



INVITED ARTICLE

IDENTIFICATION OF A BIOMARKER: A NECESSARY APPROACH IN HERBAL INDUSTRY

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Abstract

Herbs have now become a source of medicinal drugs that can be used as supplements or as - drugs for ailments of various disorders. Moreover, complementary medicines (i.e a combination of standard drug and herbal drug) may help in reducing side effects and increasing the drug potency. The market for herbal drugs is growing rapidly due to its use in different industries like medicinal, nutraceutical, cosmetic and textile. Due to the large scale usage of herbal drugs, government and private organizations are searching for ways to determine their quality, consistency, efficacy and safety. Hence, in the preliminary stage herbal ingredients have to be standardized and potential biomarkers in these herbs needs to be identified. Also, research is being conducted to find low cost detection methods using common spectroscopic instruments for specific biomarkers. This review provides a brief overview of the importance of biomarkers in the herbal industry.

Keywords: *Biomarker, consistency, herbal drug, identification, standardization*

Abbreviations: World Health Organization, WHO; Department of Ayurveda, Yoga and Neuropathy, Unani, Siddha and Homeopathy, AYUSH; Indian Pharmacopeia, IP; United States Pharmacopeia, USP; European Pharmacopeia, EU; Therapeutic Good Administration of Australia, TGA

Introduction

Herbs are different in its own unique way; each herb has its own physiological, chemical, biological characteristics with a unique cultivation method required for each. Earlier some crops were only available in regions that were best suited for it, regions that had high yield and high active chemical constituents.

But, human beings changed the habitat of crops and consequently the genes of the seeds also changed, resulting in an increase in the chemical constituent content and a reduction in the growth period of these plants. Herbal drugs were foremost used in ancient times for treating various ailments and these drugs had a rapid onset of action and targeted specific efficacy. Nowadays, these herbs do not show such significant effects in clinical assessments. There are many reasons that may be causing a reduction in potency such as spurious seeds, non-favorable cultivation environments, usage of toxic chemical pesticides during cultivation, adulterated or spurious herbal drugs, inability to identify the correct solvent for extraction, herb-herb interaction and many more [1]. To overcome these limitations it is important to identify biomarkers.. A biomarker helps to identify a given herb both qualitatively and quantitatively. Moreover, the biomarker helps in identifying that the sample is the same as the prescribed by comparing with the said standard of the same species and this process may help in determining the presence of adulterated or spurious drugs. A biomarker can be easily identified by simple spectroscopic analysis, a cost effective method.[2].

Herbs are also identified by their physical characteristics (macroscopically and microscopically), chemical analysis and other physicochemical parameters [3]. There are many agencies that have standards available for these parameters such as the Indian Pharmacopeia (IP), United States Pharmacopeia (USP), European Pharmacopeia (EU) and Therapeutic Goods Administration of Australia (TGA). Recently, the Department of Ayurveda, Yoga and Neuropathy, Unani, Siddha and Homeopathy (AYUSH), under the Ministry of Health and Family Welfare(Government of India) has started developing monographs for herbs and herbal extracts by collaborating with different companies such as Green Chem, Bangalore, India. This will help in setting up a database that could be used as the standard for determining the herbs [4]. The World Health Organization (WHO) has also given different standards for research and evaluation in traditional medicine for different herbs [5].

Herbal fingerprinting

Research on herbal medicine is carried out to check the consistency, safety, quality, efficacy and its mode of action. Herbal drugs have been proved to have significant drug activity in different formulations but its consistency is sometimes questionable. To overcome this problem some standards need to be followed in steps such as identifying required species, maintaining the consistency of plant source (plant environment and cultivation pattern),

selecting the season of collection of plant parts and washing and storing these herbs. Herbal drugs are generally considered to be safe due to its natural origin. But, in today's world the use of chemical pesticide and different chemicals for the faster germination of crops with higher quantity output is generally preferred to increase profits. Due to the use of these chemicals the plant may absorb some of these chemicals and become toxic and the plant needs to be checked for its microbial load, heavy metal analysis and toxicity level and drug-drug interaction before usage [6]. In the health care system quality is an important criterion that has to be maintained.

WHO has given different standard monographs of different plant drugs to maintain the quality standard of a given plant drug.

Efficacy of a plant extract or a plant drug depends on the above characteristics of consistency, safety and quality. Various analyses should be carried out to know the effectiveness of the drug for a given symptom. Herb-Herb interactions and Herb-Drug interactions; if present, need to be specified to avoid adverse drug reactions. Also, it is conceptualized that the slow mode of actions of herbal drugs may be due to fact that the above criteria are not followed [7]. Moreover, the active chemical constituent from the plant for the required activity needs to be isolated. This will help in determining the higher efficacy and identification of the constituent giving the said activity [8].

Application of Biomarkers

Biomarkers help in the identification of a given disorder and detect the presence of a compound in a given product. In the herbal industry, biomarkers play an important role in identifying herbs and in identifying the chemical constituent giving the respective herb activity. In herbal drugs, sometimes adulterated and spurious drugs are also used. The low quality/sub-standard drugs are generally mixed with the pure drugs to increase the profit margin. In order to identify the correct drug and its constituent, the biomarkers play an important role [9]. Biomarkers ensure that the distributor is providing the correct sample. There are various detection methods for identification of biomarkers such as the ultraviolet visible spectra, high performance thin layer spectroscopy spectra, high performance liquid chromatography spectra, infrared spectra and many more. The simpler the method, the faster and more cost effective it is.

Herbal drugs have complex constituents and identification of these active constituents can be difficult. There are some markers that are present in all the species of one genus so identification of the correct biomarker is important [10].

Regulatory Requirement

Regulations may vary from country to country as they are influenced by their environmental conditions. Earlier the herbal industry didn't have any regulatory body. Nowadays, with use of plant hybridization techniques and other

chemicals for growth of herbs, the regulations have become necessary to maintain the safety and efficacy of these drugs [11].

The WHO has set guidelines to detect the botanical characters, sensory evaluation, foreign organic matter, microscopic, histological, histochemical assessment and quantitative measurement. The WHO has also set guidelines for, the physical and chemical identity, fingerprints chromatography, ash values, extractive values, moisture content, volatile oil and alkaloids tests. Also guidelines for the quantitative estimation protocols, estimation of biological activity, the values of bitterness, astringency hemolytic index, a factor swelling, foaming index, detail-toxicity pesticides residues, heavy metals, microbial contamination as viable count, total pathogens such as *E. coli*, *Salmonella*, *P. aeruginosa*, *S. aureus*, *Enterobacteriaceae*, microbial contamination and radioactive contamination needs to be followed. In India, the herbal products must satisfy the requirements specified by the Department of AYUSH, a department that is preparing the standards for herbs and herbal extracts. The other requirements that need to be followed are specified in the Food, Drug and Cosmetic Act. Now, regulatory authorities have started to be focused on labeling requirement such as the botanical source of the herbs, the quantity used and the expiry of the same [4].

In the United States, herbal drugs come under the purview of the Dietary Supplement Health and Education Act,

which states that any herb, botanical and natural concentrate, metabolite and constituent of extract, is classified as a dietary supplement. Moreover, dietary supplements do not require approval from Food and Drug Administration (US FDA). USFDA considers dietary supplements safe and only requires that the label is not misleading or adulteration/spurious drugs are not added. The label should specify all the GLP criteria like the drug intended use, side effect if any, drug-herb interaction and dosage of the product [12]. The European Directive provides the guidelines for the use of herbal medicines pertaining to Europe. European laws are very stringent towards the use of herbal medicine. They have stringent measures such as mandating that the herbal medicinal products need to be medically used for at least a period of 30 years in the European Union, at least 15 years within the EU and 15 years elsewhere for products outside the EU.

The monographs of the products should also be attached with comparison to the standards [13].

Perspective

Since ancient times, herbs have been used as medicines for treating various disorders and as supplements for prevention of the disorder. Medications currently available are generally derived from plants or from the bases of plant drugs [14]. So, it is necessary to prove the safety and efficacy of these herbs with scientific evaluations. Due to different plant cultivation regions and hybridization of plant parts, the identification of the plant material is

important for better efficacy and activity [15]. Also, the consistency of the herbs needs to be evaluated with the available spectroscopic techniques. For this reason, a biological fingerprinting or a biomarker is required to ensure the consistency, safety, quality, efficacy and mode of action of these herbs. Ayurveda knowledge and traditional usage information are excellent, but using these in a scientific way and incorporating a pharmaceutical approach will be more meaningful to ensure the safety of consumers.

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