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Chapter 11

Herbal Medicine

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Additional information is available at the end of the chapter

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Abstract

Herbal medicine has gained cumulative popularity in today's medical practice. These treatments are the synthesis of therapeutic experiences of generations of traditional physicians for over hundreds of years. However, most of these applications are unorthodox, with over 80% of the world's population depending on some form of traditional medicine. The increase in the use of herbal products is due to their cultural acceptability, availability, affordability, efficacy and safety claims. This upsurge has led to the improvements in the quality and analysis of herbal products to be made with clinical research advancements in their safety and efficacy. The World Health Organization has recognized the importance of herbal medicine to the health of many people. Therefore, developing guidelines to evaluate herbal medicine by using modern control procedures and applying suitable standards. The current review aims to describe the present state and the projected future of herbal medicine.

Keywords: herbal medicine, safety and toxicity, regulations

1. Introduction

The practice of herbal medicine is the oldest form of healthcare which has been used for decades in developing and developed countries. Primitive people have depended on nature for food, shelter, clothing and medicine to cure ailments. These humans distinguished useful herbs with beneficial effects from those that were inactive or toxic [1]. According to literature approximately 50,000 plant species are stated to have medicinal properties [2]. Thus, the basis of modern medicinal drugs such as aspirin, morphine, digitoxin and quinine were synthesized through scientific validation of herbal medicine [3, 4]. Plant based drugs awareness advanced gradually and has been passed on, therefore setting a foundation for many traditional medicine systems around the globe [1].

Today herbal medicine is still the primary healthcare system for about 80% of the world's population, especially in the developing countries [1, 5, 6]. There has been also a sudden increase in the utilization of herbs as prescription drugs in developed countries such as France and Germany [3, 7]. However, there is a concern that not all herbal medicines are safe as reported [8]. Over the years the use of traditional medicine has provided us with valuable formulas on the selection, preparation and application of herbal remedies. The same vigorous method clinically and scientifically must be implemented to verify the effectiveness and safety of curative products, to be viable alternative to western medicine [4].

2. Herbal medicine

The World Health Organization (WHO) defines herbal medicine as a practice which includes herbs, herbal materials, herbal preparations and finished herbal products, that contain as active ingredients parts of plants, or other plant materials, or combinations [9]. These herbs are derived from plant parts such as leaves, stems, flowers, roots, and seeds [10].

Herbal drugs contain active ingredients, plant parts or plant materials in the processed or crude state with certain excipients, i.e., dilutions, solvents or preservatives [10, 11]. These active ingredients protect plants from damage and diseases and contribute to the plants aroma, flavor and color. Scientifically, they are known as phytochemicals which include several classes such as saponins, flavonoids, glycosides, tannins, alkaloids and terpenoids [12]. Phytochemicals have been scientifically validated over the years to provide health benefits for humans [13]. For example herbal remedies used as sedative and stomachic mixtures contain mainly aromatic plant species which have therapeutic essential oils, possessing antibacterial, stomach-soothing and antispasmodic properties. Plant species which have a high tannin content are used in mixtures for diarrhea and stomach ulcers; generally showing antimicrobials, astringents and anti-inflammatory activities [14, 15]. Bioactive and disease preventing phytochemicals present in medicinal plants are shown in **Table 1**.

Class	Characteristic	Use	Pharmacological activity	Reference
Alkaloids	Organic nitrogenous bases, bitter taste, colorless/yellow, crystalline solids, liquids	Biosynthesis of pharmaceuticals	Anticancer, antimicrobial, amoebicidal, anti-inflammatory,	[16, 17]
Saponins	Soap-like forming property, bitter taste,	Detergent, wetting and emulsifying agent	Antifeedant, antifungal, antiobesity, antioxidant	[18]
Tannins	Water-soluble, leather hides,	Used for cationic dyes, production of ink,	Antimutagens, anticarcinogens, antimicrobial,	[12, 19]
Flavonoids	Free radical scavenger	Prevents microbial infection,	Anti-inflammatory, antimicrobial, antibacterial, antioxidant	[20]

Table 1. Properties of some major constituents of medicinal plants.

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3. Historical perspective of herbal medicine

The use of plants as medicines dates 60,000 years ago according to ancient Babylon reports. In Egypt and China written material on herbal medicine dates approximately 5000 years back, in Asia Minor and Greece it dates 2500 years ago [21]. There are various herbal medicinal systems, the practices and philosophy of each are influenced by the region within which it first evolved [22]. In China, they have their own system known as the Traditional Chinese medicine which has been used throughout history [23]. The oldest known herbal book in the world *The Devine Farmer's Classic of Herbalism* was compiled in China about 2000 years ago, numerous herbal pharmacopeias and various monographs on specific herbs exist through the composed information on herbs [3]. Ayurveda, a healthcare system that has been used in India for over 5000 years, that was founded by ancient Hindu healers and saints. Its *materia medica* provides a comprehensive description of over 1500 herbs and 10,000 formulations. The Indian government has recognized Ayurveda to be a complete healthcare system in comparison to western medicine [24]. Kampo medicine, the Japanese herbal medicine dates back over 1500 years with approximately 148 formulations [25].

4. Common herbal medicines

4.1. *Echinacea purpurea*

Echinacea has an extensive history on the use as medicines, mainly for infections such as septic wounds and syphilis, also as an anti-toxin for snakebites [26]. The species *Echinacea purpurea* from this genus is a well-known medicinal plant used in treating snake bites, toothache, skin disorders, bowel pain, chronic arthritis, seizure and cancer, traditionally [27]. *E. purpurea* possesses secondary metabolites including caffeic acid derivatives, alkamides, glycoproteins and polysaccharides alleged to be biologically and pharmacologically active [26, 27]. Allergic reactions can occur and are usually mild, but individuals with a history of asthma, atopy, or allergic rhinitis may experience severe allergic reactions that include dyspnea and anaphylaxis [26, 28]. Other adverse effects include abdominal pain, urticarial, nausea, erythematous, rash and pruritus [26].

4.2. Garlic

Traditionally, garlic (*Allium sativum*) has been used to treat colds, chronic bronchitis, coughs, respiratory catarrh, bronchitic asthma and influenza [26]. Additionally it is used mainly to manage hypertension and hypercholesterolemia. It contains alliin, which upon chopping or crushing is activated by alliinase in the absence of acid or heat [8, 28]. Allicin produces both hydrophilic (cysteine) and lipophilic (sulfides, ajoene) sulfur compounds which are accountable for pharmacologic effects. Garlic is administered via oil-filled capsules, condensed dried powder, and enteric-coated tablets and capsules; it is also aged in aqueous alcohol [28]. Adverse effects of garlic extract include burning sensation in the gastrointestinal tract, diaphoresis, nausea, and light headedness. The extract may also cause contact dermatitis and excessive ingestion may cause morbid spontaneous spinal epidural hematoma [8, 28].

4.3. Ginkgo

Ginkgo (*Ginkgo biloba*) and its leaf extracts contain active compounds which have been found to improve circulation and cognition. The extracts are sold in both solid and liquid forms and appear to be relatively safe [28]. Medicinal use of ginkgo dates back 2800 BC, the seeds are used as an expectorant, antitussive and anti-asthmatic, and the leaves aid in asthma and cardiovascular disorders [26]. The most common side effects are dizziness, headache, restlessness, vomiting, nausea, diarrhea and dermal sensitivity. Cross-allergenicity with poison ivy has been reported. Ginkgo as an inhibitor of platelet-activating factor may alter bleeding times, therefore it may cause an upsurge of the anticoagulant effect of aspirin and warfarin [28].

4.4. Ginseng

Ginseng (*Eleutherococcus senticosus*) is the fourth most extensively used Chinese medicinal herb, treating a variety of conditions. It is used as a general tonic and is claimed to increase the body's resistance against stress and builds up general vitality besides treating diabetes, depression and hypertension [29]. Products are made from dehydrated roots, such as extracts, elixirs and tea, also tablets and capsules. Numerous active constituents, ginsenosides, respectively have specific pharmacologic effects that sometimes compete with each other, thus the whole root is used in preparations [28]. Excessive doses of ginseng have been reported to cause insomnia, agitation and elevation of blood pressure, mastalgia and vaginal bleeding have been detected at acclaimed doses [8].

4.5. Kava

Kava (*Piper methysticum*) is believed to be beneficial for health by soothing nervous illnesses, inducing sleep and relaxation, reducing weight and counteracting fatigue. It is often used to treat asthma, urinary infections, fever, headaches, syphilis, rheumatism and gonorrhea, it is also used as a stomachic and diuretic [26]. Kava is commonly known as an anxiolytic agent. Reported side effects include dizziness, gastrointestinal discomfort, headaches and localized numbness after oral ingestion. Long term use at high doses may cause scaly, dry skin and discoloration of nails and the skin, eye redness and photosensitivity. Diplopia and photophobia may also occur after excessive consumption. Interaction of central nervous system depressants and kava may lead to a comatose state [8, 28].

4.6. St John's wort

St John's wort (*Hypericum perforation*) is specified to possess astringent and sedative properties. It has been used for neuralgia, excitability, fibrositis, menopausal neurosis, sciatica, wounds, depression and anxiety. Modern interest is focused on its antidepressant use [26]. St John's wort possesses active compounds such as hyperforin, hypericin and melatonin. It is reported to have side effects which include fatigue, constipation, nausea, vomiting, dry mouth, headaches, dizziness and photosensitivity [8].

4.7. Ma huang

Ma huang (*Ephedra sinica*) is a medicinal plant traditionally used to treat hay fever, bronchial asthma, colds, coughs, enuresis, myasthenia gravis, narcolepsy, rheumatism and chronic postural hypotension. It contains a number of alkaloids including ephedrine and pseudoephedrine [26]. Ma huang is not considered as a safe herb, with adverse effects including insomnia, dizziness, headaches, nervousness, stroke, seizures, hypertension, psychosis, irritability, myocardial infarction, premature ventricular contraction and death [28].

4.8. Valerian

Valerian (*Valeriana officinalis*) is a medicinal plant commonly used as a mild sedative and anxiolytic. Numerous constituents are found in the root of this plant, valerenic acid (C15 sesquiterpenoid) and valerena-4,7(11)-diene have been suggested to possess the active ingredients accountable for the sedative effect [30]. Valerian has been reported to cause excitability, headache, gastrointestinal complaints and ataxia. An oral overdose may result in abdominal cramps, onset of fatigue, light headedness, chest tightness, and tremors of feet and hands [28].

5. Why people use herbal medicine?

5.1. Accessibility and affordability

The documentation of medicinal plants of numerous cultures is extensive, these plants have been used in treating various diseases even without the knowledge of their constituents and accurate functions [31]. The high practice of herbal medicine is due to cultural acceptability, as plant remedies have been around for centuries [32]. In countries such as Zambia, Tanzania and Uganda the ratio of herbal medicine practitioners to the population was found to be 1:200–1:400. However, the ratio of western medicine practitioners is 1:20,000 or less [33]. A survey conducted in 1991 revealed that traditional practitioners in sub-Saharan Africa out number western practitioners by 100 to 1 [34]. Herbal medicine has remained affordable in comparison to high cost western medicine [35]. In over populated countries such as India, the rural population has almost no access to modern medicine, therefore, they are compelled to rely on herbal medicine for their basic healthcare needs [36].

5.2. An alternative approach to healthcare

Plants are perceived to be healthier than conventional biosynthetic drugs. Reports on conventional drugs adverse effects has been found to be much higher compared to herbal toxicity reports [4]. Other reasons for the use of herbal medicine include: (i) several claims on the efficacy and safety of plant medicines [11], (ii) improvements in the quality of herbal medicines with the development of scientific evaluation [21], (iii) to relieve symptoms related to chronic or

terminal illnesses [37], such as HIV/AIDS, malaria, diabetes and sickle-cell anemia [38]. A survey conducted in the USA showed that 78% of patients living with HIV/AIDS use some form of herbal medicine. In such cases, western medicine is perceived to have failed the public [4].

6. Challenges facing the use of herbal medicine

6.1. Safety and toxicological concerns of herbal medicine

The products of herbal medicine have a long history of being safe [39], however the misuse of these medicines may have side effects due to toxic constituents [29]. In some countries, toxicological assessment of herbal medicine and associated products are not employed before placing them in the market [8]. Herbal medicine of a single plant may contain hundreds of constituents and mixed products may contain numerous times that number. The time required to isolate every single active ingredient from every herb would be tremendous [22]. Moreover, these countries lack operative machinery to legalize manufacturing quality standards and practices. Thus making hazardous herbal products continually available to consumers [8]. A study related on the use of traditional eye medicine reported that it caused 26% of childhood blindness in Malawi and Nigeria, and 25% of corneal ulcer in Tanzania [4]. Pyrrolizidine alkaloids have been reported to be fatal, these are molecules within certain plants causing hepatotoxicity through a veno-occlusion illness [10]. Nausea and probably vomiting can occur with some herbs such as ephedra and echinacea. Herbs consumed as teas have been reported to cause diarrhea and hematologic, cardiac and gastrointestinal effects [40]. Herbal products from Asia have been reported to be problematic since it contains numerous contaminants. A study on the assessment of 260 Asian patent medications reported that 25% of these products contained high levels of heavy metals and 7% contained undeclared drugs, decisively and unlawfully added to produce desired effects [41].

6.2. Challenges of quality control

Quality control of herbal drugs and their formulations is of vital importance in order to justifying their acceptability in modern system of medicine. A major concern facing the herbal drug market is the unavailability of the source and quality of herbal materials and their formulations [42]. Other factors such as the temperature, use of fresh plants, light exposure, nutrients, water availability, period and time of harvest, method of harvesting, drying, packing, storage and transportation of raw herbal material, etc., can critically affect the beneficial value of medicinal plants and quality. Some plant elements are heat labile and the plants containing them need to be dried at low temperatures [11].

6.3. Lack of knowledge about herbal medicine within government regulations

Herbal remedies can be sold as supplements, for supporting, maintaining, stimulating and promoting health in many countries. These supplements require a label that defines the ingredients are intended to affect the functions within humans in line with Act 101 of 1965 and amendments (2002) [14]. The evidence on the efficacy, safety and quality of such herbal products is unknown, therefore, raising a concern on the safety of these herbal medicines [8].

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6.4. Need for scientific and clinical evaluation of herbal medicine

The concern surrounding safety of herbal medicinal products is increasing [8]. In order to allay these concerns and achieve public reliance on herbal medicine, manufacturers, researchers and regulatory authorities must follow inclusive clinical trials and vigorous scientific methodologies to ensure the quality and safety of herbal products [41]. The safety evaluation of any herbal drug considers two important factors; the nature and significance of the adversarial effect. Toxicity screening can disclose some of the risks related to the use of herbal medicine [43]. In 1991, WHO issued guidelines for the assessment of herbal medicine which include: (i) Quality assessment: crude plant material; plant preparation; finished product. (ii) Stability: shelf life. (iii) Safety assessment: documentation of safety based on experience or toxicology studies. (iv) Assessment of efficacy: documented evidence of traditional use or activity determination (animals, human) [6].The US Food and Drug Administration (FDA), the International Conference on Harmonization (ICH) and the United States Pharmacopeia (USPC, 1994–2001) follow these guidelines to validate herbal products [1].

7. National policies of herbal medicine

A national policy on herbal medicine may include the following: a defining role of herbal medicine in the health care system, provision for the necessary regulations and laws, contemplation of intellectual property concerns [22]. National policies vary from country to country regarding herbal medicine. Herbal medicines are classified as either prescription or non-prescription medicines. The Working Party on Natural and Nutritional Supplements was established by the Australian Parliament to evaluate the safety, efficacy, quality and labeling of herbal products (Therapeutic Good Act, 1990). The act states "that traditional claims for herbal remedies be allowed, providing general advertising requirements are complied with and providing such claims are justified by literature references" [11]. Herbal medicine in Canada must meet the terms of the National Health Products Regulations. In accordance to these regulations, a product license is required for all herbal products to be sold in Canada. The recommended use, potency, comprehensive information on the medicinal constituents, source and nonmedicinal constituents need to be provided in order for a license to be granted. The companies that manufacture, pack, label and import herbal medicine also need a site license [3].

The Dietary Supplement Health and Education Act (DSHEA) of 1994, states that any herb, natural and botanical concentrate, constituent and metabolite of extract, is categorized as a dietary supplement. These supplementations do not need any sanction from the FDA. Herbal medicine which is categorized as dietary supplements under DSHEA, are alleged to be safe and the FDA does not have the authority to require them to be approved for efficacy and safety before they enter the market. However, manufacturers of these herbal products are required to provide purity and identification standards, and confirm that claims made concerning their products are precise [39, 44].

In Chile the Unidad de Medicina Tradicional was established in 1992, with the aim of incorporating herbal medicine with established efficacy into health programs (Law No. 19.253,

October 1993). Directive No. 435/81 defines herbal drugs with therapeutic proposed claims and/or dosage recommendations as being medications, restricted from being sold in drugstores and pharmacies. Registration for marketing authorization is required for herbal products. These products are lawfully distinguished as follows: (1) drugs intended to alleviate, cure or prevent disease; (2) food products with therapeutic properties and for medicinal use, and (3) food products with nutritious purposes [11].

In Europe, the European Directive 2004/24/EC released in 2004 by the European Parliament and by the Council of Europe provides the guidelines for the use of herbal medicines. The guidelines state that for herbal medicine to be released in the market, it needs authorization from the national regulatory authorities of each country in Europe and the herbal products must have a standard level of efficacy and safety. The registration of herbal products from outside the European Union (EU) require substantial evidence of their medicinal use, at most a period of 15 years within EU and 15 years elsewhere [3]. In Germany, more than 300 monographs on medicinal plants have been regulatory evaluated, and in France more than 200 herbs have been recorded as acceptable ingredients of herbal medicine [4].

The widespread use of herbal medicine in Brazil is favored by two present public policies i.e. the National Policy on Integrative and Complementary Practices in the Public Health System (PNPIC) and the National Policy on Medicinal Plants and Herbal Medicines (PNPMF), through the Law 971/2006 and the Declaration 5813/2006, respectively. Currently, 382 herbal medicines are registered in Brazil, 357 of these are single medicines and the other 25 are composed of more than one medicinal plant [45].

8. The market for herbal medicine in the developed world

Herbal medicine has gained increasing popularity in the last two decades in industrialized countries. The congress of the United States of America (USA) established the Office of Alternative Medicine in the year 1989 within the National Institute of Health (NIH). This was formed to interest scientists in the field of medicinal plants [3]. According to the 2007 NIH survey, 4 out of 10 adults (38.8%) and 1 out of 9 children (11.8%) used some form of herbal medicine [37]. In USA, presently about 25% of prescription drugs contain at least one plant derived ingredient [21], the herbal market in this country has doubled from $4 billion since 1996 [6]. In 1989, the European Scientific Cooperative on Phytotherapy was formed with an aim to advance herbal medicine [3]. The herbal medicine market in European countries has been growing steadily from $6 billion in 1991 to over $20 billion currently, particularly in Germany, France and Italy [4, 6]. In Germany, herbal medicine is identified as one of the elements of naturopathy [46], approximately 600–700 plant derived medicines are accessible and prescribed by approximately 70% of German physicians [47]. In 2011, 20% of herbal drugs were sold as prescriptions and 80% over the counter in Germany [46]. In the year 2005, The National Centre for Complementary and Alternative Medicine at the National Institutes of Health in the USA spent about US$ 33 million on herbal medicine, the National Canadian Institutes disbursed approximately US$ 89 million for research in traditional therapies in 2004. These scientific evaluations have led to an upsurge in the investment of herbal medicine [3].

9. Future prospects of herbal medicine

In the past decade, about 121 pharmaceutical products have been formulated based on herbal medicine knowledge [42]. According to literature at least 25% of modern medicines are derived from plants, such as aspirin, picrotoxin and numerous others are synthetic analogues built on prototype compounds isolated from plants [48]. Because of the increase in the acceptance of plant derived drugs, the use of plants in medicine as a source of therapeutic agents will expand rapidly in the future [42]. This has extremely increased international trade of herbal medicine, attracting a number of pharmaceutical companies, including the multinationals [11]. The interest of WHO by documenting the use of medicinal plants used by ethnic groups, has increased scientific validation of the use of these plants. This will make people better informed concerning the effectiveness and safety of the treatment [21]. The regulation of herbs has assisted in improving herbal products, however additional changes need to be applied to advance and indorse high quality research [10].

10. Conclusion

The use of herbal medicine is not restricted to developing countries. Over the years, there has been an escalating interest in the use of herbal medicine worldwide. This has greatly expanded the demand for plant products, since herbal medicine has an advantage of being inexpensive with minimal side effects compared to synthetic medicines. The growth of the herbal drug market has attracted pharmaceutical companies which in turn have driven scientific validation and clinical studies on herbal medicines. Thus far, few programs have been established to study the safety and efficacy of herbal medicines as originally proposed by the WHO Guidelines for the assessment of herbal medicines. These guidelines have been helpful in establishing the role of herbal medicine in the health care industry. However, the data to provide a precise assessment on the safety, quality and efficacy of herbal medicine is inadequate generating concerns regarding the use of herbal products.

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