled in Internship Education Program (IEP). These two questions, however, were not grouped together with another two questions asking participants' past work experience in either healthcare or food service field. One participant (n=1) indicated that it was difficult for her follow the logic from question to question and suggested that these four questions are inter-related and should be grouped together.

3.4.3 Specificity and Sufficiency

Being specific is an important standard for questionnaire development (214). Being specific in content, such as by providing specific and detail explanations or examples, can improve the readability of questions and can also lead to providing sufficient response options. Based on the feedback comments, some questions in the draft and the second version of NHP-Q were not specific enough. It negatively affected the readability of the questionnaire. For example, several questions asked participants to categorize themselves as “full-time student”, “part-time student”, “transfer student”, or “international student”

without providing clear explanations for these response options. Some participants commented that clear explanations should be provided to define “full-time student” and “part-time student” due to the fact that course load varies among different students. Also, some students might have transferred from a different program within the same university, or from a different program in another university, or from a similar program in another university. They might not categorize themselves as “transfer students”. The feedback comments suggested that clear explanation should be provided regarding what “transfer student” means. Also, for the question “*Do you currently have dependents living in your household?*”, one participant (n=1) indicated that she did not understand the meaning of the word “dependents”.

Based on the feedback comments, several explanatory notes were added under these questions (such as what “full-time student”, “part-time student”, “transfer student” and “dependents” mean) to assist participants to make correct choices.

Three nutrition student participants (n=3) also indicated that the question “*Are you currently enrolled in the Department of Applied Human Nutrition—Internship Education Program?*” was confusing to them, because some of them were enrolled in the Applied Human Nutrition program but not in Internship Education Program yet. They suggested that the question should provide specific explanation regarding whether it includes students who are still planning to be enrolled in the Internship Education Program. This suggestion was, therefore, incorporated into the revised version.

Some participants indicated that the response options in several questions were confusing. They suggested that providing specific examples for these response options could help them choose answers correctly. For example, four nutrition student participants (n=4) commented that the response options for the question “*Have you taken any of the listed nutritional supplements below within the past year?*” did not provide specific examples. They indicated that it was difficult for them to differentiate the response options without examples provided for each of them. Indeed, the response options for this question involve a list of NHPs, some of which might not be familiar to the participants. In the revised version, each response option was, therefore, followed by some examples (provided in a pair of brackets) to help participants understand and make correct choices.

Furthermore, some participants commented that several questions did not cover sufficient response options. For example, for the question asking participants' ethnic background, a total of five health professional participants (n=5) indicated that the response options provided were not sufficient. Based on the suggestions from the participants, several more options regarding ethnicity were added into the response option list along with specific examples provided for each response option. After the revised question was presented again to nutrition student participants, none of them (n=0) indicated that the question did not provide complete response options. This means that after revision, the response option list for this question has covered most potential answer choices.

3.4.4 Ambiguity

Minimal ambiguity is the second important standard for questionnaire development. Some words in the draft and second version of NHP-Q were ambiguous and could be interpreted differently by different people. Words with high ambiguity and cause confusion and decrease the understandability (214). For example, for the question "*What is the highest level of education you have received?*", five participants (n=5) commented on the word "received" in the question and indicated that people could interpret this word differently. Some participants believed that it should include their current level of education (Applied Human Nutrition program at MSVU), whereas some other participants believed that it should be the highest level of education they had completed prior to their enrollment into Applied Human Nutrition program at MSVU. The ambiguity of this word caused confusion to the participants. Based on these comments, the word "received" was replaced with "completed" and the question was revised to "*What is the highest level of education you have completed prior to the enrollment of your current program at Mount Saint Vincent University?*".

For another example, in the question "*Do you have work experience in any of the following fields?*", the words "work experience" can also be interpreted differently by different people. Some participants counted their volunteer experience as "work experience", whereas some other participants only counted paid-job experience as "work experience". Based on the suggestions from participants, an explanatory note was added

under the question explaining what “work experience” in the question refers to (paid job experience, in this case).

3.4.5 Precision and Redundancy

Being brief is another important standard for questionnaire development. All the questions in the questionnaire should ideally contain less than 20 words or less than 3 commas so that people with low literacy level can read the questionnaire (214). This standard, therefore, requires the wording of the questionnaire to be simple, precise and not redundant. Based on the feedback comments, some questions in the draft and second version of NHP-Q were too wordy. For example, for the first question in NHP-Q asking about participants’ age, three participants (n=3) suggested that the question should be worded as simple as possible, such as “*What is your current age?*”, or “*How old are you?*”. (214).

Another example is that in the NHP-Q draft, Question 13 asked participants if they had professional experience in healthcare and health research field, and Question 14 asked participants if they had experience in food service and administration related field. A total of five participants (n=5) commented that these two questions were redundant and only one question could suffice. Based on the feedback comments, all the response options from these two questions were combined under one question.

3.4.6 Relevancy

Being relevant to the goal and objectives of the study is also an important standard for questionnaire development (214). This means that questions in the questionnaire should be able to yield meaningful results that are highly relevant to the goal and objectives of the study. If a question does not produce meaningful results, it should be removed from the questionnaire. For example, one health professional participant (n=1) indicated that Question 6 in Section B (“*Is ginseng a Natural Health Product?*”) was an unnecessary question, because at this point of the questionnaire, all participants will have already known (based on the previous content of the questionnaire) that ginseng is an example of NHPs and will certainly choose the “Yes” response option. The data result, therefore, will

not be meaningful or relevant to the goal of this study. In the revised version of NHP-Q, this question has been deleted from the questionnaire.

This sub-study is to investigate nutrition students' knowledge and perception of as well as interest in NHPs. One important element of the study objectives is to investigate nutrition students' "interest" in NHPs. One nutrition participant (n=1) pointed it out, however, that there was no question in NHP-Q asking nutrition students' interest in learning NHPs. The feedback comment was "*I think it would be beneficial to have a few questions relating to the students' personal interest in the field of Natural Health Products, if there are certain products they have a particular interest in, etc.*" It is necessary to design a question that can cover this study objective. In the final version of NHP-Q, therefore, one last question was added in Section C—"*Is there any Natural Health Products that you are particularly interested in learning?*"

3.4.7 Jargons and Technical Words

Avoiding jargons and highly technical words is another standard for questionnaire development (214). People who read this questionnaire might have low literacy level and might not be able to understand some jargons. For example, one participant (n=1) suggested that in the question "*Do you think that ginseng has a role to play in chronic disease management?*", the word "chronic" might be difficult for some people to understand, especially for many first-year undergraduate nutrition students who usually do not know yet which conditions should be considered as "chronic" conditions. Based on the feedback comments, the word "chronic" was removed from the question.

Also, one participant (n=1) indicated that in the question "*Do you think knowledge and information in the field of Natural Health Products should be integrated into undergraduate nutrition courses offered at MSVU?*", the word "integrated" was hard for her to understand. Based on this feedback, the word "integrated" is replaced with the word "covered".

For another example, the question "*Do you think that consuming ginseng can have side effects?*" might be challenging for participants to think of any answers. Two participants (n=2) indicated that "side effects" in the question are highly technical words, and it is unrealistic for young nutrition students to think of any specific side effects

associated with consuming ginseng. Based on the suggestion from the participants, this question is revised to an opinion-based question—*"Do you think ginseng is safe to consume?"*

3.4.8 Leading Question

Being objective and unbiased is the last important standard for questionnaire development. This means that any question in NHP-Q should not suggest an answer to the participants or lead the answer toward a desired direction (214). In other words, leading question should be avoided. Several questions in the draft and second version of NHP-Q tended to lead the participants to choose "Yes" instead of "No" response option. For example, two participants (n=2) indicated that for the following questions in NHP-Q, participants would most likely choose "Yes" instead of "No" response option due to the way the questions were stated:

"Do you think that clients should tell their Registered Dietitian if they are using Natural Health Products?"

"Do you think Registered Dietitian has a role to play in recommending Natural Health Products to their clients based on nutritional assessment?"

"Do you think that Registered Dietitian has a role to play in advising clients to use Natural Health Products correctly?"

"Do you think that nutrition students should learn about Natural Health Products as part of their training/education?"

For these questions, the way the questions were stated gave people a feeling that choosing "Yes" would be the "correct" answer, just as the feedback comment stated—*"The questions sound like people would say 'Yes', even if people did not believe so."* In addition, these questions were grouped together, and it could induce a tendency for participants to choose "Yes" instead of "No" for all of them—after participants chose "Yes" as the answer for the first question, they tended to choose "Yes" for the rest of the questions because they were stated in a similar way.

To break this tendency (that would lead participants to choose "Yes"), these questions were revised to an opinion-based question format, for example, *"Do you agree with the following statement—'Registered Dietitians usually play very little role in*

recommending specific Natural Health Products to their clients based on nutritional assessment' _____ *Agree* _____ *Disagree* _____ *I have no opinion / I am not sure*". In the revised version, "Yes" and "No" response options were replaced with "Agree", "Disagree" and "I have no opinion / I am not sure" response options. Furthermore, the questions were revised from a positive statement (such as "*Registered Dietitians play an important role*") to a negative statement (such as "*Registered Dietitians usually play very little role*"). This revision can induce the participants to think about the question carefully and then express their own opinions faithfully.

3.4.9 Limitations

This study (Phase One) has two limitations. First, the feedback was provided on a separated feedback form. The participants had to match the response options of each feedback question on the feedback form with the actual question numbers in NHP-Q. After they chose a specific response option on the feedback form, they had to provide comments to justify their choice on the separated lines below. This process might potentially have induced some mismatches between the response options on the feedback form and the actual question numbers on NHP-Q, if the participants did not pay close attention to the question numbers. Some nutrition student participants indicated that this process was confusing for them, and they had hard time with constantly looking for the correct question number on NHP-Q to match with the response option provided on the feedback form. Also, if a participant chose several response options for a specific feedback question, many comments they provided below (to justify their choices) were very general and did not specify which comment was to justify which response option. This has created difficulty for the research investigator to match the response options with the feedback comments, and might potentially have induced some mismatches. Furthermore, some participants simply did not provide feedback comments to justify the response options they chose on the feedback form. These problems have rendered some insistency between the quantitative data and the qualitative data.

Second, since the feedback comments are subjective data based on the participants' personal opinions, some comments from different participants were contradictory to each other. The decisions on how to revise the questions were often based on subjective

judgement. For example, for the question asking participants' ethnic background, some participants suggested to expand the response options (to make them more inclusive) and provide specific examples for each response option. Whereas some other participants suggested that since ethnic identity is such a complex topic, this question should be revised to an open-ended question format and simply ask participants to write down their ethnic identities by themselves and categorize their answers later during data analysis stage. In this case, which side of suggestion should be adopted was based on subjective judgement. The former suggestion (expanding the response options with specific examples provided for each of them) was eventually adopted, since multiple-choice was the main chosen format for this questionnaire.

3.5 Conclusion

The revision of NHP-Q based on the feedback data collated from both health professional and nutrition student participants has brought three major improvements:

(a) It has improved the overall structure and content flow of the questionnaire. The questionnaire is now divided into three main sections to facilitate the content flow: Section A (demographic questions), Section B (participants' personal experience with NHPs), and Section C (participants' knowledge and perception of as well as interest in NHPs). And all questions related to a similar field have been grouped together.

(b) The response options of many questions have become more inclusive and more specific, especially in the questions related to ethnic background, student status, and examples of NHPs. Also, many unnecessary jargons and technical words have been removed or attached with explanatory notes.

(c) To avoid leading the audience to favor a specific response option over others, some questions have been revised to opinion-based questions, especially in the questions regarding Registered Dietitians' role in providing consultation service in the field of NHPs.

These three major improvements have increased the understandability, readability and objectivity of the questionnaire for the target audience (nutrition students). The final version of NHP-Q (Appendix 7) is a face-content validated measuring tool and can now be used as an administration tool during *Phase Two* and *Three* of the study.

4. THESIS SUMMARY AND DISCUSSION

As highlighted at the beginning (the Introduction section) of the thesis, five questions are the center of the thesis:

- (1) What have been known regarding ginseng's (an example of NHPs) therapeutic effects in T2DM management?
- (2) What is the knowledge gap regarding ginseng's therapeutic effects that still needs to be explored, especially from nutritional perspective?
- (3) What do nutrition students know about NHPs and ginseng?
- (4) Do nutrition students perceive NHPs differently from other health professionals?
- (5) Are nutrition students interested in learning NHPs/ginseng related knowledge?

According to the estimations summarized by Diabetes Canada, approximately 25-57% of people living with T2DM report using NHPs (217-220). Ginseng, as an example of NHPs, has been used as a traditional therapeutic intervention to help with glycemic control among people living with T2DM, especially in Asian culture (127,128). Previous sections in the Literature Review Chapter have discussed the main active components (ginsenosides) of ginseng and their main functions (at cellular level) in helping with glycemic control. Numerous animal studies and human trials have been conducted in past to explore the true effect of ginseng on glycemic control. Some of them showed positive results. For examples, as highlighted in *Section 1.3.4*, several clinical trials conducted by Vuksan et al. (2000-2001) and Sievenpiper et al. (2006) showed significant effect of ginseng on reducing postprandial blood glucose concentration among people living with T2DM (160,161,163,165,166,170). Based on the literature review, the relationship between ginseng consumption and satiety in people living with T2DM was identified as a knowledge gap, as highlighted in *Section 2.1*. This knowledge gap might be particularly interesting to Dietitians and nutrition and foods students due to its dietetic focused nature. Study 1, therefore, focused on the relationship between ginseng consumption and satiety in people living T2DM. The Literature Review chapter and Study 1 chapter, therefore, addressed the first two questions above.

In Study 1, a secondary data analysis study (based on a KWG double-blind, randomize-controlled, cross-over trial completed at St. Michael's Hospital, Toronto, ON) was conducted, investigating the acute dose-dependent effect of KWG on blood glucose concentration and satiety within a sample of participants living with T2DM. The results

from Study 1 showed that administration of 1g, 3g and 6g of KWG did not have significant impact on either postprandial blood glucose concentrations or appetite scores. Although the significant correlations between KWG doses and blood glucose concentrations as well as between KWG doses and appetite scores were not observed, *Section 2.4.2* has discussed the potential reasons behind the insignificant correlations, which include:

- KWG doses being too low comparing to the doses used in existing literature;
- Results being potentially complicated by the anti-hyperglycemic and antihypertensive medications the participants were taking at the time of the study;
- KWG treatment not being continuous: KWG was administrated only on the day of visit, as opposed to being consumed on daily basis over a prolonged period (such as weeks or months).

As discussed in *Section 1.4.2*, KT plays an important role in effectively disseminating new research findings to a group of audience and in helping health professionals gain new knowledge and engage in evidence-based practice (187). Without effective KT, patients/clients will fail to benefit from new research findings and might receive unnecessary or even potentially harmful treatment (186,188). For the purpose of this thesis and shown in figure 2 in *Section 1.4.2*, Study 1 represents the “knowledge inquiry and knowledge synthesis” (the inner-core) of the Knowledge-to-Action cycle. The results of Study 1 supplement the existing research evidence regarding the clinical utility of ginseng, especially regarding its short-term effect. Shown in figure 9 below, according to the Bench-to-Bedside model (the American version of the Knowledge-to-Action cycle model), new research studies are built on the identification of research gaps from the existing research findings, as well as the recognition of the importance of the new research findings to current clinical practice (215,216). Efforts should be made by Scientists to ensure that novel information be translated in an effective way to those (such as healthcare professionals) who will educate the knowledge end-user (215,216). Patients are the knowledge end-user who eventually benefit from the knowledge dissemination process (215,216).

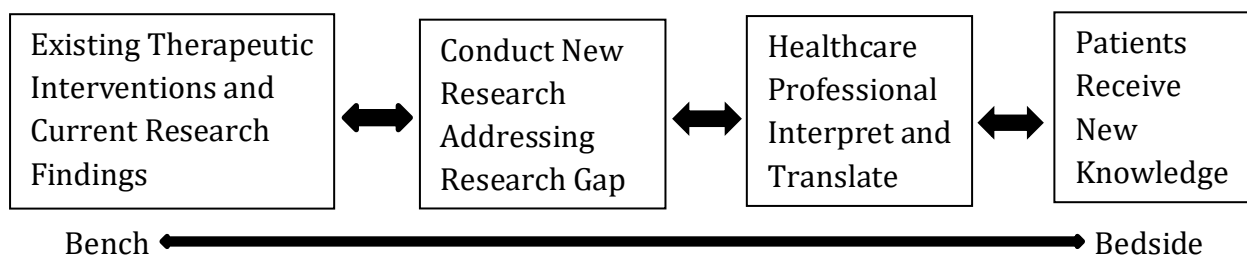


Figure 9. Bench-to-Bedside

(215,216)

Although significant correlations between KWG doses and blood glucose concentrations as well as between KWG doses and appetite scores were not observed in Study 1, the potential reasons behind these results (as highlighted above) have implied that more studies in the future with different methodologies are needed to further investigate the short-term efficacy of KWG on postprandial blood glucose concentration and satiety. This is in line with the suggestion highlighted by Diabetes Canada CPG—more clinical trials are needed regarding the short-term efficacy of ginseng (217). Results from all studies investigating the short-term efficacy of ginseng (including Study 1 of this thesis) will add to the existing knowledge pool and synthesize with each other to give a better picture regarding ginseng’s overall efficacy in glycemic control, in both long-term and short-term.

The results of Study 1 might be an interesting topic for nutrition and foods students, especially if they plan to become health professionals (such as Registered Dietitian) in the future specializing in T2DM management. If the results from Study 1 and these potential reasons behind the results (as discussed above) can be effectively delivered to Dietitians and nutrition students, they will then be able to synthesize the novel information with the knowledge from existing literature to make informed decisions regarding the clinical utility of KWG. The clinical utility can include whether they should recommend KWG to their patients living with T2DM and how to recommend, or whether they want to pursue further research studies in the future by adopting different methodologies, such as increasing the dosage of KWG, or administrating the doses on daily basis over a prolonged period.

Since approximately 25-57% of people living with T2DM report using NHPs, effective knowledge translation and dissemination (regarding how to use NHPs

appropriately) from healthcare professionals to people living with T2DM has become very important (217-220). The question here is how research findings in the field of NHPs (such as ginseng in this case) can be effectively disseminated to the target audience. The answer still lies in KT. As discussed in *Section 1.4.2*, the “knowledge application” (the out-circle) of Knowledge-to-Action cycle includes eight phases:

- (1) “Identifying a problem that needs to be addressed”;
- (2) “Identifying, reviewing and selecting knowledge or research findings relevant to the problem”;
- (3) “Adapting the new research findings or knowledges to the local context”;
- (4) “Assessing barriers to knowledge use”;
- (5) “Selecting, tailoring and implementing interventions that promote the dissemination of knowledge to the target audience”;
- (6) “Monitoring the process of KT”;
- (7) “Evaluating the outcomes of KT”;
- (8) “Sustaining the ongoing use of knowledge”. (186)

Study 2 intends to address the last three questions listed at the beginning of this chapter. Study 2, therefore, involves the “knowledge application” of the Knowledge-to-Action cycle. Its goal is to facilitate the effective dissemination of knowledge and new research findings in the field of NHPs and ginseng to nutrition and foods students. To effectively disseminate knowledge and research findings to the target audience, investigating their current knowledge and perception of as well as interest in NHPs has become the first step down the path. In other words, whether nutrition students (the future health professionals) have the initiatives in learning knowledge related to NHPs determines if these research findings can be disseminated to them effectively.

Phase One of Study 2 focused on the development of a face and content validated questionnaire that can help with investigating nutrition and foods students’ knowledge and perception of as well as interest in NHPs during the next study phase. The process was based on asking feedback from two sub-samples (health professionals sample and nutrition students sample) regarding the understandability and readability of a pre-designed NHP-Q and making revision on NHP-Q based on their feedback. The revision of NHP-Q based on

the feedback data from these samples has brought improvements to the questionnaire from three main aspects: structure, specificity and objectivity.

This final version of NHP-Q can now be used as the face and content validated administration tool during *Phase Two* (pre-testing the questionnaire on a small sample size) and *Phase Three* (administrating the questionnaire on a large sample size) at MSVU and St.FX (not included in this thesis). Through administrating this questionnaire during the next study phases, the results can help health educators identify whether there is any problem that needs to be addressed regarding integrating NHPs related knowledge into nutrition education at universities. Health educators then can select, tailor or adapt NHPs related knowledge and new research findings based on the requirements of nutrition science and nutrition education (adapting to local context). It can also help health educators assess the barriers to disseminating NHPs related knowledge to nutrition and foods students. In return, it will further help them select and tailor knowledge before disseminating it to the audience. *Phase One, Two and Three* of Study 2 together involve the first four phases of the Knowledge-to-Action cycle highlighted above.

After completion of *Phase Three* of the study, it will then enter the fifth phase of the Knowledge-to-Action cycle—"selecting, tailoring and implementing interventions that promote the dissemination of knowledge to the target audience". The Applied Human Nutrition department at MSVU currently offers Natural Health Products course as an elective to nutrition students, but St.FX does not have such course offer currently. Some faculty members of the Department of Human Nutrition at St.FX have indicated the interest in incorporating NHPs related knowledge in their future nutrition courses depending on the survey results. The results of *Phase Three*, therefore, will help MSVU and St.FX plan NHPs related curriculum in their nutrition programs, which involves finding effective strategies and educational tools of translating and disseminating NHPs/ginseng knowledge to their nutrition students.

The Knowledge-to-Action cycle is a dynamic process, and each phase in the knowledge application cycle can influence each other and send feedback to the core—knowledge inquiry and knowledge synthesis, requiring constant knowledge adjustment (186). It is, therefore, necessary to constantly assess how effectively the knowledge are disseminated to nutrition and foods students, and its subsequent impact on their

understanding of and attitudes toward NHPs (the sixth phase of the cycle). It is also important to evaluate the knowledge application in their future healthcare and health research practice, as well as whether the NHPs related knowledge they have learned makes a difference in health outcomes during their practice (the seventh phase of the cycle). The eighth phase of the cycle involves establishing a long-term feedback loop from nutrition students and practicing Dietitians assessing new emerging problems and knowledge gaps to promote sustained knowledge creation and knowledge use.

APPENDIX

Appendix 1
VAS Questionnaire

VAS QUESTIONNAIRE

KWG Study
REB: 12-300

PARTICIPANT #: _____
DATE: _____

Visit Number: 1 2 3 4 5 6 (Circle)

Time: 0 min 60 min 120 min 180min 240 min (circle)

These questions relate to your physical assessment at this time. Please rate your feelings by placing a vertical line across the line at the point which best reflects your present feelings.

1. How strong is your desire to eat?

Very weak _____ Very strong

2. How hungry do you feel?

Not hungry at all _____ As hungry as I have ever felt

3. How full do you feel?

Not full at all _____ As full as I have ever felt

4. How much do you think you could eat now?

Nothing at all _____ A large amount

Appendix 2

SYMPTOMS QUESTIONNAIRE

KWG Study
 REB: 12-300
 PARTICIPANT #: _____
 DATE: _____

To be completed by the participant

Visit Number: 1 2 3 4 5 6 (Circle)

Please indicate if you have any of the following symptoms during the study visit:

SYMPTOMS	PRESENCE	SEVERITY	Time	Comm- ents
Bloating	<input type="checkbox"/> Yes <input type="checkbox"/> No	Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High		
Belching	<input type="checkbox"/> Yes <input type="checkbox"/> No	Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High		
Diarrhoea	<input type="checkbox"/> Yes <input type="checkbox"/> No	Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High		
Flatulence (gas)	<input type="checkbox"/> Yes <input type="checkbox"/> No	Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High		
Excessive urination	<input type="checkbox"/> Yes <input type="checkbox"/> No	Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High		
Nausea	<input type="checkbox"/> Yes <input type="checkbox"/> No	Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High		
Headache	<input type="checkbox"/> Yes <input type="checkbox"/> No	Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High		
Dizziness	<input type="checkbox"/> Yes <input type="checkbox"/> No	Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High		
Disorientation	<input type="checkbox"/> Yes <input type="checkbox"/> No	Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High		

Examination of the Ginseng Utility from the Perspective of the Nutrition Professional

<p>Nervousness (Anxiety)</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>	<p>Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High</p>		
<p>Insomnia</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>	<p>Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High</p>		
<p>Numbness</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>	<p>Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High</p>		
<p>Impaired vision</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>	<p>Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High</p>		
<p>Other (specify): _____</p>		<p>Low 1-----2-----3-----4-----5-----6-----7-----8-----9-----10 High</p>		

Appendix 3

Letter of Invitation

Nutrition Students' Knowledge and Perception of Natural Health Products and Ginseng Questionnaire Development

[Insert date]

Dear [Insert Full Name],

My name is Haoliang He, a graduate student in Department of Applied Human Nutrition at Mount Saint Vincent University (MSVU). I am developing a questionnaire to help us better understand MSVU undergraduate nutrition students' knowledge and perception of Natural Health Products (NHPs) and ginseng.

I am contacting you now to ask you if you are willing to provide feedback on the *Natural Health Products and Ginseng Questionnaire (NHP-Q)*. This questionnaire was drafted using questions in the published literature modified for nutrition students. The original questions were developed to query medical students', Nurses', Pharmacists' or Registered Dietitians' knowledge and perception of NHPs.

If you would like to participate to provide feedback on the questionnaire, please reply to this email (ccing my supervisor, Dr. Shannan Grant) within five business days of receiving this message. If you decide to help me, you will receive a second email from me. Attached to this email will be the NHP-G-Q and a feedback form. You will be given directions, including a request for 10-day turnover. The feedback form can be completed electronically and the whole process should take 20 minutes to one hour.

Your feedback will be used to improve the quality of the questionnaire, which can be used as a measuring tool to investigate MSVU undergraduate nutrition students' knowledge and perception of NHPs and ginseng. The results of this study will be used as evidence to help Department of Applied Human Nutrition at MSVU develop NHPs and ginseng related undergraduate nutrition course content

Sincerely,

Haoliang He
MSc. AHN
Mount Saint Vincent University
Email: Haoliang.he@msvu.ca

Supervisor's email: Shannan.grant2@msvu.ca

Appendix 4



Natural Health Products and Ginseng Questionnaire Feedback Form

Directions:

Please read each question making up the Natural Health Products and Ginseng Questionnaire (NHP-Q) and provide your feedback using this feedback form. If you also wish to write feedback directly on the questionnaire, you are welcome to do so. We will take feedback on the questionnaire as either MS WORD Track Changes and Comments or handwritten feedback on a hardcopy of the questionnaire, scanned to PDF and emailed. If you choose to include feedback on the questionnaire, we still would like you to fill out the feedback form.

After preparing your feedback, please email it to haoliang.he@msvu.ca.

Examination of the Ginseng Utility from the Perspective of the Nutrition Professional

1. Write an "X" on the line left of each NHP-Q question that you found hard to understand.

Section A: Getting to Know You

- Question 1 Question 2 Question 3 Question 4
 Question 5 Question 6 Question 7 Question 8
 Question 9 Question 10 Question 11 Question 12
 Question 13 Question 14 Question 15 Question 16
 Question 17 Question 18 Question 19 Question 20
 Question 21 Question 22

Section B: What Do You Know and Think About Natural Health Products and Ginseng?

- Question 1 Question 2 Question 3 Question 4
 Question 5 Question 6 Question 7 Question 8
 Question 9 Question 10

I do not think any questions in the NHP-Q are hard to understand.

If you marked "X" next to any of the above question numbers, please provide more detail on the line below. For instance, tell us why question 2 was hard to understand.

2. Write an "X" on the line left of each NHP-Q question that you think contains words that might be interpreted differently by different people.

Section A: Getting to Know You

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9 _____ Question 10 _____ Question 11 _____ Question 12
_____ Question 13 _____ Question 14 _____ Question 15 _____ Question 16
_____ Question 17 _____ Question 18 _____ Question 19 _____ Question 20
_____ Question 21 _____ Question 22

Section B: What Do You Know and Think About Natural Health Products and Ginseng?

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9 _____ Question 10

_____ I do not think any questions in the NHP-Q contain words that might be interpreted differently by different people.

If you marked "X" next to any of the question numbers, please provide rationale for your response on the lines below.

3. Write an "X" on the line left of each NHP-Q question that you think contains offensive words.

Section A: Getting to Know You

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9 _____ Question 10 _____ Question 11 _____ Question 12
_____ Question 13 _____ Question 14 _____ Question 15 _____ Question 16
_____ Question 17 _____ Question 18 _____ Question 19 _____ Question 20
_____ Question 21 _____ Question 22

Section B: What Do You Know and Think About Natural Health Products and Ginseng?

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9 _____ Question 10

_____ I do not think any questions in the NHP-Q contain offensive words.

If you marked "X" next to any of the question numbers, please provide rationale for your response on the lines below.

4. Write an "X" on the line left of each NHP-Q question that you think is constructed in a way that a particular answer is favored over others.

Section A: Getting to Know You

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9 _____ Question 10 _____ Question 11 _____ Question 12
_____ Question 13 _____ Question 14 _____ Question 15 _____ Question 16
_____ Question 17 _____ Question 18 _____ Question 19 _____ Question 20
_____ Question 21 _____ Question 22

Section B: What Do You Know and Think About Natural Health Products and Ginseng?

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9 _____ Question 10

_____ I do not think any NHP-Q questions/answers are constructed in a way that a particular answer is favored over others.

If you marked "X" next to any of the question numbers, please provide rationale for your response on the lines below.

5. Write an "X" on the line left of each NHP-Q question that you think does not provide sufficient response options.

Section A: Getting to Know You

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9 _____ Question 10 _____ Question 11 _____ Question 12
_____ Question 13 _____ Question 14 _____ Question 15 _____ Question 16
_____ Question 17 _____ Question 18 _____ Question 19 _____ Question 20
_____ Question 21 _____ Question 22

Section B: What Do You Know and Think About Natural Health Products and Ginseng?

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9 _____ Question 10

_____ I think each question in the NHP-Q provides sufficient response options.

If you marked "X" next to any of the question numbers, please provide rationale for your response on the lines below.

6. a. Do you think the general content flow from question to question in NHP-Q is easy to follow?

_____ Yes

_____ No

6. b. Please provide rationale for your response above and / or additional feedback in the lines below.

7. a. Do you think the font size of NHP-Q is suitable?

Please write an "X" on the line next to the response that best represents your answer to the question.

_____ Yes

_____ No

7. b. Please provide rationale for your response above and / or additional feedback in the lines below.

8. a. Does the questionnaire have enough “white space”?

_____ Yes

_____ No

8. b. Please provide rationale for your response above and / or additional feedback in the lines below.

9. Do you have any additional feedback on the NHP-Q? If yes, please include it on the lines provided below.

10. Do you have any feedback on your experience as a study participant? If yes, please include it on the lined provided below.

**End of feedback form.
Thank you for your input.**

Appendix 5

Letter of Invitation

October 25th, 2017

Dear Department of Applied Human Nutrition Undergraduate Student,

We are currently developing a questionnaire to collect information on your knowledge and perception of natural health products and ginseng. We have made the first draft of the *Natural Health Products and Ginseng Questionnaire* and would like your feedback.

If you are interested in learning more about this study, please contact the study coordinator by email (Haoliang.he@msvu.ca) to set up a time to review the consent form with a member of our research team.

We look forward to hearing from you.

Sincerely,

Haoliang He
MSc. AHN
Mount Saint Vincent University
Email: Haoliang.he@msvu.ca

Supervisor's email: Shannan.grant2@msvu.ca

Appendix 6



Natural Health Products and Ginseng Questionnaire Feedback Form

Directions:

Thank you for agreeing to provide us with feedback on the Natural Health Products and Ginseng Questionnaire (NHP-Q). This feedback form has been developed to help you provide us with your feedback and is made up of two sections (1 and 2). Directions for each section are provided below. After completing this feedback form, please email it to haoliang.he@msvu.ca, or you can drop a hardcopy off at EV422 (a cardboard box with a slot in the top is where you will submit the hard copy of your NHP-Q Feedback Form).

Section 1:

Complete the NHP-Q. The purpose of our asking you to complete the questionnaire is to see how much time it takes you to complete it. You will write the amount of time (minutes and seconds) that it took you to complete the NHP-Q in Section 1 of this feedback form. You do not need to email us the completed NHP-Q.

On the line below, please write how much time it took you to complete the NHP-Q.

_____ (minutes: seconds)

Section 2:

Complete the feedback questions about the NHP-Q: Close-end (e.g. multiple choice, yes or no) and Open-end (written answers) responses will be collected in this section.

1. Write an "X" on the line left of each NHP-Q question that you found hard to understand.

Section A: Getting to Know You

_____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9 _____ Question 10 _____ Question 11 _____ Question 12
_____ Question 13

Section B: Getting to Know You More

_____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6

Section C: How Do You Think about Natural Health Products and Ginseng?

_____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9

_____ I do not think any questions in the NHP-Q are hard to understand.

If you marked "X" next to any of the above question numbers, please provide more detail on the line below. For instance, tell us why question 2 was hard to understand.

2. Write an "X" on the line left of each NHP-Q question that you think contains words that might be interpreted differently by different people.

Section A: Getting to Know You

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9 _____ Question 10 _____ Question 11 _____ Question 12
_____ Question 13

Section B: Getting to Know You More

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6

Section C: How Do You Think about Natural Health Products and Ginseng?

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9

_____ I do not think any questions in the NHP-Q contain words that might be interpreted differently by different people.

If you marked "X" next to any of the question numbers, please provide rationale for your response on the lines below.

3. Write an "X" on the line left of each NHP-Q question that you think contains offensive words.

Section A: Getting to Know You

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9 _____ Question 10 _____ Question 11 _____ Question 12
_____ Question 13

Section B: Getting to Know You More

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6

Section C: How Do You Think about Natural Health Products and Ginseng?

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9

_____ I do not think any questions in the NHP-Q contain offensive words.

If you marked "X" next to any of the question numbers, please provide rationale for your response on the lines below.

4. Write an "X" on the line left of each NHP-Q question that you think is constructed in a way that a particular answer is favored over others.

Section A: Getting to Know You

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9 _____ Question 10 _____ Question 11 _____ Question 12
_____ Question 13

Section B: Getting to Know You More

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6

Section C: How Do You Think about Natural Health Products and Ginseng?

- _____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9

_____ I do not think any NHP-Q questions/answers are constructed in a way that a particular answer is favored over others.

If you marked "X" next to any of the question numbers, please provide rationale for your response on the lines below.

5. Write an "X" on the line left of each NHP-Q question that you think does not provide sufficient response options.

Section A: Getting to Know You

_____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9 _____ Question 10 _____ Question 11 _____ Question 12
_____ Question 13

Section B: Getting to Know You More

_____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6

Section C: How Do You Think about Natural Health Products and Ginseng?

_____ Question 1 _____ Question 2 _____ Question 3 _____ Question 4
_____ Question 5 _____ Question 6 _____ Question 7 _____ Question 8
_____ Question 9

_____ I think each question in the NHP-Q provides sufficient response options.

If you marked "X" next to any of the question numbers, please provide rationale for your response on the lines below.

6. a. Do you think the general content flow from question to question in NHP-Q is easy to follow?

_____ Yes

_____ No

6. b. Please provide rationale for your response above and / or additional feedback in the lines below.

7. a. Do you think the font size of NHP-Q is suitable?

Please write an "X" on the line next to the response that best represents your answer to the question.

_____ Yes

_____ No

7. b. Please provide rationale for your response above and / or additional feedback in the lines below.

8. a. Does the questionnaire have enough “white space”?

_____ Yes

_____ No

8. b. Please provide rationale for your response above and / or additional feedback in the lines below.

9. Do you have any additional feedback on the NHP-Q? If yes, please include it on the lines provided below.

10. Do you have any feedback on your experience as a study participant? If yes, please include it on the lines provided below.

End of feedback form.
Thank you for your input.

Appendix 7

Table-8 and Table-9 Legend Explanations

Table-8 NHP-Q Question

Section A

- Q2—"Which response option best represents your marital status?"
- Q4—"Which ethnic group(s) do you identify with?"
- Q6—"Which of the following options best represents your current program at Mount Saint Vincent University?"
- Q7—"Do you plan to become a Registered Dietitian in the future?"
- Q13—"Do you have professional experience in any of the following fields?"
- Q14—"Do you have professional experience in the following fields?"
- Q15—"Have you taken nutritional supplements within past year?"
- Q16—"Have you taken herbal products within past year?"
- Q17—"Have you taken ginseng root within past year?"
- Q18—"What form of ginseng do you use?"
- Q19—"Have you taken ginseng products within past year?"
- Q20—"What form of ginseng products do you use?"
- Q22—"Have you recommended ginseng products to other people (such as friends, family members, clients, customers, etc.)?"

Section B

- Q1—"Do you think that clients should tell their Dietitians if they are using Natural Health Products?"
- Q2—"Do you think Dietitians should recommend Natural Health Products to their clients based on nutritional assessment?"
- Q3—"Do you think that Dietitians have a role to play in ensuring clients use Natural Health Products correctly (such as time and dose)?"
- Q5—"Which of the following options are your main source of information on Natural Health Products?"
- Q7—"Do you think that ginseng has a role to play in chronic disease management?"
- Q8—"Do you think that consuming ginseng can have side effects?"

Q9—"From which course at Mount Saint Vincent University you learned ginseng?"

Q10—"Are you interested in taking a course that teaches you about Natural Health Products?"

Table-8 and Table-9 NHP-Q Feedback Form Question

FQ1—"Write an "X" on the line left of each NHP-Q question that you found hard to Understand."

FQ2—"Write an "X" on the line left of each NHP-Q question that you think contains words that might be interpreted differently by different people."

FQ3—"Write an "X" on the line left of each NHP-Q question that you think contains offensive words."

FQ4—"Write an "X" on the line left of each NHP-Q question that you think is constructed in a way that a particular answer is favored over others."

FQ5—"Write an "X" on the line left of each NHP-Q question that you think does not provide sufficient response options."

FQ6—"Do you think the general content flow from question to question in NHP-Q is easy to follow?"

FQ7—"Do you think the font size of NHP-Q is suitable?"

FQ8—"Does the questionnaire have enough 'white space'?"

Appendix 8

Natural Health Products Questionnaire Revision Based on Feedback from Health Professional Participants

- In Section A, switched Question 7 and 8 to being after Question 12.
- Under Section A title, revised the original note with “Select the option that best applies to you (by writing an “X” on the line next to the option)”;
- In Section A, added “Prefer not to answer” to each question’s response options;
- Added a new Section after Section A, called “Getting to Know You More”, and divided NHP-Q into three sections—Section A, B and C;
- Replaced all “dietitian” with “Registered Dietitian”
- For Section B: replaced “I do not know the answer to this question” with “I have no opinion” in all questions that involve this response option.

Section A

- Question 1: revised the question with “What is your current age?”;
- Question 2: expanded the response options based on the comments;
- Question 3: deleted the “under the age of 18 years” in the brackets within the question;
- Question 4: reorganized and expanded the response options based on comments, as well as provided specific example for each response option;
- Question 5: replaced the word “finished” in the question with the word “received”, and replace the fourth response choices with “Graduate or professional degree”;
- Question 7: added “I don’t know yet” as one response option.
- Question 10: changed the question and response options to: “*What is your current student status? _____ Full time student _____ Part time student*” and added a note (brackets) explaining what “full time” and “part time” mean;
- Question 11: added a note explaining what “transfer student” means.
- Question 12: added a note explaining what “international student” means;

- Question 13 and 14: changed “professional experience” to “work experience” in the question, combined Question 13 and Question 14 into one question, and replaced the word “Clinical” in the response options with “Providing healthcare or counselling to patients / clients”, and combined the two response options “Food service” and “Food administration” into one response option “Food service and administration”;
- Question 15, 16 and 17: revised and expanded the response options based on the comments to make them more specific, and added notes (brackets) explaining what what herbal products mean and what ginseng root is;
- Question 18: deleted this question;
- Question 19 and 20: combined Question 19 and 20 into one question;
- Question 21 and 22: Replaced the word “recommended” with “encourage” in the question;
- Question 22: replaced “ginseng products” with “ginseng products other than ginseng root” in the question.

Section B

- Question 2: replaced the words “should recommend” with “may have a role to play in recommending”;
- Question 3: replaced the words “ensuring clients use” with “advising clients to use”, and revised the content in the Note brackets to clearly explain what “using NHPs correctly” means;
- Question 4: added a note under the question explaining what specific knowledge and information in the field of Natural Health Products can possibly be included in the education program;
- Question 5: added several response options based on the comments;
- Question 6: deleted this question;
- Question 7 and 8: moved the question along with Question 8 to the top of this section, and removed the word “chronic” from the question;
- Question 8: moved the question along with Question 7 to the top of this section, and replaced the question with “Do you think ginseng is safe to consume?”;

Examination of the Ginseng Utility from the Perspective of the Nutrition Professional

- Question 9: replaced the question with: “*Have you learned about ginseng from any courses you took at Mount Saint Vincent University? _____ Yes _____ No _____ I do not remember*”;
- Question 10: revised the question into: “*Do you think knowledge and information in the field of Natural Health Products should be integrated into undergraduate nutrition courses offered at Mount Saint Vincent University? _____ Yes _____ No _____ I have no opinion*”.

Appendix 9

Table-30 and Table-31 Legend Explanations

Table-30 NHP-Q Question Number

Section A

Q1--What is your current age?

Q2--What is your current marital/living status?

Q3--Do you currently have dependents living in your household?

Q4--Which ethnic group(s) do you identify with?

Q5--What is the highest level of education you have received?

Q6--Which of the following options best represents your current program at Mount Saint Vincent University?

Q7--Which academic year of your program are you currently in?

Q9--Are you a transfer student?

Q10--Are you an international student?

Q12--Are you currently enrolled in the Department of Applied Human Nutrition— Internship Education Program?

Q13--Do you have work experience in any of the following fields?

Section B

Q1--Have you taken any of the listed nutritional supplements below within the past year?

Q2--Have you taken herbal products within the past year?

Q3--Have you consumed ginseng root within the past year?

Q5--Excluding ginseng root, have you taken any of the listed ginseng products below as a supplement within the past year?

Q6--Have you encouraged other people to take ginseng products other than ginseng root?

Section C

Q1--Do you think that ginseng has a role to play in disease management?

Q2--Do you think ginseng is safe to consume?

Q3--Do you think that clients should tell their Registered Dietitian if they are using Natural Health Products?

- Q4--Do you think Registered Dietitian has a role to play in recommending Natural Health Products to their clients based on nutritional assessment?
- Q5--Do you think that Registered Dietitian has a role to play in advising clients to use Natural Health Products correctly (such as taking them at correct time during the day and at correct dose)?
- Q6--What is your main source of information on Natural Health Products?
- Q7--Have you learned about ginseng from any courses you took at Mount Saint Vincent University?
- Q8--Do you think that nutrition students should learn about Natural Health Products as part of their training/education?
- Q9--Do you think knowledge and information in the field of Natural Health Products should be integrated into undergraduate nutrition courses offered at Mount Saint Vincent University?

Table-30 and Table-31 NHP-Q Feedback Form Question Number

- FQ1—"Write an "X" on the line left of each NHP-Q question that you found hard to Understand."
- FQ2—"Write an "X" on the line left of each NHP-Q question that you think contains words that might be interpreted differently by different people."
- FQ3—"Write an "X" on the line left of each NHP-Q question that you think contains offensive words."
- FQ4—"Write an "X" on the line left of each NHP-Q question that you think is constructed in a way that a particular answer is favored over others."
- FQ5—"Write an "X" on the line left of each NHP-Q question that you think does not provide sufficient response options."
- FQ6—"Do you think the general content flow from question to question in NHP-Q is easy to follow?"
- FQ7—"Do you think the font size of NHP-Q is suitable?"
- FQ8—"Does the questionnaire have enough 'white space'?"

Appendix 10

Natural Health Products Questionnaire Revision Based on Feedback from Nutrition Student Participants

- Changed the format of question order, for example, using 4(a) instead of 4.a.
- Changed the response option “*I have no opinion*” to “*I have no opinion / I am not sure*” in all questions involving this response option.
- Added a last question (Question 10) in Section C to facilitate the content flow:
“*Is there any Natural Health Product that you are particularly interested in learning?*
_____ *Yes* _____ *No* _____ *I am not Sure*”.

Section A of NHP-Q

- Question 2: divided this question into two sub-questions: “*(a) What is your current marital status? (b) What is your current living status?*”, and deleted the response option “*living with support person*”;
- Question 3: added a note under the question, explaining what “dependents” means;
- Question 4: provided more examples for each response option;
- Question 5: revised the question to: “*What is the highest level of education you have completed prior to the enrolment of your current program at Mount Saint Vincent University?* _____ *High school or high school equivalent* _____ *College certificate or diploma* _____ *Undergraduate degree* _____ *Graduate or professional degree* _____ *Other* _____ *Prefer not to Answer*”;
- Question 7 and 8: switched the order of Q7 and Q8;
- Question 12: added a note under the question explaining what “being enrolled in IEP program at MSVU” means;
- Question 13: added a note under the question specifying that work experience does not include volunteer experience.

Section B of NHP-Q

Examination of the Ginseng Utility from the Perspective of the Nutrition Professional

- Question 1: added some extra response options and provided examples for each response option;
- Question 3: added a picture of ginseng root, and the Note brackets, specified that it refers to pure “root” form;
- Question 4: added a note under the question explaining what ginseng products include;
- Question 5: added “ginseng tea-bag” as one response option, and added a note explaining what ginseng products mean.

Section C of NHP-Q

- Question 1: revised the question to: *“Do you think that ginseng can be used in disease management?”*;
- Question 3: revised the question and replaced the “Yes” or “No” response option format with a more specific response option format: *“Which of the listed healthcare professionals do you think that clients should tell if they are using Natural Health Products?”*;
- Question 4: revised the question and replaced the “Yes” or “No” response option format with a more opinion-based response option format: “Agree”, “Disagree” or “I have no opinion / I am not sure”;
- Question 6: added several more response options;
- Question 8: revised the question and replaced the “Yes” or “No” response option format with a more opinion-based response option format: “Agree”, “Disagree” or “I have no opinion / I am not sure”;
- Question 9: replaced the word “integrate” with the word “cover”.

Appendix 11

Date Completed: ____/____/____
Day/ Month/ Year



Natural Health Products and Ginseng Questionnaire (final version)

Section A: Getting to Know You

Select the option that best applies to you (by writing an "X" on the line next to the option)

1. What is your current age?

- 18 to 25
- 26 to 35
- 36 to 45
- Above 45
- Prefer not to answer

2. (a) What is your current marital status?
(Please select all options that apply to you.)

- Single
- Married
- Common Law
- Divorced
- Separated
- Widowed
- Other
- Prefer not to answer

2. (b) What is your current living status?
(Please select all options that apply to you.)

- Living with immediate family
- Living with extended family
- Living with partner
- Living alone
- Living with friends/ roommates
- Other
- Prefer not to answer

3. Do you currently have dependents living in your household?

(Note: "Dependent" means a person who relies on other people, such as family members, for aid and support.)

- Yes
- No
- Prefer not to answer

4. (a) Which of the following ethnic group(s) do you identify with?
(Please select all options that apply to you.)

- Indigenous/Aboriginal/First Nation (such as Metis, Inuit, etc.)
- European/Caucasian (such as Scottish, Irish, English, German, Russian, etc.)
- African/Caribbean (such as African, Haitian, Jamaican, Somali, etc.)
- Chinese
- Korean
- Japanese
- South Asian (such as Indian, Pakistani, Sri Lankan, Burmese, Bangladeshi, Cambodian, Laotian, Thai, Vietnamese, Malaysian, Filipino, Indonesian, etc.)
- Arab/Middle Eastern (such as Armenian, Iranian, Lebanese, Moroccan, etc.)
- Latin American
- Other
- Prefer not to answer

4. (b) If your answer was "Other" in 4(a), please specify your response on the line below.

5. (a) What is the highest level of education you have completed prior to the enrolment of your current program at Mount Saint Vincent University?

- High school or high school equivalent
- College certificate or diploma
- Undergraduate degree
- Graduate or professional degree
- Other
- Prefer not to answer

5. (b) If your answer was "Other" in 5(a), please write your response on the line below.

6. (a) Which of the following options best represents your current program at Mount Saint Vincent University?

- Applied Human Nutrition Major
- Applied Human Nutrition Minor
- Other

6. (b) If your answer was "Other" in 6(a), please write your response on the line below.

7. What is your current student status?

- Full-time student
- Part-time student

(Note: Full-time means taking three or more than three credit courses per semester. Part-time means taking less than three credit courses per semester.)

8. (a) Which academic year of your program are you currently in?

- 1st Year
- 2nd Year
- 3rd Year
- 4th Year
- Other

8. (b) If your answer was “Other” in 8(a), please write your response on the line below.

9. Are you a transfer student?

(Note: Transfer student means a student who transferred from another program or from another university)

_____ Yes

_____ No

10. Are you an international student?

(Note: International student means a student who is not a permanent resident or citizen of Canada, but lives to Canada for the purpose of study.)

_____ Yes

_____ No

11. Do you plan to become a Registered Dietitian in the future?

_____ Yes

_____ No

_____ I do not know yet / have not decided yet

12. Are you currently enrolled in the Department of Applied Human Nutrition—Internship Education Program (IEP)?

(Note: Being enrolled in IEP means that you have been accepted into the dietetic internship program at Mount Saint Vincent University and guaranteed an internship spot.)

_____ Yes

_____ No

13. Do you have work experience in any of the following fields?
(Please select all options that apply to you.)

(Note: It does not include volunteer experience)

- Providing healthcare or counselling to patients/clients
- Engaging in human healthcare research studies
- Providing health education
- Herbal products store
- Pharmacy
- Food service and/or administration
- I do not have any work experience in the above fields

Section B: Getting to Know You More

1. (a) Have you taken any of the listed nutritional supplements below within the past year?
(Please select all options that apply to you.)

(Note: Nutritional supplements are commonly in the form of tablet, capsule, powder, or liquid extract.)

- Vitamin supplements (e.g. vitamin A, B, C, D, E, folic acid supplements, etc.)
- Mineral supplements (e.g. calcium, zinc, magnesium, iron supplements, etc.)
- Multi-vitamin & mineral complex supplements
- Amino acid supplements (e.g. glutamine, taurine, glycine, leucine, arginine, Alanine, branched-chain amino acids supplements, etc.)
- Fatty acid supplements (e.g. omega-3, flaxseed oil, salmon fish oil, etc.)
- Protein supplements (e.g. protein powder, protein capsule, protein bar, etc.)
- Fiber supplements (containing dietary fiber that helps with the digestion)
- Energy boost supplements (e.g. Ensure, energy bar, etc.)
- Enzyme supplements (e.g. coenzyme, digestive enzyme supplements, etc.)
- Probiotic supplements (supplements containing live gut friendly bacteria that can help the digestive system absorb nutrients—often called “good” bacteria)
- Other
- I have not taken any of the listed supplements above
- Prefer not to answer

1. (b) If your answer was “Other” in 1(a), please specify your answer on the line below.

2. Have you taken herbal products within the past year?

(Note: Herbal products are products derived from seeds, berries, roots, leaves, bark, or flowers of plants. They can be used as supplements for therapeutic purposes. They can also be produced in the form of tablet, capsule, powder, liquid extract, or tea bag)

- Yes
 No
 Prefer not to answer

3. Have you consumed ginseng root (in pure “root” form) within the past year?

(Note: Ginseng root is the fleshy root of a kind of slow-growing plant. In some cultures, ginseng root is also called “Man Root” or “Ren Sheng”. One common cultural practice is slicing ginseng root into thin slices, and mixing them with hot water to make ginseng tea, or using them as one ingredient in soup recipes)



- Yes
 No
 Prefer not to answer

4. Have you encouraged other people to consume ginseng root (in pure “root” form)? (Such as your friends, family members, clients, customers, etc.)

- Yes
 No
 Prefer not to answer

5. (a) Excluding ginseng root, have you taken any of the listed ginseng products below as a supplement within the past year?
(Please select all options that apply to you.)

(Note: ginseng products are products on the market that are processed from ginseng root. They can be taken as a supplement, and are commonly produced in the form of tablet, capsule, liquid extract, tea-bag, etc.)

- Ginseng tablets (containing ingredients extracted from ginseng)
- Ginseng capsules (containing ginseng powder)
- Ginseng liquid extract (containing ingredients extracted from ginseng)
- Ginseng tea-bag (commercially produced tea-bags that contain ginseng)
- Ginseng candies (containing ingredients extracted from ginseng)
- Over-the-counter medicine that contains ginseng ingredients
- Other
- I have not taken any of the listed ginseng products above
- I am not sure
- Prefer not to answer

5. (b) If your answer was "Other" in 5(a), please specify your answer on the line below.

6. Have you encouraged other people to take ginseng products other than ginseng root?
(Such as your friends, family members, clients, customers, etc.)

- Yes
- No
- Prefer not to answer

Section C: What Do You Think about Natural Health Products and Ginseng?

In Canada, Natural Health Products (NHPs) include vitamin and mineral supplements, herbal medicines, homeopathic medicines, traditional medicines, probiotics, and other products such as essential fatty acids and amino acids supplements

1. (a) Do you think that ginseng can be used in disease management?

- Yes
- No
- I have no opinion / I am not sure

1. (b) If your answer was “Yes” in 1(a), please specify on the line below which diseases you think that ginseng can be used to manage:

2. (a) Do you think ginseng is safe to consume?

- Yes
- No
- I have no opinion / I am not sure

2. (b) If your answer was “No” in 2(a), please specify your reason on the line below.

3. (a) Which of the listed healthcare professionals do you think that clients should tell if they are using Natural Health Products?
(Please select all options that apply to you.)

- Physician
- Naturopath Doctor
- Pharmacist
- Registered Dietitian
- Nurse
- Other
- Clients do not need to tell any healthcare professional
- I have no opinion / I am not sure

3. (b) If your answer was "Other" in 3(a), please specify your answer on the line below.

4. Do you agree with the following statement?

"Registered Dietitians usually play very little role in recommending specific Natural Health Products to their clients based on nutritional assessment."

_____ Agree

_____ Disagree

_____ I have no opinion / I am not sure

5. Do you think that Registered Dietitians have a role to play in advising clients on how to use Natural Health Products correctly (such as taking them at correct time during the day and at correct dose)?

_____ Yes

_____ No

_____ I have no opinion / I am not sure

6. (a) What is your main source of information on Natural Health Products?

(Please select all options that apply to you.)

_____ Professional reference books (such as textbooks)

_____ Scientific journals

_____ Health Canada website

_____ Dietitians of Canada online courses on supplements

_____ Nutrition professional articles and blogs

_____ Courses taken at university (including online courses)

_____ Reference database

_____ Social media

_____ Magazines

_____ Television shows

_____ YouTube videos

_____ Herbal products stores

_____ Pharmacies

_____ Healthcare professionals (such as Doctors, Pharmacists, Dietitians, etc.)

_____ Families / friends / colleagues

_____ Other

_____ I do not pay attention to Natural Health Products information

6. (b) If your answer was "Other" in 6(a), please specify your answer on the line below.

7. (a) Have you learned about ginseng from any courses you took at Mount Saint Vincent University?

- Yes
- No
- I do not remember

7. (b) If your answer was "Yes" in 7(a), please write the course number or course name on the line below.

8. Do you agree with the following statement?

"Nutrition students do not necessarily need to learn knowledge and information about Natural Health Products as part of their training/education."

(Note: Knowledge and information in the field of Natural Health Products can include regulations, research findings, and packaging/labelling, etc.)

- Agree
- Disagree
- I have no opinion / I am not sure

9. Do you think undergraduate nutrition courses offered at Mount Saint Vincent University should cover more knowledge and information in the field of Natural Health Products?

- Yes
- No
- I have no opinion / I am not sure

10. (a) Is there any Natural Health Product that you are particularly interested in learning?

- Yes
- No
- I am not sure

10. (b) If your answer was “Yes” in 10(a), please specify your answer on the line below.

End of Questionnaire.

Thank You for Your Participation.

Appendix 12



Consent to Provide Feedback on Natural Health Products and Ginseng Questionnaire

Study Title

Evaluating Applied Human Nutrition Undergraduate Students' Knowledge and Perception of Natural Health Products and Ginseng (Phase One—Questionnaire Development)

Introduction

We would like to invite you to give feedback on a questionnaire that has been made to collect applied human nutrition students' knowledge and perception of natural health products (NHP) and ginseng. This consent form provides you with an overview of the study so you can make an informed decision about if you would like to participate. Before agreeing to take part in this study, it is important that you read and understand this consent form. If you have any questions, contact one of the study investigators listed below. Please do not sign this form until you are sure you understand the information in it. You will be given a copy of this consent form to keep for your own records, if you choose to participate.

Study Investigators

Principal Investigator:

Shannan Grant, MSc, RD, PhD Assistant Professor	Department of Applied Human Nutrition Mount Saint Vincent University Phone: (902) 457-6256 Email: shannan.grant2@msvu.ca
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Co-Investigators:

Haoliang He, MSc Student Study Coordinator	Department of Applied Human Nutrition Mount Saint Vincent University Email: haoliang.he@msvu.ca
Chelsey Purdy, BSc Student Research Assistant	Department of Applied Human Nutrition Mount Saint Vincent University
Antonia Harvey, PDt, MSc Candidate Research Assistant	Department of Applied Human Nutrition Mount Saint Vincent University

Potential Conflict of Interest

This study is to be completed as part of Haoliang He's M.Sc. degree requirements, under the supervision of Dr. Shannan Grant. Outside of Mr He's aim to complete an MSc, there are no conflicts to report.

Study Sponsor

This study is conducted by investigators who are members of Mount Saint Vincent University. Funding for this study will not be received from any outside organization.

Study Background

In Canada, NHPs include vitamin and mineral supplements, herbal medicines, homeopathic medicines, traditional medicines, probiotics, and essential fatty acids and amino acids supplements. Dietitians (PDts) can play an important role in educating the public on NHPs. If PDts choose to play this role, they must be knowledgeable about NHPs and NHPs role in health and disease. Not all university-based Dietitian-training programs in Canada have courses that teach this information in detail. If this knowledge is not obtained post-undergraduate training, PDts may not have sufficient knowledge to engage in NHP education.

There are currently no Canadian studies published that examined nutrition students' knowledge, perception and interest in NHPs. There is also limited information available on nutrition student's knowledge and perception of ginseng, an example of a NHP. Ginseng's therapeutic effects are well documented and it can be found as an ingredient in many foods, drinks, and over-the-counter products.

Purpose of the Study

The purpose of this study is to investigate undergraduate students' knowledge and perception of NHPs and ginseng.

Study Overview

This consent form describes phase one of a three phase study called "Evaluating Applied Human Nutrition Undergraduate Students' Knowledge, Perception and interest in Natural Health Products". Phase one is the Natural Health Products and Ginseng Questionnaire (NHP-G-Q) development phase, while phase two and three will be the NHP-G-Q administration phase. The feedback given during phase one will be used to improve the NHP-G-Q for future phases.

Participants

If you choose to sign this consent form, you are consenting to volunteer for Phase One of the study. You will be one of 20 undergraduate students recruited from the Department of Applied Human Nutrition, Mount Saint Vincent University.

Study Activities

If you choose to sign this consent form, you will be asked to review the NPHG-Q and give feedback to us using a feedback form. You will be asked to give us feedback on questionnaire content, format and readability (e.g. are the questions clear? Is the questionnaire easy to read?). This feedback will be used to improve the NPH-G-Q for phases two and three. Participating in this study will take about 30 to 75 min of your time - This is a time estimation and can vary by participant.

You will be emailed two attachments:

- (1.) The Natural Health Products and Ginseng Questionnaire (NHP-G-Q)
- (2.) A NHPG-Q Feedback Form

And

the following step-by-step directions:

Step 1: Please complete the NHP-G-Q. Use the NHP-G-Q Feedback Form to tell us how much time it took for you to complete the NHP-G-Q.

Step 2: Complete NHP-G-Q Feedback Form (instructions on the form). The NHP-G-Q Feedback Form includes 10 questions designed to collect your feedback on questionnaire content, format and readability.

Step 3: After the NHP-G-Q Feedback Form, drop a hardcopy off at EV422. A cardboard box with a slot in the top is where you will submit your NHPG-Q Feedback Form. You do not need to submit the NHP-G-Q.

Step 4: Once the Study Coordinator (Mr. He) confirms that the total number of NHP-G-Q Feedback Forms have been received, you will be asked to delete all electronic copies of study materials and shred all hard copies.

The NPH-G-Q Feedback Form will not ask for your personal information (e.g. name) or include a study code. Once the Study Coordinator (Mr. He) receives your feedback, it will be stored with other feedback in a locked cabinet until analysis occurs.

Potential Harms (Injury, Discomforts or Inconvenience)

There are no known harms associated with participating in this study. If you feel uncomfortable with answering any of our questions, you can choose not to answer them.

Potential Benefits

You will not benefit directly from taking part in this study, but will provide feedback that will benefit Phase Two of this study.

Protecting Your Information

Your signed consent form will be kept in a locked filing cabinet in the Principal Investigator's office. Your feedback form will be kept in hard copy in a locked filing cabinet within the Principal Investigator's office. Your feedback will also be kept in electronic form on the MSVU server. The Research Team will know your name during the study, but will not include an identifier on your feedback form. This means that data taken from your feedback form and entered into an excel spreadsheet will never be linked back to you. Only these anonymous data will be taken off campus by Mr. He for analysis and thesis writing purposes.

Potential Costs and Reimbursement to the Participant

There will be no costs charged to you if you choose to participate in this study. There will be no reimbursement for participating in this study.

Participation and Withdrawal

Participation in this study is voluntary. You may choose to stop being in the study at any time without any negative consequences. If you withdraw from the study, the study data/information collected from you up to that time will be used.

Research Ethics Board Contact

Before agreeing to take part in this research study, it is important that you read and understand this consent form. If you have questions about how this study is being conducted and wish to speak with someone not involved in the study, you may contact the Chair of the University Research Ethics Board (UREB) c/o MSVU Research Office, at 457-6350 or via e-mail at research@msvu.ca

The ethical components of this research study have been reviewed by the University Research Ethics Board and found to be in compliance with Mount Saint Vincent University's Research Ethics Policy.

Declaration of Consent

I acknowledge that the details described above have been explained to me and that any questions that I have asked have been answered to my satisfaction. I have been informed of the alternatives to participation in this study, including the right not to participate and the right to withdraw. As well, the potential risks, harms and discomforts have been explained to me. I understand that I will not receive compensation for my time spent participating in the study.

I hereby agree and give my authorized consent to participate in the study and to treat confidential information in a restrictive manner as described above. I will be given a copy of the consent form to keep for my own records.

Participant Name
(Please Print)

Signature of Participant

Date
(Day-Month-Year)

I confirm that I have explained the nature and purpose of the study to the participant named above. I have answered all questions asked about the study.

Name & Position of Person
Conducting Consent Discussion

Signature of Person
Conducting Consent Discussion

Date
(Day-Month-Year)

Appendix 13

Questionnaire Feedback Comments Theme Codebook

Level			Theme
1	2	3	
100			No Comments
200			Questionnaire Content
	201		Content of Questions
		201.1	Choosing precise / appropriate words or terms
		201.2	Unnecessary / redundant question
		201.3	Controversy on ethnic identity
		201.4	Gramma / spelling mistake
		201.5	Being less intrusive
		201.6	Defining / explaining terms clearly
		201.7	Using consistent terms / language
		201.8	Being more specific when asking a question
		201.9	Making question more realistic or easier to answer
		201.10	Being more inclusive
		201.11	Avoiding leading-question
	202		Content of Response Options
		202.1	Providing broader / appropriate response options
		202.2	Being less intrusive
		202.3	Controversy on ethnic identity
		202.4	Choosing precise / appropriate words or terms
		202.5	Gramma / spelling mistake
		202.6	Defining / explaining terms clearly
		202.7	Being more specific in response options
		202.8	Redundant response options
		202.9	Too many response options
300			Questionnaire Structure
	301		Content flow
		301.1	Switching specific questions' order
		301.2	Adding extra section heading
		301.3	Inserting extra question
		301.4	Dividing into two questions
400			Questionnaire "Face"
	401		Font Size
	402		White Space
		402.1	Space between lines
		402.2	Page space density
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