Botanical Extraction: An Insider's Look

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The botanical medicine market is experiencing continued growth due to an increased consumer interest in personal health and wellness. In an aging population more and more people are looking to preventative and alternative measures to positively influence their health. The Food and Agriculture Organization (FAO) of the United Nations estimates that over 50,000 plant species may have medicinal uses.[1]

This increasing consumer demand for botanical extracts has had many impacts; primarily on the development of new extraction process technologies, but also on the creation of new standardized extracts.

Botanical medicines contain many different bioactive compounds (also known as marker compounds), which can vary significantly in products of different manufacturers. The reason for this is mainly because the manufacturing processes used by the different companies can extract varying levels of specific compounds, partly by molecular weight and hydrophilic or –phobic nature of the compounds, and partly due to the differences in raw materials. To overcome this, the industry has focused on "standardizing" ingredients based upon a specific marker compound. However herbs have numerous active compounds, some of which may not even have been identified.

The production of botanical extracts involves six major processes; cultivation, identification, extraction, drying, formulation and testing.

Cultivation

The majority of botanical medicines are harvested from their natural habitat (known as 'wildcrafting'), which has led to environmental consequences such as over harvesting leading to species endangerment and loss of genetic diversity.[1,2] Over harvesting is not limited to a specific region of the world and has been seen in the U.S. in the case of American ginseng and yew trees (*Taxus* species) including Pacific yew native to the U.S. and Chinese yew which are used to product the anti-cancer drug, Taxol. Some botanical species sought for their medicinal properties, such as hoodias, ginseng, and goldenseals, are listed by the Convention on International Trade in Endangered Species of Wild Fauna and Flora as endangered species due to over harvesting.[3] *C. wightii*, (locally know as guggul), is commonly found in Northern India but may grow in regions from Northern Africa to Central Asia. The oleo-gum of *C. wightii* has historical use in obesity and lipid metabolism disorders and is harvested by tapping the branches by incision. Due to the slow-growing nature of *C. wightii*, poor germination rate and excessive tapping for its gum resin, however, the plant has been listed in the data deficient category of the International Union for Conservation of Nature's (IUCN) 'Red List' of Threatened Species™.[4] The IUCN Red List evaluates conservation status of plants and animals using a scientific approach to determine risk of extinction and is recognized by both the World Health Organization and various governmental and non-governmental agencies worldwide. Harvesting of species listed on the Red List must be conducted in accordance with national and/or regional legislation.

With a recent rise in consumer environmental awareness, some manufacturers are turning to organic cultivation and offer "organic certified" botanical extracts. At present, however, there are very few certified organic extracts available to consumers. In order to be certified organic, a manufacturer must produce a finished product which is grown organically and is manufactured using water or certified organic grain alcohols as solvents. Some challenges in producing organic certified botanical extracts include avoiding synthetic chemical inputs such as pesticides, solvents used in extraction and preservatives, use of farmlands free from chemicals for three or more years and maintaining physical separation of organic products from non-certified products, which ultimately leads to increased manufacturing costs.

Identification

Good agricultural practices and good collection practices should be followed to ensure that correct species of botanicals are collected.[5] At minimum a visual inspection should be performed to prevent cross-contamination by unwanted plants and/or plant parts as well as evaluation for appearance, damage, size, and other organoleptic qualities. Some regulatory agencies (e.g., Health Canada), require botanical extracts to be identified using physical and chemical identification tests including macroscopic or microscopic techniques, DNA fingerprinting (genetic profiling) and spectral fingerprinting (chemical profiling) via Ultra Violet (UV), Infrared (IR), Mass Spectroscopy (MS) or chromatographic methods, such as High Performance Liquid Chromatography (HPLC), Thin Layer Chromatography (TLC) or Gas Chromatography (GC) to prevent

misidentification of the herb.[6] Misidentification, leading to use of incorrect plant parts or substitution of different species can lead to serious health consequences. This is the case for the Chinese herbal preparations of *Aristolochia fanghi* and *Podophyllum emodi* where misidentification of plant constituents in therapeutic products have been linked to sequelae as serious as nephropathy and urothelial carcinoma.[7,8,9] Once the plant/plant part has been identified and sorted, processing techniques such as extraction, standardization and drying may commence.

Extraction and Standardization

Botanical extracts are prepared in various forms including, but not limited to, essential oils, fluid extracts, solid extracts, native extracts, tinctures, and spray-dried extracts. Extraction from plant or plant materials (i.e., roots, stems, leaves) may be achieved through processes such as percolation or maceration.[10] Percolation involves reducing plant material to suitable size, mixing with solvent and transferring to a percolator. The mixture is allowed to percolate slowly and become concentrated. In the case of maceration, plant material is reduced to suitable size and solvent added. With frequent agitation, the soluble matter is dissolved and filtered prior to concentration. These processes may involve the use of relatively benign solvents such as water, ethanol and methanol or volatile organic chemicals such as benzene, chloroform or acetone. Note: some solvents such as chloroform and benzene are not allowed for use in some countries. The solvent is then evaporated or removed and the resulting extract may be standardized to meet final specifications for the ingredient. Standardization refers to adjusting the content of a characterized bioactive constituent by increasing the active compound, decreasing unwanted constituents or both. Contrary to popular belief, however, standardization does not necessarily mean a stronger product; the author has had tested through HPLC analysis at third party accredited laboratories, 8:1 extracts of lemon balm and 10:1 bugleweed have significantly lower rosmarinic acid, lithospermic acid than using unprocessed dry lemon balm or bugleweed directly from the garden. Standardization may be achieved in various ways, such as, mixing raw material lots, varying extraction conditions, varying extraction ratio of plant material to solvent or normalizing by varying the quantities of excipients among others.[10] Additionally, some botanical extracts may be fortified (or 'spiked') with another marker or ingredient and are not standardized products. A fortified product will normally be labelled in an unambiguous manner such as 'rose hips with added vitamin C'.[6]

In order to improve physical characteristics of the botanical extract, diluents (a filler or thinner such as water or microcrystalline cellulose), and in some cases, anti-microbial agents or preservatives, may be added. Natural health products (NHPs) containing extracts often present an extract ratio on the label (e.g., 4:1, 1:20). The ratio does not indicate the amount of the particular herb, but rather the ratio used in preparing the extract. In the case of tinctures, this ratio indicates the solute to solvent ratio, whereas in the case of spray dried extracts, the ratio is indicates the amount of inputted plant material to output. For example, a label stating "Licorice root extract (4:1), 20mg" indicates that 20mg of the extract is present in the finished product, but was prepared from 80mg of licorice root. Thus when assessing the safety and efficacy of the ingredient and potential contraindications, NDs should consider the product as having 80mg of licorice, in this case, or whichever plant compound is listed on the label.

Drying

Powdered botanical extracts used in natural products are almost always spray dried. Spray drying produces free flowing powders. The main reason for spray drying is to create a powdered extract that can be encapsulated. Without spray drying, botanical extracts would remain as a liquid in the form of a tincture or fluid extract. Spray drying usually involves five steps: concentration, atomization, droplet-air contact, droplet drying and separation. The botanical extract is usually concentrated prior to introducing in the spray dryer. The second stage, atomization, creates prime conditions to evaporate a product to desired characteristics. The atomized liquid is then brought into contact with the drying medium, most commonly hot air and allowed to continue until the desired moisture content is obtained at which time the particles are separated from the air. Particles may be separated utilizing specific properties of the compound of interest such as filtration or electrostatic precipitation.[11,12,13,14]

Formulation of the Finished Product

The finished NHP may be a single botanical extract or a combination of botanical extracts or other natural ingredients. In most cases, ingredients are blended together and either tabletted or encapsulated. Encapsulation involves filling the ingredients into a capsule shell. Non-medicinal agents may be added for a variety of purposes including lubrication, binding, coating and diluting.

Product Specifications and Analysis

Products may be tested at the ingredient stage, finished product stage or both by the manufacturer of the ingredient and/or finished product or by third party contract laboratories. Testing can be done in-house and does not always involve a third party. Most of the manufacturers of finished products provide their own test results to Health Canada in product applications.

Testing requirements depend on the type or nature of the ingredient or finished product and regulatory mandates. Botanical extracts (ingredients and/or finished products) are required by Health Canada to be tested for residual solvents, especially in cases where potentially toxic or carcinogenic solvents are used (e.g. styrene divinyl benzene, acetone, carbon tetrachloride), pesticide residues, heavy metals and microbes, however this may not always be the case as there are still numerous botanicals on the market in Canada that have not been assessed and approved by Health Canada.[6,9] Though not common practice, it may be necessary to sterilize raw materials or finished products to reduce microbial loads where found to exceed pharmacopeial limits to meet regulatory requirements. In such cases, pasteurization or

irradiation may be used. Though irradiation is not approved for use in the United States, it may be permitted by the Natural Health Products Directorate of Health Canada as a method of reducing microbiological loads or as a sterilization procedure for plant materials.[6] When irradiation is used as a means of sterilization, testing is imperative to ensure residual radioactivity is below the upper allowable regulatory limits. Currently, labelling of irradiated products is voluntary, and if labelled, will bear a statement to the effect "Treated with irradiation," "Treated by irradiation" or "irradiated".[6]

Pesticide Use

Most cultivated botanical species are grown with conventional agriculture methods using various pesticides and herbicides. There are no global regulations on the use of pesticides and thus testing requirements on botanicals is necessary to ensure consumer safety. Many pesticides contain chlorine and are referred to as organochlorides (examples include DDT, endosulfan and endrin). Many organochlorides have been banned in various countries, however only few have been banned worldwide (DDT and endosulfan to be banned globally in 2012). The continued allowance of pesticides such as 2,4- Dichlorophenoxyacetic acid in many regions including the U.S. and E.U., has consequences on watersheds and soils, those involved in the farming (farmers and agriculture workers) and manufacturing (those involved in extraction of the compounds) and ultimately those using these products. The state of Wisconsin regulates the amount and type of chemicals which may be sprayed on ginseng farms, although pesticides may still be used. Other countries cultivating ginseng, however, including China and South Korea, do not impose strict guidelines on pesticide use. An analysis conducted by ConsumerLab reported the presence of quintozene (pentachloronitrobenzene or PCNB) and hexaclorobenzene in some samples of East Asian ginseng. These pesticides are banned from most crop use throughout the world, including in Wisconsin, as they are possible carcinogens.[17,18] Ginseng, in this example, illustrates the critical importance for dispensaries and consumers to know the quality and source botanical extracts used in the dietary supplements. One such method may include reviewing NHPs to determine if they have been assessed and approved for use/sale in regulated countries such as Canada.

As the NHP industry continues to grow, manufacturers will need to review and evaluate current collection and manufacturing procedures in order to ensure well characterized, efficacious, safe, environmentally conscious products are available to consumers and medical professionals. Emphasis must be placed on the correct identification and characterization of botanicals used to prevent potential serious health consequences. Naturopathic doctors, as well, should be able to inform their patients on the safe use of NHPs. However, individual NDs can also play an important role by requesting both certified organic extracts and independent testing, which ensures that toxic solvents and processes are not used. In order to do this, the industry in turn must be more transparent with the methods employed to manufacture their finished products and unambiguously detail all ingredients and their amounts in the finished product.

About the Author

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