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1.1 HERBAL MEDICINE

Ever since the birth of humanity, there has been a relationship between life, disease and plants. Primitive men started studying diseases and treatments\textsuperscript{1}. There is no reflect that people in ancient set interest synthetic medicament for their ailments but they tested to make interest of the things they could gently procure. The most ordinary clothes they could find was there in surrounding i.e. the sapling and animals\textsuperscript{2}. They embarked on using plants and establish that the majority of plants were suitable as food, where as other were either poisonous or medicinally useful\textsuperscript{3}.

By their experience, this knowledge of herbal remedies was transferred to generation as family medicine. So the history of herbal medication is equally old as human history. Most of these plant-derived drugs were originally identified through the subject of traditional remedies and folk knowledge of indigenous people and some of these could not be substituted despite the tremendous progress in synthetic chemistry. Therefore, plants can be depicted as a major source of medicines, not merely as isolated active principles to be doled out in standardized dosage form but also as crude drugs for the population. Modern medicines and herbal medicines are complimentary being used in areas for health care program in various developing countries including India\textsuperscript{4}.

Herbs had been practiced by all cultures throughout history, but India has one of the oldest, most productive and most diverse cultural living traditions associated with the role of medicinal plants. In the present scenario, the demand for herbal products is growing exponentially throughout the globe and major pharmaceutical companies are currently carrying on extensive research on plant materials for their potential medicinal value\textsuperscript{5,6}. 
Nevertheless, the folkloric use of crude drugs has been often empirical and is founded on observation from clinical trials without experimental support. The need for exhaustive systemic research into indigenous drugs cannot be overemphasized.

Plants have always acted as a major part in the handling of human and animal diseases. World-wide interest in the use of medicinal and aromatic plants is increasing. In spite of the great advances observed in modern medical specialty in recent decades, plants still make an significant donation to health care. Natural products have been our single most successful source of medicines. Every plant is like a factory capable of blending an infinite number of highly complex and uncommon chemical substances.

India delivers very long, safe and continuous usage of many herbal drugs in the officially documented alternative systems of health viz., Ayurveda, Unani, Siddha and Homoeopathy. These systems have fairly existed side by side with Allopathy and are not ‘in the field of obscurity’. Herbal drugs are regularly used as spices, home remedies and health foods as well as over-the-counter (OTC) as self-medication or prescribed in the non-allopathic systems.

The progression of high-throughput screening and the post-genomic era provided more than 80% of drug substances, which are obtained from natural products or inspired by a natural compound. More than one hundred natural invention resulting compounds are presently enduring clinical trials and around 100 similar projects are in preclinical development.

A diffusive number of plants used in the traditional practice have now turn into a part of the modern health overhaul system either as a whole or a product obtained from the plant expedient. A series of natural products isolated from higher plants became clinical agents and are still in use today. Quinine and quinidine from Cinchona bark, morphine and codeine from the latex of Papaver somniferum, digoxin from Digitalis leaves, atropine and hyoscine from plants of the Solanaceae family continues to be in clinical use.
1.2 Ethnopharmacology

The scientific contemplation of traditional plant medicament can be considered as a major part of ethnopharmacology, a condition introduced in 1967. Ethnopharmacology can be explain as the expert meditation of materials utility by heathen and cultural nest as elixir’ and in most token this is synonymous with the meditation of old-fashioned medicines. The influence of traditional plant medicines to isolate active constituents have been significant and some evident instance are isolation of atropine (Atropa belladonna), caffeine (Coffea arabica, Thea sinensis), digoxin (Digitalis purpurea), ephedrine (various species of Ephedra), ergometrine (Claviceps purpurea), pilocarpine (Pilocarpus jaborandi), reserpine (Rauwolfia serpentina) etc.16.

1.3 A research approach to develop products using ethnopharmacology

The revelation process of herbal products is composed of several steps. The first stage must be the stated use of a naturally occurring material for curative purpose. If there is a sign of a remedial effect, then the material necessarily to be recognized and characterized according to scientific nomenclature. It can then be composed for trial studies followed by biological study associated to the isolation and structure determination of any chemicals which might be amenable for some bioactivity. The active compounds are usually espy by several cycles of fractional process of the extract associated to testing for action of each fraction, until pure compounds are separated from the active fractions. After establishing molecular structure, active compounds serve as the leads for the progression of clinically useful products.17.

Reverse Pharmacology is explained as the science of integrating documented clinical/experiential hits, into leads by transdisciplinary experimental studies and more emerging these into drug candidates by experimental and clinical examination. The identification of structures with unique biodynamic effects can also lead to an innovative chemical entity trail for drug development. The scope of Reverse Pharmacology is to understand the mechanisms of action at diverse stages of biological organization and to make optimal safeness, effectiveness and acceptableness of the leads in natural products, based on relevant science.17.
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There are two discrete forms of research on medicinal plants. In the first segment, the choice of plant is mainly based on their genuine use and reputation in the Indian traditional system of medicine, although in second stage, more extensive base, in which screening of a large number of natural products for biological activity is commenced, irrespective of the circumstance whether these plants are being used by the traditional system of medicine or not\textsuperscript{18}.

Herbal medicines include herbs, herbal materials, herbal formulations and finished herbal products. Herbs include crude plant material, such as leaves, flowers, fruit, seeds, stems, wood, bark, roots, rhizomes or other plant parts, which may be entire, fragmented or powdered. Herbal materials include, in addition to herbs, fresh juices, gums, fixed oils, essential oils, resins and dry powders of herbs. In several countries, these materials may be treated by various local processes, such as steaming, roasting or stir-baking with honey, alcoholic beverages or other materials.

Herbal preparations are the basis for finished herbal products and may comprise powdered herbal materials, or extracts, tinctures and fatty oils of herbal materials. They are formed by extraction, fractionation, purification, concentration, or other physical or biological processes. They also include preparations prepared by steeping or heating herbal ingredients in alcoholic beverages and/or honey or in other materials. Finished herbal products consist of herbal preparations made from one or more herbs. If more than one herb is used, the term “mixture herbal product” can likewise be applied. Finished herbal products and mixture herbal products may contain excipients in addition to the active ingredients\textsuperscript{19}.

1.4 Standardization

As commercialization of the herbal medicine has occurred, certainty of safeness, peculiarity and potency of medicinal plants and herbal products has become an essential issue. The herbal raw material is susceptible to a lot of variation due to some issues, the important ones being the identity of the plants and periodic dissimilarity, the ecotypic, genotypic and chemotypic differences, drying and storage conditions and the existence of xenobiotic\textsuperscript{20}. 
1.5 Guidelines for the standardization of herbal drugs

The guidelines set by WHO:

Botanical characters, sensory evaluation, foreign organic matter, microscopic, histological, histochemical assessment, quantitative measurements, physical and chemical identity, fingerprints chromatography, ash values, extractive values, moisture content, volatile oil and alkaloids tests, quantitative estimation protocols, Estimation of biological activity, the values of bitterness, hemolytic index, swelling index, foaming index, pesticides residues, heavy metals, microbial contamination as total viable count, pathogens such as E.coli, Salmonalla, P.aeroginosa, S.aureus, Enterobacteriaceae, Microbial contamination and radioactive contamination are evaluated\(^\text{21}\).

1.6 Chromatographic Fingerprinting and Marker Compound Analysis

A chromatographic fingerprint of a Herbal Medicine is a chromatographic pattern of the extract of certain common chemical components of pharmacologically active and or chemical constituents. This chromatographic contour should be highlighted by the essential attributions of “reliability” and “fuzziness” or “similarity” and “differences” so as to chemically represent the herbal medicine explored. It is proposed that with the help of chromatographic fingerprints acquired, the confirmation and identification of herbal medicines can be precisely conducted (reliability) even if the amount and/or concentration of the chemically characteristic components are not exactly the identical for diverse samples of herbal medicine (hence, “fuzziness”) or, the chromatographic fingerprints could validate both the “sameness” and “differences” among several samples magnificently. Hence, we should universally reflect various components in the herbal medicine extracts, and not independently consider only one and/or two marker components for estimating the quality of the herbal medicine products. However, in several herbal medicine and its extract, there are hundreds of anonymous constituents and many of them are in little amount. Furthermore, they are generally occurs variability inside the same herbal materials. Therefore it is very significant to achieve reliable chromatographic fingerprints that characterize pharmacologically active and chemically distinctive constituents of the herbal medicine.
1.7 TLC

Thin layer chromatography is one of the most acceptable and modest chromatographic technique used for separation of compounds. In the phytochemical appraisement of herbal drugs, TLC is being use widely for the following reasons:

1. It facilitates rapid analysis of herbal extracts with minimum sample requirement.
2. It offers qualitative and semi quantitative information of the resolved compounds.
3. It facilitates the quantification of chemical components.

In TLC fingerprinting, the data that can be recorded using a high-performance TLC (HPTLC) scanner includes the chromatogram, retardation factor (Rf) values, the color of the separated bands, their absorption spectra and $\lambda_{\text{max}}$ of all the resolved bands. All of these, together with the profiles on derivatization with different reagents, represent the TLC fingerprint profile of the sample. The data thus generated has a potential application in the designation of an authentic drug, in excluding the adulterants and in upholding the tone and consistency of the drug. HPLC fingerprinting includes recording of the chromatograms, retention time of individual peaks and the absorption spectra with different mobile phases.

Likewise, GLC is used for producing the fingerprint profiles of volatile oils and fixed oils of herbal drugs. Furthermore, the modern methodologies of applying hyphenated chromatography and spectrometry such as High-Performance Liquid Chromatography–Diode Array Detection (HPLC–DAD), Gas Chromatography–Mass Spectroscopy (GC–MS), Capillary Electrophoresis– Diode Array Detection (CE-DAD), High-Performance Liquid Chromatography–Mass Spectroscopy (HPLC–MS) and High-Performance Liquid Chromatography–Nuclear Magnetic Resonance Spectroscopy (HPLC–NMR) could provide the supplementary spectral information, which will be very useful for the qualitative analysis and even for the on-line structural elucidation$^{22,23}$. 
1.8 HPTLC

HPTLC method is extensively used in the pharmaceutical industry in process development, recognition and detection of adulterants in herbal products and supports in identification of pesticide content, mycotoxins and in quality control of herbaceous plants and health foods\(^24\). It has been well documented that various samples can run simultaneously by use of a smaller quantity of mobile phase than in HPLC\(^25\). It has been stated that mobile phases of pH 8 and above can be used for HPTLC. Another advantage of HPTLC is the repeated exposure of the chromatogram with the same or different conditions. Subsequently, HPTLC has been explored for simultaneous assay of several components in a multi-component formulation\(^26\). Through this technique, authentication of various species of plant is also possible\(^27\).

1.9 HPLC

Preparative and analytical HPLC are extensively useful in the pharmaceutical industry for separating and purifying of herbal compounds. There are essentially two types of preparative HPLC: low pressure HPLC (typically under 5 bars) and high pressure HPLC (pressure >20 bar)\(^28\). The essential factors to be considered are resolution, sensitivity and fast analysis time in analytical HPLC however both the degree of solute purity as well as the amount of compound that can be produced per unit time i.e. throughput or recovery in preparative HPLC\(^29\). In preparative HPLC (pressure >20 bar), larger stainless steel columns and packing materials (particle size 10-30 \(\mu\)m) are required. The examples of normal phase silica columns are Kromasil 10 \(\mu\)m, Kromasil 16 \(\mu\)m, Chiralcel AS 20 \(\mu\)m while for reverse phase are Chromasil C18, Chromasil C8. The objective is to separate or purify compounds, however in analytical work the aim is to acquire information about the sample. This is certainly significant in the pharmaceutical industry of nowadays because fresh products (Natural, Synthetic) have to be taken out to the marketplace as quickly as possible. Because of such a great purification technique, it is possible to save time on the synthesis condition\(^30, 31, 32\).
1.10 *Oldenlandia corymbosa*

*Oldenlandia corymbosa* syn. *Hedyotis corymbosa* (Rubiaceae) is a weedy annual herb, found specifically during rainy season in fields throughout India, Sri Lanka, tropical East Asia to Java and the Phillipines. It is usually identified as “Parppatakappullu” in traditional medicine in Kerala. The plant is known to clear heat and toxins, activate blood circulation, promote diuresis and relieve strangury. It is also known to act on lymphosarcoma and carcinoma of the liver and larynx. It is also active against appendicitis, hepatitis, pneumonia, cholecystitis, urinary infection, cellulites and snake bite. Chinese folk medicine describes the plant to treat skin sores, ulcers, sore throat, bronchitis, gynecologic infections and pelvic inflammatory diseases.

It is given in jaundice and other diseases of the liver, heat eruptions, vitiated conditions of pitta, hyperdypsia, giddiness, indigestion, gas, constipation, helminthiasis, leprosy, skin diseases, cough, bronchitis, necrosis, nervous depression caused by deranged bile and hepatopathy. The important preparations of the drug are Amritarishtam, Candanasavam, Mahatiktaghrtam, Jatyadi tailam, Aranyatulasyadi coconut oil etc.

**Taxonomic classification**

Kingdom: Plantae

Phylum: Angiosperms

Class: Dicotyledonae

Subclass: Asteridae

Order: Gentianales

Family: Rubiaceae

Subfamily: Rubioideae

Genus: Oldenlandia

Species: corymbosa
**Vernacular Name**

In different parts of India *O. corymbosa* is known by different names\(^{39}\).

**Sanskrit:** Parpata, Parpataka

**English:** Diamond flower

**Hindi:** Daman pappar, Pitpapra

**Malayalam:** Parpatakapullu, Parpatakam

**Geographical distribution:** *Oldenlandia corymbosa* is native to Africa and India, but also found throughout Malaysia\(^{40}\).

**Morphology:**

It is an annual slender herb up to 40 cm tall. Stem is 4-angled to flat, glabrous and angles are thick to wing. Leaves are simple, sub-sessile or very short petiole. They are linear, narrowly lanceolate or narrowly elliptic. The size of leaf is 0.8-2 cm long and 0.1-0.5 cm wide. The base and apex is acute, margin is entire, secondary veins are not visible, stipules fused to petiole bases.

Inflorescence axillary, usually cymose and contains 2-5-flowers. Pedicels are slender and 2-12 mm long. Calyx is glabrous. Hypanthium portion is subglobose to narrowly ellipsoid. Corolla is white or pink, funnel form to rotate, tube 0.8-1 mm, inside pubescent or glabrous. Fruit capsular, subglobose, ovoid, 1.2-2×1.2-2.2 mm size, dehiscent through flat to broadly rounded apex, beak when present to 0.5 mm, peduncles and pedicels usually extending promptly and prominently as the fruit develops. Seeds are smooth and dark brown\(^{41,42}\).
1.11 *Grangea maderaspatana*

*Grangea maderaspatana* is a weed usually known as Madras carpet commonly budding in sandy lands and waste places. It is reported to have flavonoids, diterpenes, sesquiterpenoids, steroid and essential oil. It is a medicinal plant extensively used in the Indian traditional system of medicine for curing several ailments. The herb is worthy for pain in the eyes and ears. The root is an appetizer, astringent to the bowels, diuretic, anthelmintic, emmenogogue, galactogogue, stimulant, beneficial in gripping, in troubles of the chest and lungs, headache, paralysis, rheumatism in the knee joint, piles, pain in the muscles, diseases of the spleen and the liver, reduces sweating. The plant is stomachic and uterine stimulant

**Taxonomy of *Grangea maderaspatana* (L.) Poir**

Kingdom: Plantae
Subkingdom: Planta Tracheophyta
Subdivision: Spermatophyta
Division: Magnoliophyta
Class: Magnoliopsida (Dicotyledons)
Subclass: Asteraeidae
Order: Asterals
Family: Asteraceae

**Synonyms:**

*Grangea maderaspatana*, *G. adansonia*, *Artemesia maderaspatana*

**Vernacular name:**

**Gujarati:** Jhinkimundi, Nahanigora, Khamundi

**Hindi:** Mukhatari, Mustaru

**Malayalam:** Nelampala

**Marathi:** Mashipatri

**Tamil:** Mashipatri
Telugu: Machi-Patri
Urdu: Afsantin
Kannada: Dodda gaadaari

**Occurrence and distribution:**
It is a weed habitually growing in sandy lands and waste places. It is dispersed all over India, Baluchistan, Ceylon, tropical and subtropical Asia and Africa.

**Macroscopical characters**¹⁴³⁻⁴⁵
It is a prostrate, ascending to erect annual herb, which is up to 55 cm tall, split from base with a taproot. Stems are numerous, prostrate, spreading from the center, 10-30 cm long, haired with soft white hairs.

**Leaves:** Leaves are numerous, sessile, 2.5-6.3 cm long, sinuately pinnatifid with 2-4 pairs of opposite or subopposite lobes smaller towards the base and largest towards the terminal lobe, margins coarsely serrate-dentate, pubescent on both sides.

**Flowers:** The inflorescence is terminal, truncate spherical head, 6-10 mm in diameter, solitary or 2-3 together, yellow and many flowered. The peduncle is 1-4 cm long.

**Fruits:** The fruit is turbinate and compacted while the truncate achene is about 2mm long, smooth and sparingly glandular. The pappus consists of a ciliate cup. The hypocotyls are 2-2.5 mm long. The cotyledons are subsessile and elliptical to widely elliptical while epicotyl is absent.
1.12 Psychopharmacological activity:

Psychopharmacology is the systematic study of the effects of drugs on mood, sensation, thinking and behavior\textsuperscript{46}. Psychiatry denotes to a field of medicine focused specifically on the mind, aiming to study, prevent, and treat mental disorders in humans\textsuperscript{47}. The condition often co-exists with other chronic ailments that amount to even greater morbidity and mortality rates. According to the WHO, disability due to mental illnesses is greater than cancer and heart disease in developed countries\textsuperscript{48}.

Public concern on mental health has noticeably increased given the high prevalence of neuropsychiatric disorders. WHO reports approximately 450 million of people suffer by mental or behavioral disorder\textsuperscript{49}. Two-thirds of the anxious, depressed or psychotic patients react to the currently available treatments; but their clinical uses are limited by their side effects such as psychomotor injury, potentiation of other central depressant drugs and dependence liability. In the hunt for novel therapeutics for the management of neurological disorders, medicinal plant research has also contributed by demonstrating pharmacological effectiveness of different herbs in various animals models\textsuperscript{50,51}.

Herbal treatments are gaining emergent attention because of their cost-effective, eco-friendly features and true relief from illness. Since antique tense the herbal remedies are effective in the control of some complaints. Various plants have a folklore claim in the dealing of some dreadful syndromes, but they are not scientifically exploited and/or incorrectly used. Thus, these plant dose demerit particularised contemplation in the luster of neoteric cure\textsuperscript{52}.
References:


