Evidence Based Validation of Indian Traditional Medicine – Way Forward

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ABSTRACT

Evidence based validation of the ethno-pharmacological claims on traditional medicine (TM) is the need of the day for its globalization and reinforcement. Combining the unique features of identifying biomarkers that are highly conserved across species, this can offer an innovative approach to biomarker-driven drug discovery and development. TMs are an integral component of alternative health care systems. India has a rich wealth of TMs and the potential to accept the challenge to meet the global demand for them. Ayurveda, Yoga, Unani, Siddha and Homeopathy (AYUSH) medicine are the major healthcare systems in Indian Traditional Medicine. The plant species mentioned in the ancient texts of these systems may be explored with the modern scientific approaches for better leads in the healthcare. TM is the best sources of chemical diversity for finding new drugs and leads. Authentication and scientific validation of medicinal plant is a fundamental requirement of industry and other organizations dealing with herbal drugs. Quality control (QC) of botanicals, validated processes of manufacturing, customer awareness and post marketing surveillance are the key points, which could ensure the quality, safety and efficacy of TM. For globalization of TM, there is a need for harmonization with respect to its chemical and metabolite profiling, standardization, QC, scientific validation, documentation and regulatory aspects of TM. Therefore, the utmost attention is necessary for the promotion and development of TM through global collaboration and co-ordination by national and international programme.

Key words: Indian traditional medicine, AYUSH, Ayurveda, Chemical profiling, Plant metabolomics

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INTRODUCTION

TM has a long history of cultural heritage and ethnic practices. TM has been defined as skills and a practice based on the theories, believes and experiences indigenous to different cultures and maintenance of healthcare as well as in the prevention, diagnosis and treatment of physical and mental illnesses[1]. Some evidences of efficacy, safety and quality, if they exist, for herbal medicines, are considered to be anecdotal or empirical at best and rarely it is subjected to the rigorous prospective randomized controlled trial. Until 1899, when Bayer introduced aspirin, traditional and ethno-medicine was the basis of healthcare for humankind. Through a slow process of clinical trial and error, each culture developed a local, natural resource-based tradition of healing. These systems of TM, today, provide the basis of global implementation of an evidence-based regulatory approach to biomarker-driven drug discovery and development. TMs are an integral component of alternative health care systems. India has a rich wealth of TMs and the potential to accept the challenge to meet the global demand for them. Ayurveda, Yoga, Unani, Siddha and Homeopathy (AYUSH) medicine are the major healthcare systems in Indian Traditional Medicine. The plant species mentioned in the ancient texts of these systems may be explored with the modern scientific approaches for better leads in the healthcare. TM is the best sources of chemical diversity for finding new drugs and leads. Authentication and scientific validation of medicinal plant is a fundamental requirement of industry and other organizations dealing with herbal drugs. Quality control (QC) of botanicals, validated processes of manufacturing, customer awareness and post marketing surveillance are the key points, which could ensure the quality, safety and efficacy of TM. For globalization of TM, there is a need for harmonization with respect to its chemical and metabolite profiling, standardization, QC, scientific validation, documentation and regulatory aspects of TM. Therefore, the utmost attention is necessary for the promotion and development of TM through global collaboration and co-ordination by national and international programme.

All patients have the right to expect that a medicine will “work”, i.e., that it will be safe, effective and consistent. Ethically, it should not matter whether the medicine is an approved prescription product, over-the-counter medication, dietary supplement, phyto-pharmaceutical, or traditional medicine when human health is at stake. To diminish that right is to diminish the value of one human life over another. Global implementation of an evidence-based regulatory foundation for TMs and dietary supplements is essential to ensure healthcare for all[3]. Scientific validation and QC of TMs are critical and essential aspects to ensure therapeutic efficacy, safety and rationalization of their use in healthcare. Quality assurance (QA) is the thrust area for traditional formulations in Indian TM like churnas (herb powder), bhasmas (calcined metallic ashes), Kwath (liquid orals) and Lekhas (oral supplements)[4]. Chromatographic finger printing and marker compound analysis are getting momentum for the standardization of traditional medicinal formulations. This technique helps not only in establishing the correct botanical identity but also helps in regulating the chemical profile of the herbs[5]. TMs have been regarded as stronghold in drug discovery and drug development as they offer unmatched chemical diversity with structural complexity and novel biological interactions. Searching for the TMs in untapped source can lead us to new horizons where we can find novel, potent and selective lead compounds. Such leveraging innovations in the development of traditional medicine products (TMPs) suggested an immense growth potential in future for their validation. The European Medicines Agency (EMEA) defines chemical markers as chemically defined constituents or groups of constituents of herbal medicinal product, which are of interest for QC purposes in spite of whether or not they possess any therapeutic activity[6].

Wisdom and compassion, global collaboration and leadership are essential to change the contemporary paradigms and develop new strategies for the promotion of TMs. From the history on discovery and development of drugs, it is understood that with adequate support, an important health outcome of the evidence-based approach to the study of
TMs has developed several safe and effective medicines\(^1\). The rich secondary metabolite resources of medicinal plants are widely accepted for their unique chemical and biological features. They are gaining global acceptance because they offer natural ways of treatment and promote healthcare. Scientists around the world are emphasizing on medicinal plants as alternative medicine and their commercial potential in healthcare\(^7\).

**INDIAN SYSTEM OF MEDICINE (ISM)**

India has an ancient heritage of traditional system of medicine. Indian *Materia-Medica* provides a huge knowledge base on folklore practices of traditionally inspired medicine. Indian traditional medicine is based on AYUSH, with the emerging interest of the world in adopting and studying traditional systems, and in exploiting their potential from different healthcare perspectives, the Ministry of AYUSH, Government of India has initiated several attempts to explore the possibility of evaluating TMs for their therapeutic potential as originally practiced, as well as to generate data to put them in national healthcare programs. The Ministry of AYUSH regulates education, practice and encourages research in these systems. The National Medicinal Plant Board (NMPB) deals with conservation, cultivation, post-harvest technology and related issues on medicinal plants\(^8\). The detailed profile of Ministry of AYUSH, Govt. of India is given in Table 1.

India has approximately 47,000 plant species and about 15,000 medicinal plants, among them 7,000 plants used in Ayurveda, 700 in Unani medicine, 600 in Siddha medicine. The 65% population in rural India is using Ayurvedic medicines. Traditionally, 2,000 species in Ayurveda, Siddha and Unani medicine (ASU) are used by classical traditions. Traditional village practitioners are practicing 4,500-5,000 species. A tribal and other traditional community uses 8,000 plant species. The details of herbs used in Indian system of medicine have been described in Figure 1. Medicinal Plants Division of the Indian Council of Medical Research has brought out thirteen volumes in a series of publications entitled “Reviews on Indian Medicinal Plants” consolidating multidisciplinary scientific published research work on 3679 Indian medicinal plant species with 56964 citations on various aspects including pharmacognostic, ethnobotanicals, Ayurvedic, phytochemical, pharmacology and toxicology.

Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homeopathy (AYUSH) are the official Indian traditional systems of medicine. The department of Indian systems of Medicines and Homoeopathy (ISM & H) was established in March, 1995 as a separate department in the Indian Ministry of Health and Family Welfare and re-named as Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH) in November, 2003 with a view to providing focused attention to development of Education and Research in Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy systems. The Department has been

![Figure 1. Traditional medicine used in Indian system of medicine](image)

Table 1. Various organizations of Ministry of AYUSH, Govt. of India for exploration and development of TM\(^9\)

<table>
<thead>
<tr>
<th>Organizations</th>
<th>Particulars</th>
</tr>
</thead>
</table>
| **Research councils** | Central Council for Research in Ayurvedic Sciences (CCRAS), New Delhi, India  
Central Council for Research in Siddha (CCSR), Tamil Nadu, India  
Central Council for Research in Unani Medicines (CCRUM), New Delhi, India  
Central Council for Research in Homoeopathy (CCRH), New Delhi, India  
Central Council for Research in Yoga & Naturopathy (CCRYN), New Delhi, India |
| **Board** | National Medicinal Plant Board (NMPB) |
| **Educational institutions** | National Institute of Ayurveda (NIA), Jaipur  
National Institute of Naturopathy (NIN), Pune  
National Institute of Unani Medicine (NIUM), Bangalore  
National Institute of Siddha (NIS), Chennai  
National Institute of Homoeopathy (NIH), Kolkata  
Institute of Post Graduate Teaching & Researchin Ayurveda (IPGTRA), Jamnagar (Gujarat)  
Rashtriya Ayurveda VidyaPeeth (RAV), New Delhi  
Morarji Desai National Institute of Yoga (MDNIY), New Delhi  
The Central Council of Indian Medicine (CCIM), New Delhi  
The Central Council for Homoeopathy (CCH), New Delhi |
| **Statutory organizations** | Indian Medicine Pharmaceutical Corporation Ltd. (IMPCL), Almora, Uttarakhand  
Pharmacopoeial Laboratory for Indian Medicine (PLIM), Ghaziabad, U.P.  
Homoeopathic Pharmacopoeia Laboratory (HPL), Ghaziabad, U.P. |
| **Manufacturing unit** | |
| **Laboratories** | |

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elevated to an independent Ministry w.e.f. 09.11.2014. The ministry continues to lay emphasis on up-gradation of AVUSH educational standards, QC and standardization of drugs, improving the availability of medicinal plant material, research and development and awareness generation about the efficacy of the products of the systems[9].

Under the Ministry of AYUSH, there are 5 research councils, 1 board, 8 educational institutions, 2 statutory organizations, 1 drug manufacturing unit, 2 laboratories, and 11 national institutes established at national level for promoting current research, clinical practices and related aspects[9]. Various sectors of Ministry of AYUSH, Govt. of India for promotion and development of TM are given in the above Table 1.

1. Ayurveda

Ayurveda, the “Science of life”, is accepted as one of the oldest treatises on medical systems came into existence in about 900 B.C. According to Indian Hindu mythology, there are four Vedas written by the Aryans - Rig veda, Shama veda, Yajur veda, and Atharva veda. Among these, Rig veda, the oldest, was written after 1500 B.C. The Ayurveda is said to be an Upaveda (part) of Atharva veda, whereas the Charaka Samhita (1900 B.C.) is the first recorded treatise fully devoted to the concepts of practice of Ayurveda[10]. According to Ayurveda, a human being is a replica of nature and everything, which affects the human body and influences the macrocosm. Along with these panchamahabhutas, the functional aspect like movement, transformation and growth is governed by three biological humors, viz. vata (space and air), pitta (fire and water) and kapha (water and earth), respectively. This phenomenon may be attributed to the philosophy in Ayurveda known as Ashtanga Ayurveda. In Ayurveda, major disciplines are Ayurveda Siddhanta (fundamental principles of Ayurveda), Ayurveda Samhita (dealing with Ayurvedic classics), Sharira Rachna (anatomy), Sharira Kriya (physiology), Dravya Guna Vigyan (Materia Medica and pharmacology), Rasa Shastra (metal and minerals processing), Bhaishajya Kalpana (pharmaceuticals), Kaumabhritya (pediatrics), Prasuti Tantra (obstetrics and gynecology), Swasthavritta (social and preventive medicine), Kayachikitsa (internal medicines), Roga Nidana (etiopathology), Shalya Tantra (surgery), Shalkya Tantra (eye and ENT), Manasa Roga (psychiatry), Agada Tantra (toxicology and forensic medicine), Sangaharana (anesthesia), and Panchakarma (cleansing for rejuvenation therapy). Ayurveda is widely respected for its uniqueness and global acceptance as it offers natural ways to treat diseases and promote health[1,11]. The major discipline in Ayurveda has been explained in Figure 2.

Ayurveda is health care in continuity since Indus Valley Civilization (2300-1750 B.C.). We must consider human being as a whole with body, mind and soul to be healthy; healthy life is ensured by the harmony of these three entities. In life, we must have satisfaction of mind and tranquility of spirit. In Ayurveda all recipes have been given; one has to find out the right things in the right directions. Ayurveda considers individual as a whole, the object of treatment, and

![Figure 2. Major disciplines in Ayurveda](image)
not merely a particular expression of that system. In order to understand Ayurveda, we need scientific thinking which in turn will answer various healthcare issues[11].

The backbone of Ayurveda can be traced to the beginning of cosmic creation. In the earth, everything is composed of matter (substance), and as per the Ayurveda, all matter consists of five basic elements (Panchamahabhutas): the first element is space (Akasha), and the remaining four elements are air (Vayu), water (Jala), fire (Agni), and earth (Prithivi) exist within the space. Both the systems, human (microcosm) and universe (macrocosm) are linked permanently, since both are built from the same elements. Thus, humans are miniatures of the universe, a replica of nature, and everything that affects human beings also influences the macrocosm. Hence, the evolution of life and the creation of the universe can be concerned with Ayurveda. Along with these Panchamahabhutas, functional aspects like movement, transformation, and growth are governed by three biological humors, viz. Vata (space and air), Pitta (fire and water), and Kapha (water and earth), respectively. These three bodily humors usually known as Tridhatus regulate every physiological and psychological processes in the living organism. The knowledge base of Ayurveda includes Ayurvedic medicine, Ayurvedic principles, therapeutic modalities Panchakarma, and preventive aspect through Rasayana and veterinary use[11].

2. Siddha
The Siddha is one of the ancient systems of traditional Indian medicine. The term ‘Siddha’ means achievement and the ‘Siddhars’ were saintly figures who achieved results in medicine through the practices. The system is believed to be developed by 18 ‘Siddhars’, who glorified human being as the highest form of birth and believed that preserving the human body is essential to achieve the eternal bliss. The principles and concepts of this system are closely similar to those of Ayurveda, with specialization in iatro-chemistry. As in Ayurveda, this system also considers the human body as a conglomeration of three humors, seven basic tissues and the waste products. The equilibrium of humors is considered as health and its disturbance or imbalance leads to disease or sickness. The system describes 96 chief constituents of a human being, which include physical, physiological, moral and intellectual components. When there is any change or disturbance in functioning of these principals, body as a system deviates towards the cause of disease. The diagnosis methodology in the Siddha system is eight-fold, including examination of pulse, tongue, complexion, speech, palpatory findings, and so forth. Perception has a great role in this venture; this can be achieved by sensory organs, by mind, by yoga, by pain and pleasure. The Siddha system is a psychosomatic system, where attention is given to minerals and metals along with plant constituents[7].

3. Unani
The Unani system of medicine owes its origin in Greece. In India, Arabs introduced the Unani system of medicine, which was developed and blended with the Indian culture under the Mughal Emperors. The Greek philosopher-physician Hippocrates (460-377 B.C.), Greek and Arab scholars like Galen (131-212 A.D.), Raazes (850-0925 A.D.) and Avicenna (980-1037 A.D.) enriched this system considerably. Unani considers the human body to be made up of seven components. Arkanelements, Mizaj-temperaments, Aklath-humors, Ana organs, Arawh-spirits, Quo-faculties and Afal-functions, each of which has a close relationship with the state of health of an individual. A physician takes into account all these factors before diagnosing and prescribing treatment. In Unani medicine, single drugs or their combinations are preferred over compound formulations. The naturally occurring drugs used in this system are symbolic of life and are generally free from side effects. Such drugs, which are toxic in crude form, are processed and purified in many ways before use[7].

In Unani system of medicines, the diseases are considered as a natural process, and their symptoms are the reaction of the body. Therefore, the chief function of the physician is to aid the natural forces of the body. This system believes that every person has a unique humor constitution, which represents his healthy state. Hippocrates was the first physician to introduce the method of taking medical histories, which gave rise to the development of ‘humoral theory’ and presumed the presence of several humors such as Dam (blood) ‘Balgham’ (phlegm), ‘Safra’ (yellowbile) and ‘Sauda’ (black bile) in the body. The Unani system believes that every person has a unique humoral constitution that represents its healthy state. There is power of self preservation or adjustment called the ‘medicatrix nature’ or the defense mechanism, which strives to restore disturbances within the limit prescribed by the constitution of an individual and imbalance in the humor systems lead to several diseases[7].

4. Homoeopathy
Homoeopathy as it is practised today was evolved by the German physician, Dr. Samuel Hahnemann (1755-1843). The word ‘Homoeopathy’ is derived from two Greek words, ‘Homeos’ meaning similar and ‘pathos’ meaning suffering. Homoeopathy simply means treating diseases with remedies, which are capable of producing symptoms similar to the disease when taken by healthy people. Homoeopathy is being practised since ≥150 years in India. It has blended so well into the roots and traditions of the country that it has been recognized as one of the system of medicine and plays an essential role in boosting human healthcare largely[7].

LEVERAGING APPROACHES FOR VALIDATION OF TRADITIONAL MEDICINE
The practices and public interest in natural therapies and TM have increased dramatically. This has increased international trade in herbal medicine and attracted number of pharmaceutical companies. A few years ago, only small companies had interest in the marketing of TM, now multinational companies have started showing interest in commercializing herbal drugs[12].
In traditional systems of medicine, the medicinal plants play a major role and constitute their backbone. Indian Materia Medica includes about 2000 drugs of natural origin almost all of which are derived from different traditional systems and folklore practices.[13] According to WHO reports the populations in developing countries like India (70%), Rwanda (70%), Uganda (60%), Tanzania (60%), Benin (80%) and Ethiopia (90%) use traditional and alternative medicines for health care. In developed countries like Belgium (31%), USA (42%), Australia (48%), France (49%), Canada (70%), a significant percentage of the population has used traditional and alternative remedies for healthcare.[14] The global market of trade related to medicinal plants is estimated around US $60 billion per year and is growing at the rate of 7% annually with varying shares of developed and developing countries.[15]

Discovery of new drug is facing serious challenges due to reduction in number of new drug approvals coupled with excessive increasing cost. Combinatorial chemistry provided new expectation of higher achievement rates of new chemical entities (NCEs) but this scientific development has failed to improve the success rate in novel drug discovery. This scenario has prompted researchers to come out with a novel approach of integrated drug discovery. The starting point for plant-based new drug discovery should be identification of the right candidate plants by applying traditional documented use, tribal non-documented use, and exhaustive literature search. Bioassay-guided fractionation of the identified plant may lead to standardized extract or isolated bioactive compound as the new drug. This integrated approach could enhance success rate in drug discovery.[16] The development of TM requires the convergence of modern techniques and integrated approaches related to their evidence based research in various fields of science through national and international coordination.[17] The integrated strategies of drug development from TM have been enumerated in Figure 3.

![Figure 3](image-url)
APPROACHES FOR RESEARCH AND DEVELOPMENT IN TRADITIONAL MEDICINE

Around 25,000 effective plant based formulations are used as folk medicine in different rural communities of India and about 95% of medicinal plants are obtained from wild sources, among them only 150 species are used commercially. Approximately, 5-15% of the total 250,000 species have been validated scientifically. The annual turnover of the Indian herbal medicinal industry is about Rs. 2,300 crore as against the pharmaceutical industry’s turnover of Rs. 14,500 crores with a growth rate of 15 percent. There are over 1.5 million traditional practitioners and approximately 7000 medicinal drug-manufacturing units, which are using medicinal plants for prevention and treatment of different ailments.

Major thrust areas of research in TM includes: (i) phyto-chemical & pharmacological screening, (ii) chemo-profiling, (iii) DNA-bar coding, (iv) phyto-informatics, (v) metabolomic study, (vi) phyto-equivalence, (vii) reverse pharmacology, (viii) high-throughput screening, (ix) safety evaluation, (x) value added drug delivery system; (xi) quality control and standardization, (xii) clinical evaluation etc. Traditional use of medicinal plants needs to be systematically investigated and standardized with respect to quality, safety and efficacy. Macroscopic and microscopic studies, genetic fingerprinting methods, analytical chemical fingerprinting techniques e.g., high performance liquid chromatography (HPLC), high performance thin layer chromatography (HPTLC), capillary electrophoresis (CE), or gas chromatography LC-MS/MS are preferred tools for standardization. Although there has been an increase in interest in science based research into herbal medicine, some of the research to date has been overwhelmed by studies conducted using unauthenticated and uncharacterized products.

In reverse pharmacology, researchers start with the final product, a clinically useful compound for example, and work backwards to find out what it contains and how it functions. This can offer clues about how particular medicines work, and where they act in the body. High-throughput screening is the advanced screening technology that relies on high-speed data processing and sensitive detectors to conduct millions of biochemical, genetic or pharmacological tests in a few minutes. The process can quickly identify active compounds that affect particular biological pathways. Systems biology deals with the holistic approach to know different chemicals and metabolic processes to interact within the body. Since traditional medicines often have numerous active ingredients, it could be used to measure the whole body’s response to the mixture of compounds.

Metabolomics study reveals to the quantitative and qualitative estimation of “whole-set of metabolites” formed in a cellular/organism system. It may be defined as the systemic study of the individual chemical fingerprints that definite cellular process leaves behind and even more particularly, the technique of the metabolite profile of molecules in an organism. The combined data of all the metabolites in a biological system, which are the final products of its gene expression, is known as metabolome. These approaches deal with the study of genomics, transcriptomics and proteomics of biological systems.

Herbal medicine are complex products because a single medicinal plant constitutes a hundreds of phytoconstituents and their pharmacological properties are influenced by the time of collection, area of plant origin, and environmental conditions so special attention is needed for its cultivation and collection for quality of products. Therefore, above mentioned strategies regarding various issues are needed for validation of TM.

CHEMICAL PROFILING AND STANDARDIZATION OF INDIAN TRADITIONAL MEDICINE

Chemical profiling of traditional herbal preparations is essential in order to assess the quality of drugs. It deals with bioactive compound quantification, spurious drug determination, comparative fingerprint analysis, standardization of herbs, stability of formulations and quality consistency of TMPs. Botanicals are mostly obtained from wild sources and have the greatest challenges for ensuring consistent product quality. There are so many environmental factors including soil conditions, availability of light and water, temperature variations, nutrients, and geographical location affect the phyto-constituents present in plants. Further cultivation and harvesting techniques and storage methods also influence the physical appearance and chemical constituents of the plant. This means quality parameters should be set not only for the plant material but also for plant extracts and final product. Botanical extracts made directly from crude plant material show substantial variation in composition, quality and therapeutic effects. The standardization of herbal drugs includes authentication, harvesting the best quality raw material, assessment of intermediate, finished product. As the genetic composition is unique for each species and is not affected by age, physiological conditions and environmental factors DNA based markers are also used in identification of inter/intra-species variation.

Standardized extracts are high-quality extracts containing consistent levels of specified compounds and they are subjected to rigorous quality controls during all phases of the growing, harvesting, and manufacturing processes. When the active principles are unknown, marker substance should be established for analytical purposes and standardization. Marker substances are chemically defined constituents of herbal drug that are important for the quality of the finished product. Ideally, the chemical markers chosen should be bioactive.

Marker compound selection is generally based upon a variety of different factors including stability, ease of analysis, time and cost of analysis, relevance to therapeutic effect and indicator of product quality or stability. Various chemical markers have been described for the validation of TM including therapeutic components, bioactive components, synergistic components, characteristic components, main component, correlative components, toxic components and...
Chemical constituents of medicinal plants are commonly used in the identification/authentication of herbal drug components\cite{26,28}. Marker based standards are becoming popular for the quality control of raw materials, while biomarkers may be defined as pharmacologically active metabolites from natural resources\cite{50}. There are several well documented examples of the use of metabolomics in pharmaceutical and nutraceutical research\cite{52}. The use of metabolomics in drug discovery has renewed interest in the biological activity of herbal products, beginning in the early 19th century with the isolation of morphine from opium.

A study involved in the characterization of a set of defined metabolites is known as “targeted” metabolomics and usually combine NMR-MS techniques, which is applied for such type of analysis\cite{53}. Thousands of metabolites can be detected by this method in a single elute and it is the global approach that is leading the way to major revelation in our understanding of cell biology, physiology and medicine\cite{54}. Metabolomics study has diverse field of application and can be divided into four areas: (i) target compound analysis – the quantification of specific metabolites, (ii) the metabolomic profiling – the quantitative and qualitative estimation of a set compounds, (iii) metabolite chemo-analysis – the qualitative and quantitative analysis of all metabolites and (iv) metabolomic fingerprinting – sample classification by rapid global analysis\cite{55}. These approaches emphasize the phytomedicine research that may assist evidence-based phytotherapeutics, and such research may lead to a change of paradigm in the development and application of multicomponent botanical therapeutics (MCBT)\cite{56}.

Chemo profiling of the metabolites can help to identify the metabolites and to compare the nature of compounds. The output of sensors (analytical detectors) are known as ‘profiling’ which are classified and statistically analyzed to marks out their differences\cite{57}. It involves identification of metabolites as the analysis is based on their spectral peaks and calibration curves. Metabolome investigation comprehensively examines entire range of metabolites in a sample by the mutual application of various analytical techniques\cite{58}. Metabolomics allows an overall calculation of a cellular system, in regards to the gene regulation, modulated enzyme kinetics, and variations in metabolic reactions. In difference to the genomics or proteomics, metabolomics reveals the phenotypic changes in the function\cite{49}. However, it is important to mention here that the ‘omic’ sciences are corresponding as “upstream” changes in genes and proteins are considered “downstream” as changes in physiological function. The divergent of metabolomics is that it is a terminal view of the biological system, not allowing for demonstration of the increased or decreased genes and proteins\cite{59}. The markers used for the standardization, chemical and DNA fingerprinting, bioassays, metabolomics approach and the emerging field of phytomics provide mechanisms for assuring consistent quality and efficacy of herbal medicine\cite{24}. Several Indian traditional medicines such as Curcuma longa, Boerhavia diffusa, Glycyrrhiza glabra, Echinacea angustifolia, Saraca asoca, Withania somnifera, Psoralea corylifolia, Zanthoxylum armatum, Tinospora cordifolia and Commiphora wightii have been established for the different therapeutic activities and their metabolite profiling, which has been described in Table 3.

**CONCLUSION**

Medicinal plants are not only a major resource base for the traditional medicine and herbal industry but also provide livelihood and health security to a large segment of Indian
<table>
<thead>
<tr>
<th>Traditional medicine</th>
<th>Parts used</th>
<th>Active constituents</th>
<th>Biological activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Allium sativum</em>[^29^]</td>
<td>Bulb</td>
<td>Allicin</td>
<td>Hypolipidaemic, antiatherosclerotic, hypoglycaemic, anticoagulant, antihypertensive, antimicrobial, anticancer, antidote (for heavy metal poisoning), hepatoprotective and immunomodulatory</td>
</tr>
<tr>
<td><em>Aloe vera</em>[^30^]</td>
<td>Leave (gel)</td>
<td>Emodin</td>
<td>Wound healing, Anti-inflammatory, antifungal, hypoglycemic and gastroprotective</td>
</tr>
<tr>
<td><em>Andrographis paniculata</em>[^31^]</td>
<td>Leave</td>
<td>Andrographolide</td>
<td>Treatment of fever, inflammation, common cold, upper respiratory tract infection, tonsilitis, pharyngitis, laryngitis, pneumonia, tuberculosis, pyelonephritis and hepatic disorder</td>
</tr>
<tr>
<td><em>Bacopa monnieri</em>[^32^]</td>
<td>Whole plant</td>
<td>Bacoside</td>
<td>Used as memory enhancer, brain tonic, antiasthmatic and antipyretic</td>
</tr>
<tr>
<td><em>Boswellia serrata</em>[^33^]</td>
<td>Gum resin</td>
<td>Boswellic acids</td>
<td>Used in inflammatory bowel disease, rheumatoid arthritis, osteoarthritis and asthma</td>
</tr>
<tr>
<td><em>Calendula officinalis</em>[^34^]</td>
<td>Flower</td>
<td>Rutin</td>
<td>anti-inflammatory, antioxidant, wound healing, UV-screening, antiaging and antimutagenic</td>
</tr>
<tr>
<td>Traditional medicine</td>
<td>Parts used</td>
<td>Active constituents</td>
<td>Biological activity</td>
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<td>----------------------</td>
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</tr>
<tr>
<td><em>Camellia sinensis</em>[^35^]</td>
<td>Leave</td>
<td><img src="image1.png" alt="" /> Epicatechin</td>
<td>Antiageing, antidiabetic, neuroprotective, antimutagenicity, anti-obesity, antibacterial and anti-HIV</td>
</tr>
<tr>
<td><em>Capsicum annum</em>[^36^]</td>
<td>Fruit</td>
<td><img src="image2.png" alt="" /> Capsaicin</td>
<td>Analgesic, counterirritant, rheumatism, lumbago, neuralgia, to treat hoarseness, atonic dyspepsia, loss of appetite and flatulence</td>
</tr>
<tr>
<td><em>Centella asiatica</em>[^37^]</td>
<td>Leave</td>
<td><img src="image3.png" alt="" /> Asiaticoside</td>
<td>Anti-wrinkle, used in wound healing and antihistimincs</td>
</tr>
<tr>
<td><em>Coffea arabica</em>[^38^]</td>
<td>Seed</td>
<td><img src="image4.png" alt="" /> Ferulic acid</td>
<td>Antioxidant, antiageing, hepatoprotective, antiatherogenic, antimutagenic, anti-inflammatory, anticancer, anti-diabetic, neuroprotective and cardioprotective activities</td>
</tr>
<tr>
<td><em>Crocus sativus</em>[^39^]</td>
<td>Flowering tops</td>
<td><img src="image5.png" alt="" /> Crocetin</td>
<td>Potent antioxidant, anticancer and photoprotectant</td>
</tr>
<tr>
<td><em>Curcuma longa</em>[^40^]</td>
<td>Rhizome</td>
<td><img src="image6.png" alt="" /> Curcumin</td>
<td>Antitumour, antioxidant, antiarthritic, antimyloid, Anti-ischemic and anti-inflammatory</td>
</tr>
<tr>
<td><em>Emblica officinalis</em>[^41^]</td>
<td>Fruit</td>
<td><img src="image7.png" alt="" /> Gallic acid</td>
<td>Hepatoprotective, anti-oxidant, anti-diabetic, anti-tumor and immunomodulatory</td>
</tr>
<tr>
<td><em>Eugenia caryophyllata</em>[^42^]</td>
<td>Flower bud</td>
<td><img src="image8.png" alt="" /> Eugenol</td>
<td>Anti-inflammatory, antioxidant, carminative, anti-spasmodic, antiseptic and anti-microbial agent</td>
</tr>
<tr>
<td>Traditional medicine</td>
<td>Parts used</td>
<td>Active constituents</td>
<td>Biological activity</td>
</tr>
<tr>
<td>----------------------</td>
<td>----------------------------------</td>
<td>---------------------</td>
<td>-------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><em>Ginkgo biloba</em></td>
<td>Leave</td>
<td>Ginkgolide A</td>
<td>Used in peripheral circulatory insufficiency, cerebrovascular disorders, geriatric complaints alzheimer dementia, antioxidant and anticancer</td>
</tr>
<tr>
<td><em>Glycine max</em></td>
<td>Seed</td>
<td>Ginkgolide B</td>
<td>Antioxidant, anti-carcinogenic and antiaging</td>
</tr>
<tr>
<td><em>Glycyrrhiza glabra</em></td>
<td>Root and rhizome</td>
<td>Genistein</td>
<td>Anti-inflammatory and antiulcer, hepatoprotective, antiallergic, anti-arthritic, anti-arrhythmic, antibacterial, antiviral and antiasthmatic</td>
</tr>
<tr>
<td><em>Hypericum perforatum</em></td>
<td>Aerial parts</td>
<td>Glycyrrhizin</td>
<td>Antidepressants, antimicrobial, antifungal and other CNS disorder</td>
</tr>
<tr>
<td>Traditional medicine</td>
<td>Parts used</td>
<td>Active constituents</td>
<td>Biological activity</td>
</tr>
<tr>
<td>----------------------</td>
<td>------------</td>
<td>---------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td><em>Nelumbo nucifera</em>[^46]</td>
<td>Rhizome</td>
<td><img src="image1" alt="Betulinic acid" /></td>
<td>Used in pharyngopathy, pectoralgia, leucoderma, strangury, dysentery, cough, haematemesis, tissue inflammation, cancer, skin diseases and diabetes</td>
</tr>
<tr>
<td><em>Ocimum sanctum</em>[^47]</td>
<td>Leave</td>
<td><img src="image2" alt="Carvacrol" /></td>
<td>Antioxidant, antibacterial antihypertensive and to treat respiratory complications</td>
</tr>
<tr>
<td><em>Piper longum</em> and <em>Piper nigrum</em>[^23]</td>
<td>Fruit</td>
<td><img src="image3" alt="Piperine" /></td>
<td>Antiageing, revitalizing, memory enhancing, adaptogenic, anti-diarrhoeal, antispasmodic, immunomodulatory, remedies for cough, cold, fever, asthma and other respiratory problems</td>
</tr>
<tr>
<td><em>Punica granatum</em>[^44]</td>
<td>Fruit</td>
<td><img src="image4" alt="Ellagic acid" /></td>
<td>Antioxidant, antiaging and anti-inflammatory</td>
</tr>
<tr>
<td><em>Silybum marianum</em>[^43]</td>
<td>Fruit</td>
<td><img src="image5" alt="Ellagic acid" /></td>
<td>Used in a whole range of liver and gall bladder conditions including hepatitis and cirrhosis. Anti-oxidant, anti-carcinogenic and anti-inflammatory</td>
</tr>
<tr>
<td><em>Terminalia belerica</em>[^41] and <em>Terminalia chebula</em>[^48]</td>
<td>Fruit</td>
<td><img src="image6" alt="Gallic acid" /></td>
<td>Anti-atherosclerotic, hepatoprotective, cardioprotective, cytoprotective, cardiotonic, antimutagenic and antifungal</td>
</tr>
<tr>
<td><em>Zingiber officinale</em>[^23]</td>
<td>Rhizome</td>
<td><img src="image7" alt="Gingerol" /></td>
<td>Antiviral (hRSV), antiinflammatory, bronchitis and other respiratory tract infections</td>
</tr>
</tbody>
</table>
population. Ministry of AYUSH, Government of India has taken several initiatives for promotion and development of TM.

**ACKNOWLEDGMENT**

We would like to dedicate this article in memory of our beloved Prof P. K. Debnath for his blessing, support and guidance to explore Ayurveda worldwide. Prof Debnath was a renowned scientist for exploring the science of Ayurvedic medicine. Unfortunately, he passed away on April 25, 2015; we pay our deep respect to his departed soul. The authors are thankful to the Department of Biotechnology, Government of India, New Delhi, for financial support through Tata Innovation Fellowship (D.O. No. BT/HRD/35/01/04/2014) to Dr. Pulok K. Mukherjee.

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### Table 3. Metabolite fingerprinting of some Indian traditional medicinal plants.

<table>
<thead>
<tr>
<th>Medicinal plant</th>
<th>Metabolomics approach</th>
<th>Metabolites</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Curcuma longa</em>[^60^]</td>
<td>LC-ESI-MS/MS</td>
<td>Curcumin; Demethoxycurcumin; Bisdemethoxycurcumin; 1,7-Bis(4-hydroxyphenyl)-3,5-heptanediol; 5-Hydroxy-1,7-bis(3,5-dimethoxyphenyl)-3-heptanone; 1,7-Bis(4-hydroxy-3-methoxyphenyl)-4,6-heptadien-3-one; 1-(4-Hydroxy-3-methoxyphenyl)-7-(4-Hydroxy-3,5-dimethoxyphenyl)-4,6-heptadien-3-one; 5-Hydroxy-1,7-bis(3,4-dihydroxyphenyl)-1-hepten-3-one; 4-Hydroxybisdemethoxycurcumin</td>
</tr>
<tr>
<td><em>Boerhavia diffusa</em>[^61^]</td>
<td>HS-SPME-GC-MS</td>
<td>Phellandrene; α-Pinene; 3 Limonene; Camphor; Isothemone; Menthol; Geranylacetone; cis 4-Hexen-1-ol; trans 2-Octanal; 2-Nonen-1-ol; 2-Decen-1-0; Methylpyrrole; 3-Phenyl-2-(20-pyridyl)-indole; Eugenol; Vanillin; β-Cyclocitral; β-Ionone; Dihydroadantoinolide; Linalyl antranilide; 4-Oxoisophorone; Resorcinol monoacetate; Benzothiazol; Benzophenone</td>
</tr>
<tr>
<td><em>Glycyrrhiza</em> species (Glycyrrhiza glabra, Glycyrrhiza uralensis, Glycyrrhiza inflata and Glycyrrhiza echinata)[^62]</td>
<td>1H NMR, GC-MS , LC-MS and PCA</td>
<td>Glycyrrhizin; Sucrose; Liquiritin; Liquiritigenin; Isoliquiritigenin; 4-Hydroxyphenyl acetic acid; Licochalcone; Rhamnose (glycosides)</td>
</tr>
<tr>
<td><em>Echinacea</em> species (Echinacea purpurea, Echinacea pallida and Echinacea angustifolia)[^63]</td>
<td>HPLC/ESI/MS, GAP, Biplot</td>
<td>Undeca-2Z(E),4E(Z)-dien-8,10-diynoic acid- isobutylamide; Trideca-2E,7Z-dien-10,12-diynoic acid-isobutylamide; Dodeca-2Z,4E(E)-dien-8,10-diynoic acid-isobutylamide; Dodeca-2Z,2E,E-dien-8,10-diynoic acid-isobutylamide; Dodeca-2Z,4E,8Z-trienoic acid- isobutylamide; Undeca-2E(Z)-en-8,10-diynoic acid- isobutylamide; Dodeca-2E-en-8,10-diynoic acid-isobutylamide; Undeca-2Z-en-8,10-diynoic acid-2-methylbutylamide; Pentadeca-2E-en-8,10-diynoic acid-2-methylbutylamide; Pentadeca-2E,ZS-dien-12,14-diynoic acid-isobutylamide; Pentadeca-1,8-diene; pentadeca-1,8,11-trienn; Heptadeca-1,8,11-triene; Pentadeca-8Z-en-2-one; Pentadeca-8Z-11Z-dien; Pentadeca-8Z-en-11,13-dyn-2-one; Aromadendrene; Germacrene-D; β-Gurjunene; p-Menth-1-en-6-0l</td>
</tr>
<tr>
<td><em>Saraca asoca</em>[^64]</td>
<td>UPLC-QTOFMS</td>
<td>(R) Prunasin; Sn-Glycero-3-phosphocholine; Delphinidin; O-Phosphocholine; Procyandin B1; (-) Epicatechin</td>
</tr>
<tr>
<td><em>Withania somnifera</em>[^65]</td>
<td>GC-MS, HPLC and NMR</td>
<td>Palmitic acid; Oleic acid; Linoleic acid; Linolenic acid; Citric acid; Fructose-5 TMS; Fructose-5 TMS; Fructose-5 TMS, Fumaric acid (L); GABA (L &amp; R); Galactose (L &amp; R); Glycerol (R); Glutamate (L &amp; R); 2 O-Glutamine (L &amp; R); α-Glucose (L &amp; R); β-Glucose (L &amp; R); Glycine (L); Myo-Inositol (L); Isoleucine (L); Lactic acid; Lysine; Leucine (L); Succinate (L &amp; R); Malic acid 3 TMS; N-Acetyl- Glucosamine (L); Phenyl alanine (L); Tryptic acid (L); Benzozic acid (L &amp; R); Butandioic acid (L); Phenylacetic acid (L &amp; R); p-Hydroxy, phenyl ethanol (L); p-Hydroxy, phenyl acetic acid (R); 3,4,5-Trihydroxy cinnamic acid (R); β-Sitosterol (L)</td>
</tr>
<tr>
<td><em>Psoralea corylifolia</em>[^66]</td>
<td>GC/MS, HPLC/UV–MS</td>
<td>Psorale; Stignasta-5-en-3-ol; Stignasta-5,22-dien-3-ol; Daidzein; Neophytdiene; 2-Furancarboxaldehyde,5-(hydroxymethyl); Myristic acid; Caryophyllene oxide; Phytol; Bakuchiol; 1,2-Benzenedicarboxylic acid; 2,6-Dimethylohexanol; 2,8-Diisopropyl-peri-xanthenoxanthene-4,10-quinoine; Linoleic acid; Palmitic acid; Stearic acid; 1-Ecosanol</td>
</tr>
<tr>
<td><em>Zanthoxylum armatum</em>[^67]</td>
<td>UPLC-DAD-ESI-QTOF-MS/MS</td>
<td>Rubemamin; Zanthoxin; N-(4-methoxy-phenethyl)-3,4-dimethoxy-cinnamamide; Eudesmin; Magnolin or epimagnolin; Isomer of hydroxy-sanshool; Armatamide; Horsfieldin; Hydroxysanshool; Xanthoxylin; Dioxamin; Kobusin; Fargesin; Sesamin; Asarinin</td>
</tr>
<tr>
<td><em>Tinospora cordifolia</em>[^68]</td>
<td>UPLC-QTOFMS</td>
<td>Jatrorrhizine; Mangoflorine; Menisperine; Columbamine; Berberine; Tinosporoside</td>
</tr>
<tr>
<td><em>Commiphora wightii</em>[^69]</td>
<td>NMR, GC–MS, HPLC</td>
<td>Guggulsterone E and Z; D-limonene; β-Myrcene; α-Caryophyllene; β-Caryophyllene; δ-Cadiene; β-Elemene; Guaiacol; Isoeugenol; Verticil; Quinic acid; myo-Inositol; α-Tocopherol; N-Methylpyrrolidone; trans-Farnesol; Prostaglandin F2; Protocatechuic; Gallic acid; Cinnamic acids</td>
</tr>
</tbody>
</table>
CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES


