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Herbal Medicines: Benefits and Risks

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ABSTRACT

The popularity of herbal medicines is growing, mainly because they are perceived as low risk and are often used over the counter in alternative and complementary medicine in the framework of primary health care. But, medicinal plant preparations should be used with caution, because they contain hundreds of active biomolecules with potential beneficial or even detrimental effects for health and disease. These active substances are often capable of modifying vital functions of the body and interacting with other medications the patient is on, with significant impact on the effectiveness and toxicity of pharmacotherapy. Herbal preparations may also contain pesticides, microbes, heavy metals, solvents and other contaminations that increase their toxicity potential. Misidentification of plant species and excessive amounts used in herbal preparations are also responsible for toxicity. Therefore, authentication of medicinal plant species and removal of harmful phytochemicals by producers combined with broad knowledge of regulatory authorities, health care professionals and the community on their pharmacological and toxicity activities, constitute a prerequisite that ensures the effectiveness and safety of herbal medicines as complementary or alternative therapies in the framework of primary health care.

Keywords: Herbal remedies; Herbal supplements; Healthcare; Herb-drug interactions

INTRODUCTION

For millennia medicinal plants have been used in traditional, alternative and complementary medicine including Siddha, Ayurveda and Chinese medicine for health maintenance, the prevention, diagnosis, alleviation of symptoms, as well as the improvement or even the treatment of various diseases.

(http://www.who.int/medicines/areas/traditional/definitions/en/). Currently, many herbal medicines and supplements are available over the counter and widely used by the general population, although there is no scientific evidence of their efficacy and safety. Notably, in the majority of African and Asian countries (~70-80%) their unique medical system was built on empirical and mounting knowledge on the use of herbal preparations for medical purposes. In particular, according to the records of the World Health Organization (WHO), over 80% of the world's population, mainly of developing countries including China, Cambodia, Thailand, Vietnam, India, Jordan, Chile and Saud Arabia use herbal preparations for medicinal purposes. Complementary and alternative medicines based on herbal preparations are now becoming main stream in several developed countries, such as the USA, the UK, France, Australia and Canada [1-7] (https://apps.who.int/gb/ebwha/pdf_files/WHA56/ea5618.pdf).

There are various reasons of the increasing use of herbal preparations in general population. In the developing countries, they constitute the main or sometimes the only source of health care, because they are accessible, trusted and culturally acceptable. Their affordability also makes them attractive in a universal environment of soaring health-care costs and austerity [8,9]. Feeling uncomfortable in discussing their medical problems and the fear of lacking confidentiality in handling their personal and health information, along with that of misdiagnosis and incorrect treatment in particular, in cases of non-verified symptoms or general malaise, are among the main reasons of the extensive use of herbal medicines and supplements by patients [3].

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The broad use of herbal medicines in the form of food, supplements and drugs [4], is based on the fact that the medicinal plants offer a vast repertoire of chemical diverse substances that are active molecules, capable of interacting with various macromolecules including proteins and DNA, thus exhibiting significant biological functions that are of therapeutic importance. It should be noted that in a total 56% of the prescribed drugs, the 24% are derivatives from medicinal plants, 9% are active molecules modelled from plant products and 6% are compounds directly extracted from herbs [10]. One should bare in mind though that herbs also contain biomolecules displaying detrimental effects for health and disease [1,11].

In recent years, pharmaceutical industry has turned its interest again to medicinal plants for the identification of novel molecules to treat mainly rare diseases and those resistant to known synthetic drugs. The mounting knowledge over the ages on the use of medicinal plants consists the basis for the development of new drugs displaying improved pharmacological and toxicity profiles. The last decades, the revolutionary evolution in analytical and computational chemistry, biochemistry, molecular biology, pharmacogenomics and the high-throughput screening techniques of plants contributed decisively in the isolation and identification of numerous active biomolecules from the plants that along with the *de novo* computational or biotechnological synthesis of new molecules provide valuable therapeutic tools for the treatment of various diseases, including diabetes, hypertension, arthritis, heart failure, inflammation, infectious diseases, depression and cancer, among others [1]. Therefore, it is of paramount significance, the scientific community to acknowledge the value of medicinal plants and therefore, to work for the preservation of their biodiversity along with the wise and safe use of herbal medicines for therapeutic purposes, especially when the patient is already on medication that may interact with the active molecules included in herbal preparations exposing them to harmful side effects and modified drug efficacy [1,11]. This later issue is critical because, unlike modern medicines, clinical practitioners do not have enough scientific data on the risks and benefits of herbal medicines as rigorous clinical trials and post-approval surveillance are no mandatory to assess their effectiveness and safety [7]. Hence, herbal medicines are now in the centre of concern among health-regulatory authorities, health professionals and the community, imposing the readjustment of the framework of herbal medicines use and control (http://www.who.int/medicines/areas/traditional/definitions/en/) [7].

THERAPEUTIC APPLICATIONS OF HERBAL MEDICINES

Currently, thousands of herbal medicines and supplements are available over the counter for the general population in the USA and worldwide and they are used in the framework of complementary and alternative medicine under the term “integrative medicine” [12]. They are extensively used over the years to treat or prevent several diseases including arthritis, breathing and heart problems, stroke, obesity, gastro-oesophageal reflux disease, nasopharyngeal cancer, resectable gastric cancer, viral infections, stress, anxiety, dementia, hypertension, dyslipidemia and diabetes, just to name a few [2]. Although Surveys on the demographic characteristics of patients using herbal remedies have several methodological limitations (e.g. size of sample, sex, race and age of participants), some findings are very informative. It appears that white women and old people having higher education use herbal supplements more often than general population [12]. Patients mainly, with chronic diseases appear to seek alternative treatments based on herbal preparations, when their conventional disease treatments are challenging, and they do not guarantee their complete recovery [2,3]. Furthermore, over the counter and online/mail-order drug users, as well as patients with stroke use herbal medicines more often than others [2,12]. There is also a strong belief among many people that consuming herbal supplements favours health and longevity [2,4,6].

The last decades there is an increasing intense research on the potential beneficial effects of plant-based extracts and plant-derived substances on various diseases. In particular, several research groups worldwide have been engaged on intense research on their effects on brain functions, including *Olea europea*, *Salvia spp*, *Coffea arabica*, *Cannabis sativa*, *Ginkgo biloba L. Myrtillus* and *Withania somnifera*, among others [13]. They focus mainly on their effects on depression and the cognitive functions in patients with neurodegenerative disorders [14-17]. More information on these effects is available in the online recourses: Enethogen.com, erowid.org, botanical.com, maps.org, heffter.org, http://kidb.cwru.edu, http://mediplantepirus.med.uoi.gr

Since ancient times, several herbs, such as *Laurus nobilis*, *Arnica Montana*, *Helichrysum italicum ssp*, *Hypericum perforatum* and many others, containing alkaloids, steroids, flavonoids, polyphenolics and terpenoids with anti-inflammatory properties have been widely used for the alleviation of pain and other inflammatory disorders [18]. Nowadays, research focuses on identifying new molecules of herbal origin with efficient anti-inflammatory activity and better toxicity profiles than the currently used synthetic anti-inflammatory drugs [18].

Several plants contain compounds that directly affect blood vessels and the functional integrity of heart, including *Digitalis spp*, *Crataegus oxycantha*, *Inula racemosa* and *Commiphora mukul*, among others [19]. Preparations of these herbs administered alone or in combination, have been used for the treatment of heart failure, hypertension, angina and their lipid-lowering effects [19]. Preclinical studies reported also that various plant-derived substances and mainly, alkaloids [19,20], proanthocyanindins, saponins, glycosides, polyphenols and flavonoids exhibit also cardioprotective properties [21-27].

Since 1950 to day, except vinca alkaloids (vincristine and vinblastine), various plant-derived molecules with significant anticancer properties, such as taxanes (paclitaxel, docetaxel), podophyllotoxin, anthracyclines (doxorubicin, epirubicin, daunorubicin, idarubicin) and camphotechin have been included in standard anticancer treatment protocols [28]. Furthermore, several dietary phytochemicals, such as resveratrol, curcumin, genistein, allicin and lycopene appear to display anticancer properties [28]. The last decades, anticancer research focuses on identifying new lead plant-derived anticancer molecules, more effective and less toxic than the current widely used

anticancer drugs.

It should be noted also that several phytochemicals are effective against a broad spectrum of pathogens including bacteria, mycobacteria, fungi, viruses and protozoa. The plant-derived antimicrobials are in most cases, secondary plant metabolites belonging to the family of flavonoids, flavones, flavonols, quinones, alkaloids polypeptides, phenols, tannins, coumarins, terpenoids and essential oils, present in species of *Ranunculaceae*, *Mentha suaveolens*, *Pinaceae*, *Apiaceae*, *Cupressaceae*, *Futua pilosa*, *Capsicum annuum*, *Mangifera indica*, *Coffea arabica*, *Allium sativum* and *Daucus carota*, among others [29-47].

There is also a broad experience worldwide in the use of various medicinal plant formulations in popular medicine for the treatment of Type II diabetes [48,49] and the management of hepatic and gastro-intestinal disorders, such as ulceration and gastritis [50-53].

DISCUSSION

Toxicity and Complications from the Use of Herbal Medicines

There is a widespread belief in the community that herbal medicines and dietary supplements are natural and therefore, safe [7] and this belief is largely associated with the sex, race, education level, the income and place of residence [54]. Although indeed, several herbal medicines are of promising potential and have been widely used, there is no monitoring of their effectiveness and safety regarding their effective dose, side effects and toxicity. Therefore, knowledge on their safe and effective use is very limited thus making the promotion of their rational use difficult [3]. The safety of herbal preparations is also compromised by their inadequate labelling, the lack of their appropriate quality control and patient information [3]. It should be also mentioned here that the presence of various external factors in the herbal preparations including pesticides, microbial and mycotoxins contamination, radioactive contamination, fumigation agent residues, residual solvents and high levels of heavy metals can be a source of herbal-induced toxicity [55,56]. Many cases of toxicity have been also attributed to misidentification of plant species and the excessive amounts of them used in herbal preparations [56].

Numerous of scientific reviews reveal mild adverse effects associated with the use of herbal medicines, but some of them may constitute severe health and life threats. In the broad array of side effects related to herbal preparations belong the pain, headache, allergic reactions, burning sensation, dermatitis, fatigue, confusion, dizziness, epilepsy, loss of consciousness, diarrhoea, gastrointestinal upset, constipation, nausea and vomiting, menstrual disturbances, loss of appetite, coagulation abnormalities, severe multi-organ hypoxic injury, carcinoma, congestive heart failure, tachycardia, coma and liver failure, among others [57].

The toxicity and adverse reactions of herbal preparations is closely related to the presence of various bioactive molecules and their toxic potential [58], and it can be more excessive in complex herbal mixtures containing hundreds of active compounds [56] potentially displaying hepatotoxic, genotoxic, cytotoxic, phototoxic, carcinogenic, nephrotoxic, neurotoxic and embryotoxic properties, among others [55,59-61]. These active substances may also interact with other drugs and supplements the patient may simultaneously receive, thus affecting their efficacy and toxicity profiles and the functional integrity of vital organs, such as the liver, brain and heart [56,62].

Here, several paradigms of herbal medicine-drug interactions are summarized. It is reported that garlic alters the pharmacokinetic profile of paracetamol and increases the risk of bleeding when it is concomitantly used with warfarin [63]. It is also reported that patients treated with aspirin or warfarin had severe spontaneous bleeding following *Gingo biloba* ingestion, whereas another patient with Alzheimer's disease on trazodone fell into coma [63]. Insomnia and nausea were reported in patients received influenza vaccine and ginseng. It also reported that echinacea potentially decreases the effects of immune-suppressants [64]. Interestingly, the St John's-wort (*hypericum perforatum*) appears to reduce the plasma concentrations of warfarin, oral contraceptives, cyclosporine, amitriptyline, digoxin, Indinavir and many more other drugs, thus reducing their effectiveness [63,65].

Therefore, standardization/quality control of medicinal plants used in herbal preparations, broad knowledge of medical practitioners and pharmacists, and community awareness of their use and safety are of immense importance to ensure the effective and safe use of herbal medicines in primary health care (PHC) [1,11,56].

CONCLUSION

The growing popularity of herbal medicinal preparations that are used without prescription in alternative and complementary medicine in the framework of PHC, requires assurance of their efficacy, quality and safety. Health care professionals and community should bear in mind that herbal preparations should be used with caution, because they contain hundreds of active compounds with potential beneficial or even detrimental effects for health and disease. They can modify vital functions of the body and interact with other medications the patient is on with determinant impact on the outcome and toxicity of pharmacotherapy. Therefore, herb-drug interaction is a serious challenge to human health and life and healthcare professionals should be aware of this potential.

At present, there is no monitoring and sharing information system among countries, health care authorities, practitioners and consumers on herbal medicine effectiveness, quality and safety (pharmacopoeia, education, research, recorded local traditional knowledge, websites, seminars, workshops etc.) that could assist enormously the effectiveness and safety of integrated medicine in PHC. As a consequence of this information deficit is the inadequate knowledge on herbal medicine's mode of action, potential side effects, interactions with other drugs and contraindications. It is conceivable though that only the rational use of high quality, efficacy and safety herbal medicines should be promoted. In addition, more robust preclinical and clinical studies to establish the efficacy and safety profiles of herbal medicines used in PHC should be encouraged. A major problem in the use of herbal remedies

in PHC is also the insufficient training of pharmacists, clinical and traditional practitioners on the accurate and safe handling of herbal remedies, who should be adequately trained. This training could be feasible in the framework of organized studies at a Bachelor's or Master's degree or through seminars and workshops. A subject on the use of herbal medicines in integrative medicine could be also added in the curriculum of modern Medical and Pharmacy Schools. Until then, Advisory committees on traditional/herbal medicine could guide health care practitioners in their decision-making process. Education of herbal medicine providers and patients/consumers is also crucial in order to prevent potential serious risks from the misuse of herbal remedies.

Based on available information and experience, it is mandatory, as it happens with other drugs for human and animal use, that the use of herbal medicines and supplements is covered worldwide by a drug regulatory framework to ensure that they meet the required standards of quality, efficacy and safety. Leading role in this regulatory readjustment should have the European Medicines Agency (EMA) in European Union, the Food and Drug Administration (FDA) in the USA, and the national drug administrations of the other countries, ideally in collaboration.

Therefore, the authentication of medicinal plant species, the removal of harmful phytochemicals from them, the thorough investigation of their pharmacological and toxicity activities in well-designed preclinical and clinical studies and the adequate training of health care practitioners, is imperative for the scientific community, the producers and regulatory authorities, who are responsible to disclose all essential information to the healthcare professionals and the community, in order to ensure the efficiency, quality and safety of herbal medicines in the context of PHC.

AUTHOR CONTRIBUTION

None.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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