

Chapter 2

Food and Nutraceutical Applications of Chinese Herbal Products

Priya Kathirvel, Phillip Joy and Bohdan L. Luhovyy

2.1 Introduction

Traditional Chinese medicine (TCM) is undergoing rapid growth and development in China and worldwide. Risks and benefits associated with Chinese herbal products, that are consumed as functional foods or nutraceuticals, requires further understanding before entering new markets including Canada. A recent market report indicates that China exports 240,000 tonnes of Chinese medicine annually, of which 200,000 tonnes are raw herbs that accounts for 20 % of the country's annual harvest [1]. The growth in demand of Chinese herbs can be attributed to the rise in use of complementary and alternative medicine in the U.S., which has increased from 36 % of population in 2002 to 38.3 % in 2007 [2]. Nutritional Business Journal's Supplement Report for 2012 shows that herbs (botanicals) represented 17 % of dietary supplement sales in 2011 and the industry grew by 7 % in the U.S in the same time period [3]. While many Chinese herbal remedies have been used for more than 5000 years [4], their efficacy and safety needs to be evaluated using evidence-based approaches including double-blinded randomized clinical trials and toxicological studies. Another important issue is the lack of uniform regulations for herbal remedies (other terms are *herbal supplements*, *herbal substances*, *botanicals*, and others) which vary significantly between jurisdictions [5].

P. Kathirvel · P. Joy · B.L. Luhovyy (✉)
Department of Applied Human Nutrition, Mount Saint Vincent University,
Halifax, NS, Canada
e-mail: bohdan.luhovyy@msvu.ca

2.2 Regulation of Dietary Use of Herbal Remedies in Canada, USA and European Union

2.2.1 Natural Health Product Regulation in Canada

In Canada, herbal remedies and traditional Chinese medicine products (TCM) are regulated as Natural Health Products (NHP). In 2013, NHP market includes more than 50,000 products authorized for sale by Health Canada [6] including 2000 TCM [7]. According to Ipsos Reid 2010 report, 73 % of Canadians regularly take natural health products. While vitamin, minerals and essential fatty acids represent the most widely consumed NHP (71 %), herbal products are typically used as a tea (11 %), herbal remedies (10 %) and Echinacea (7 %) [8]. There is no distinction between dietary and non-dietary (i.e. medicinal) herbs in Canadian Regulations even though the earlier version of NHP regulation was intended to distinguish between dietary and medicinal herbs [9]. The consumption pattern of NHP in Canada and other countries does not account for the ethnic and cultural specifics which influence the choice and type of NHP consumed. The study conducted with Canadians of Chinese and white backgrounds revealed that the responders of Chinese descent were more inclined to use herbal medicine compared to their white counterparts. Furthermore, their motivation to use herbal products was different. Thus, for Chinese responders the main factor to choose herbal medicine was the presence of chronic disease while for white responders it was perceived higher safety of herbal products compared to pharmaceuticals [10]. This indicates the substantial gaps in consumers' knowledge and provides the opportunities for nutritionists and other health care practitioners to translate the available scientific data and promote at least those products with proven safety and clinical efficacy.

While the main purpose of NHP is to: prevent, treat, mitigate a disease, disorders or abnormal physical state or its symptoms, or restore, correct or modify organic functions and overall maintain and promote human health [9], the Food and Drug Act prohibits to advertise and label any food, drug, cosmetic or device as a treatment preventative or cure for any of the diseases listed in Schedule A [11]. This list includes the following conditions: acute alcoholism, acute anxiety state, acute infectious respiratory syndromes, acute, inflammatory and debilitating arthritis, acute psychotic conditions, addiction (except nicotine addiction), appendicitis, arteriosclerosis, asthma, cancer, congestive heart failure, convulsions, dementia, depression, diabetes, gangrene, glaucoma, haematologic bleeding disorders, hepatitis, hypertension, nausea and vomiting of pregnancy, obesity, rheumatic fever, septicemia, sexually transmitted diseases, strangulated hernia, thrombotic and embolic disorders, thyroid disease, and ulcer of the gastro-intestinal tract. In 2007, NHP were exempted from preventative claim prohibition in respect to Schedule A listed diseases, while the previous conditions regarding the treatment and mitigation remain in force [12]. Considering that in Canada TCM are regulated as NHP, these regulations pertain to Chinese herbs as well. In order to better understand the issues related to TCM including traditional and novel TCM products, their sale,

importation and use in Canada, the Advisory Council on Traditional Chinese Medicines represented by stakeholder groups including industry, consumers and patients, health care professionals and academics was established by Health Canada in 2011.

2.2.2 Botanical Products and Their Regulation in the U.S. and European Union

In the U.S., herbal products are regulated under the Federal Food, Drug, and Cosmetic Act either as foods, botanical drugs or dietary supplements. While the herbs consumed as foods primarily due to their taste, aroma or nutritive value are regulated as foods, dietary supplements are regulated under the Dietary Supplement Health and Education Act (DSHEA) of 1994 and may not claim to: diagnose, mitigate, treat, cure, or prevent a specific diseases. Instead, dietary supplements may claim a benefit related to a classical nutrient deficiency disease, describe the benefits for structure or function of human body and the mechanisms of thereof. If a botanical product is intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in humans, such product is regulated as a drug. Both botanical drug products and herbal dietary supplements can be manufactured in the form of herbal tea and non-food forms such as concentrates, powder, tablet, capsule, elixir and other forms. Another type of products that are not regulated as drugs and do not require prescription are called *medical foods* intended to meet specific nutritional requirements of a disease or condition and must be used under medical supervision. The regulation of botanical products and medical foods in the U.S. is enforced by U.S. Food and Drug Administration [13].

In the European Union, the use of herbal products is regulated under the Directive 2004/24/EC of the European Parliament and of the Council enacted in 2004. Article 31 of the Directive defines *herbal substances* as mainly: whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually dried, form, but sometimes fresh. This definition also includes certain exudates that have not been subjected to a specific treatment. Article 32 defines *herbal preparations* as preparations obtained by subjecting herbal substances to treatments such as: extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include: comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates [14]. According to the Directive, each Member State has to set up a simplified registration for herbal medicines that have been traditionally used for at least 30 years including 15 years within the EU. In 2004, the Committee on Herbal Medicinal Products (HMPC) was established and aimed to assist the harmonisation of procedures and provisions concerning herbal medicinal products laid down in EU Member States, and further integrating herbal medicinal products in the European regulatory framework. HMPC serves as a scientific body and provides its opinion on herbal medicinal

products to EU Member States, establishes ‘Community list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products’, and Community herbal monographs [15]. In respect to botanicals intended for use in food applications, European Food Safety Authority (EFSA) has issued the “Compendium of botanicals reported to contain naturally occurring substances of possible concern for human health when used in food and food supplements”. The Compendium covers about 900 botanicals, their scientific name, common synonyms and safety concerns [16].

2.3 Randomized Clinical Trials Using Dietary Herbs and/or Active Ingredients and Their Limitations

Dietary Chinese herbs have long been used in Traditional Chinese Medicine (TCM) for disease prevention, treatment and to enhance the overall wellbeing of human beings. However in the recent years, an increased focus on clinical and pharmacological-evidence based investigation on the efficacy of herbs and their active ingredients can be noticed. Based on a study published in the Chinese Medical Journal, the four major health categories where the application of Chinese medicine and natural products were more pronounced included: cancer, cardiovascular, oral & gastrointestinal as well as inflammatory/immune disorders [17]. Other categories consisted of neurological disorders, stroke, skin diseases, metabolic disorders, reproductive health, mental health and metabolic or endocrine disorders [17].

A wide range of disparity exists in the use of Chinese herbs for therapeutic purposes in modern medical practice. Traditional Chinese medicine practitioners use herbal combinations rather than single herbs in which each herb plays a specific role in addressing the patterns of symptoms. The inclusion of one herb may enhance the activity of the other or reduce the risk of short-term or long-term side effects of another herb [18, 19]. When herbal combinations/decoctions are subjected to preliminary studies, characterization of the principal component and/or adjuvant phytochemical constituents responsible for the curative action becomes impossible [20]. This is extremely essential when studies are to be applied to human subjects in various clinical trials. However, such an approach is not compatible with the basic theories of TCM including ‘treating the patient as a whole’ where the interaction of forces and energies both within and outside the individual is given importance [21].

Conducting randomized, controlled clinical trials in human subjects using dietary herbs becomes difficult due to: various factors including herb quality issues, improper processing and manufacturing practices, variations in active herbal components and interactions between herbs as well as with administered drugs [22]. The chemical composition of TCM and natural products are mostly governed by growing conditions such as rainfall, length of cultivation, soil nutrients and geography. A change in any one of these factors inevitably affects the content of chemical constituents present in herbal products. Even though the products are

standardized for content of their known active ingredients, there could be differences in the content of other components. Such variations can pose problems while conducting preclinical, pharmacological and clinical assessment of herbal formulations/products. Studies by Fitzloff et al. [23] showed that 26 % of the ginseng products marketed in North America did not meet the label claims of ginsenoside content of *Panax ginseng* and *Panax quinquefolius* products. An extensive study by Gilroy et al. [24] reported the reduced contents of active ingredients echinacoside or cichoric acid in Echinacea products marketed in the United States. Lack of quality control/quality assurance requirements for the dietary ingredient suppliers have been indicated as the cause of adulteration, substitution or low quality of materials being incorporated in the dietary herbal supplements [25]. In addition to this, various herb-herb interactions (incompatibilities and counteracting abilities) have been documented [26]. Also, interactions of herbal medicines with drugs such as warfarin, aspirin, midazolam, digoxin and irinotecan have been reported [27, 28]. Hence, understanding these pitfalls and taking remedial measures are crucial while integrating herbal medicine into evidence-based clinical practice. Preclinical and pharmacological assessment of herbal medicines conducted using animal model systems might sometimes not prove useful in humans as biological responses may not be species transferable. It is possible to have a positive effect of a drug/active ingredient in animals whereas it may be completely inactive in humans. Testing the toxicity levels and manifestations of a certain drug in animal models is particularly useful while assessing drug safety issues. Moreover, testing the presence of heavy metals such as arsenic, lead, copper and mercury in herbal ingredients is necessary to avoid possible adverse effects while conducting trials in humans [22]. The Consolidated Standards of Reporting Trials (CONSORT) checklist developed by the CONSORT group (www.consort-statement.org) provides a solid basis for conducting and reporting randomized controlled trials (RCT). This includes documentation of various aspects of RCT's including randomization, blinding and analysis along with detailed descriptions on patient eligibility criteria, experimental objectives and hypotheses, sample size calculation, implementation of the study and statistical methods used [29, 30]. However at times, implementing herbal medicinal trials pose problems due to their distinguishable organoleptic properties compared to placebo which could have a confounding effect on the efficacy of the treatment. In such cases, strategies adopted to control this possible bias should be well documented so as to facilitate replication of treatments by other investigators.

Although it is uncommon among the TCM practitioners to use single herbs, some specific herbs have gained attention and have been investigated for their potential to be used in the development of treatments or as therapeutic interventions. A large number of trials on herbs and their active ingredients can be retrieved from The Cochrane Central Register for Controlled Trials (www.cochranelibrary.com) and PubMed. Few examples of randomized, single/double blinded, placebo-controlled clinical trials of Chinese herbs and active ingredients for various diseases/disorders are shown in Table 2.1.

Some clinical trials on herbs provide promising results, where as some do not show any significant difference between the treatment and the placebo. In such

Table 2.1 List of few randomized, single/double blinded, placebo-controlled clinical trials of Chinese herbs and active ingredients for various diseases/disorders

Scientific name	Active ingredients (if investigated)	Health category	References
<i>Curcuma longa</i> L.	Curcumin	Colorectal cancer, Type-2 diabetes, Type-2 diabetic nephropathy, Gall bladder function Inflammation, Cardiovascular	[46–52]
<i>Gingko biloba</i> L.	Gingkolide-B	Sepsis, Multiple sclerosis, Acute ischemic stroke, Alzheimer’s disease, Mild cognitive impairment, Hypertension, Diabetic nephropathy	[53–59]
<i>Cinnamomum cassia</i> Presl		Diabetes, Lipid profile	[60–63]
<i>Panax ginseng</i> C.A Mey., <i>Panax notoginseng</i> (Burk.) F.H. Chen, <i>Panaxquinquefolius</i>	Ginsenoside-Rd	Acute ischemic stroke, Type-2 diabetes, Erectile dysfunction, Psychomotor function, Neurocognitive function	[64–69]
<i>Zingiber officinale</i> Rosc.		Nausea, Vomiting, Hyperlipidemia	[70, 71]
<i>Salvia miltiorrhiza</i>		Oxidative stress, Hypertension	[5, 72]
<i>Morus alba</i> L	Mulberry 1-deoxynojirimycin (DNJ) Mulberry extract oil	Diabetes mellitus Melasma	[73] [74]
<i>Astragalus membranaceus</i> (Fisch.)	Purified extract PG2	Allergic rhinitis Hemorrhagic stroke Cancer-related fatigue	[75, 76] [77]
<i>Angelica sinensis</i> (Oliv.)		Menopausal symptoms	[78, 79]

cases, investigators are led to conclude that more randomized controlled trials are recommended to understand the benefits. However, extensive research reviews on the scientific validity of clinical trials of TCM are available, which points out the various drawbacks of the studies and also provide recommendations for proper future trials [31]. Publication bias resulting from selective outcome reporting has been projected as one of the drawbacks that could diminish the strength of evidence while making informed decisions about a treatment [31]. In order to increase the transparency of randomized clinical trials and to improve the quality of trials, registration of prospective trials in international clinical trials registry such as *ClinicalTrials.gov* and International Clinical Trial Registry Platform (ICTRP) (<http://www.who.int/ictrp/en/>) established by World Health Organization has been highly warranted.

2.4 Market Trends in the Functional Foods and Natural Health Products Industry

The functional foods and natural health products industry is expanding with major financial implications on the world stage and shows growth in all areas including firms, sales and new product development. In 2004, the World Bank estimated the functional foods and natural health products industry to be worth 30–60 billion US dollars with estimates of it reaching \$130 billion US dollars by 2015, which corresponds to 1–3 % of the total food market [32]. Three leading markets dominate this industry, the U.S, Japan and Europe, with over 90 % of the total sales for functional foods and natural health products [33]. The expansion of these markets is expected to continue over the next few years with markets also growing in China, India, and the Asia-Pacific countries [32].

An overview of the leading markets reveal that in the United States, the retail value of the functional foods and natural health products industry was \$59 billion in 2007 with the natural health product segment accounting for 26.4 % of the total US health food sales [32]. The number of products on the market is increasing steadily, with new introductions increasing from 200 to 800 between 2006 and 2008 [34]. Several factors contribute to the growth of this industry including the increased awareness between health and diet, an aging population, the increasing cost of health care, increasing competition in the food industry for novel products, and the challenges consumers face while trying to meet their nutritional needs using conventional foods [32, 34]. The estimated value for functional foods and natural health products in Japan was estimated to be 16.4 billion US dollars in 2007 [32]. In Europe, the market was estimated at 8 billion US dollars, with the natural health product segment accounting for 6 billion US dollars [32]. The European Union is also the largest importer of medical plants with an estimated 100,000 tonnes of plant material being imported in 2000 [32].

Canada has a small portion of the global functional food and natural health product market which constitutes only about 1 % of the total global market. Although Canada's market share is small, it is increasing with further demands for novel products from Canadian consumers. Within Canada, the functional food and natural health product industry generates \$3.7 billion in revenue with \$1.7 billion coming from firms producing only natural health products [35]. The Canadian functional foods and natural health product industry has also expanded from 389 food and natural health product companies to over 680 companies between 2005 and 2007 producing over 22,062 product lines [32, 35]. Canadian firms who specialize in natural health products are targeting four main health areas: vascular health, weight control, energy and general nutrition. There is also a focus on the health of the immune system, the eyes, the bones, the urinary tract, the prostate and the gut as well as diabetes, cancer, arthritis, menopause, anxiety and other mental health issues and sexual health and performance [32, 35].

2.4.1 Patents with Herbs

Patents granted by world governments are used in the food industry to protect the exclusive rights of the inventors or applicants of a novel product for a limited amount of time. According to the 2007 results from the Functional Foods and Natural Health Products Survey, there was a total of 999 existing patents worldwide for functional food and natural health products with another 1005 pending approval [35]. As with the overall industry, the number of patents in this sector is also expanding. For example, in the European Union functional foods and natural health patents grew from 3.2 to 7.7 % between 1994 and 2000 [32]. The United States and Canada, are also experiencing an increase in functional foods and natural health products patents. In the United States, the growth in patent applications is driven by the regulatory approval of many health claims [32]. Patents are granted by the United States Patent and Trademark Office in United States and by the Canadian Intellectual Property Office in Canada. An inventor in the United States must demonstrate that the invention is useful and new within the patent application whereas in Canada the invention must not only be first in the world or show “novelty” but also be functional and operative or have “utility” and show “ingenuity” in order for the application to be successful [32]. Patent regulation within Japan is based on the similar concept of novelty as in Canada. Between 1994 and 2001, Japan held over 22 % of the global patent applications with a major focus on dairy-based functional foods [32, 36, 37].

The majority of successful functional foods and natural health patents have been in the area of extraction and purification techniques of plants and plant parts [32]. For example, one patent provides a method of β -carotene extraction from the genus *Momordica* and yields an oil rich in β -carotene [38]. The patented process is done without the use of organic solvents and provides a stable source of β -carotene that can be used in products as a nutritional supplement for human and animal consumption as well as for pharmaceuticals and cosmetics [38]. Another process patent describes a low-temperature extraction process for several species of plants including *Zingiber officinale* (ginger), *Curcuma longa* (turmeric), *Cinnamomum cassia* (Chinese cinnamon), and *Mentha* (Mint) species for producing heat stable flavorings used in bakery applications [39]. An emulsion of edible oil, water and an emulsifier is created with the plant material and than separated to produce the liquid flavorings fraction. This fraction is then encapsulated and dried into a heat-stable powder [39]. Patents have also been obtained for the production technique used for enhancing the physico-chemical properties of beverages. Mennett et al. [40] described a method for enhancing the foam properties of a number of beverages including fermented malt beverages, beer, cappuccino, flavored coffee, tea, hot chocolate, and carbonated soft drinks by incorporating foam-enhancing formulations comprising plant materials from the mint family either to the finished beverage or into a step in the beverage manufacturing process.

2.4.2 Food Products with Added Herbs

Patents dealing with actual food products are less common but still exist. Morazzoni et al. [41], holds a patent for a medicament or a dietary supplement with ginkgo derived from the plant *Ginkgo biloba*, complexed with phosphatidylserine for the enhancement of cognitive function and to alleviate mental fatigue. The authors state that the product is “to improve the speed of memory and memory quality, to increase accuracy and attention in activities in normal healthy subjects, to prevent deterioration of the speed and quality of memory in people with decreased cognitive functions and to counteract cognitive fatigue, having also an influence on the mood, particularly in healthy children, young adults, middle-aged and/or old people” [41]. A dietary supplement comprised of fibre, whey and plant parts from plants of the genus *Capsicum* and *Mentha* and aimed for regulating appetite was patented [42]. It induces satiety by occupying the stomach and sending satiety signals to the brain and involve some other metabolic mechanisms. The herb *Angelica sinensis* is patented in the use of a fermented herbal drink which is effective in treating the symptoms of menopause [43]. The herb is extracted with yeast and water which allows the yeast to ferment the crushed herb. This fermentation process is carried out over seven days at 10–20 °C and is then filtered [43]. One more example of successful application of patents using herbs as part of the food product is described by Adachi et al. [44] as a flavor deterioration inhibitor for foods, drinks and/or oral care products. This product is made by extracting *Angelica keiskei*, avocado, *Cassia tora*, *Plantago asiatica*, hawthorn, fermented tea leaves with water, an organic polar solvent, and a deterioration smell inhibitor. The addition of the flavor deterioration inhibitor to foods will improve storage life by maintaining the product’s flavor [44].

2.4.3 Natural Health Products Based on Herbal Remedies: What Is on the Market?

Health Canada with its Natural Health Product Database provides consumers with a means to search for licensed natural health products available in Canada, including vitamin and mineral supplements, herb and plant-based remedies, traditional Chinese and Indian medicines, omega 3 and essential fatty acids, probiotics, homeopathic medicines and many oral and personal hygiene products. These licensed products have been assessed by Health Canada and have been found to be of high quality, effective, and safe under the recommended usage of the products. Consumers can find information such as product name, product licence holder, Natural Product Number (NPN) or Homeopathic Medicine Number (DIN-HM), product’s medicinal ingredients, product’s non-medicinal ingredients, product’s dosage, product’s recommended use, and cautions, warnings, contra-indications and known adverse reactions with the product’s use (Health Canada, 2013) [45]. Several examples of natural health products in Canada using selected Chinese herbs are given in Table 2.2.

Table 2.2 Examples of natural health products in Canada using selected Chinese herbs

Selected Chinese herb	Natural product number (NPN):	Brand name(s)	License holder	Dosage form	Recommended route of administration	Recommended use or purpose	Cautions and warnings	Contra-Indications
<i>Angelica dahurica</i> , <i>Poria cocos</i>	2,230,977	Huohsiang Chengchi Pill	Wing Quon Enterprises Ltd.	Tablet	Oral	Traditional herbal medicine for relief of diarrhea and associated nausea and bloating	If diarrhea persists for more than 2 days or in the presence of high fever, consult a physician. For adults only	Do not use if pregnant
<i>Angelica sinensis</i>	1,995,987	Genestra Brands™ Multi Gyn; Genestra Brands™ Formula Gyn	Seroyal International	Tablet	Oral	Helps the body to metabolize carbohydrates, fats and proteins and helps in tissue formation; helps in the development and maintenance of bones and teeth and helps to maintain proper muscle function	If symptoms persist or worsen; if you are breastfeeding or if you have a liver disorder or develop symptoms of liver trouble, consult your health care practitioner prior to use	If you are pregnant; if you have had breast, uterine or ovarian cancer or taking oral contraceptive medication, do not use
<i>Cassia obtusifolia</i> , <i>Gardenia jasminoides</i> , <i>Polygonum multiflorum</i>	80,036,033	Jiangzhi Paidu Capsule	T.C. Unicorn Ltd	Capsule	Oral	This Traditional Chinese Medicine helps clear toxic heat and regulate qi	Do not use if you are pregnant or breastfeeding. Consult a health care practitioner if symptoms persist or worsen. Please consult a health care practitioner before consumption. Do not use if the cap or seal is damaged. Keep out of reach of children	Do not use if you are experiencing loose stool due to deficiency of the spleen

(continued)

Table 2.2 (continued)

Selected Chinese herb	Natural product number (NPN):	Brand name(s)	License holder	Dosage form	Recommended route of administration	Recommended use or purpose	Cautions and warnings	Contra-Indications
<i>Chrysanthemum morifolium</i> , <i>Dendrobium nobile</i> , <i>Panax ginseng</i> , <i>Prunus armeniaca</i>	80,025,795	ShihuYeguang Wan	T.C. Unicorn Ltd	Pill	Oral	This traditional Chinese medicine helps replenish yin of the kidney, quench the liver-fire and improve eyesight. It is used for yin deficiency of the liver and the kidney with flaming-up of fire causing impaired vision	Consult a health care practitioner prior to use if you have liver disorders. Do not use if you have hypokalemia, high blood pressure, or a kidney or cardiovascular disorder. Consult a health care practitioner prior to use if you are taking other medications. Do not use if you are pregnant or breastfeeding. If condition persists for more than 7 days, worsens, or clears up and occurs again in a few days, discontinue use and consult a TCM practitioner. Do not use if cap or seal is damaged. Keep out of reach of children	None

(continued)

Table 2.2 (continued)

Selected Chinese herb	Natural product number (NPN):	Brand name(s)	License holder	Dosage form	Recommended route of administration	Recommended use or purpose	Cautions and warnings	Contra-Indications
<i>Curcuma longa</i>	80,000,032	KrippsTumeric	Kripps Pharmacy Ltd.	Capsule	Oral	Traditionally used as an anti-inflammatory	Consult a health care provider if you have a history of gallstones, biliary tract obstructions, stomach ulcers or are taking blood thinners	Do not use if you are pregnant or breastfeeding
<i>Gardenia jasminoides</i>	2,236,749	Ammien Tablets	Wing Quon Enterprises Ltd.	Tablet	Oral	Traditional herbal medicine helps to relieve jitteriness due to feeling of fatigue and occasional insomnia	May cause drowsiness. Don't engage in activities requiring alertness. Avoid alcoholic beverages. Do not exceed recommended dose except on the advice of a doctor. If sleepiness persists continuously for more than two weeks, consult your physician. Insomnia may be a symptom of serious underlying medical illness	None

(continued)

Table 2.2 (continued)

Selected Chinese herb	Natural product number (NPN):	Brand name(s)	License holder	Dosage form	Recommended route of administration	Recommended use or purpose	Cautions and warnings	Contra-Indications
<i>Lonicera japonica</i>	2,239,977	Yin Chiao Herbal Tablets For Cold	Classical Remedia Ltd.	Tablet	Oral	Traditional Chinese Medicine used to provide temporary relief for symptoms of colds and flus: sore throat, fever and productive cough	Do not use when pregnant or breastfeeding. Consult a doctor if cough worsens, lasts more than 7 days accompanied by high fever or sore throat persists for more than 2 days. Do not exceed dosage	None
<i>Panax notoginseng</i>	2,238,959	PienTze Huang Tablets	Classical Remedia Ltd.	Tablet	Oral	Traditional Chinese Medicine: Analgesic—for pain relief	None	Do not use if pregnant or breastfeeding
<i>Phyllanthus emblica</i>	80,019,321	Triphala Plus-Sewanti.Ayurvedic Series	Padmashri Naturals Inc.	Capsule	Oral	Traditionally used in Ayurvedic medicine in the treatment of indigestion, constipation, and to strengthen the eyes	Do not use if pregnant or breastfeeding. Consult a health care practitioner prior to use if you have a liver disorder. Do not use if you are taking thiazide diuretics, corticosteroids, stimulant laxatives or other medications which may aggravate electrolyte imbalance. Discontinue use if persistent abdominal cramps, spasms, and/or pain	None

(continued)

Table 2.2 (continued)

Selected Chinese herb	Natural product number (NPN):	Brand name(s)	License holder	Dosage form	Recommended route of administration	Recommended use or purpose	Cautions and warnings	Contra-Indications
Prunella vulgaris	80.017,024	Jiang YaPian	T.C. Unicorn Lid	Tablet	Oral	This traditional Chinese medicine helps clear away the heat and reduce fire to help calm the liver. It is used for dizziness, vertigo and headache due to blood rising and flaming up of excessive fire of the liver	<p>occur. Consult a health care practitioner prior to use if you have abdominal pain, nausea, fever, vomiting, and hemorrhoids, or if you have a chronic gastrointestinal disorder</p> <p>Consult a health care practitioner prior to use if you are taking other medications. Consult a health care practitioner if symptoms persist or worsen. Consult a health care practitioner prior to use if you have a liver disorder or develop symptoms of liver trouble (such as abdominal pain, dark urine or jaundice). Consult a health care practitioner prior to use if you have an iron deficiency. Not recommended for use in cases of diarrhea</p>	Do not use if pregnant or breastfeeding

2.5 Conclusion

Growing market for dietary and medicinal herbs including TCM requires the harmonization of food and supplement regulations between jurisdictions. The new unified standards for herbal products and their clinical efficacy and safety evaluations need to be implemented in order to provide both healthcare providers and consumers with transparent and explicit information. The creation of a global database using the existing platforms (e.g., WHO, FAO, Codex Alimentarius, etc.) may provide a unique opportunity to consolidate all available information on herbal products and their nomenclature, efficacy, toxicity, applications, origin, territorial regulation and approval status.

References

1. Helmut Kaiser Consultancy (2013) Traditional Chinese Medicine (TCM) In China and Worldwide. Available at <http://www.hkc22.com/ChineseMedicine.html>. Accessed on 06 Aug 2013
2. Nutrition Business Journal (2008) Integrative medicine stakeholders organize to address healthcare crisis integrative medicine is on the rise in the United States. *Nutr Bus J XII* 11:1–13
3. Nutrition Business Journal (2012) 2012 Supplement Business Report. Executive summary available at <http://newhope360.com/site-files/newhope360.com/files/uploads/2013/04/TOCSUMM120928.sup%20report%20FINAL%20standard.pdf>. Accessed on 08 Aug 2013
4. National Center for Complementary and Alternative Medicine (2009) Traditional chinese medicine: An introduction. Available at <http://nccam.nih.gov/health/whatiscam/chinesemed.htm#examples>. Accessed on 22 Sept 2013
5. Qian et al (2012) Effect of salvia miltiorrhiza hydrophilic extract on antioxidant enzymes in diabetic patients with chronic heart disease: a randomized controlled trial. *Phytotherapy Res* 26(1):60–66. doi:10.1002/ptr.3513
6. Health Canada (2013) A new approach to natural health products. Available at: <http://www.hc-sc.gc.ca/dhp-mps/prodnatur/nhp-new-nouvelle-psn-eng.php#fnb1-ref>. Accessed on 05 Aug 2013
7. Health Canada (2013) Harper Government Continues to Engage with Traditional Chinese Medicine Community in Canada. Available at: http://www.hc-sc.gc.ca/ahc-asc/media/nr-cp/_2013/2013-44-eng.php. Accessed on 05 Aug 2013
8. Health Canada (2011) Natural Health Product Tracking Survey—2010 Final Report. Prepared by: Ipsos Reid. Available at <http://epe.lac-bac.gc.ca/100/200/301/pwgsc-tpsgc/por-ef/health/2011/135-09/report.pdf>. Accessed on 21 Sept 2013
9. Government of Canada (2003) Natural Health Products Regulations (SOR/2003-196), Canada Gazette Part II, vol 137, no 13. Available at <http://publications.gc.ca/gazette/archives/p2/2003/2003-06-18/pdf/g2-13713.pdf>. Accessed on 22 Sept 2013
10. Quan et al (2008) Complementary and alternative medicine use among Chinese and white Canadians. *Can Fam Physician* 54(11):1563–1569. doi:10.54/11/1563 [pii]
11. Government of Canada (1985) Food and Drugs Act (R.S.C., 1985, c. F-27). Available at <http://laws-lois.justice.gc.ca/eng/acts/F-27/page-14.html#h-21>. Accessed on 22 Sept 2013
12. Government of Canada (2007) Regulations Amending Schedule A to the Food and Drugs Act and the Medical Devices Regulations—Project 1539 (SOR/2007-288). Canada Gazette Part II,

- vol 141, no 26. Available at <http://publications.gc.ca/gazette/archives/p2/2007/2007-12-26/pdf/g2-14126.pdf>. Accessed on 22 Sept 2013
13. U.S. Food and Drug Administration (2004) Botanical Drug Products. Guidance for Industry. Available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070491.pdf>. Accessed on 22 Sept 2013
 14. The European Parliament and the Council of the European Union (2004) Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004 amending, as regards traditional herbal medicinal products. Official J Eur Union 47:85–90
 15. European Medicines Agency (2013) The Committee on Herbal Medicinal Products Overview. Available at http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000122.jsp&mid=WC0b01ac0580028e7d. Accessed on 22 Sept 2013
 16. European Food Safety Authority (2012) Compendium of botanicals reported to contain naturally occurring substances of possible concern for human health when used in food and food supplements. *EFSA J* 10(5):2663
 17. Collins (2011) A ten-year audit of traditional Chinese medicine and other natural product research published in the Chinese Medical Journal (2000–2009). *Chin Med J* 124(9):1401–1408. doi:10.3760/cma.j.issn.0366-6999.2011.09.023
 18. Boik (ed) (1995) *Cancer and natural medicine: a textbook of basic science and clinical research*. Oregon Medical Press, Princeton
 19. Wang et al (2006) Study on combination components and effectiveness of Chinese traditional herbal formulas. *China J Chin Mat Med* 31(1):5–9
 20. Fong et al (2006) Evidence-based herbal medicine: challenges in efficacy and safety assessments. *Curr Rev Chin Med* 2:11–26. doi:10.1142/9789812774019_0002
 21. Zhu and Woerdenbag (1995) Traditional Chinese herbal medicine. *Pharm World Sci* 17(4):103–112. doi:10.1007/bf01872386
 22. Fong (2002) Integration of herbal medicine into modern medical practices: issues and prospects. *Integr Cancer Ther* 1(3):287–293
 23. Fitzloff et al (1998) Perspectives on the quality assurance of ginseng products in North America. In: *Advances in Ginseng Research—Proceedings of the 7th International Symposium on Ginseng*, Seoul, Korea
 24. Gilroy et al (2003) Echinacea and truth in Labeling. *Arch Intern Med* 163(6):699–704. doi:10.1001/archinte.163.6.699
 25. Liva (2009) Controlled testing: the cornerstone of all quality natural products. *Integr Med* 8(2):40–42
 26. Tang et al (2009) Modern understanding for “eighteen incompatible medicaments” and “nineteen medicaments of mutual restraint” in TCM. *Chin J Exp Trad Med Formulae* 15(6):79–82
 27. Ulbricht et al (2008) Clinical evidence of herb-drug interactions: a systematic review by the natural standard research collaboration. *Curr Drug Metab* 9(10):1063–1120
 28. Zhou et al (2007) Identification of drugs that interact with herbs in drug development. *Drug Discovery Today* 12(15–16):664–673. doi:10.1016/j.drudis.2007.06.004
 29. Gagnier et al (2006) Recommendations for reporting randomized controlled trials of herbal interventions: explanation and elaboration. *J Clin Epidemiol* 59(11):1134–1149. doi:10.1016/j.jclinepi.2005.12.020
 30. Gagnier et al (2006) Reporting randomized, controlled trials of herbal interventions: an elaborated CONSORT statement. *Ann Intern Med* 144(5):364–367
 31. Liu et al (2013) Prospective registration, bias risk and outcome-reporting bias in randomised clinical trials of traditional Chinese medicine: an empirical methodological study. *BMJ open* 3(7):e002968. doi:10.1136/bmjopen-2013-002968
 32. Malla et al (2013) Assessing the functional foods and natural health products industry: a comparative overview and literature review. Canadian Agricultural Innovation and Regulation (CAIRN) Network. Available at http://www.ag-innovation.usask.ca/cairn_briefs/publications%20for%20download/Publication. Accessed on 30 Aug 2013

33. Kaur, Das (2011) Functional foods: an overview. *Food Sci Biotechnol* 20(4):861–875. doi:10.1007/s10068-011-0121-7
34. Evani (2009) Tendances du marché américain en matière d'aliments, de boissons et d'ingrédients fonctionnels. Institute of Food Technologists. Available at <http://www.agrireseau.qc.ca/Marketing-Agroalimentaire/documents/Tendances%20aliments%20fonctionnels%20-%20USA%20-%20AAC%2007-2009.pdf>. Accessed on 26 July 2013
35. Cinnamon (2007) Results from the Functional Foods and Natural Health Products Survey - 2007. Statistics Canada. Available at <http://www.statcan.gc.ca/pub/88f0006x/88f0006x2009001-eng.htm>. Accessed on 01 July 2013
36. Stein AJ, Rodriguez-Cerezo E (2008) Functional Food in the European Union, Institute for Prospective Technological Studies (IPTS), Technical report series EUR 23380 EN-2008. Available at <http://ftp.jrc.es/EURdoc/JRC43851.pdf>. Accessed on 30 Aug 2013
37. Trueman (2009) Functional foods. Patents and health claims, IP Strategist Publication, Nerac Inc
38. Vuong (2004) Obtaining a quantity of ripen fruits of *Momordica cochinchinensis* plant (spiny melon), collecting aril and seeds from the cavity of the fruit, separating aril from the seeds, drying wet aril, extracting oil from the aril. Patent Publication number US20040024275 A1, Publication date 5 Feb 2004
39. Green R, Owusu-Ansah YJ (1999) Natural heat stable flavorings for bakery applications. Patent Publication number US5902622 A, Publication date 11 May 1999
40. Menett et al (2004) The use of labiatae herb preparations for foam enhancement of beverages. Patent Publication number CA2538766 A1, Publication date 31 March 2005
41. Morazzoni et al (2005) Use of ginkgo complexes for the enhancement of cognitive functions and the alleviation of mental fatigue. Patent Publication number CA2554760 A1, Publication date 18 Aug 2005
42. Nielsen SVS, Teisen-Simony C (2011) Appetite regulating dietary supplement. Patent Publication number CA2781740 A1, Publication date 3 June 2011
43. Kong (2002) Fermented herbal drink. Patent Publication number CA2325751 A1, Publication date 2 May 2002
44. Adachi et al (2011) Flavor deterioration inhibitor and inhibitor for the generation of citral deterioration smell. Patent Publication number CA2489390 C, Publication date 19 July 2011
45. Health Canada (2013) Licensed natural health products database. Available at <http://www.hc-sc.gc.ca/dhp-mps/prodnatur/applications/licen-prod/lnhpd-bdpsnh-eng.php>. Accessed on: 30 Aug 2013
46. Carroll et al (2011) Phase IIa clinical trial of curcumin for the prevention of colorectal neoplasia. *Cancer Prevent Res* 4(3):354–364. doi:10.1158/1940-6207.ccrp-10-0098
47. Chuengsamarn et al (2012) Curcumin extract for prevention of type 2 diabetes. *Diabetes Care* 35(11):2121–2127. doi:10.2337/dc12-0116
48. Khajehdehi et al (2011) Oral supplementation of turmeric attenuates proteinuria, transforming growth factor-beta and interleukin-8 levels in patients with overt type 2 diabetic nephropathy: a randomized, double-blind and placebo-controlled study. *Scand J Urol Nephrol* 45(5):365–370. doi:10.3109/00365599.2011.585622
49. Mohammadi et al (2013) Effects of supplementation with curcuminoids on dyslipidemia in obese patients: a randomized crossover trial. *Phytotherapy Res* 27(3):374–379. doi:10.1002/ptr.4715
50. Rasyid, Lelo (1999) The effect of curcumin and placebo on human gall bladder function: an ultrasound study. *Aliment Pharmacol Ther* 13(2):245–249
51. Satoskar et al (1986) Evaluation of antiinflammatory property of curcumin (diferuloyl methane) in patients with postoperative inflammation. *Int J Clin Pharmacol Ther* 24(12):651–654
52. Wongcharoen et al (2012) Effects of curcuminoids on frequency of acute myocardial infarction after coronary artery bypass grafting. *Am J Cardiol* 110(1):40–44. doi:10.1016/j.amjcard.2012.02.043

53. Albrecht et al (2004) Efficacy and safety of the platelet-activating factor receptor antagonist BN 52021 (Ginkgolide B) in patients with severe sepsis—a randomised, double-blind, placebo-controlled, multicentre trial. *Clin Drug Investig* 24(3):137–147. doi:[10.2165/00044011-200424030-00002](https://doi.org/10.2165/00044011-200424030-00002)
54. Brinkley et al (2010) Effect of ginkgo biloba on blood pressure and incidence of hypertension in elderly men and women. *Am J Hypertens* 23(5):528–533. doi:[10.1038/ajh.2010.14](https://doi.org/10.1038/ajh.2010.14)
55. Brochet et al (1995) Double blind placebo controlled multicentre study of ginkgolide B in treatment of acute exacerbations of multiple sclerosis. The ginkgolide study group in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 58(3):360–362
56. Oskouei et al (2013) The effect of ginkgo biloba on functional outcome of patients with acute ischemic stroke: a double-blind, placebo-controlled, randomized clinical trial. *J Stroke Cerebrovasc Dis* 22(8):E557–E563. doi:[10.1016/j.jstrokecerebrovasdis.2013.06.010](https://doi.org/10.1016/j.jstrokecerebrovasdis.2013.06.010)
57. Vellas et al (2012) Long-term use of standardised ginkgo biloba extract for the prevention of alzheimer's disease (GuidAge): a randomised placebo-controlled trial. *Lancet Neurol* 11(10):851–859. doi:[10.1016/s1474-4422\(12\)70206-5](https://doi.org/10.1016/s1474-4422(12)70206-5)
58. Zhang et al (2013) Ginkgo biloba extract for patients with early diabetic nephropathy: a systematic review. *Evid Based Complement Altern Med eCAM* 2013:689142–689142. doi:[10.1155/2013/689142](https://doi.org/10.1155/2013/689142)
59. Zhao et al (2012) Effects of ginkgo biloba extract in improving episodic memory of patients with mild cognitive impairment: a randomized controlled trial. *J Chin Integr Med* 10(6):628–634
60. Khan et al (2003) Cinnamon improves glucose and lipids of people with type 2 diabetes. *Diabetes Care* 26(12):3215–3218. doi:[10.2337/diacare.26.12.3215](https://doi.org/10.2337/diacare.26.12.3215)
61. Leach MJ and Kumar S (2012) Cinnamon for diabetes mellitus. *Cochrane Database Syst Rev* 9. doi:[10.1002/14651858.CD007170.pub2](https://doi.org/10.1002/14651858.CD007170.pub2)
62. Mang et al (2006) Effects of a cinnamon extract on plasma glucose, HbA(1c), and serum lipids in diabetes mellitus type 2. *Eur J Clin Invest* 36(5):340–344. doi:[10.1111/j.1365-2362.2006.01629.x](https://doi.org/10.1111/j.1365-2362.2006.01629.x)
63. Vanschoonbeek et al (2006) Cinnamon supplementation does not improve glycemic control in postmenopausal type 2 diabetes patients. *J Nutr* 136(4):977–980. doi:[10.1364/977](https://doi.org/10.1364/977) [pii]
64. de Andrade et al (2007) Study of the efficacy of Korean red ginseng in the treatment of erectile dysfunction. *Asian J Androl* 9(2):241–244. doi:[10.1111/j.1745-7262.2007.00210.x](https://doi.org/10.1111/j.1745-7262.2007.00210.x)
65. Hong et al (2002) A double-blind crossover study evaluating the efficacy of Korean red ginseng in patients with erectile dysfunction: a preliminary report. *J Urol* 168(5):2070–2073. doi:[10.1097/01.ju.0000034387.21441.87](https://doi.org/10.1097/01.ju.0000034387.21441.87)
66. Liu et al (2012) Ginsenoside-Rd improves outcome of acute ischaemic stroke—a randomized, double-blind, placebo-controlled, multicenter trial. *Eur J Neurol* 19(6):855–863. doi:[10.1111/j.1468-1331.2011.03634.x](https://doi.org/10.1111/j.1468-1331.2011.03634.x)
67. Scholey et al (2010) Effects of American ginseng (*Panax quinquefolius*) on neurocognitive function: an acute, randomised, double-blind, placebo-controlled, crossover study. *Psychopharmacology* 212(3):345–356. doi:[10.1007/s00213-010-1964-y](https://doi.org/10.1007/s00213-010-1964-y)
68. Vuksan et al (2008) Korean red ginseng (*Panax ginseng*) improves glucose and insulin regulation in well-controlled, type 2 diabetes: Results of a randomized, double-blind, placebo-controlled study of efficacy and safety. *Nutr Metab Cardiovasc Dis* 18(1):46–56. doi:[10.1016/j.numecd.2006.04.003](https://doi.org/10.1016/j.numecd.2006.04.003)
69. Ziemba et al (1999) Ginseng treatment improves psychomotor performance at rest and during graded exercise in young athletes. *Int J Sport Nutr* 9(4):371–377
70. Alizadeh-Navaei et al (2008) Investigation of the effect of ginger on the lipid levels a double blind controlled clinical trial. *Saudi Med J* 29(9):1280–1284
71. Zick et al (2009) Phase II trial of encapsulated ginger as a treatment for chemotherapy-induced nausea and vomiting. *Support Care Cancer* 17(5):563–572. doi:[10.1007/s00520-008-0528-8](https://doi.org/10.1007/s00520-008-0528-8)
72. Yang et al (2012) A randomized, double-blind, placebo-controlled study to evaluate the efficacy and tolerability of Fufang Danshen (*salvia miltiorrhiza*) as add-on antihypertensive

- therapy in taiwanese patients with uncontrolled hypertension. *Phytotherapy Res* 26(2):291–298. doi:[10.1002/ptr.3548](https://doi.org/10.1002/ptr.3548)
73. Kimura et al (2007) Food-grade mulberry powder enriched with 1-deoxynojirimycin suppresses the elevation of postprandial blood glucose in humans. *J Agric Food Chem* 55(14):5869–5874. doi:[10.1021/jf062680g](https://doi.org/10.1021/jf062680g)
 74. Alvin et al (2011) A comparative study of the safety and efficacy of 75 % mulberry (*morus alba*) extract oil versus placebo as a topical treatment for melasma: a randomized, single-blind, placebo-controlled trial. *J Drugs Dermatol* 10(9):1025–1031
 75. Chen CC et al (2012) Chinese herb astragalus membranaceus enhances recovery of hemorrhagic stroke: double-blind, placebo-controlled, randomized study. *Evidence-Based Complementary and Alternative Medicine*. doi: [10.1155/2012/708452](https://doi.org/10.1155/2012/708452)
 76. Matkovic et al (2010) Efficacy and safety of astragalus membranaceus in the treatment of patients with seasonal allergic rhinitis. *Phytotherapy Res* 24(2):175–181. doi:[10.1002/ptr.2877](https://doi.org/10.1002/ptr.2877)
 77. Chen et al (2012) A novel infusible botanically-derived drug, PG2, for cancer-related fatigue: a phase II double-blind, randomized placebo-controlled study. *Clin Invest Med* 35(1):E1–E11
 78. Al-Bareeq et al (2010) Dong Quai (*Angelica sinensis*) in the treatment of hot flashes for men on androgen deprivation therapy: results of a randomized double-blind placebo controlled trial. *Cuaj-Can Urol Assoc J* 4(1):49–53
 79. Hirata et al (1997) Does dong quai have estrogenic effects in postmenopausal women? A double-blind, placebo-controlled trial. *Fertil Steril* 68(6):981–986