Herbal Medicine Use in Adult Dental School

Patients at the University of Toronto

by

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A thesis submitted in conformity with the requirements for the degree of Master of Science

Graduate Department of Paediatric Dentistry
University of Toronto

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Abstract

**Background:** Some herbal medications (HM) may have potential adverse drug interactions and may impact dental treatment. To date, there is a dearth of information on the use of HM among dental patients. **Objectives:** The primary goal of this study is to determine the prevalence of HM usage among patients in the clinic at the Faculty of Dentistry – University of Toronto. Also, this study will determine the prevalence of recording of HM use in the medical records of the same institution. **Materials and Methods:** The primary method to assess the prevalence of HM use is by a survey of dental school patients and chart review. **Results:** 65% of patients currently use one or more HM, while their use is recorded in only 8% of the dental charts. **Conclusion:** There is a significant difference between the prevalence of HM use and their recording in the dental charts.
Acknowledgments

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1 Literature Review

1.1 Introduction

Complementary and alternative medicine (CAM) is a group of diverse medical and health care systems, therapies, and products that are not considered to be part of conventional medicine (Barnes, 2002). Complementary medicine can be considered as adjuncts to conventional medicine; however, alternative medicine is used in place of conventional medicine. The National Institutes of Health (NIH) established the National Center for Complementary and Alternative Medicine (NCCAM) to provide guidance to the public regarding the use of CAM (Najm, 2001).

There are 5 major categories of Complementary and Alternative Medicine:

The first category is alternative medical systems. These systems include homeopathic medicine, naturopathic medicine, Traditional Chinese medicine (TCM), and Indian Ayurveda. Homeopathic medicine is based on the concept that “like cures like”. For example, when a substance is given at a higher or more concentrated dose, then it would cause a set of symptoms, but then a small, highly diluted quantity of the same medicinal substance is given to cure those symptoms. Naturopathic medicine involves the natural healing forces within the body. The primary goal is to help the body heal from disease and achieve better health. This type of alternative medicine can include dietary modifications, massage therapy, exercise, and acupuncture. Traditional Chinese Medicine has its basis that disease is the result of a disturbance in the natural environment of the body, and the purpose is to restore the balance of the Yin and the Yang. This balance is restored by the administration of herbs, acupuncture, and massage. Once the balance of Yin and Yang is achieved, it will allow the Qi (vitality) to flow through the channels of the body. Finally, Ayurveda is a type of medical system that has been practiced mainly in India. Its components include diet and herbal remedies, and focuses the use of the body, mind, and spirit in disease prevention and treatment.

The second category is mind-body interactions such as biofeedback, meditation, prayer, mental healing, and music or art therapies.
The third category is energy therapies, and this group includes Qi Gong, Reiki, and bioelectromagnetic therapies. Qi Gong is a component of traditional Chinese medicine. It combines meditation, exercise, and regulation of breathing to enhance the flow of the vital energy known as the \textit{Qi}. This \textit{Qi} flows throughout the body to improve circulation and enhance immune function. Reiki is the Japanese word for universal energy. The basis of Reiki is that the spiritual energy is channeled through a Reiki practitioner to heal the patient’s spirit, and consequently it will heal the physical body.

The fourth category is body-based methods, which includes chiropractic and osteopathic treatments and massage therapy. For example, massage therapy involves manual or mechanical pressure acting on the body. It can promote relaxation and well-being.

The fifth and final category is natural products, such as herbs, vitamins, and dietary supplements. The majority of natural products come from plants (herbal medications), and a minority come from animals, such as a honey-bee, or minerals, such as sulphur (Eldin, 1999).

Herbal medicines (HM) are a type of CAM. They are also known as phytochemicals or botanical medicines because their source is plant-based. In Canada, they are classified as Natural Health Products; whereas, in the United States, they are classified as Dietary Supplements.

1.2 \textbf{Prevalence of Herbal Medications}

According to The Fraser Institute, in 2006, 54\% of Canadians reported using at least one alternative therapy in the past 12 months. In contrast, in 1997, 50\% of Canadians reported using at least one alternative therapy in the past 12 months. This 4\% increase was found to be statistically significant (Esmail, 2007).

Lindau (2008) investigated the use of prescription and over-the-counter medications and natural supplements in older adults. The research demonstrated that 49\% of Americans used dietary supplements; however, they included minerals, vitamins, animal products, and herbal medications in this category. In this study, professional interviewers conducted in-home interviews of 3005 adults, aged 57-84 years old, from across the United States. Data collected on medications were done by direct observation of medication bottles; participants were asked to
show the interviewer the containers of all the medications they are currently taking, including prescription, over-the-counter, vitamins, herbal, and alternative medications. Although this method does not rely on recall, interview bias is still a main factor because there may be a systematic difference between each interviewer on how the data was solicited, recorded, or interpreted. For example, as part of the protocol, interviewers asked participants to provide medications used “on a regular schedule, like every day or every week.” There may be confusion with “prn or as needed medications”. Are those medications omitted simply because they are not taken on a regular schedule? Also, the methodology does not state how the interviewers were standardized, and the only aspect that was stated about the interviewers were that they were “professional interviewers”.

Looking specifically at the prevalence of herbal medication use, they are most commonly used to treat allergies, digestive problems, insomnia, and lung problems (Eisenberg, 1998). Additional studies showed that they are used for treating asthma, depression, and rheumatological disorders (Barnes, 2000 and Gyorik, 2004).

A Canadian study demonstrated that 17% of patients with cardiovascular disease used herbal medications (Pharand, 2003). This study looked at 306 individuals with a diagnosed cardiovascular disease, such as coronary artery disease and hypertension. Pharmacists from eight teaching hospitals across Canada recruited participants. The hospital pharmacist used a standardized survey with the patients. However, the methods did not indicate if the pharmacists themselves were standardized in the way they interviewed the participants and recorded the data. Even though the research was a national study, two provinces were not included in the sample: British Columbia and Newfoundland. The results may not be generalized to all of Canada. Finally, the survey did not specifically ask about herbal medications, such as St. John’s Wort, *Ginkgo biloba*, and saw palmetto. These popular HMs are important to include in the survey so that individuals can recognize them as HMs rather than relying on memory recall. Thus, the prevalence of HM use may be under-reported.

A study in British Columbia demonstrated that 34% of pre-surgical patients at a day care unit reported using a herbal medication (Lennox and Henderson, 2003). The researchers collected data on HM use by employing a written survey. The survey was provided in both English and Chinese. The surveys were distributed to patients while waiting for their surgery in the day-
surgery unit at Vancouver General Hospital. The patients were initially asked on the survey if they take a herbal medication. If the answer was ‘yes’ then they continued to fill out the remainder of the questionnaire. There are several limitations to this study. First, there was no mention of how or who distributed the surveys to the patients. This lack of standardization may bias the recruitment of the participants. Also, the surveys were provided in either English or Chinese. This method selectively biases the sample population to those who understand either English or Chinese. The sample population was patients waiting for their surgery in the outpatient surgical unit. This sample may not represent the average Canadian. All of these patients have a medical condition, and this may confound the results because this sample may skew the results of the prevalence of HM use. Finally, the researchers assessed the prevalence by simply asking if the patient had taken a herbal medication prior to completing the survey. The researchers are relying on the patient’s definition of what a herbal medication is. This may under-report the prevalence because they did not provide examples of herbal medications, because some participants may not consider HMs such as garlic or aloe vera as herbal medications. Thus they may have potentially missed some affirmative responses.

A survey in 2005 found that approximately 11% of Canadians take herbal medicines (Ipsos/Reid, 2005). The Fraser Institute found that 10% of Canadians in 2006 used an herbal medication in the past 12 months, and 15% of Canadians reported using herbal medication at some point in their lives (Esmail, 2007). The researchers employed Ipsos Reid to conduct the survey. The surveyors interviewed 2000 adults across Canada using a computer generated random telephone number. The surveyors were standardized and read from a script. However, the study did not mention any inclusion or exclusion criteria, but instead only discussed whether or not they were able to reach a potential participant and if the participant had a language barrier. Another limitation was selection bias because they only selected for people who had a landline to the house.

In the context of dental patients, only one study was done in Canada. A paper survey was conducted in six private dental practices in Thunder Bay, Ontario regarding the use of herbal medications. According to the results, 38% of the dental patients reported using herbal medications (Polek, 2006). Although a one-page questionnaire was distributed to 1400 patients, the methodology did not describe how the participants were selected. There may have been a
selection bias in asking participants to complete the survey. In addition, as the authors acknowledged, no information was collected about ethnicity. Ethnicity is important because literature has shown that Caucasians have a higher prevalence of HM use (Leung, 2001). According to the 2006 Census (Statistics Canada, 2006), there were 109,140 people living in Thunder Bay. Approximately 86.2% of the population was Caucasian. Also of note, Thunder Bay has the highest concentration of Finnish people per capita and second most Finnish population in Canada. In addition, Thunder Bay has a large Aboriginal population, and they comprise about 8.2% of the population.

Delbanco (1993) discovered that only 3% of a nationwide telephone survey respondents took HMs in the past twelve months. They interviewed 1539 adults across the United States. They were selected by a random digit dialing. The interviewers asked the participants questions regarding their health care practices. Although the participants were randomly selected, only those with a telephone number were selected. This systematic selection bias may not be representative of the population.

Kessler (1998) compared the prevalence of HM use between 1990 and 1997 in the United States. In 1990, 2.5% of the respondents used HM, but increased to 12.1% in 1997. This increase was statistically significant. Although a large sample size was used, 1539 adults in 1990 and 2055 adults in 1997, to do a national survey, there were several biases. First, the surveys were conducted using random-digit dialing to select households across the United States. This is a selection bias because it only selected for people who had a landline to the house. Second, the surveys were conducted as interviews. The methodology states that investigators from Harvard Medical School conducted the interviews, but there were no details on whether the interviews were standardized, or how the information was solicited. Interviewers may be biased in how the information was recorded or interpreted. Third, no stipend was provided to participants in the 1990 survey, but in 1997, a financial incentive ($20 USD) was given to participants. Furthermore, to entice non-respondents, a second round of survey requests were made with an increased honorarium of $50 USD. This change in methodology of recruiting participants may bias the selection of participants because the financial incentive may systematically bias which participants take the survey.
Tsen and colleagues (2000) found that 22% of pre-surgical patients used HM. Surveys were distributed at the patient’s pre-operative visit with either an anaesthesiologist or a certified registered nurse anaesthetist. The methods did not clearly outline how the patients were recruited or whether the surveyors were standardized. In addition, the authors stated that with patients who did not speak English or patients who could not read or write were provided assistance to complete the survey. There are no details on how or what type of assistance was provided. Lack of standardization on data collection may lead to problems with how the data are solicited, recorded and interpreted. For example, anaesthesiologists take detailed medical histories, including medications. Hence, their penchant for recording all prescription medications, over-the-counter medications, and other medications, such as herbal medications, may systematically increase the prevalence of HM use among their sample. Another weakness with this study is that the responses relied on self-reporting and the participants may not remember all of their previous HM use. Finally, only two demographic data were collected: age and gender. There is no way to assess if the sample was representative of the population.

An American study looked at dental patients in a dental school setting, and they found that 26.6% of dental patients had used herbal medicines at some point in their life and 16.9% had used it in the past 12 months (Spector, 2012). Although this study collected information on ethnicity, the sample population was more homogeneous than other published research. The Caucasian respondents made up 92.8% of the sample population. This sample may have been as a result of selection bias.

1.3 **Table of Evidence**

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Type of Survey</th>
<th>Results</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eisenberg et al. 1993</td>
<td>1539 adults (5158 contacted)</td>
<td>Telephone interview (random digit dialing)</td>
<td>3% had used herbal medicine in the past 12 months; 34% reported using at least one unconventional therapy in the past year</td>
<td>The frequency of use of unconventional therapy in the US is higher than previously reported, and medical doctors should ask their patients about their use</td>
</tr>
<tr>
<td>Study</td>
<td>Sample Size</td>
<td>Study Design</td>
<td>Findings</td>
<td>Notes</td>
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<tr>
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</tr>
<tr>
<td>Eisenberg et al. 1998</td>
<td>1539 adults (1990) 2055 adults (1997)</td>
<td>Telephone (random-digit dialing), &gt;18 years old across United States</td>
<td>2.5% (1990) 12.1% (1997) used herbal medication; 39.8% (1990) 38.5% (1997) discussed with their physician</td>
<td>Statistically significant increase in herbal medication use between 1990 and 1997</td>
</tr>
<tr>
<td>Tsen et al. 2000</td>
<td>3106 adults (3842 distributed)</td>
<td>Written survey to presurgical patients over an 11 week period</td>
<td>22% of patients used herbal medication</td>
<td>Alternative medicine use is common in the pre-operative period</td>
</tr>
<tr>
<td>Pharand et al. 2003</td>
<td>306 adults</td>
<td>Written survey</td>
<td>17% of patients with cardiovascular disease took HM</td>
<td>Patients with cardiovascular disease take HMs, and clinicians should be aware of their use</td>
</tr>
<tr>
<td>Lennox and Henderson 2003</td>
<td>485 adults (575 adults approached)</td>
<td>Written survey</td>
<td>34% of patients at a surgical day care unit took HMs</td>
<td>Patients undergoing day surgery have a higher prevalence of HM use than previously reported</td>
</tr>
<tr>
<td>Poleck et al. 2006</td>
<td>1320 adults in 6 private dental clinics (1400 distributed)</td>
<td>Written survey (non-randomized)</td>
<td>38% of dental patients use herbal medications</td>
<td>Use of herbal medications is relatively common among patients in private dental clinics in Thunder Bay, ON</td>
</tr>
<tr>
<td>Qato et al. 2008</td>
<td>3005 adults (57-84 years old) (4400 contacted)</td>
<td>In-home interviews, (cross-sectional of the United States)</td>
<td>49% of elderly adults used dietary supplements; among prescription medication users, 52% of the elderly were concurrent users of dietary supplements</td>
<td>There is a high prevalence of older adults using prescription medication with dietary supplements, and this presents a potential risk for a major drug-drug interaction</td>
</tr>
</tbody>
</table>
### 1.4 Disclosure of Herbal Medication Use

In terms of disclosure of CAM use, approximately 28-37% of people using CAM disclose this information to their physician or other healthcare professionals (Eisenberg, 2001). Currently, there are only three studies on disclosure of herbal medications by patients to their physicians. A Canadian study showed that 46% of patients had informed their family doctor that they were taking HMs (Lennox, 2003). An American study demonstrated that almost 70% of people taking dietary supplements did not tell their health care providers that they are using them (Gardiner, 2006). Another American study surveyed CAM users and showed that only 33.3% of HM users disclosed their use to their health care providers (Chao, 2008).

The reason for lack of disclosure is multi-factorial. From the patients’ perspective, the major reason for non-disclosure was their fear of a negative reaction by the clinician (Robinson, 2004). Also, some patients assume that because herbal medications are natural, they are beneficial and do not have any adverse effects. In addition, the patients perceive that telling their healthcare provider about the use of HMs is irrelevant because they are not conventional medical products. Another reason may be due to the patients’ view that either the clinician lacks interest or knowledge in HMs (Robinson, 2004). Finally, patients do not disclose the use of HMs because their clinicians did not ask (Robinson, 2004).

From the healthcare providers’ perspective, their lack of knowledge in HMs is a major reason for not asking their patients about HM use (DTB, 2013). In a 2010 Drug and Therapeutics Bulletin (DTB) survey of 164 physicians, none of them felt that their knowledge about HMs was “very good”. In the same survey, only 1.8% of the respondents reported that physicians were “well informed” about HMs, and 89% of physicians admitted that their knowledge of HMs was “much

<table>
<thead>
<tr>
<th>Spector et al. 2012</th>
<th>402 adults in a dental school</th>
<th>Written survey of adults in the waiting room</th>
<th>Lifetime prevalence: non-vitamin herbal 26.6%, topical herbal oral 9.5%; past 12 months prevalence: non-vitamin herbal 16.9%, topical herbal oral 6.2%</th>
<th>A higher rate of CAM usage was found in this specific type of population than previously reported in a general population</th>
</tr>
</thead>
</table>
poorer” than their knowledge of prescription medication (DTB, 2013). Furthermore, 77% of physicians are concerned that their patients may not be disclosing their herbal medication use, and the same DTB survey revealed that 9% of the physicians never asked about herbal medication use, 47% occasionally asked, 27% asked most of the time, and only 13% always asked (DTB, 2013). This evidence suggests that because the physicians do not possess the knowledge, they are less inclined to ask their patients about the use of HM. Similar to their patients, clinicians also think that because HMs are natural, they do not have any health risks, such as drug and HM interactions. Also, physicians have a biased view that HMs lack therapeutic effect and those are not “real” medications (DTB, 2013).

1.5  Pharmacokinetics of Herbal Medications

1.5.1  Biotransformation

We are exposed to a wide variety of chemicals by way of percutaneous absorption, inhalation, and more commonly ingestion. These chemicals may include prescription medications, recreational drugs, nutritional products, and environmental toxins. Our bodies are capable of eliminating these compounds through enzyme-catalyzed reactions called drug biotransformation. Herbal medicines, like any other foreign chemical, undergo biotransformation. One of the goals of drug biotransformation is to make the chemical more water-soluble in order to facilitate elimination (Riddick, 2007 and Katzung, 2015). There are two types of reactions: phase I and phase II reactions. Phase I reactions consist of hydrolysis, reduction, and oxidation processes, which may add or reveal a functional group, for example a hydroxyl or amine (Katzung, 2015). These functional groups make the drug more polar or water-soluble. Phase II reactions involve conjugation processes which combines an endogenous molecule, for example glutathione or glucuronic acid, with the functional group obtained from Phase I reactions (Katzung, 2015). This results in a highly polar drug conjugate. The liver is the most important organ of biotransformation (Riddick, 2007).

There are several sequences in which a drug undergoes biotransformation. First, the parent drug may simply be eliminated without the need for any reactions and is excreted unchanged. Second, the parent drug may first pass through Phase I and then Phase II before being eliminated. Third, the drug may either only go through Phase I or Phase II, and then excreted. Finally, the chemical
may be metabolized by Phase II reactions first before moving onto Phase I reactions, and then eliminated. Within each phase, there are specific types of reactions (Riddick, 2007 and Katzung, 2015).

As mentioned earlier, Phase I reactions include oxidation, reduction, and hydrolysis. Oxidation reactions are an important component of drug metabolism, and they are mostly facilitated by a group of enzymes called cytochrome P450 (Guengerich, 2003). These proteins are located in the phospholipid membrane of the endoplasmic reticulum. It functions as the terminal oxidase in the catalytic pathway. Specifically, the cytochrome P450’s hemoprotein is initially in the oxidized ferric state (Fe$^{3+}$). When the chemical substrate binds with the cytochrome P450 to form a complex, an electron is donated by nicotinamide adenine dinucleotide phosphate (NADPH) to reduce the complex to its ferrous state (Fe$^{2+}$) (Thummel, 1998). Then through a series of poorly understood reactions, a hydroxyl group is added to the chemical substrate and the cytochrome P450 is returned to its initial ferric state (Guengerich, 2005). The hydroxylated product is polar, and thus is more water-soluble. The cytochrome P450 enzymes are capable of handling a variety of chemical substrates. There are two reasons for this ability. First, there are a variety of molecular configurations of cytochromes P450. Second, each of the cytochrome P450 enzymes can catalyze a large number of substrates. Of the cytochrome P450 enzymes, CYP3A4 plays the largest role.

Another Phase I reaction is reduction. Cytosolic and microsomal enzymes are involved in catalyzing azo linkages (RN=NR’), nitro groups (RNO$_2$), and carbonyl groups (RCOR’). As discussed earlier, although cytochrome P450 enzymes participate in oxidation reactions, they can also perform reduction reactions. For example, quinone-containing compounds can undergo a reversible reaction to produce a semi-quinone. This reaction is catalyzed by cytochrome P450. In addition to cytochrome P450, NAD(P)H-quinone oxireductase reduces quinone into hydroquinone, a more polar product, which is eventually eliminated (Oppermann, 2000).

A third Phase I reaction is hydrolysis. Drugs containing ester groups (RCOOR’) and amides (RCONHR’) are hydrolyzed by esterases and amidases respectively. Hydrolysis involves the introduction of a water molecule to break apart a chemical. These chemical compounds are initially metabolized into epoxide intermediates, and then hydrolyzed by epoxide hydrolase into more water-soluble products (Morisseau, 2005).
In contrast, Phase II reactions involve conjugation of a drug or its metabolite and an endogenous substance. The first type is glucuronidation, and this reaction conjugates the drug with glucuronic acid, an endogenous substance. This reaction is a three-step process because free glucuronic acid cannot bind to drugs. Instead, uridine diphosphate glucuronic acid (UDPGA) will conjugate with drugs. UDPGA is synthesized in a two-step process from glucose-1-phosphate. The third step is catalyzed by UDP-glucuronosyltransferase, and this enzyme conjugates the glucuronic acid from UDPGA with the drug (Kroemer, 1992). This conjugate can be excreted by urine or bile.

The second Phase II reaction is glutathione conjugation. Glutathione is a tripeptide, and is made up of glutamine, cysteine, and glycine. The conjugation of the drug with glutathione is catalyzed by glutathione S-transferase (Hayes, 2005). Although the conjugation of the drug with glutathione is an important step in detoxification, it is not the final product. The conjugate undergoes further metabolism to produce mercapturic acid end-products, which are then eliminated.

Another Phase II reaction is sulfation. This reaction is a three-step process, because inorganic sulfate must be activated to 3’-phosphoadenosine-5’-phosphosulfate (PAPS). Activation is a two-step process, and the third step is the sulfation reaction whereby a sulfotransferase catalyzes the conjugation of the drug with the activated sulfate to form a sulfate ester (Glatt, 2001).

### 1.5.2 Drug Interactions

Drug interactions are an important aspect of any medication, and herbal medications are no exceptions to this rule. Herb-drug interactions are a complex issue because of the complexity of herbal medications (Lanca, 2013). For example, some HMs may contain several active chemical compounds, which may make it difficult to determine which ingredient is pharmacologically responsible for the interaction (Lanca, 2013). In addition, due to lack of standardization, there may be contaminants, questionable botanical source, and variation in potency of the HM (Lanca, 2013). These factors may play a role in increasing or decreasing the activity of the other drugs that the HM may interact with.
1.6 **Drug Development**

Drug development in Canada is highly standardized and scrutinized. These steps are in place to ensure that a drug is not only effective, but also safe. Prior to clinical trials, there are preclinical trials, which are conducted in a laboratory. The primary goal of a preclinical trial is to test the drug molecule candidate in animal models or *in vitro* with human cells and determine the toxicity of the drug (Katzung, 2015). The drug candidate undergoes a battery of toxicity test, such as acute toxicity, chronic toxicity, effect on reproductive performance, carcinogenic potential, and mutagenic potential (Katzung, 2015). These experiments help pharmaceutical companies decide whether or not a drug is suitable for further studies into clinical trial. If the drug candidate has scientific merit for further development as a new drug, then it moves onto the clinical trials. There are four phases in clinical trials: Phase I, II, III, and IV (Katzung, 2015).

Phase I answers the question, “Is the drug safe?” It tests the drug on healthy volunteers to determine the safe clinical dose range, and only a small number of participants (20 to 100) are tested. This phase determines whether or not the drug is safe to check for efficacy. Although this may have been tested at the preclinical trials, it is often difficult to predict the efficacy and toxicity based on laboratory tests alone. Phase I trials are often non-blinded experiments, which means that both the investigators and the participants know what they are receiving. However, sometimes the trials may be blinded and have a control group, which means that both the investigators and the participants do not know whether they are receiving the experimental drug or a placebo. In addition to determining the clinical dose range, pharmacokinetic measurements are done, such as absorption, bioavailability, half-life, and excretion (Evans, 2007; Lee, 2005; and Ng, 2008).

Phase II answers the question, “Does the drug work?” The drug is tested on patients with the target disease to assess its efficacy. A therapeutic dose is used on a larger number of participants (100 to 300). At this stage, it is assumed that the drug has no therapeutic effect, and the trials must show that the drug has a beneficial effect. If either no therapeutic effect is observed or the drug has toxic effects at therapeutic doses, then the new drug fails and the development process stops. If the new drug candidate is deemed safe and efficacious, then it proceeds to the next stage. Usually, phase II trials are conducted as a single-blind, placebo-control, and an established active drug (which serves as a positive control) (Evans, 2007; Lee, 2005; and Ng, 2008).

Phase III is a large-scale test. It answers the question, “Does the drug work in double-blind studies?” The goal is to further evaluate the drug’s therapeutic effect on a larger
number of patients with the target disease (300 to 3000). These studies are randomized controlled multicentre trials, and they are used to compare with the current “gold standard” treatment. Also, this phase further establishes and confirms the efficacy and toxicity. These trials are very expensive, difficult to design and run, and time-consuming. Once a drug has shown satisfactory results in Phase III, the new drug candidate can be submitted for regulatory submission for review for approval (Evans, 2007; Lee, 2005; and Ng, 2008). Finally in Phase IV, also known as post-marketing surveillance, the drug is available to the public. The main goal is to observe the drug’s long-term adverse effects, interactions with other drugs, and effects on certain population groups such as pregnant women. Unfortunately, neither in Canada nor in the United States, none of these trials for drug approval are required for herbal medications (Evans, 2007; Lee, 2005; and Ng, 2008).

1.7 Relevance for Dental Practice

Determining the prevalence of herbal medication usage is important for dental clinicians. HMs may have potential adverse interactions with other HMs, over-the-counter medications or prescription medications. These adverse interactions may be a complication for dental treatment. For example, there may be an increased risk for bleeding with certain HMs. Garlic can increase the risk of bleeding. One component of garlic is allicin, and it inhibits platelet activity by inhibiting the production or release of platelet aggregating factor (Abebe, 2002). In addition, allicin inhibits platelet activity in vitro without affecting other enzymes, such as cyclooxygenase and lipoxygenase (Makheja, 1990 and Mayeux, 1988). Another component of garlic is ajoene, and it is an unsaturated sulfoxide disulfide. This molecule irreversibly inhibits platelet function (Ang-Lee, 2001). It is thought that ajoene inhibits platelet aggregation through inhibition of granule release and fibrinogen binding (Rendu, 1989). Another mechanism by which garlic can increase bleeding risk is reducing the synthesis of thromboxane and promoting the synthesis of prostacyclin (Pierre, 2005). These two changes decrease platelet aggregation. There have been several case reports that have linked garlic with spinal epidural hematoma (Rose, 1990 and Rowin, 1996), spontaneous post-operative bleeding (German, 1995), and increased INR with concomitant use of warfarin (Izzo, 2001).

Ginkgo biloba can also increase the risk of bleeding. The main chemical responsible for this risk is terpene ginkgolide B (Sierpina, 2003). This molecule is a platelet activating factor (PAF)
antagonist, which means that it displaces the PAF from its receptor binding site; therefore, reducing platelet aggregation (Chung, 1987). There have been several case reports of associating *Ginkgo biloba* with bleeding. For example, a 61-year-old man had spontaneous subarachnoid hemorrhage due to consuming *Ginkgo biloba* for 6 months (Vale, 1998). Another example was a 40-year-old woman who suffered from subdural hematoma after taking *Ginkgo biloba* for 2 months (Evans, 2000).

Bleeding is not the only complication with HMs. Risk of hypotension is also possible with HMs. For example, black cohosh has been associated with risk of hypotension. Cimifugic acid, which is an active component of black cohosh, produced vasodilatation *in vitro* (Noguchi, 1998). When black cohosh is concomitantly used with an anti-hypertensive medication, such as valsartan or bisoprolol, then this herb-drug interaction may make the patient hypotensive. Another example of herb-drug interaction is St. John’s wort. It is used to manage mild to moderate depression (De Smet, 2005). Hyperforin is the active compound in St. John’s wort (Barnes, 2001). It has shown to reduce the anticoagulant effect of warfarin (Brazier, 2003). Also, St. John’s wort can significantly induce the cytochrome P450 enzyme CYP 3A4 (Markowitz, 2003). Since cytochrome P450 enzymes are involved in metabolizing many exogenous substances, including medications, then St. John’s wort may reduce the effects of many drugs, such as warfarin. Hence, results of this study will highlight the significance and the importance of herbal medication use by dental patients and determine if clinicians are asking their patients if they use it or not. To date, there is a dearth of information in the literature regarding herbal medication use among dental patients. Furthermore, we do not know if dental clinicians are recording the use of these medications by their patients.

1.8 **Hypothesis**

Null hypothesis: there is no difference between the prevalence of HMs use among adult dental patients and the prevalence of recording of their use in medical records.

1.9 **Objectives**

The first objective was to determine the prevalence of herbal medicine use among adult patients of the dental school clinic at the University of Toronto. The second objective was to determine the prevalence of recording the use of herbal medicine in the patient’s medical chart.
2 Materials and Methods

Objective 1: To determine the prevalence of herbal medication use among adult patients, the University of Toronto Faculty of Dentistry’s patient population was recruited for the study. A sample size was calculated based on a precision of 5%, a 95% confidence interval, and a sampled proportion of 10% (Spector, 2012). The sample size estimate was 140, but was increased to 150 for convenience. This research was approved by the Research Ethics Board of the University of Toronto (REB #31529). Surveys were conducted between May 8, 2015 and May 29, 2015. Participants were invited to participate in the study by an in-person invite by researcher EY. The prospective individuals were approached while in the waiting area near the clinic or in the clinic. There was only one person involved in recruiting participants, recording and interpreting the responses. The inclusion criteria for the study were: had to be an active patient of the dental school at the University of Toronto, over the age of 18 years, and able to read and comprehend English at a basic level. Participants were excluded if they did not meet the above criteria. If the participant was amenable to taking the survey, then the participants were instructed to read the information letter and sign the consent form (Appendix A) prior to starting the survey. If the participant consented to taking the survey, then a four-page survey (Appendix B), similar to the one used by Tsen et al. at Harvard University (Tsen, 2000), was provided to the participant. The survey was filled out with researcher EY. It took the form of a guided interview, whereby the participants were allowed to ask questions for clarification. It took approximately 5-10 minutes to complete. The survey collected data on demographics, use of herbal medications, types of herbal medications, route of administration, frequency of use, reason for use, and type of disclosure of use (either voluntary disclosure or response to the clinician’s inquiry). Participants’ responses were kept strictly confidential and reporting did not identify individual participants. Additionally, participants were advised that all data collected during the study would remain anonymous. In all, 150 surveys were completed, and none of the participants withdrew from the study. Afterwards, the participant was given a debrief form to provide some information regarding the research study (Appendix C). No compensation was provided to the participants of the study. Completed surveys were placed in an envelope and sealed. The data were tabulated into Microsoft Office Excel 2008, and stored on a USB flash drive that was encrypted and password protected. In addition, a back-up copy was stored on a
password-protected account on the Faculty of Dentistry's Server. Only members of the research committee had access to the files.

The prevalence of herbal medication use was calculated by determining the number of patients who took herbal medication divided by the total number of patients surveyed. Data analysis included descriptive statistics (proportions at 95% confidence interval). Prevalence of herbal medication use was compared among different age groups, ethnicity, gender, type of disclosure of HM use, knowledge of herb-drug interactions, and knowledge of HMs impacting dental care using Chi-squared analysis. Statistical tests were interpreted at 5% significant level using Statistical Package for the Social Sciences (SPSS). In addition, the proportion of respondents who reported type of disclosure, reasons for taking herbal medication, knowledge of herbal medications as pertaining to dental treatment, and who recommended the herbal medication were summarized by descriptive statistics.

Objective 2: To determine the rate of recording in the dental chart of herbal medication use by patients, the active charts at the Faculty of Dentistry were reviewed between May 7, 2015 and May 25, 2015. Active charts are defined as patients having had a new patient exam in the past two years, or a recall examination in the past year. Due to the large volume of active charts at the Faculty of Dentistry, a fractionated sampling method was used to choose which charts would be reviewed. Since the entire patient population at the dental school was included in the sampling process, we arbitrarily chose the first chart in the chart room. The charts were already arranged in alphabetical order, and every fifth chart was chosen to be reviewed. The total number of charts reviewed was 844. Patients’ charts were reviewed and looked for evidence at either the new patient examination or recall examinations. The clinicians’ notes were searched for any written record of HM use or evidence that the information was asked to the patient. For example, in the medication list, either an herbal medication was listed or “patient is not taking any herbal medications” or a similar phrase was recorded. According to the Royal College of Dental Surgeons of Ontario’s Guidelines for Record Keeping, if the information was not recorded, then it never happened (RCDSO, 2008). Data, such as Chart ID, age, whether or not HM use was recorded, type of HM (if patient was taking HMs), adverse reactions, and potential drug interactions, were recorded into Microsoft Excel 2008. The potential drug interactions were identified by accessing Lexicomp Online: Interactions program on June 17, 2015. Drug fields
were filled out by listing all the herbal medications, prescription and non-prescription medications that a patient was taking. The program analyzed all the drugs with its database, and produced a result of drug interactions. The drug interactions were labeled as “no known interaction” (A), “no action needed” (B), “monitor therapy” (C), “consider therapy modification” (D), and “avoid combination” (X). The drug-drug combinations and type of interactions were recorded. The data were kept secured in an encrypted USB flash drive and backed up on a password-protected account on the Faculty of Dentistry’s server. The prevalence of herbal medication use by patients was calculated by taking the number of charts that have a recording of herbal medication divided by the total number of charts reviewed.
3 Results

3.1 Objective 1: Prevalence of HM use Among Adult Dental Patients

In total, 150 surveys were completed. Among those participants who agreed to participate, none withdrew from the study. Table 1 describes the characteristics of the survey respondents. The majority (60.7%) of the survey respondents were older than 60 years old. There was an almost even split between males and females (46.7% and 53.3% respectively). More than half (54.0%) of the participants were non-Hispanic white. The next two largest ethnic groups were Afro-Caribbean and South Asian (14.7% and 11.3% respectively).

Table 1: Demographic data displaying the number and percentage of adult dental patients who completed the herbal medication survey (N = 150)

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>4</td>
<td>2.7</td>
</tr>
<tr>
<td>25-29</td>
<td>3</td>
<td>2.0</td>
</tr>
<tr>
<td>30-34</td>
<td>6</td>
<td>4.0</td>
</tr>
<tr>
<td>35-39</td>
<td>5</td>
<td>3.3</td>
</tr>
<tr>
<td>40-44</td>
<td>7</td>
<td>4.7</td>
</tr>
<tr>
<td>45-49</td>
<td>10</td>
<td>6.7</td>
</tr>
<tr>
<td>50-54</td>
<td>13</td>
<td>8.7</td>
</tr>
<tr>
<td>55-59</td>
<td>11</td>
<td>7.3</td>
</tr>
<tr>
<td>60-64</td>
<td>22</td>
<td>14.7</td>
</tr>
<tr>
<td>65-69</td>
<td>24</td>
<td>16.0</td>
</tr>
<tr>
<td>70-74</td>
<td>25</td>
<td>16.7</td>
</tr>
<tr>
<td>75+</td>
<td>20</td>
<td>13.3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>150</td>
<td>100</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>70</td>
<td>46.7</td>
</tr>
<tr>
<td>Female</td>
<td>80</td>
<td>53.3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>150</td>
<td>100</td>
</tr>
<tr>
<td><strong>Ethnicity (self-reported)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African</td>
<td>6</td>
<td>4.0</td>
</tr>
<tr>
<td>Afro-Caribbean</td>
<td>22</td>
<td>14.7</td>
</tr>
<tr>
<td>East-Asian</td>
<td>7</td>
<td>4.7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>6</td>
<td>4.0</td>
</tr>
<tr>
<td>Middle-Eastern</td>
<td>8</td>
<td>5.3</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>81</td>
<td>54.0</td>
</tr>
<tr>
<td>South-Asian</td>
<td>17</td>
<td>11.3</td>
</tr>
<tr>
<td>Mixed</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>150</td>
<td>100</td>
</tr>
</tbody>
</table>
According to the survey responses, 65% of the participants reported using one or more HMs currently. Table 2 describes the most common HM, in terms of current or past use, was chamomile (52.6%). The next most common HMs were peppermint (46.0%), aloe vera (38.0%), Echinacea (35.3%), and ginger (34.0%). In terms of current use, the most common HM was chamomile (35.3%). The next most common HMs were peppermint (33.3%), ginger (26.7%), aloe vera (15.3%), and Echinacea (10.0%). Table 2 not only summarizes the prevalence of specific types of HMs, both as current or past use, but also their routes of administration. The most common ways that HMs are taken are either as pills or teas. The only remarkable topical route is the aloe vera.

Table 2: Current and previous use of herbal medications and their route of administration
(N = 150)

<table>
<thead>
<tr>
<th>Herbal Medication</th>
<th>% ‘Yes’</th>
<th>% Current</th>
<th>% Past</th>
<th>Route of Administration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Topical</td>
</tr>
<tr>
<td>Aloe Vera</td>
<td>38.0</td>
<td>15.3</td>
<td>22.7</td>
<td>32.7</td>
</tr>
<tr>
<td>Andrographis</td>
<td>0.7</td>
<td>0</td>
<td>0.7</td>
<td>0</td>
</tr>
<tr>
<td>Chamomile</td>
<td>52.6</td>
<td>35.3</td>
<td>17.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Clove Oil</td>
<td>4.7</td>
<td>4.7</td>
<td>0</td>
<td>4.0</td>
</tr>
<tr>
<td>Echinacea</td>
<td>35.3</td>
<td>10.0</td>
<td>25.3</td>
<td>0</td>
</tr>
<tr>
<td>English Ivy Leaf</td>
<td>0.7</td>
<td>0</td>
<td>0.7</td>
<td>0</td>
</tr>
<tr>
<td>Garlic</td>
<td>16.7</td>
<td>4.7</td>
<td>12.0</td>
<td>0</td>
</tr>
<tr>
<td>Ginger</td>
<td>34.0</td>
<td>26.7</td>
<td>7.3</td>
<td>0</td>
</tr>
<tr>
<td><em>Ginkgo biloba</em></td>
<td>18.7</td>
<td>4.7</td>
<td>14.0</td>
<td>0</td>
</tr>
<tr>
<td>Ginseng</td>
<td>28.0</td>
<td>7.3</td>
<td>20.7</td>
<td>0</td>
</tr>
<tr>
<td>Goldenseal</td>
<td>2.6</td>
<td>1.3</td>
<td>1.3</td>
<td>0</td>
</tr>
<tr>
<td>Gotu Kola</td>
<td>2.0</td>
<td>0.7</td>
<td>1.3</td>
<td>0</td>
</tr>
<tr>
<td>Kava-kava</td>
<td>3.4</td>
<td>0.7</td>
<td>2.7</td>
<td>0</td>
</tr>
<tr>
<td>Marijuana Oil</td>
<td>0.7</td>
<td>0.7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Melatonin</td>
<td>19.4</td>
<td>6.7</td>
<td>12.7</td>
<td>0</td>
</tr>
<tr>
<td>Peppermint</td>
<td>46.0</td>
<td>33.3</td>
<td>12.7</td>
<td>0</td>
</tr>
<tr>
<td>Primrose Oil</td>
<td>14.0</td>
<td>3.3</td>
<td>10.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Saw Palmetto</td>
<td>5.3</td>
<td>0</td>
<td>5.3</td>
<td>0</td>
</tr>
<tr>
<td>Soy</td>
<td>2.6</td>
<td>1.3</td>
<td>1.3</td>
<td>0</td>
</tr>
<tr>
<td>St. John’s Wort</td>
<td>12.0</td>
<td>0.7</td>
<td>11.3</td>
<td>0</td>
</tr>
<tr>
<td>Valerian</td>
<td>12.0</td>
<td>3.3</td>
<td>8.7</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>14.0</td>
<td>10.7</td>
<td>3.3</td>
<td>3.3</td>
</tr>
</tbody>
</table>
The source of the recommendation was also asked to the patients. The most common source was from the advice of a relative (30.0%) (Table 3). Nearly a quarter (24.0%) of the respondents said they took HMs on the advice from a friend, and 22.7% said they self-initiated the use of HMs. These responses were not mutually exclusive, and so an individual may have reported more than one source. When patients were asked about disclosure of HM use, only 10.0% of them reported disclosing their use to the clinician (Table 3). Looking specifically at how the information was disclosed, approximately half of the patients disclosed this information because the clinician asked, and the other half disclosed their use because the patient initiated the conversation. When patients were asked about their knowledge of HMs having potential drug interactions, approximately 80% knew that HMs could have potential drug interactions. However, when patients were asked regarding herbal medications impacting dental treatment, only 16% responded ‘yes’ (Table 3).

**Table 3: A summary of the source of recommendations, method of herbal medication use disclosure, and patients’ knowledge of drug interaction and dental impact of herbal medications (N = 150)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>Percent ‘Yes’</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendation</strong>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health-care Professional</td>
<td>19</td>
<td>12.7</td>
</tr>
<tr>
<td>Friend</td>
<td>36</td>
<td>24.0</td>
</tr>
<tr>
<td>Relative</td>
<td>45</td>
<td>30.0</td>
</tr>
<tr>
<td>Self</td>
<td>34</td>
<td>22.7</td>
</tr>
<tr>
<td>Advertisement</td>
<td>20</td>
<td>13.3</td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
<td>4.7</td>
</tr>
<tr>
<td><strong>Information Disclosure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>135</td>
<td>90.0</td>
</tr>
<tr>
<td>Yes, Provider Asked</td>
<td>8</td>
<td>5.3</td>
</tr>
<tr>
<td>Yes, Patient Provided</td>
<td>7</td>
<td>4.7</td>
</tr>
<tr>
<td><strong>Patients’ Knowledge</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1: Drug Interaction</td>
<td>119</td>
<td>79.3</td>
</tr>
<tr>
<td>Q2: Impact on Dental Treatment</td>
<td>24</td>
<td>16.0</td>
</tr>
</tbody>
</table>

*Percentages do not add up to 100 because responses were not mutually exclusive.

When patients were asked for reasons they were taking the HMs, the most common reason was to help them sleep (26.7%) (Table 4). The next most common reasons were digestive problems (23.3%), skin problems (18.7%), health and well-being (15.3%), and cold prevention (14.7%). Also, 6% of the patients used HM to help with tooth and gum pain.
Table 4: Dental patients’ reasons for taking herbal medications expressed as percentages
(N = 150)

<table>
<thead>
<tr>
<th>Reason*</th>
<th>Percent ‘Yes’</th>
</tr>
</thead>
<tbody>
<tr>
<td>To help sleep</td>
<td>26.7</td>
</tr>
<tr>
<td>Breathing problems</td>
<td>0.0</td>
</tr>
<tr>
<td>Asthma</td>
<td>1.3</td>
</tr>
<tr>
<td>To help with heart problems</td>
<td>4.7</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>3.3</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>2.0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.7</td>
</tr>
<tr>
<td>Anxiety</td>
<td>3.3</td>
</tr>
<tr>
<td>Depression</td>
<td>4.7</td>
</tr>
<tr>
<td>Joint problems or pain</td>
<td>10.0</td>
</tr>
<tr>
<td>To help skin problems</td>
<td>18.7</td>
</tr>
<tr>
<td>To help vision</td>
<td>0.7</td>
</tr>
<tr>
<td>To help memory</td>
<td>5.3</td>
</tr>
<tr>
<td>To help prevent cancer</td>
<td>2.7</td>
</tr>
<tr>
<td>For allergies</td>
<td>1.3</td>
</tr>
<tr>
<td>Digestive problems</td>
<td>23.3</td>
</tr>
<tr>
<td>To help live longer</td>
<td>4.0</td>
</tr>
<tr>
<td>To prevent cold</td>
<td>14.7</td>
</tr>
<tr>
<td>Relaxation</td>
<td>12.0</td>
</tr>
<tr>
<td>For health and well-being</td>
<td>15.3</td>
</tr>
<tr>
<td>Tooth or gum pain</td>
<td>6.0</td>
</tr>
</tbody>
</table>

*Percentages do not add up to 100 because responses were not mutually exclusive.

3.2 **Objective 2: Prevalence of Recording in Charts**

As mentioned in Materials and Methods, a total of 844 active were reviewed. Of these, only 64 charts (7.6%) contained written evidence of herbal medication use or denial (Table 5). For example, an herbal medication, such as *Ginkgo biloba*, was listed in the medication list of the medical history or a phrase, “patient not taking any herbal products” was written in the chart. The most common herbal medication was marijuana (37.5%). The next most common HMs were *Ginkgo biloba* (6.3%), evening primrose, garlic, and saw palmetto (4.7%) (Table 5). Seven patients who were taking herbal medications have a potential adverse herb-drug or herb-herb interaction. There were two categories of adverse reactions: bleeding issues and hypotensive risk. Herb-drug and herb-herb combinations responsible for bleeding issues were white willow-acetylsalicylic acid, evening primrose-celexa, evening primrose-acetylsalicylic acid, garlic-citalopram, ginger-licorice, white willow-arhrotec, and garlic-*Ginkgo biloba*. Herb-drug
combinations responsible for hypotensive risks were black cohosh-bisoprolol and black cohosh-valsartan.

**Table 5: Herbal medication use recorded in dental charts and their frequency**

<table>
<thead>
<tr>
<th>Herbal Medication</th>
<th>n/N</th>
<th>Percent Taking</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OVERALL</strong></td>
<td>64/844</td>
<td>7.6</td>
</tr>
<tr>
<td><strong>Out of those taking (n=64)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bella donna</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Echinacea</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Hydrastis</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Bryonia</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Chinese herb</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Digesta</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Evening primrose</td>
<td>3</td>
<td>4.7</td>
</tr>
<tr>
<td>Black cohosh</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Flaxseed</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Garlic</td>
<td>3</td>
<td>4.7</td>
</tr>
<tr>
<td>Ginkgo biloba</td>
<td>4</td>
<td>6.3</td>
</tr>
<tr>
<td>Lakota</td>
<td>2</td>
<td>3.1</td>
</tr>
<tr>
<td>Marijuana</td>
<td>24</td>
<td>37.5</td>
</tr>
<tr>
<td>Nettles</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Saw palmetto</td>
<td>3</td>
<td>4.7</td>
</tr>
<tr>
<td>St. John’s wort</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>None reported but evidence that it was asked</td>
<td>6</td>
<td>9.4</td>
</tr>
</tbody>
</table>

### 3.3 Statistical Analysis

We compared different demographic variables to see if there were any significant correlates among current users of HM. Chi-squared analysis was done to assess the correlates of sex, age, and ethnicity (Table 6). There was a significant correlation between males and females (p=0.021). In fact, females were twice as likely as males to currently take HMs (OR=2.23; 95% CI=1.12-4.43). There was no significant correlation among different age groups (p=0.294). There was significant correlation among the different ethnic groups (p=0.032), which means that among current users of HM, certain ethnic groups were more likely to take HMs versus other ethnic groups. Using non-Hispanic white as the reference ethnic group, the only statistically significant ethnic group was the Afro-Caribbean (p=0.003). They were approximately seven times more likely to take HMs than non-Hispanic whites (Table 7).
Table 6: Demographic correlates of current herbal medication use

<table>
<thead>
<tr>
<th>Correlate</th>
<th>n</th>
<th>% Yes (n)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>70</td>
<td>55.7 (39)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>80</td>
<td>73.8 (59)</td>
<td>0.021</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-39</td>
<td>18</td>
<td>72.2 (13)</td>
<td></td>
</tr>
<tr>
<td>40-59</td>
<td>41</td>
<td>73.2 (30)</td>
<td></td>
</tr>
<tr>
<td>60+</td>
<td>91</td>
<td>60.4 (55)</td>
<td>0.294</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African</td>
<td>6</td>
<td>50.0 (3)</td>
<td></td>
</tr>
<tr>
<td>Afro-Caribbean</td>
<td>22</td>
<td>90.9 (20)</td>
<td></td>
</tr>
<tr>
<td>East-Asian</td>
<td>7</td>
<td>42.9 (3)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>6</td>
<td>66.7 (4)</td>
<td></td>
</tr>
<tr>
<td>Middle-Eastern</td>
<td>8</td>
<td>87.5 (7)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>81</td>
<td>56.8 (46)</td>
<td></td>
</tr>
<tr>
<td>South Asian</td>
<td>17</td>
<td>76.5 (13)</td>
<td>0.032</td>
</tr>
</tbody>
</table>

* Chi-squared test

Table 7: Odds ratios of different ethnic groups taking HMs

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Taking HM % (n)</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic White</td>
<td>56.8% (46)</td>
<td>1.00 (ref)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>African</td>
<td>50.0% (3)</td>
<td>1.31</td>
<td>0.25-6.91</td>
<td>1.000*</td>
</tr>
<tr>
<td>Afro-Caribbean</td>
<td>90.9% (20)</td>
<td>7.61</td>
<td>1.67-34.74</td>
<td>0.003**</td>
</tr>
<tr>
<td>East-Asian</td>
<td>42.9% (3)</td>
<td>1.75</td>
<td>0.37-8.34</td>
<td>0.695*</td>
</tr>
<tr>
<td>Hispanic</td>
<td>66.7% (4)</td>
<td>1.52</td>
<td>0.26-8.79</td>
<td>1.000*</td>
</tr>
<tr>
<td>Middle-Eastern</td>
<td>87.5% (7)</td>
<td>5.33</td>
<td>0.63-45.31</td>
<td>0.136*</td>
</tr>
<tr>
<td>South-Asian</td>
<td>76.5% (13)</td>
<td>2.47</td>
<td>0.74-8.24</td>
<td>0.132**</td>
</tr>
</tbody>
</table>

* Fisher’s Exact Test
** Pearson Chi-Square

There was no correlation among patients who use HM and those who do not and the method of disclosure (p=0.782). In other words, if a patient was taking HMs, he or she was not more likely to disclose this information to the clinician or the clinician asking the patient (Table 8). Seventy-nine percent of the survey respondents said that they knew that HMs could potentially interfere with prescription medications. However, there was no correlation among patients who use HM and those who do not and their knowledge that herbal medications may potentially interfere with other prescription medications (p=0.340). This means that patients who use HMs are not more likely to know that HMs could potentially interfere with prescription medications than patients who do not take HMs (Table 9). Only 16% of the survey respondents reported that they knew
that HMs could potentially impact how dental care is provided. However, there was no
correlation among patients who use HM and those who do not and their knowledge that herbal
medications may potentially impact how dental care is provided (p=0.432). This means that
patients who use HMs are not more likely to know that HMs could potentially impact dental
treatment than patients who do not take HMs (Table 10).

Table 8: Herbal medication use and type of disclosure (either not disclosed, ‘yes’ the dental
provider asked the patient about herbal medication, or ‘yes’ the patient gave information
to the dental provider)

<table>
<thead>
<tr>
<th>Herbal Medication Use</th>
<th>% ‘No’ (n)</th>
<th>% ‘Yes’, Asked (n)</th>
<th>% ‘Yes’, Gave (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>92.3 (48)</td>
<td>3.8 (2)</td>
<td>3.8 (2)</td>
</tr>
<tr>
<td>Yes</td>
<td>88.8 (87)</td>
<td>6.1 (6)</td>
<td>5.1 (5)</td>
</tr>
<tr>
<td>Total</td>
<td>90.0 (135)</td>
<td>5.3 (8)</td>
<td>4.7 (7)</td>
</tr>
<tr>
<td>P-value*</td>
<td></td>
<td>0.782</td>
<td></td>
</tr>
</tbody>
</table>

* Chi-squared test

Table 9: Herbal medication use and the patients’ knowledge of herbal medications
potentially interfering with other prescription medications

<table>
<thead>
<tr>
<th>Herbal Medication Use</th>
<th>% ‘No’ (n)</th>
<th>% ‘Yes’ (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>25.0 (13)</td>
<td>75.0 (39)</td>
</tr>
<tr>
<td>Yes</td>
<td>18.4 (18)</td>
<td>81.6 (80)</td>
</tr>
<tr>
<td>Total</td>
<td>20.7 (31)</td>
<td>79.3 (119)</td>
</tr>
<tr>
<td>P-value*</td>
<td></td>
<td>0.340</td>
</tr>
</tbody>
</table>

* Chi-squared test

Table 10: Herbal medication use and the patients’ knowledge of herbal medications
potentially impacting how dental care is provided

<table>
<thead>
<tr>
<th>Herbal Medication Use</th>
<th>% ‘No’ (n)</th>
<th>% ‘Yes’ (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>80.8 (42)</td>
<td>19.2 (10)</td>
</tr>
<tr>
<td>Yes</td>
<td>85.7 (84)</td>
<td>14.3 (14)</td>
</tr>
<tr>
<td>Total</td>
<td>84.0 (126)</td>
<td>16.0 (24)</td>
</tr>
<tr>
<td>P-value*</td>
<td></td>
<td>0.432</td>
</tr>
</tbody>
</table>

* Chi-squared test

Based on ethnicity, the most popular HMs currently used are: ginger (African and South-Asian),
peppermint (Afro-Caribbean and Middle-Eastern), ginseng (East-Asian), and chamomile
(Hispanic and Non-Hispanic White) (Table 11). The most popular HMs overall are: ginger (African), peppermint (Afro-Caribbean, Middle-Eastern, and South-Asian), ginseng (East-Asian), and chamomile (Hispanic and Non-Hispanic White) (Table 12).

**Table 11: The current top three most common herbal medications used based on ethnic group**

<table>
<thead>
<tr>
<th>Ethnic Group</th>
<th>n</th>
<th>Most Common % (n)</th>
<th>2\textsuperscript{nd} Most Common % (n)</th>
<th>3\textsuperscript{rd} Most Common % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>African</td>
<td>3</td>
<td>Ginger 100 (3)</td>
<td>Chamomile 33 (1)</td>
<td>Peppermint 33 (1)</td>
</tr>
<tr>
<td>Afro-Caribbean</td>
<td>20</td>
<td>Peppermint 90 (18)</td>
<td>Ginger 60 (12)</td>
<td>Chamomile 55 (11)</td>
</tr>
<tr>
<td>East-Asian</td>
<td>3</td>
<td>Ginseng 66 (2)</td>
<td>Peppermint 66 (2)</td>
<td>Chamomile 66 (2)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>4</td>
<td>Chamomile 75 (3)</td>
<td>Peppermint 75 (3)</td>
<td>Aloe Vera, Echinacea, Ginger, \textit{Ginkgo biloba}, Soy, Valerian 25 (1)</td>
</tr>
<tr>
<td>Middle-Eastern</td>
<td>7</td>
<td>Peppermint 57 (4)</td>
<td>Ginger 57 (4)</td>
<td>Aloe Vera 57 (4)</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>46</td>
<td>Chamomile 67 (31)</td>
<td>Peppermint 39 (18)</td>
<td>Ginger 28 (13)</td>
</tr>
<tr>
<td>South-Asian</td>
<td>13</td>
<td>Ginger 31 (4)</td>
<td>Peppermint 23 (3)</td>
<td>Chamomile, Garlic, \textit{Ginkgo biloba}, Melatonin 15 (2)</td>
</tr>
</tbody>
</table>

**Table 12: The overall top three most common herbal medications used based on ethnic group**

<table>
<thead>
<tr>
<th>Ethnic Group</th>
<th>n</th>
<th>Most Common % (n)</th>
<th>2\textsuperscript{nd} Most Common % (n)</th>
<th>3\textsuperscript{rd} Most Common % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>African</td>
<td>3</td>
<td>Ginger 100 (3)</td>
<td>Chamomile 33 (1)</td>
<td>Peppermint, Melatonin, \textit{Ginkgo biloba} 33 (1)</td>
</tr>
<tr>
<td>Afro-Caribbean</td>
<td>20</td>
<td>Peppermint 90 (18)</td>
<td>Ginger 70 (14)</td>
<td>Chamomile 70 (14)</td>
</tr>
<tr>
<td>East-Asian</td>
<td>3</td>
<td>Ginseng 100 (3)</td>
<td>Peppermint 66 (2)</td>
<td>Ginger, Aloe Vera, Echinacea 66 (2)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>4</td>
<td>Chamomile 100 (4)</td>
<td>Peppermint 75 (3)</td>
<td>Echinacea, Ginger 50 (2)</td>
</tr>
<tr>
<td>Middle-Eastern</td>
<td>7</td>
<td>Peppermint 86 (6)</td>
<td>Ginseng 86 (6)</td>
<td>Aloe Vera, Chamomile, Ginger 71 (5)</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>46</td>
<td>Chamomile 83 (38)</td>
<td>Aloe Vera 70 (32)</td>
<td>Echinacea 63 (29)</td>
</tr>
<tr>
<td>South-Asian</td>
<td>13</td>
<td>Peppermint 46 (6)</td>
<td>Ginger 31 (4)</td>
<td>Chamomile, Echinacea, Melatonin 23 (3)</td>
</tr>
</tbody>
</table>
Finally, when comparing the prevalence of HM use among dental patients to the prevalence of recording its use in the dental charts, there was a statistically significant difference between the prevalence of those two groups (p<0.0001). This means that we can reject the null hypothesis and report that the difference in the prevalence of HM uses among dental patients (65%) and the prevalence of recording its use in the dental charts (8%) is highly significant.
4 **Discussion**

4.1 **General Discussion**

In our study, 65% of the respondents currently use herbal medicines. This prevalence is higher than other previously reported in the literature. The reason may be due to the method of collecting the data. Previous studies used a written survey, which was distributed to patients. The surveys asked patients if they take herbal medications, and if so, to check them off a list. The participants were left alone to answer the questions. This method unfortunately requires participants to recall from memory, and there may be recall bias. In our study, the surveyor sat with the individual participants and went through the survey together with the participant in the form of a guided interview. This allows for the participants to ask questions for clarification. For example, a patient may ask about aloe vera, and the surveyor can describe the plant and explain the different routes of administration. This may help to improve the memory of the participant.

Also, the surveys from other studies listed only one name for the herbal medication. Herbal medications transcend cultural boundaries, and the same HM may have multiple names depending on the locale or culture. For example, St. John’s wort has different names around the world. It can be called Tipton’s weed, Rosin rose, Goatweed, Chase-devil, or Klamath weed. Our survey had multiple names, when appropriate, for each HM. This method allows the participant to recognize HMs more readily and may help avoid missing potential positive responses.

Among the patients who use HM, there was a significant correlation between genders. Females were more likely than males to take HMs. This result is consistent with previous literature. In fact, our results show that women were twice as likely than males to take HMs. With respect to age groups, there was no significant correlation. A reason for this may be due to easier access to HMs. Previously, HMs were expensive and only available at specialty health stores; however, with recent surge of advertising campaign by the natural product industry and wellness shows in the media, HMs are commonplace. People from any age group are able to obtain and take HMs. Looking at ethnicity, there was a significant correlation between different ethnic groups. Certain ethnic groups were more likely to take HMs than others. For example, although non-Hispanic whites had the highest overall absolute number of people taking HMs (46 people), they only represented just over half the group’s total (56.8%); whereas, only 7 people from the Middle-
East took HMs, but they represented 87.5% of the group’s total (Table 6). Although we did not explore the role of ethnicity in detail, this study demonstrated that ethnicity is an important factor in HM usage.

Relatives were the most common source of advice (30.0%) for herbal recommendation. Friends were also another common source of recommendation (24%). It seems that most people who take HMs do so on the advice of another person whom they trust. This reason may be due to the fact that HMs are not regulated like prescription medications; therefore, safety and efficacy are assessed by anecdotal evidence. In fact, there are not many good double-blind, controlled studies on HMs, and so most HMs are taken based on the advice of someone they trust, such as a friend or family member. On the contrary, only 13% of the patients took HMs on the advice of a health-care professional. Unfortunately, this survey did not specify which type of health-care professional, and so it is not possible to determine if they were medical doctors, naturopathic doctors or homeopathic doctors. It would have been interesting to see which types of health-care professionals recommend the use of HMs.

According to our data, only 10% of the patients disclosed whether or not they use HMs to their dental provider. Approximately half of them disclosed this information because the dental provider asked them specifically about HMs and the other half of the patients initiated the conversation regarding their use of HMs. Yet, according to our survey, 65% of the patients are currently taking HMs; however, in the case of only 5.3% of patients, the dental providers asked their patients if they are taking HMs. This situation is unfortunate because some HMs have pharmacological effects on our bodies, such as increased risk of bleeding, or adverse drug interactions, such as inducing or inhibiting cytochrome P450 enzymes. Therefore, it is prudent to ask all the patients about HM use, and not just on prescription and over-the-counter medications.

There was no correlation among patients who use HM and those who do not and their disclosure (p=0.782). In other words, if a patient was taking HMs, he or she was not more likely to disclose this information to the clinician or the clinician asking the patient. It seems likely that patients who take HMs do not see the need to tell their dental provider that they are taking HMs. This observation is consistent with previous studies. As discussed earlier, there are several reasons that patients do not tell their health-care provider. First, patients think HMs are natural, and thus
perceive them as lacking any harm. Second, patient fear a negative reaction from their physician or dentist. Third, patients do not see the relevance of reporting HM to their health-care provider.

When we assessed patients’ knowledge about HMs, 79.3% of them knew that some HMs could have potential drug interactions; however, it was interesting to note that only 16% of the patients knew that some HMs could have an impact on dental treatment. However, there was no correlation among patients who use HM and those who do not and their knowledge that herbal medications may potentially interfere with other prescription medications (p=0.340). This means that patients who use HMs are not more likely to know that HMs could potentially interfere with prescription medications than patients who do not take HMs. Also, there was no correlation among patients who use HM and those who do not and their knowledge that herbal medications may potentially impact how dental care is provided (p=0.432). In other words, patients who use HMs are not more likely to know that HMs could potentially impact dental treatment than patients who do not take HMs. Basically, patients who take HMs are not more knowledgeable than those who do not take HMs when it pertains to potential adverse interactions and impacting dental treatment.

When patients were asked for reasons they were taking the HMs, the most common reason was to help them sleep (26.7%). The next most common reasons were digestive problems (23.3%), skin problems (18.7%), health and well-being (15.3%), and cold prevention (14.7%). It seems that HMs are used to help with either minor, general health issues, such as help with sleep or digestive problems, or overall health, such as well-being or cold prevention. HMs are rarely taken to “treat” a specific illness, such as diabetes (0.7%), asthma (1.3%), or hypertension (3.3%). Also, 6% of the patients used HM to help with tooth and gum pain. The HM in particular that was used to help with tooth and gum pain was clove. Interestingly, one bioactive chemical compound found in clove is eugenol, which is evidently used in dentistry as a mild topical analgesic (Civjan 1964).

According to our chart review, only 7.6% (64 out of 844 charts) of them had any evidence that HM use was recorded. Again, our survey revealed that 65% of the dental patients are currently taking HMs. This large discrepancy is disturbing. On closer examination of the charts, seven patients who were taking herbal medications have a potential adverse herb-drug or herb-herb interaction. For example, garlic and Ginkgo biloba combination may lead to increased risk of
bleeding. Since garlic inhibits platelet activity by inhibiting the production or release of platelet activating factor, and *Ginkgo biloba* is a platelet activating factor antagonist, then the interaction of the two herbs may severely inhibit the function of platelets during hemostasis. This point is crucial because if a patient is taking this combination and undergoing dental surgery, such as a tooth extraction, then peri-operative and post-operative bleeding complications may arise. It would be prudent for both the dentist and the patient to be aware of this potential complication so that both parties know what to expect and to handle the bleeding complication if it occurs. Another example, black cohosh and bisoprolol combination may lead to a hypotensive episode. Since black cohosh may cause vasodilatation, this may decrease blood pressure because there is decreased resistance in the blood vessels. Bisoprolol is a beta-blocker, more specifically it is a beta-1 antagonist. Beta-1 receptors are found on cardiac muscle cells. When these receptors are stimulated by an agonist, such as epinephrine, it increases the heart rate and force of contraction of the heart. However, if the beta-1 receptors bind with a beta-1 antagonist, such as bisoprolol, it does not stimulate the receptor, but instead it blocks the receptor from binding with an agonist. This antagonist decreases both heart rate and strength of cardiac muscle contraction; therefore, this drug is used as an anti-hypertensive. The interaction of the two compounds may result in a hypotensive episode. This example is important because if a patient is taking this combination, then he or she may experience lightheadedness or dizziness and may have an episode of syncope. These two examples highlight the importance of asking the patient if they are taking herbal medications and if so, which ones. Furthermore, the dentist should identify any precautions required with the HMs.

Of the 64 charts that had evidence of HM use recorded, 24 (37.5%) of them had recorded marijuana use. This represents 2.8% of the total sample that uses marijuana. However, in our survey, only one person (0.7%) admitted to using marijuana oil. This difference is interesting because one would expect more than one person in our survey to report using marijuana. Perhaps response bias may play a role. Due to the informal nature of our survey, patients may be reluctant to admit the use of marijuana for fear of a negative reaction from the surveyor. However, in a more formal medical and dental history taking, the patient may be more inclined to admit the use because the dental chart is confidential.
4.2 **Limitations**

There are some limitations to our study. First, it is a cross-sectional study that looked at HM use among patients at a single point in time. Perhaps a longitudinal study would have been better because we would have been able to assess HM use across a longer period of time. For example, some people use Echinacea to prevent the common cold, and perhaps its use might be increased near the winter months. Also, some people use aloe vera to treat sunburn on the skin, and its use might be increased during the summer months.

Second, our study surveyed dental patients at the Faculty of Dentistry at the University of Toronto. This sample is not completely representative of the general population; therefore, our results are not generalizable. Most patients at the dental school are older and on fixed income, and so this sample may systematically bias the survey responses.

Another limitation of our study was the use of surveys to collect data on herbal medication use. Surveys are susceptible to recall bias because they are relying on the participant’s memory. For example, they may not remember all the HM they took or they may confuse one HM for another. Response bias is another problem with surveys because respondents may want to answer the survey questions in a positive way. For example, participants may not want to reveal use of certain HMs for fear of a negative reaction, such as marijuana.

A limitation of the chart review is that there may be insufficient documentation. Although it is a standard of practice to record all pertinent details in the chart, maybe the clinician did ask about herbal medication use but neglected to record the information in the chart. This lack of recording may under-estimate the actual prevalence of recording in the chart. However, it is important to mention that according to the Royal College of Dental Surgeons of Ontario, record keeping is important for medico-legal purposes (RCDSO 2008). If there is no record in the chart, then the procedure or discussion never happened.

4.3 **Future Direction**

Since this research is a pilot study about HM use in dental patients, there are several areas of future research. One area is to conduct a multi-centre survey at different dental faculties across Canada. This may provide a more in-depth picture of HM use across Canada. Also, since there is
limited information on HM use among children, it would be interesting to survey this population group. However, care must taken when surveying this age group because some parents may be hesitant to enroll their children for fear of potential reporting to a children’s aid society. Another area of interest is to compare the prevalence of recording of HM use among the different dental specialties. For example, we can speculate that dental anaesthesiologists may have a higher prevalence of recording because they may take a more detailed medical history. In addition, since this study showed such a low prevalence of recording HM use in patient’s charts, then it would be interesting to research dental school curricula on herbal medications. Sending out surveys to dental school deans across Canada and asking them questions, such as how many lecture hours are devoted to HM, can achieve this. Another area of further study is in educational research. Since dental students are under the guidance of clinical demonstrators, it is important to assess the demonstrators’ knowledge and attitudes towards HM. Even though a student has been taught about HMs, if that knowledge is not reinforced by the clinical demonstrator, then the student may also perceive that HMs are not relevant.

4.4 Conclusion

The results of this pilot study demonstrated a high prevalence of HM use among dental school patients (65%). Also, there was a low prevalence of HM documentation in patient’s charts (7.6%).
5 **References**


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Oppermann UC, Maser E. Molecular and structural aspects of xenobiotic carbonyl metabolizing enzymes: role of reductases and dehydrogenases in xenobiotic phase I reactions. Toxicology. 2000;144:71-81.


Appendix A

Participant Consent Form

**Title of Research Project:** Herbal Medicine use in Adult Patients at the Faculty of Dentistry

**Investigator(s):**

1. **Principal investigator**  
   Dr. Edward Yoon DDS  
   M.Sc. candidate  
   Faculty of Dentistry, University of Toronto  
   124 Edward Street  
   Toronto, ON M5G 1G6  
   647-704-6764

2. **Faculty Supervisor**  
   Dr. Jose Lança MD, PhD  
   Assistant Professor  
   Department of Pharmacology  
   Faculty of Dentistry, University of Toronto  
   124 Edward Street  
   Toronto, ON M5G 1G6  
   416-979-4900 Ext4609

**Purpose of the Research:**  
The purpose of this research is to determine how frequently dental patients at the dental school take herbal medication.

**Time Commitment:**  
Approximately 5-10 minutes

**Description of the Research:**

Subject Population: Persons who are 18 years old or older and are active patients at the Faculty of Dentistry, University of Toronto.

Background: The Faculty of Dentistry at the University of Toronto is interested in making your dental visit safe and comfortable. Part of the safety factor is knowing what kinds of medications that you are on. While many people do not consider herbal and non-prescription remedies to be medications, they sometimes affect the drugs that we use in dental treatment. The study aims to determine what percentage
of the adult patients at the dental school take herbal medications and important characteristics about their use. By taking this survey, you can help us answer these questions.

Inclusion Criteria: You are an active patient at the Faculty of Dentistry, University of Toronto. You have to be at least 18 years of age or over. You must be knowledgeable of a basic level of the English language.

Exclusion Criteria: You are not an active patient at the Faculty of Dentistry, University of Toronto. You are under the age of 18 years. You do not possess a basic level of the English language.

Location: The study will be conducted at the Faculty of Dentistry, University of Toronto. The survey will be conducted in the clinic areas.

Participation: Participation in this research project is voluntary and you may refuse to participate or withdraw from the study at any time. You may withdraw even after you have handed in your survey. If you choose to withdraw, your data will be removed from the database and will not be used in this study. If you choose to withdraw after completing the survey, you may contact the principle investigator requesting that your survey be withdrawn. However, once the thesis is completed, you may not withdraw from the study because the statistical analysis has been completed. You may also decline to answer any question or participate in any part of the study without any consequences. It will not affect your treatment or access to care. Finally, it is important to note that this data is being collected for the purposes of research only, and will not be part of your clinical record.

Potential Risk, Harm, Injuries, Discomforts or Inconvenience: You may feel embarrassed about revealing your use of herbal medications, but all of the information is confidential and will not affect your overall treatment. However, if a potential adverse drug interaction is identified, then you will be advised of this interaction and recommend that you disclose this information to your dental provider.

Potential Benefits: Although there is no direct benefit, results of this study will add new information to this area of research, and may potentially benefit future patients in dental care.

Confidentiality: Your identity is kept confidential and your data are made anonymous with a study-specific ID number. Your identity will be known only to the principal investigator. All the data will be stored on a password protected computer and encrypted. The paper survey will be kept in a locked box, and only the principal investigator will have access to it. 3 years after the completion of the research, all of the data will be erased and the paper surveys will be shredded. This research may be published or presented in the future.

Contact
If you have any questions about this study, please contact:
Dr. Edward Yoon
M.Sc. candidate
Faculty of Dentistry, University of Toronto
124 Edward Street
Toronto, ON M5G 1G6
ed.yoon@mail.utoronto.ca
647-704-6764

If you have any complaints or concerns about how you have been treated as a research participant or if you have questions about your right as a participant, please contact:
Office of Research Ethics at: ethics.review@utoronto.ca or 416-946-3273
You will receive a debriefing form at the end of the survey.

By signing this form, I agree that:
The study has been explained to me. All questions were answered or concerns were addressed. Possible risks or benefits of this study have been explained to me. I understand that my participation is voluntary and that I have the right to not participate or to withdraw at any time. I have a choice to decline to answer any questions. I can ask questions about the study now or at any time in the future. I have been informed that my personal information will be kept confidential. I will receive a signed copy of this consent form. I understand that no information that could identify me will be released or printed without asking my consent first.

Participant:

Name: ______________________________
E-mail address: ______________________________

_________________________________________  ________________
Signature                                  Date

Person who obtained the consent:

Name: ______________________________
E-mail address: ______________________________

_________________________________________  ________________
Signature                                  Date
Appendix B

The Faculty of Dentistry at the University of Toronto is interested in making your dental visit safe and comfortable. Part of the safety factor is knowing what kinds of medications that you are on. While many people do not consider herbal and non-prescription remedies to be medications, they sometimes affect the drugs that we use in dental treatment. Please fill out the following questionnaire. This will only take 5-10 minutes of your time. This survey is anonymous and no identifying information will be recorded. Thank you for your help.

1) Have you taken any of the following herbal remedies (please check)?

a) Aloe (*Aloe vera*)
   - Are you taking it or did you take it?
     ( ) Now ( ) In the past
   - How do you take it?
     ( ) Topical ( ) Pill/Extract ( ) Tea ( ) Other 

b) Andrographis (Chuan Xin Lin, False Waterwillows, Periyanagai, Maha-tita, Kalmegh, Kalamegha)
   - Are you taking it or did you take it?
     ( ) Now ( ) In the past
   - How do you take it?
     ( ) Topical ( ) Pill/Extract ( ) Tea ( ) Other 

c) Chamomile
   - Are you taking it or did you take it?
     ( ) Now ( ) In the past
   - How do you take it?
     ( ) Topical ( ) Pill/Extract ( ) Tea ( ) Other 

d) Echinacea
   - Are you taking it or did you take it?
     ( ) Now ( ) In the past
   - How do you take it?
     ( ) Topical ( ) Pill/Extract ( ) Tea ( ) Other 

e) English Ivy Leaf (European ivy, Common ivy)
   - Are you taking it or did you take it?
     ( ) Now ( ) In the past
   - How do you take it?
     ( ) Topical ( ) Pill/Extract ( ) Tea ( ) Other 

f) Garlic
   - Are you taking it or did you take it?
     ( ) Now ( ) In the past
   - How do you take it?
     ( ) Topical ( ) Pill/Extract ( ) Tea ( ) Other 

g) Ginger (Ginger root)
   - Are you taking it or did you take it?
     ( ) Now ( ) In the past
   - How do you take it?
     ( ) Topical ( ) Pill/Extract ( ) Tea ( ) Other 

h) Ginko biloba (Maidenhair tree)
   • Are you taking it or did you take it?
     ( ) Now ( ) In the past
   • How do you take it?
     ( ) Topical ( ) Pill/Extract
     ( ) Tea ( ) Other ____________.

i) Ginseng
   • Are you taking it or did you take it?
     ( ) Now ( ) In the past
   • How do you take it?
     ( ) Topical ( ) Pill/Extract
     ( ) Tea ( ) Other ____________.

j) Goldenseal (Orangered, Yellow puccoon)
   • Are you taking it or did you take it?
     ( ) Now ( ) In the past
   • How do you take it?
     ( ) Topical ( ) Pill/Extract
     ( ) Tea ( ) Other ____________.

k) Gotu kola (Centella, Asiatic Pennywort, Indian Pennywort)
   • Are you taking it or did you take it?
     ( ) Now ( ) In the past
   • How do you take it?
     ( ) Topical ( ) Pill/Extract
     ( ) Tea ( ) Other ____________.

l) Kava-kava (Kava, Awa, Ava, Yaqona, Sakau)
   • Are you taking it or did you take it?
     ( ) Now ( ) In the past
   • How do you take it?
     ( ) Topical ( ) Pill/Extract
     ( ) Tea ( ) Other ____________.

m) Melatonin
   • Are you taking it or did you take it?
     ( ) Now ( ) In the past
   • How do you take it?
     ( ) Topical ( ) Pill/Extract
     ( ) Tea ( ) Other ____________.

n) Peppermint
   • Are you taking it or did you take it?
     ( ) Now ( ) In the past
   • How do you take it?
     ( ) Topical ( ) Pill/Extract
     ( ) Tea ( ) Other ____________.

o) Primrose oil (Evening primrose, Suncups, Sundrops)
   • Are you taking it or did you take it?
     ( ) Now ( ) In the past
   • How do you take it?
     ( ) Topical ( ) Pill/Extract
     ( ) Tea ( ) Other ____________.
p) Saw Palmetto
- Are you taking it or did you take it?
  ( ) Now ( ) In the past
- How do you take it?
  ( ) Topical ( ) Pill/Extract
  ( ) Tea ( ) Other ____________.

d) Soy (Golden bean, Yellow bean)
- Are you taking it or did you take it?
  ( ) Now ( ) In the past
- How do you take it?
  ( ) Topical ( ) Pill/Extract
  ( ) Tea ( ) Other ____________.

r) St. John’s Wort (Tipton’s weed, Rosin rose, Goatweed, Chase-devil, Klamath weed)
- Are you taking it or did you take it?
  ( ) Now ( ) In the past
- How do you take it?
  ( ) Topical ( ) Pill/Extract
  ( ) Tea ( ) Other ____________.

s) Valerian (Garden valerian, Garden heliotrope, All-heal)
- Are you taking it or did you take it?
  ( ) Now ( ) In the past
- How do you take it?
  ( ) Topical ( ) Pill/Extract
  ( ) Tea ( ) Other ____________.

t) Other: ________________
- Are you taking it or did you take it?
  ( ) Now ( ) In the past
- How do you take it?
  ( ) Topical ( ) Pill/Extract
  ( ) Tea ( ) Other ____________.

2) Who recommended you to take this (these) herbal medication(s) (please check)?
  ( ) Health-care professional (physician, dentist, naturopathic doctor)
  ( ) Friend
  ( ) Relative (parent, sibling)
  ( ) Self
  ( ) Advertisement (newspaper, magazine, television)
  ( ) Other: ________________.

3) Were you asked about herbal medication use at the new patient examination or regular check up (please check):
  ( ) Yes, I gave information about my herbal medication use to my dental provider
  ( ) Yes, my provider asked me about these herbal remedies
  ( ) No, I did not tell my dental provider and/or was never asked about these herbal remedies
4) Why do you take your herbal medications (please check all that apply)?

( ) To help me sleep
( ) Breathing problems
( ) Asthma
( ) To help my heart
( ) High blood pressure
( ) High cholesterol
( ) Diabetes
( ) Anxiety
( ) Depression
( ) Other: _____________________________

5) Did you know that herbal medications could potentially interfere with other prescription medications?

( ) Yes    ( ) No

6) Did you know that herbal medications could potentially impact how your dental care is delivered?

( ) Yes    ( ) No

7) Age (please check the appropriate age-range):

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8) Sex (please check):

( ) Male    ( ) Female

9) How would you describe your ethnic background (please check)?

( ) Non-Hispanic White
( ) Afro-Caribbean or African American
( ) Hispanic
( ) East-Asian
( ) South-Asian
( ) Middle-Eastern
( ) Native Canadian
( ) Other: _____________________________

Thank you.
Appendix C

Debriefing Information Sheet

Title: Herbal Medicine use of Adult Dental School Patients at the University of Toronto

Researchers: Dr. Edward Yoon (M.Sc. candidate), Dr. Jose Lança M.D. Ph.D., Dr. Herenia Lawrence D.D.S. Ph.D., Dr. Carlos Quiñonez D.M.D. Ph.D.

Overview:
Complementary and alternative medicine (CAM) is a group of diverse medical and health care systems, therapies, and products that are not considered to be part of conventional medicine. Herbal medicines are a type of CAM. Approximately 10% of Canadians in 2006 used an herbal medication in the past 12 months, and 15% of Canadians reported using herbal medication at some point in their lives. Looking at herbal medicine use among dental patients in private offices, a study in Thunder Bay, Ontario showed that 38% of dental patients had used herbal medications. Similarly, 27% of dental patients at a dental school in the United States had used herbal medications at some point in their life. Our research is aimed at finding out what percentage of dental patients at the Faculty of Dentistry, University of Toronto use herbal medication.

Objective:
Our objective is to determine what percentage of adult dental patients at the Faculty of Dentistry, University of Toronto have taken or are taking herbal medication. In addition, we would like to describe the characteristics of people who take herbal medication. This information may help us to provide a more optimal care for patients.

Thank you very much for your participation in our study.

If you would like a summary of the results, please contact the primary researcher.

Primary Researcher Contact Information:

Dr. Edward Yoon
E-mail: ed.yoon@mail.utoronto.ca
Tel: 647-704-6764

For more information:

Lanca, AJ. Herbal Medications: an evidence based review. CME Resource; July 2013: 1-52