REVIEW ARTICLE

Need of Innovative Research in Herbal Pharmacotherapy for Better Therapeutic Efficacy and Safety--a Review

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ABSTRACT

Use of traditional medicines to provide relief to mankind from various illnesses is an age-old practice widely cited in history. Nature has been serving as the basic and the strongest pillar of healthcare providing impetus to the conventional system of medicine and synthetic/allopathic medicines since prehistoric times. The revolutionary developments in the field of modern medicine almost substituted the use of traditional medicines in most of the countries. But in the current scenario, ever increasing cost and side effects are forcing people to move back towards green pharmacy. Unfortunately, less attention is paid towards pharmacovigilance of crude drugs/herbal raw material as well as herbal medicinal products (HMPs) as compared to the allopathic medicines that are prepared in pharmaceutical industries. Moreover, scientific research in this discipline has usually focused on the natural product chemistry and isolation of lead compounds from traditional medicines. Presently, modern research has started to focus on the pharmacological action and standardization of herbs and herbal formulations. However, an urgent need of innovative research exists in the fields of herbal pharmacotherapy, herbal biopharmaceutics (pharmacodynamics and pharmacokinetics), herbal toxicology, herb-herb interactions, especially in case of poly-herbal formulations, herbal bioequivalence, and other efficacy and safety related issues. This modern approach will open new horizons in the field of modern herbal pharmaceutical product development, hence better and safe means of herbal pharmacotherapy.

Key words: herbal formulations, crude drugs, herbal pharmacotherapy, herbal biopharmaceutics, plant toxicology

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عنوان: نباتات کے زریعے علاج کو مزید موثر، محفوظ اور بہتر بنانے کے لیے جدید تحقیق کی ضرورت پر ایک جائزہ۔

خلاصہ: جڑی بوٹیوں کی مدد سے مختلف بیماریوں کے روایتی علاج کے آثار تاریخ میں گہرے پائے جاتے ہیں۔ اسی لیے آج کے جدید دور میں بھی قدرتی جڑی بوٹیوں کو جدید زمانے کی ادویات سازی کے لیے ایک بنیادی اور طاقتور زریعہ سمجھا جاتا ہے۔ دواسازی کے شعبہ میں اس انقلابی ترقی نے اکثر ممالک میں روایتی ادویات کے متبادل کی حیثیت حاصل کر لی ہے۔ لیکن اس دور میں ادویات کی بڑھتی ہوئی قیمتوں اور صحت پر مختلف اثرات مرتب ہونے کی وجہ سے لوگ دوبارہ سے نباتاتی ادویات کی جانب توجہ دے رہے ہیں۔ بدقسمتی سے نباتاتی ادویات حاصل کرنے کے لیے نباتاتی خام مال کے حصول اور ان سے بنی ہوئی ادویات عدم توجہ کا شکار ہیں جبکہ ڈاکٹری دواویں جو دواساز فیکٹریوں میں تیار کی جاتی ہیں ان پر زیادہ توجہ دی جاتی ہے۔ جبکہ اس فیلڈ میں کی جانے والی سائنسی تحقیق میں قدرتی اجزاء اور روایتی قسم کی ادوایات سے بنیادی مرکبات پر زور دیا گیا ہے۔ آج کے دور میں نباتات اور ان سے حاصل ہونے والی ادوویات کے معیار اور فارما کولوجیکل اثرات کو جدید تحقیقات شروع ہو چکی ہیں۔ جبکہ ہربل فارما کوتھراپی کی فیلڈ میں اس کو مزید بہتر، موثر اور محفوظ بنانے کے لیے اختراعی تحقیق کی فوری ضرورت ہے۔ یہ نئی تحقیق نباتاتی دواسازی کے میدان میں نئے ہربل طریقہ علاج کو مزید بہتر، موثر اور محفوظ بنانے کے لئے بہترین ثابت ہو سکتی ہے۔

Historical Background

Nature is the first source that was utilized by man in order to treat various diseases and to maintain health. The history of consumption of crude drugs from natural (plants, animal, mineral, and marine) sources in the treatment and prevention of illnesses is as old as the human civilization itself. Through ages, knowledge and utilization of drugs from natural origins grew and moved towards modernization. In the 18th century, the discipline dealing with this area of drug formulation was given the name of Pharmacognosy that is considered the mother field of all other departments of pharmaceutical sciences.

Later on, the discovery of natural biosynthetic pathways in plants confirmed the presence of phytochemical

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constituents in them responsible for therapeutic activity of particular crude drugs. Isolation and structure elucidation of such biosynthetic compounds from plants resulted in the formation of their synthetic analogues that were started to be used as allopathic/conventional medicines[1,2]. The era of conventional medicines continues to grow and the modern pharmaceutical industry is still developing. New scientific and innovative ideas are emerging rapidly in pharmaceutical sciences not only in terms of providing better health services but also for improving the dosage form designs and drug delivery systems.

The revolutionary development in the field of conventional medicines had gradually replaced the use of traditional medicines in 19th century especially in the developed countries. After the advent of modern and highly technical chromatographic and spectroscopic techniques, the experts in the field of Pharmacognosy and natural product chemistry focused their research mainly on the isolation and structure elucidation of natural biosynthetic compounds from plants and other natural sources that served as lead compounds or model for the synthesis /semi synthesis of their structural analogue. On the other hand, people in the developing countries continued the use of traditional medicines under different titles. Eventually due to ever increasing side effects and some other reasons, people of the developed countries have found renewed interest in natural medicines to improve their health and well being[1-3].

Current Global Situation of the Trade and Commerce of Herbs and Related Natural Products: In the current scenario, people are interested in green pharmacy not only for the treatment and prophylactic action of diseases but also to improve their health with dietary supplements. Various forms of traditional medicines and practices have been combined under the umbrella of Complementary and Alternative System of Medicine (CAM).

As per statistics provided by World Health Organization (WHO), 70-95% population in the developing world and 70-90% in the developed countries rely on CAM[3]. Researchers from various sectors especially pharmacognosists and scientists of natural product chemistry, pharmaceutical companies, entrepreneurs, regulatory authorities, World Health Organization and other health agencies from all over the world are now paying attention towards the field of medicines and related products derived from natural sources. In Western Europe, the annual revenue of traditional medicines reached US$ 5 billion in 2003-2004, US$ 14 billion in China (2005), US$ 1 billion in Japan (2006), US$ 1.86 billion in Australia (2004–2005), and sales of US$ 160 million was estimated in Brazil in 2007. By the year 2008, the annual global market of traditional medicines was estimated as US$ 83 billion. These market estimates suggest that the rate of growth in traditional medicine product sales in recent years amounts to somewhere between 5% and 18% per annum[4].

Utilization and Scope of Herbs and Related Natural Products: Besides medicines and dietary supplements, nature, especially the plant kingdom, provides other products that improve a person's quality of life and well-being e.g. products containing pesticides of natural origins that control the spread of various vector borne diseases via eliminating their responsible vectors like mosquito repellent lotions which help in controlling malaria and dengue fever. Moreover, with the help of natural pesticides, deterioration and spoilage of herbal raw material/crude drugs as well as other edible items is minimized with lesser toxicity e.g. pyrethrum flower, derris, lonchocarpus, nux vomica, eucalyptus oil, red squill, tobacco, phytolaccca berries etc[2]. On the other hand, a variety of fibers obtained from plants, animals, and mineral origins are utilized in the production of various groups of surgical dressings i.e. gauzes, dressings, bandages, sutures, and ligatures and so on. Similarly, the base of the modern biological products including immunizing biologics, allergen immunotherapy, blood and hormonal products is also provided by nature. Last but not the least, the role of natural compounds can never be ignored in the field of cosmetology also[1,2].

However, in this review, our main emphasis will be on the new dimensions that are being practiced and the need of further innovative researches that are required in the field of herbs and the herbal medicinal products (HMPs) prepared from them. This will help in setting new goals for the production of quality herbal products under pharmaceutical guidelines as well as better and safer practice in the field of herbal pharmacotherapy.

Advancements Required in Herbal Pharmacotherapy: A lot of research work has been done and is in progress regarding the pharmacological actions and isolation of phytochemical compounds from natural source all over the world. But the popular trend of utilization of traditional medicines and its ever increasing global demand, have drawn attention towards some different parameters like the manufacturing of quality approved herbal formulation, betterment in their available dosage forms, authentication of therapeutic efficacy, and safety related issues.

Being the drug specialist, it is the responsibility of the pharmacist to ensure the efficacy, safety, and quality of herbs and herbal medicinal products (HMPs) just like in the case of conventional medicines. Innovative researchers all over the world, regulatory authorities in various countries, and different national and international health agencies and organizations recommend to prepare and standardize crude drugs as well as HMPs according to international standards and pharmacopeia-defined procedures and limits[5-13]. This practice is essential and the reason behind this is to ensure the efficacy of the traditional medicines used in herbal pharmacotherapy and to minimize the potential risk of adverse reactions and toxicities that may be associated with their use.

It is the need of the time that in addition to the valuable scientific work that is already being done in various fields of pharmacy; some other innovative ideas should also be included not only in the research of Herbs and Herbal Medicinal Products but also the manufacturing of these nature sourced phytopharmaceuticals must be carried out using modern procedures and techniques. In addition, upgradation of crude drug industry should also be done according to the WHO guidelines i.e. agriculture of herbal flora, collection of fresh medicinal plants, drying, transportation, storage, and sale should be monitored according to the quality standards. High quality crude drugs provide basis for better herbal pharmacotherapy either used alone or in combination in CAM or as a raw material to be further utilized by herbal industry for the preparation of herbal formulations. Lastly, the status of herbal pharmacotherapy and practice should also be modernized according to the global healthcare trends. These points have been summarized in figure 1

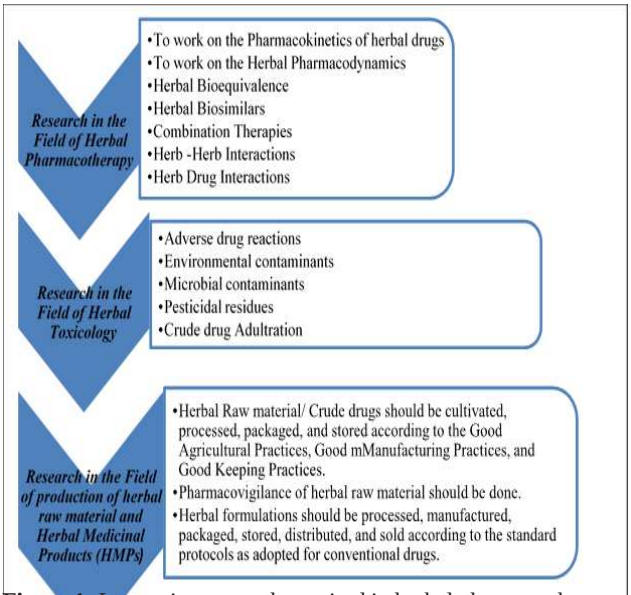

Figure 1: Innovative research required in herbal pharmacotherapy, Toxicology, and production of herbal raw material and HMPs

Innovative Research in the Field of Herbal Pharmacotherapy Need of Studies in Herbal Bio Pharmaceutics in Phytolabs: Biopharmaceutics in the field of herbs and related herbal formulation is the need of the time. To carry out studies related to the herbal bioavailability, herbal pharmacokinetics (exposure of drug to the body), and herbal pharmacodynamics (response of drug) is a very difficult task especially challenging in the case of polyherbal formulations. However, only such studies can confirm and validate the dissolution, disintegration, absorption, metabolism, and excretion of the drug in vivo[14-17]. The biosimilars and bioequivalents of herbs and herbal formulations, that will be used to replace any herbal drug with another one in case of shortage of the required herb on scientific grounds, can be found on the basis of the above information only.

Similarly, mechanisms of action of herbs and HMPs should also be investigated. Herb-drug interactions and herb-herb interaction are very important topics. Many herbs can produce synergistic or antagonistic effects on allopathic medicines. A lot of research work has already been done in this regard and should be continued in future so as to avoid any harmful effects in case of co-administration of herbs and synthetic drugs[18-20].

Innovative Research in the Field of Herbal Toxicology: It is a common misperception that since traditional medicines are derived from nature so these are safe and free from any kind of side effects. This idea is dangerously false because green pharmacy is directly related to nature so any destructive activity in nature will definitely affect the quality of the herbal traditional medicines. Due to the ever increasing rate of pollution, the natural drugs coming from plant and animal sources are also being affected by environmental contaminants[21-25]. Herbal or natural drugs may also suffer from biodiversity and gene manipulation due to global warming. There are evidences of detection of toxic heavy metals (Pb, Cd, As, Hg)[25-32], pesticide residues, radioactive elements, and microbial contaminants in crude drugs as well as in Herbal Medicinal Products (HMPs) made from them. World Health Organization (WHO) and other health agencies of the world always stress on checking the environmental contaminants in herbal drugs and provide information regarding the toxicities of these agents with especial reference to the heavy metals. It is now becoming official in the United States Pharmacopoeia (USP) to carry out necessary tests regarding the presence of heavy metals in herbal pharmaceutical products and dietary supplements[33-40].

Besides the environmental contaminants, the toxicology of the herbs itself is a big problem that should be properly addressed. Because the pharmacotherapeutic activity of the herbs and related formulations are due to the presence of active phytochemicals constituents/ secondary metabolite (alkaloids, glycosides, tannins, lignins, flavonoids etc.), therefore some side effects must be produced by these herbs. These drugs are also metabolized by the body so their degradation products or metabolites are also produced. It is also important to find out whether these drugs are metabolized in the liver or the kidneys[41-43].

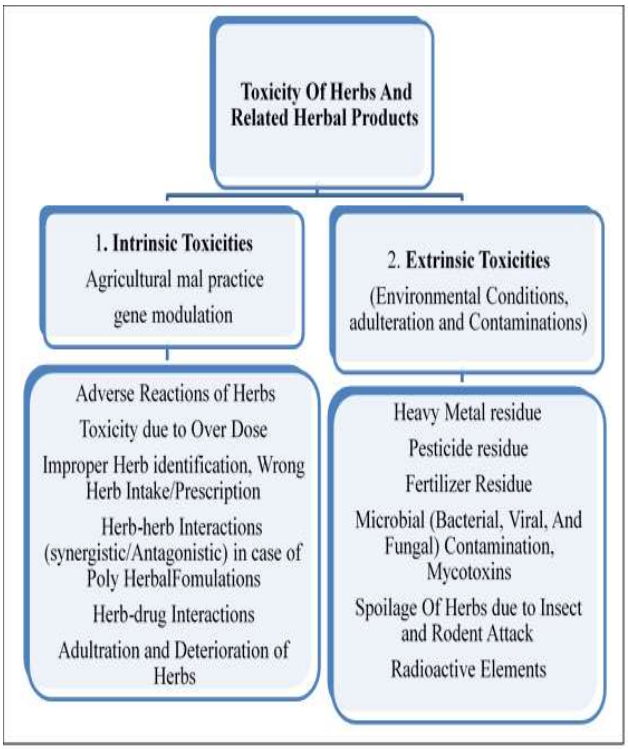

Figure 2: Factors affecting the toxicology of Herbs and related Herbal Medicinal Products

Figure 2 represents a summary of both internal as well as external factors that may lead to different types of herbal toxicities and adverse reactions; hence affect the safety parameters of traditional medicines. The practice of assessing the quality and safety parameters of herbs and related herbal products must be carried out not only for the sake of better health services provided to the patients that rely on traditional medicines, but also for the better standard of herbal drugs utilized in herbal pharmacotherapy.

Advances Required in Production of Herbal Raw Material/Crude Drugs and Herbal Formulations

Herbal formulations should be manufactured, packaged, stored, and sold in the same manner as the conventional medicines. It must be produced under strict pharmaco-vigilance according to the CGMP (Current Good Manufacturing Practices) and must pass through all quality control tests. All of these steps should be verified by Quality Assurance and proper documentation records should be maintained[44]. In addition, since the quality of the herbal formulations basically depends upon the quality of herbal raw material i.e. crude drugs that actually contain active phytochemicals that produce the required therapeutic activity of the herbal formulations, so the production of quality raw material is a prerequisite. World Health Organization not only recommends such practices but also provides scientific documents related to the good agricultural and field collection practices that must be implemented and followed by concerned herbal companies and agricultural communities involved in crude drug industry[45-46].

Genomic research is also useful for the identification of medicinal plants belonging to various families and as a tool for the discovery of new pharmaceutical agents[47-50].

Conclusion and Recommendations: In the current scenario, people are moving back towards green pharmacy to prevent and cure various illnesses with Complementary and Alternatives Medicines. Herbs and other natural substances are also utilized as crude drugs taken as home remedies. Self medication of ready to use herbal formulation is also very common worldwide. However, these crude drugs and related herbal medicinal products are generally not processed in the same manner as conventional medicines. It is the need of time to pay attention to the efficacy and safety related issues. Innovative research regarding herbal biopharmaceutics, toxicities, and contamination and adulteration should be carried out in phytolabs and followed by herbal industries. Innovative traditional medicine practice in line with the current global trends, is essential to provide quality goods and services to the consumers of Traditional Medicines. Above all, the raw or crude natural material must undergo standardization process starting from the sensory method testing to microscopy alongwith DNA sequencing.

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