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ETHNOMEDICINAL KNOWLEDGE TO EVIDENCE-BASED THERAPEUTICS: CONTEMPORARY ADVANCES IN PHARMACOGENETIC EVALUATION OF MEDICINAL PLANTS

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ABSTRACT:
Background: Metabolic syndrome is a major cardiometabolic health problem, and simple anthropometric measures may facilitate early identification of individuals at increased metabolic risk. Body mass index (BMI) reflects overall adiposity, whereas waist circumference (WC), waist-to-height ratio (WHtR), and neck circumference (NC) provide information regarding regional adiposity.
Methods: A hospital-based cross-sectional analytical study was conducted among 200 adults attending a tertiary care hospital over a six-month period. Demographic and clinical information was collected using a structured proforma. BMI, WC, WHtR and NC were measured using standardized anthropometric techniques. Blood pressure was recorded, and fasting plasma glucose, triglycerides and HDL-cholesterol were estimated. Metabolic syndrome was defined according to harmonized criteria. Descriptive and comparative analyses were performed, followed by correlation analysis, receiver operating characteristic (ROC) analysis and logistic regression. Diagnostic performance was assessed using area under the curve (AUC), sensitivity, specificity and optimal cut-off values.
Results: Metabolic syndrome was identified in 93 (46.5%) participants. BMI, WC, WHtR and NC were significantly higher among participants with metabolic syndrome than those without it ($p<0.001$ for all comparisons). All four anthropometric indices demonstrated significant positive correlations with fasting glucose and triglycerides and inverse correlations with HDL-cholesterol. WHtR demonstrated the highest discriminatory performance for metabolic syndrome, with an AUC of 0.852 (95% CI: 0.801–0.903), followed by WC (AUC 0.816), BMI (AUC 0.797) and NC (AUC 0.712). The optimal WHtR cut-off was >0.529, with 72.0% sensitivity and 86.0% specificity. In adjusted logistic regression analysis, WC demonstrated the strongest independent association with metabolic syndrome (OR 8.63, 95% CI: 4.59–16.23).
Conclusion: WHtR demonstrated the best overall discriminatory performance, while WC showed the strongest independent association with metabolic syndrome. These measures may complement BMI in identifying adults requiring further metabolic assessment, while NC may serve as an additional simple anthropometric marker.

KEYWORDS: Metabolic syndrome; obesity; body mass index; waist circumference; waist-to-height ratio; neck circumference; anthropometry; ROC curve.

INTRODUCTION

1.1 Background and Historical Context

Despite the differing geographic location of these communities, the importance of the ethnomedicinal knowledge they employ is fundamental to the cultural, economic, and social constructs of their respective societies. In sub-Saharan Africa, over 4,000 plant species have been documented as being utilized in the healing process, while in the Amazon, the indigenous tribes use the plant Uncaria tomentosa, also called "cat's claw," because of its immunomodulatory effects. In addition, the system of Siddha and Unani medicine, as used in Asia, is said to function alongside the system of Ayurveda (1). Historical records show that the Ebers Papyrus, as used by the ancient Egyptians around 1550 BCE, contains over 700 plant-based medicines, including the use of opium latex as an analgesic, while the Shennong Ben Cao Jing, as used in China around 200 BCE, contains 365 medicines and is said to be the oldest surviving pharmacopeia. The Roman Empire is also said to have contributed to the world of medicine, as evidenced by the contributions of Dioscorides, as documented in De Materia Medica, compiled around 50 CE. Evidence from the historical record shows that colonialism led to the interactions and exchanges between cultures. The example cited is the use of quinine, derived from the bark of the Cinchona plant, by Jesuit missionaries as an anti-malaria drug, illustrating the move from the use of ethnomedicine to pharmacology. In the twentieth century, plant-based precursors led to the development of drugs such as aspirin (2). The use of willow bark and the discovery and validation of the use of the Chinese herb Artemisia annua,

as used in the 1970s, show that 25-50% of the medicines now in use are derived from plants, and the renewed interest in the search for new medicines from plants is well founded.

1.2 Key Concepts

The term pharmacognosy is derived from the Greek words pharmakon, meaning “drug or poison,” and gnosis, meaning “knowledge”. It originated in the 19th century from the study of crude drugs and involves the authentication and standardization of natural products as a multidisciplinary field integrating botany, chemistry, and pharmacology (3). The primary activity of a pharmacognosist is pharmacognostic evaluation, which consists of three major components: (i) macroscopic or organoleptic evaluation, which includes the description of the color, odor, texture, and fracture of the product (e.g., the characteristic aroma of Cinnamomum camphora); (ii) microscopic evaluation, which examines cellular structures and may include powder microscopy, stomatal counting, and the study of veins, vein endings, idioblasts, and cystoliths (as observed in *Cannabis sativa*); and (iii) physicochemical evaluation, which includes the determination of total ash, acid-insoluble ash, water-soluble ash, and swelling index, as described by WHO guidelines (4). In contrast, ethnomedicine is subjective and experiential in nature and is often documented through ethnobotanical surveys, which may involve the use of the Fidelity Level (FL) index for the quantitative assessment of informant consensus. The need for therapeutic validity. However, demands a more stringent scientific approach, including the application of Roux’s principles such as randomization, controls, and replication, as well as meta-analysis and sophisticated laboratory studies. Such approaches are intended to detect biomarkers and develop a “gold standard” for herbal products. Such a “gold standard” is crucial to reduce batch-to-batch variability and to address safety concerns, including herb-drug interactions. St. John’s Wort, for example, is known to induce CYP3A4 metabolism, a potent effect on the efficacy of co-administered medications (5).

1.3 Relevance in Contemporary Healthcare

The rising problem of antimicrobial resistance, with the WHO predicting 10 million deaths per annum by 2050, and the untoward effects of synthetic drugs, as exemplified by nonsteroidal anti-inflammatory drugs (NSAIDs), responsible for an estimated 16,500 gastrointestinal deaths in the USA each year, highlight the tremendous opportunity to revive the therapeutic potential of the plant kingdom. The potential therapeutic value of over 25,000 plant species is considerable, given the wide structural diversity of secondary metabolites, as exemplified by alkaloids (e.g., vinblastine from (Catharanthus roseus) for the treatment of leukemia), terpenoids (e.g., taxol from (Taxus brevifolia) in cancer therapy), and polyphenols (e.g., resveratrol from (Vitis vinifera) with cardioprotective activity) (6). The global herbal market is expected to reach $150 billion by 2025, reflecting a compound annual growth rate (CAGR) of 7-10%. The growth is driven by the increased market potential of integrative medicine, especially among the elderly with non-communicable diseases (NCDs) such as diabetes, affecting 537 million people worldwide. India is home to over 7,500 species of ethnomedicinal plants and has tremendous potential for standardization through AYUSH. However, the pharmacognostic potential is only 15% or less, given the tremendous potential offered by the Eastern Himalayas, where 50% of the endemic plant species are found in the country. The WHO Traditional Medicine Strategy 2025-2034 and the European Medicines Agency’s issue of herbal monographs highlight the importance of pharmacognostic evaluation.

1.4 Scope and Objectives of the Review

The review is intended to illuminate the translational mechanisms involved in the process from ethnomedicinal knowledge to the practical application of therapeutics. The scope is limited to recent developments in pharmacognostics since 2015, including, but not limited to, HPLC-DAD-MS, NMR-based metabolomics, and recent developments in AI-based omics technologies (8). Ethnobotanical databases such as NAPRALERT and Dr. Duke's Phytochemical and Ethnobotanical Databases, as well as emerging technologies such as blockchain technology, are included within the scope. The major goals are to (i) compile over 200 peer-reviewed publications, such as those found on PubMed, Scopus, and Web of Science, focusing on the transition from documentation to standardization; (ii) compile over 20 pharmacognostic markers for priority medicinal plants such as Azadirachta indica (neem) for antiviral applications; (iii) determine gaps for clinical application through meta-analysis, performed according to PRISMA guidelines; and (iv) explore sustainable approaches to bioprospecting within the Nagoya Protocol, with a focus on fair and equitable sharing with indigenous communities and knowledge-holders (9).

II. ETHNOMEDICINAL FOUNDATIONS

2.1 Global Knowledge Systems of Ethnomedicine

Systems of ethnomedicine often combine biological and cultural knowledge, and this is found in a range of different ecosystems, including rainforest, desert, and high-altitude ecosystems. The holistic and experiential approaches to health and healing, as seen in these systems, perceive medicinal plants to be a part of the process for maintaining a balance among the physical, spiritual, emotional, and social aspects of human existence (10). In India, the traditional system of healing known as Ayurveda is described in ancient texts such as the "Charaka Samhita" and "Sushruta Samhita," where a number of medicinal plants are described and classified. For example, *Withania somnifera* or *ashwagandha*, a rasayana herb that rejuvenates the body, is used to treat stress, as an immunomodulator, and as a general body tonic. In the traditional system of healing known as Siddha, used in Tamil Nadu, a number of herbal and mineral preparations are commonly used. One such plant, (Terminalia chebula) haritaki, is known for its astringent and laxative properties and is traditionally employed for detoxification, purification of body systems, and longevity. Likewise, in Unani medicine, popularly known as Greco-Arabic medicine and practiced in some areas of the Deccan plateau, (Commiphora wightii) resin, referred to as guggul, is traditionally employed for maintaining metabolic balance, relieving joint stiffness and inflammation, etc. The (Shennong Bencao Jing) is considered one of the first recorded documents on the materia medica of Traditional Chinese Medicine (TCM). The medicinal plants included in this system are (Panax ginseng) Ren Shen, traditionally employed for increasing vital energy and relieving fatigue, and (Ephedra sinica) Ma Huang, traditionally

employed for relieving respiratory conditions and expelling pathogenic factors. In Mesoamerican cultures, plants such as Tagetes lucida are used to treat gastrointestinal disorders, parasitic infections, and nervous system problems. Ritual steam baths with plants such as Piper sanctum are used in curanderismo, traditional medicine based on Mayan and Zapotec cultures, to bring about physical and spiritual purification.

In every culture, traditional societies have traditionally relied on plants as a source of healing. In Africa, the San and Khoikhoi tribes used (*Sceletium tortuosum*) (kanna) to improve moods and reduce anxiety. The Maasai tribes used (*Aloe secundiflora*) to heal wounds. In the Ituri Forest, the Congolese Pygmies used (*Ancistrocladus korupensis*) to cure fever. In Madagascar, (*Rauvolfia vomitoria*) was used to cure hypertension. In Australia, the Indigenous tribes used eucalyptus leaves in inhalation therapy to cure respiratory infections and microbial diseases. In Fiji, the leaves of (*Polyscias scutellaria*) (Kowai) are traditionally used to treat infant colic and aid in the process of digestion (13). All these systems underscore the value of polyherbal synergy in which multiple herbs are used to improve the therapeutic value of the medicine. They also underscore the value of seasonal collection of herbs, the use of ritualistic practices, and the inclusion of spirituality in medicine. Most importantly, these traditional systems of medicine are serving a vital purpose in primary health care, especially in areas where access to modern medicine is difficult or too costly.

2.2 Approaches to Documentation in Ethnobotany

Ethnobotanical documentation has its own guidelines to structure qualitative and informal data into a more structured and usable one. Researchers try to reduce the subjective nature of ethnobotanical data by using a combination of different approaches, even while maintaining its informal nature. Data collection takes place through semi-structured interviews with healers and elders who possess in-depth knowledge about plants and their uses. During interviews, researchers collect “use reports”, which are related to the use of a particular plant for a specific health condition. Use reports can sometimes provide detailed descriptions of the methods of preparation of the plants, the dosage of the plants (which may vary depending on the patient and the severity of the illness), and the application of the plants (which can be taken internally, applied topically on the skin, or even used in the process of fumigation).Researchers can determine the importance of certain plants with the help of free listing and pile sorting methods, which can give a clue about the most commonly known and used plants. Quantification of the significance and use of the plants and the level of agreement are also carried out with the help of various research methods.

Other methodologies include the development of voucher specimens, which are authenticated and placed in herbarium collections, and the use of GPS devices to record the locations of the sites of collection in order to facilitate ecological monitoring and replication. Participatory rural appraisal methods are used to portray the knowledge systems of the population. The digitalization of ethnobotanical data has enabled the development of simple databases such as NAPRALERT, which links bioactive compounds with ethnomedicinal uses and Dr. Duke's Phytochemical and Ethnobotanical Databases. Other sources of information include the ethnopharmacological databases of the United States National Library of Medicine, as well as artificial intelligence-based systems which digitalize and analyze indigenous knowledge with the aim of enhancing its accessibility (16). The ethical issues continue to be an important consideration in ethnobotanical studies. The issues include Free, Prior, and Informed Consent (FPIC) for the communities, fair and equitable benefit-sharing, indigenous data sovereignty, and the prevention of exploitation of traditional knowledge, among others (17). Some interesting case studies include studies carried out in the foothills of the Himalayan Mountains, where healers' consensus was established for *Swertia chirayita* use in metabolic disorders, studies carried out in the Peruvian Amazon region for the latex use of *Croton lechleri* to control hemorrhage and wound healing, and studies carried out in the Western Ghats region for the bark use of *Holarrhena antidysenterica* to treat dysentery. These studies illustrate the use of best practices in ethnobotanical studies and are a step towards advancing reproducible pharmacognostic studies (18).

2.3 Key Medicinal Plants, Success Stories

Ethnopharmacology is an example of the role that plants have played in the development of multimillion-dollar industries, and the pharmaceutical industries are no exception. Artemisinin, derived from (*Artemisia annua*), has saved thousands of people from serious malaria and earned its discoverer, Professor Tu Youyou, the Nobel Prize. Antimalarial agent Originated in ancient Chinese medicine as a treatment for fevers and chills. Cinchona bark of *Cinchona calisaya*, brought to Europe by Jesuit missionaries, led to the discovery of quinine, the first effective antimalarial agent and precursor of a number of synthetic derivatives (19). *Digitalis lanata*, a plant used in traditional folk medicine by Romani communities, was later adapted into modern medicine for the treatment of congestive heart failure and atrial fibrillation through the use of digitalis and other cardiac glycosides. Similarly, the Sumerians referred to *Papaver somniferum* as the “joy plant,” as it is the natural source of morphine and codeine, which remain essential for pain management in surgical and palliative care settings (20). The chemotherapeutic agent paclitaxel (Taxol®), used in the treatment of ovarian, breast, and lung cancers, was partly inspired by Native American knowledge of *Taxus brevifolia* (Pacific yew), whose bark was traditionally used for pain and tumor-related conditions. Likewise, Malagasy traditional practitioners used *Catharanthus roseus* (periwinkle) for diabetes-related symptoms. This led to the discovery of vinca alkaloids such as vincristine, which revolutionized the treatment of childhood leukemia and Hodgkin’s lymphoma through their ability to inhibit cell division. In Indian traditional medicine, *Curcuma longa* (turmeric) has long been used as a wound-healing agent. Its active constituent, curcumin, is currently under clinical trials to evaluate its effectiveness for the treatment of inflammatory bowel disease, arthritis, and some neurodegenerative disorders because of its anti-inflammatory and antioxidant properties (21).

2.4 Challenges in Documentation and Transmission

This gap in indigenous knowledge is increasing due to the continuous loss of traditional knowledge, which is being exacerbated by the aging population of healers and the lack of apprentices. This knowledge loss is irreversible. This is especially true in regions that are more vulnerable to this issue, such as the Amazon region, where the Yanomami are at

risk of losing an entire knowledge system in just one generation (22). Knowledge theft on the biocultural level is also an issue. One can point to the patenting controversy of hoodia, traditionally used by the San people, and the neem plant, traditionally used in Indian traditional medicine. These are violations of the principles of equity and the legal framework set forth in the Convention on Biodiversity, leading to increasing mistrust and litigation that undermines cooperative research. However, data quality problems also exist in ethnobotanical research, and they include recall bias from leading questions, seasonality, and a focus on elite practitioners, which may neglect informal healers, gatherers, and midwives. Further, Western biomedicine does not consider the psycho-spiritual aspects of healing rituals and plant use. Threats to habitats exist in many forms and on a large scale, e.g., overharvesting and commercialization of ginseng, leading to its near depletion, and subsequently, many plant species are threatened with extinction (23). These challenges are further complicated by climate change, which influences changes in suitable zones for plant growth, and issues of access to land and socio-economic factors like rapid urbanization, which cause a loss of experienced wild harvesters and alter traditional modes of land utilization. In addition, market forces have a major impact on wild harvesting instead of promoting sustainable cultivation techniques, hence speeding up environmental degradation. There is a large information gap in ethnobotany, especially in areas like Oceania, comprising island countries, and Central Asia, comprising steppes, which are rich in biodiversity but underrepresented. These areas have invaluable traditional knowledge reservoirs, which have yet to be protected (24).

2.5 Role of Multidisciplinary Ethnobotany in Pharmacognosy

Multidisciplinary ethnobotany thus shows the potential of various disciplines being brought together, including anthropology to gain a deeper understanding of the culture of the people, linguistics to decipher the meaning of the names of the plants and the oral traditions of the people, ecology to study the aspects of sustainability, and pharmacology to assess the therapeutic value of the plants. Such source-to-clinic pathways generally start with the documentation of the ethnomedicinal claims and then the pharmacognostic evaluation and scientific validation of the plants (25). Organizations like the World Health Organization's herbal monographs and the Traditional Knowledge Digital Library of India are of utmost importance in protecting intellectual property rights and promoting scientific validation and commercialization of the traditional knowledge of the people. Conservation ethnobotany also helps to support such endeavors through the promotion of in-situ conservation practices, such as community-based botanical gardens like those in Kerala, which aid in the conservation of rare and endangered species and also facilitate intergenerational knowledge transfer. Community-based biodiversity inventories also help to empower communities and promote sustainable management practices, thus supporting global sustainability agendas such as "Life on Land". This critical knowledge base has to be preserved through the adoption of decolonized research methodologies, such as co-authoring with indigenous scholars as co-authors, not co-researchers. New technologies such as blockchain may improve the transparency and traceability of supply chains, while technologies such as metabolomics and genomics may help speed the conversion of ethnomedicinal leads into validated therapeutics (26).

III. PHARMACOGENETIC EVALUATION METHODS

3.1 Organoleptic and Macroscopic Evaluation

Organoleptic evaluation, therefore, can be thought of as the "first handshake" between a researcher and a plant. Before any complicated machinery or chemical analysis comes into play, this method entirely relies upon human senses to create a quick, holistic impression of a given sample. By merely looking at the color, touching the texture, or smelling the aroma, one can immediately evaluate what a given sample is and whether it has been kept fresh or not. For instance, if a given leaf has lost its color and turned brown rather than maintaining its original green color, then it immediately implies that this particular leaf has been kept for too long or has been dried improperly. The pungent smell of Eucalyptus or the strong resinous smell of Myrrh immediately functions as a fingerprint for immediate identification, while the snapping sound of a brittle stem or the moisture content of a thick root immediately reveals how it has been stored (27). While "vibes" might be part of this, there is also a disciplined examination of the physical architecture of the plant. One might look at the size of the leaves, the vein patterns, and the inner structure of a stem or a particular part of a flower. It's this kind of attention to detail that will help identify red flags, such as overly large leaves that could be a sign of hybridization or worse, artificial coatings to hide poor quality. The macroscopic examination, finally, is the final screening tool in the field; it's a quick and sure method of making certain that plants meet quality standards before they ever leave the field, making it a critical first step in both traditional ethnobotany and contemporary agricultural safety (28).

3.2 Microscopic and Histological Analysis

Microscopic evaluation is an extension of pharmacognostic study that involves an analysis of the cellular and tissue level organization of plant materials to show diagnostic anatomical markers with minimal chances of misidentification. The anatomical features of plant parts are examined using sections cut along the transverse and longitudinal axes using techniques such as freehand sectioning, microtome sectioning, and powder microscopy. The microscopic features include the types of stomata, e.g., paracytic stomata in Mentha piperita and anisocytic stomata in Atropa belladonna. These features are quantitatively measured using the stomatal index, calculated as the ratio of the number of stomata to the total number of epidermal cells and stomata.

Stomatal Index= Number of stomata % Number of stomata + Number of epidermal cells ×100

To really know a plant, scientists seek "security features" that are hidden at a cellular level, such as "trichomes", those tiny hair cells that vary from the simple hairs found on stinging nettles to the complex oil glands found in Cannabis. Further examination also reveals "anatomical fingerprints", such as "calcium oxalate crystals", which appear as tiny crystals in turmeric or needle-like crystals found in taro. Even further, an examination of the "plumbing and skeleton", such as "vessels", or water cells, and "stone cells", which give structure and grit to a plant, allow for a definitive

identification to be made. The microscopic details are like a "botanical serial number", a foolproof means to ensure that a material is authentic and safe to use(29). Staining techniques improve the contrast and facilitate differentiation of the tissue structures. To illustrate, the use of the phloroglucinol-hydrochloric acid stain gives a pink color to lignified tissue structures, Sudan III stains lipophilic compounds, e.g., oleoresins, orange-red, while iodine solution is used to locate starch granules, which give a blue-black color. Polarized light microscopy is employed in the differentiation of crystalline structures, e.g., druses, while crystal sands are differentiated using the same technique. Powder microscopy is advantageous in the study of commercial samples, particularly in the detection of adulterants, e.g., ginseng powder replaced with rice starch, while the "fingerprints" obtained from histological examination, when compared to the standard anatomical literature, e.g., Brain and Metcalfe's Anatomy of the Dicotyledons, facilitate the accurate identification of species, detection of adulterants, and localization of bioactive compounds, which in turn can be used to direct the selective extraction processes (30).

3.3. Physicochemical Standardization Parameters

Physicochemical evaluation of the bulk material of the plants is carried out by testing a number of batches of the material to determine the extractability and purity of the material with regard to certain physical and chemical parameters. This ensures the product meets the established pharmacopoeial standards and is of uniform quality (31). These parameters are established by international pharmacopoeial organizations such as the World Health Organization and the United States Pharmacopeia to ensure minimum variation due to environmental factors such as the composition of the soil and the climatic conditions in which the plants are grown and handled after harvesting. To get a true sense of a plant's quality, scientists move beyond the surface and run a series of "chemical health checks" to ensure it's both pure and effective. One of the most telling tests is an ash analysis; by burning a sample, researchers can see what's left behind—if there's too much gritty residue, it's a dead giveaway that the batch is contaminated with sand or dirt. They also test "extractive values" by soaking the plant in solvents like alcohol or water to measure exactly how many active, healing ingredients it can actually release. Moisture control is another big deal; using oven drying to measure "loss on drying" ensures the material isn't damp enough to grow mold or go bad. Finally, for aromatic plants like fennel, a specialized steam-distillation process is used to pull out its essential oils. If that oil yield is low, it's a sign the plant is a weak substitute rather than the potent, high-quality medicine it's supposed to be (32). Other parameters include swelling and foaming indices, especially in the case of mucilage-containing plants like Plantago ovata (psyllium), which indicate the water absorption and saponin content of the plants, respectively. Moreover, the pH of the aqueous solutions or suspensions is also evaluated, as in the case of Myristica fragrans (nutmeg) with slightly acidic properties. All these parameters are standardized according to the WHO and USP guidelines and are therefore a set of pharmacopoeial 'fingerprints' of the herbs and spices, which ensures the reproducibility and quality of the herbs and spices and compliance with the regulatory guidelines. For example, the extractive values of the Piper longum fruits are standardized to 8-12% water-soluble extractives, which ensures the consistency of the fruit's use in medicine.

3.4 Preliminary Phytochemical Screening

In preliminary phytochemical screening, qualitative color reactions are utilized to identify major classes of secondary metabolites, thus facilitating the assessment of extract potential and target selection. Alkaloids can be detected using precipitation reactions with reagents like Mayer's reagent, where a creamy precipitate is formed, and Wagner's reagent, where a reddish-brown precipitate forms, as seen in (Vinca minor). The detection of flavonoids can be done using Shinoda's test, where a magenta or pink color is formed after the addition of magnesium and hydrochloric acid; alkaline conditions can cause this color to be shifted to orange. Tannins are characterized by the formation of gelatinous sediments with protein substances and the formation of green-black or blue-black colors following the reaction with ferric chloride, depending on the type of tannins. Sterols and triterpenoids are characteristically identified using the Liebermann-Burchard test, in which acetic anhydride and concentrated sulfuric acid produce a green or blue color following the reaction (33). Anthraquinones, as found in Cassia senna, are identified using the Borntrager's test, which produces pink or red colors in the ammoniacal phase following alkaline extraction. Thin Layer Chromatography (TLC) is commonly employed as an instrumental method to separate and identify these phytochemicals. In general, the phytochemicals are defatted using nonpolar solvents (e.g., hexane), and the extracts are then treated with solvents of increasing polarity (e.g., chloroform and methanol). The separated phytochemicals are visualized under ultraviolet light or using anisaldehyde-sulfuric reagent, which shows characteristic violet or purple colors for terpenoids. These initial screening techniques are used to rapidly screen phytochemical classes, which in many cases are correlated with ethnomedicinal uses. Curcuma longa, formerly Curcuma domestica, has been linked to anti-inflammatory compounds, while members of the Corynanthe genus are linked to alkaloids with antimalarial properties. Bioassay-guided fractionation is then performed to isolate the active compounds, which are then tested for biological activity, while also allowing the detection of potentially toxic compounds, including pyrrolizidine alkaloids (34).

3.5 Customary Developments and Hyphenated Techniques

Modern developments in pharmacognosy have utilized an integrated approach in analysis, where chromatography and mass spectrometry techniques, such as LC-MS and GC-MS, have been linked with metabolomics to provide a complete chemical profile. High-performance liquid chromatography with diode array detection (HPLC-DAD) is often employed for quantitative analysis of bioactive constituents, such as curcuminoids in (Curcuma longa) at 425 nm and withanolides in (*Withania somnifera*) at 254 nm, using standard references. Ultra-performance liquid chromatography with electrospray ionization quadrupole time-of-flight mass spectrometry (UPLC-ESI-QTOF-MS) facilitates the thorough characterization of intricate polyphenolic mixtures like Camellia sinensis with the aid of mass fragmentation patterns. Further structural characterization of the bioactive constituents of the plants can be performed with the aid of nuclear magnetic resonance (NMR) spectroscopy, including ^{1}H and ^{13}C NMR spectroscopy. DNA barcoding with the help of various DNA markers like matK, rbcL, and ITS2 can also be performed to authenticate the plant materials and resolve

taxonomic uncertainties of traded plants like Ginkgo biloba and Sophora japonica (35). Recent advances in the development of artificial intelligence technologies have made it possible to carry out automated image analysis for the quantification of microscopic parameters, e.g., stomatal indices using microphotographs. The use of multivariate statistical tools, such as Principal Component Analysis (PCA), is used to differentiate genuine samples from adulterated ones. These tools, in accordance with ICH Q2(R1) guidelines for validation, have transformed pharmacognosy from an entirely descriptive science to one that is predictive and very standardized. This justifies in-depth analytical studies on starting materials, as discussed in the subsequent sections(36).

IV. PHYTOCHEMICAL PROFILING AND ISOLATION

4.1 Extraction Methodologies and Solvent Selection

Extraction of secondary metabolites is done using solvents that are usually selected on the basis of their polarity, while the preservation of thermolabile metabolites and the achievement of the highest yield from plant parts are taken into account. The traditional methods of plant extraction include the following:

Maceration is the method in which powdered plant material is treated with solvents, ethanol, or methanol, and the mixture is left to soak for a few days with occasional shaking, and the solution is filtered to extract the bioactive compounds, such as glycosides from the roots of (*Glycyrrhiza glabra*) licorice. The process can be improved through percolation, in which the solution is allowed to percolate through the plant material, such as alkaloids from the roots of (*Rauwolfia serpentina*) (37). The Soxhlet method is an extraction technique that uses reflux, thus creating continuous solvent circulation. The method is applicable in the exhaustive extraction of lipophilic substances, waxes, and triglycerides from Ricinus communis, commonly referred to as Castor. The most commonly used solvents are non-polar, such as petroleum ether, followed by the application of polar solvents. Modern methods have improved the efficiency and selectivity of the process. The application of supercritical fluid extraction (SFE) is applicable in the extraction of essential oils from Lavandula angustifolia, wherein the solvent leaves no residue. The application of ultrasound assisted extraction (UAE) is applicable in the extraction of phenolic compounds, as seen in the case of Vitis vinifera, commonly referred to as Grape skins. Likewise, microwave-assisted extraction (MAE) utilizes a form of dielectric heating to improve the extraction of polyphenols from *Camellia sinensis* (tea) leaves (38). Sequential fractionation is often used to separate compounds according to their polarity. This usually starts with a defatting step involving non-polar solvents such as hexane, followed by extraction with increasingly polar solvents such as chloroform for moderately polar compounds such as sesquiterpenes, ethyl acetate for flavonoids, n-butanol for glycosides, and finally water for polysaccharides. Such a strategy follows the principle of “like dissolves like” and, in many cases, may also be validated by a preliminary thin layer chromatography (TLC) study. Classical approaches like infusions and decoctions are also important, especially when extracting water-soluble constituents such as mucilage from Aloe vera plants. This approach not only follows ethnomedicinal practices but also helps in streamlining downstream processes by following the solubility pattern of the target compound (39).

4.2 Separation and Purification Techniques

In order to take the raw plant extract and turn it into a pure and useful drug, the isolation process is treated as if it's a high-stakes game of sorting. Liquid-liquid partition is one of the most powerful methods, and the idea behind it is that certain chemicals have a "preference" for certain environments, so if you shake the turmeric mixture with the right solvents, the curcumin will "choose" the correct side and become much easier to separate. Another basic tool is column chromatography, which is like a race through an obstacle course on a microscopic scale. By pouring an extract through a column of silica gel and washing it with various solvents, different compounds like terpenoids in sweet wormwood pass out of the column at different rates. By the time the liquid drips out of the column, the once complex mixture is separated into individual components ready for medical study. But when speed is the main goal, they have flash chromatography, where the power of the pressurized air is harnessed to "push" the extracts through the system, rapidly isolating the desired active ingredients, such as the Withanolides found in Ashwagandha. For very small, sensitive operations, they have preparative thin-layer chromatography, where very small quantities of the substance are spread out on a plate and are detected by being made to glow under ultraviolet light before being physically removed from the plate. At the other end of the scale, if the quantity being processed is large, then the solution is vacuum liquid chromatography, as the faster method, where the power of the vacuum is harnessed to draw solvents through the substance. Whether using the power of the press or the power of the UV, the goal is the same: to rapidly remove the noise and find the desired medicinal ingredients hidden within the plant. High-performance liquid chromatography (HPLC), especially when using a reversed-phase C18 column and an acetonitrile/water gradient, is commonly employed for semi-preparative separation of compounds like hyperforin from Hypericum perforatum. Size-exclusion chromatography with a Sephadex LH-20 column has been successfully employed for separation of polyphenolic compounds, while ion-exchange resins are employed for separation of charged alkaloids like berberine from Berberis aristata. Countercurrent chromatography, a liquid-liquid partition chromatography technique, has been successfully employed for separation of labile compounds like anthocyanins from berries. In bioassay-guided fractionation, the process of separating chemicals is coupled with the bioassay, which allows the identification of the active compounds. In this regard, the antioxidant activity can be determined using the DPPH method in fractions of *Ocimum sanctum*. This approach allows the isolation of the bioactive compounds, which are then relevant to the therapeutic use (40).

4.3 Advanced Analytical Techniques for Structural Elucidation

Hyphenated techniques in analysis and multidimensional dereplication approaches allow for the integration of data from individual components, thus enabling rapid identification of known compounds and discovery of new molecular scaffolds. For instance, gas chromatography–mass spectrometry (GC–MS) is a hyphenated technique commonly employed for analyzing volatile mixtures. Trimethylsilylated terpenoids present in Eucalyptus oils can be separated

using gas chromatography and subjected to analysis using electron impact ionization, where fragmentation patterns can be correlated with existing libraries such as the NIST library. In this case, a compound like 1,8-cineole contains a molecular ion at 154m/z (41). Liquid chromatography-mass spectrometry (LC-MS), especially in negative ion mode, is widely used for the analysis of polyphenols such as quercetin-3-glucoside. The use of tandem mass spectrometry (MS/MS) helps to cleave the sugar moiety, and this is very useful for structural confirmation. The use of high-resolution quadrupole time-of-flight mass spectrometry (QTOF-MS) is important for the analysis of complex molecules such as taxoids present in Taxus brevifolia. Nuclear magnetic resonance (NMR) spectroscopy continues to be an important tool in the structural elucidation process. Proton NMR (^{1}H NMR) can be used to locate characteristic proton signals, such as the enolic hydroxyl proton signal in curcumin, which appears at 14 ppm, while carbon NMR (^{13}C NMR) can give structural details about carbon skeletons, including quaternary carbon signals, which usually appear in the 150-170 ppm region for aromatic rings. Two-dimensional NMR techniques have also been employed in the structural analysis of compounds. In the case of Panax ginseng, the ginsenosides are characterized using 2D NMR techniques, namely HSQC and HMBC. Nuclear Overhauser Effect Spectroscopy (NOESY) is employed to elucidate the stereochemistry of compounds, based on the interaction of protons in close proximity to one another (42). Infrared spectroscopy, or FTIR, can be employed to elucidate the presence of certain groups, based on the stretching frequencies of certain bonds, including the O-H stretching frequency, which is approximately 3400 cm^{-1}, corresponding to the presence of phenolic groups, as well as the C=O stretching frequency, which is approximately 1700 cm^{-1}, corresponding to the presence of carbonyl-containing compounds, including lactones. Infrared spectroscopy (FTIR) is utilized as an identifying technique, and the absorption bands are characteristic, with O–H stretching bands at 3400 cm^{-1}, indicating the presence of phenolic groups, and C=O stretching bands at 1700 cm^{-1}, indicating the presence of lactones. X-ray crystallography, along with the Cambridge Structural Database, is the ultimate structural characterization technique, and this is applicable to the structural elucidation of artemisinin and other phytochemical leads (43).

4.4. The Markers for the Various Compounds Quantitatively

Quantitative analytical approaches relate standardization to pharmacopoeia markers through validated HPLC-UV methods following ICH Q2(R1) guidelines. Quantitation occurs within a range of 20-200 µg/mL, and linearity is obtained with correlation coefficients (R^2 values) > 0.999, using replicate samples and internal standards such as gallic acid for quantitation of tannins. For instance, in Curcuma longa, quantitation of curcumin occurs at 425 nm with a retention time of ~15 minutes using a gradient C18 system. For Ginkgo biloba, flavonoids such as quercetin and kaempferol glycosides are detected at 370 nm, while for Valeriana officinalis, valerenic acids are detected at 220 nm, and this is done through reverse-phase HPLC. Ultra-performance liquid chromatography (UPLC) reduces the time required for analysis to less than 5 minutes, making the process even more efficient for quality assurance purposes (44). Other quantitative methods involve enzyme-linked immunosorbent assays (ELISA), through which substances such as ginsenosides can be measured. High-performance thin-layer chromatography (HPTLC) with detection at 254 nm is generally used to obtain the fingerprint profile of the flavonoids and other bioconstituents of the plant material. Safety evaluation can be performed with the help of inductively coupled plasma mass spectrometry (ICP-MS) to detect and quantify the heavy metal impurities present in the compounds (45). In addition, stability-indicating methods are required, which include forced degradation studies on the compounds with the help of stress conditions like heat, light, and acids. This approach ensures the specificity of the methods by monitoring the degradation products of the compounds. Curcumin epimerization can be monitored at 420 nm. The resultant analytical data are compiled into a Certificate of Analysis (CoA), which is provided by accredited laboratories. Compliance with Good Manufacturing Practices (GMP) also entails batch-to-batch quality, such as minimum thresholds, e.g., not less than 3% andrographolide in Andrographis paniculata (46). Phytochemical profiling also allows for the exploration of structure-activity relationships (SAR), thus providing mechanistic insights into ethnomedicinal uses. For example, prenylated flavonoids in Artocarpus heterophyllus have been reported to show anti-inflammatory activity through NF-κB pathway inhibition, withanolides in *Withania somnifera* have been reported to modulate the hypothalamic-pituitary-adrenal axis, leading to adaptogenic activity, and sesquiterpene lactones in Vernonia amygdalina have been reported to show antimalarial activity through protein alkylation. Metabolomic techniques, coupled with statistical analysis such as Principal Component Analysis, can be utilized for the differentiation of genuine and adulterated plant materials, for example, distinguishing *Piper longum* from *Piper sarmentosum* based on *Piper longumine* profiles. The mechanism of phytochemicals targeting multiple targets has been further explained by network pharmacology, especially in complex systems such as Traditional Chinese Medicine (TCM) formulae. Dereplication using tools such as Reaxys and Dictionary of Natural Products has also sped up the identification process, along with early-stage PAINS filtering, which helps to reduce false positives. Along with this, drug-likeness evaluation using Lipinski's Rule of Five has also helped in identifying potential phytochemical candidates for further pharmacological evaluation (47).

V. IN VITRO AND IN VIVO VALIDATION

5.1 Bioactivity Screening Assays: In Vitro

Bioactivity assays are very important in assessing the therapeutic activity of plant extracts. These assays mimic the biotargets in an in vitro environment, hence circumventing ethical issues with in vivo testing. Many initial screenings are focused on antioxidant activity. The DPPH method, also known as the 2,2-diphenyl-1-picrylhydrazyl method, is used to evaluate the free radical scavenging activity based on the reduction of the stable purple DPPH free radical to a colorless one after the donation of hydrogen to the free radical. This reduction in absorbance is measured using spectrophotometry, usually at 517 nm, and often using ascorbic acid as a standard compound. For example, extracts from Curcuma longa (turmeric) have shown strong antioxidant activity using this method. The Ferric Reducing Antioxidant Power (FRAP) test is based on the reduction of Fe^{3+} to Fe^{2+}, which forms a blue-colored complex that is

measured at 593 nm. This method is often used to test extracts that are rich in polyphenols, such as Camellia sinensis (tea) (48). Antimicrobial activity is usually measured using techniques such as the disk diffusion method and the broth microdilution method, which detect zones of inhibition and minimum inhibitory concentrations (MIC), respectively. For example, the extracts from *Azadirachta indica* (neem) have shown inhibitory activity against microbial agents, including Staphylococcus aureus. Cytotoxicity is often determined using the MTT test (3-(4,5dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide), in which the MTT reagent is reduced to purple formazan crystals by the action of mitochondrial dehydrogenases in viable cells. The absorbance is measured at 570 nm, and the method is useful in the determination of selective cytotoxicity against cancer cell lines, such as the HeLa cell line. Anti-inflammatory activity can be tested using LPS-stimulated RAW 264.7 macrophages. Nitric oxide production can be measured using the Griess reagent, which produces a pink azo dye with an absorbance maximum at 540 nm. In addition, TNF-α can be measured using an ELISA, and NF-κB luciferase reporter assays can be employed for evaluating pathway inhibition, such as in Boswellia serrata-derived compounds (50). In enzyme inhibition assays, the focus is on specific therapeutic targets. For instance, in the α-amylase or α-glucosidase enzyme inhibition assay, the focus is on the evaluation of the antidiabetic effect of compounds, including charantin from *Momordica charantia*, which acts by inhibiting the enzyme in the hydrolysis of the substrate, measured at 405 nm. Acetylcholinesterase inhibition assays, relevant to neurodegenerative diseases, are usually performed using Ellman's method, where the rate of thionitrobenzoate production is measured at 412 nm, and the flavonoids from Ginkgo biloba have been found to have acetylcholinesterase inhibitory activity. The bioactivity assays are usually done in triplicate, and the inhibitory concentrations (IC_{50}) are calculated using nonlinear regression analysis. Overall, the bioactivity assays are important in prioritizing the bioactive fractions and identifying potential off-target effects (51).

5.2 Cell-Based and Organotypic Models

In vitro models give a platform for assessing the biological activity of plant extracts with a high degree of accuracy. For wound healing, human dermal fibroblasts and keratinocytes are commonly used cell types. For assessing cell migration and gap closure, scratch assays, also known as wound-healing assays, are employed, while other assays such as MTT assays are used for assessing cell proliferation, and collagen staining is used for assessing extracellular matrix deposition, among others. For instance, polysaccharides from Aloe vera have been shown to enhance wound healing. Three-dimensional cell culture models, including 3D cell lines such as HeLa and MCF-7, are more similar to in vivo tumors. These cell cultures typically involve embedding cells in a matrix, such as Matrigel, and then measuring invasion using a transwell assay, and metabolic activity using luminescent assays, such as CellTiter Glo. Neuroprotective cell culture models often involve SH-SY5Y neuronal cells and oxidative stress induced by glutamate. The cytotoxicity is measured through lactate dehydrogenase (LDH) release assays, and the results are measured through a spectrophotometric method (e.g., 490 nm). The protective activity, such as that shown by withanolides found in *Withania somnifera*, is through the activation of antioxidant pathways, including the Nrf2 pathway. The hepatoprotective activity is measured through cell lines such as HepG2, exposing the cells to oxidative stress (e.g., tert-butyl hydroperoxide). The restoration of glutathione levels, measured through a DTNB assay, indicates the protective activity of phytoconstituents (52). Co-culture systems are used to simulate the co-operative effects of polyherbal formulations. For example, extracts of Ocimum sanctum (Tulsi) and Zingiber officinale (Ginger) have been found to augment the anti-viral interferon response in Vero cell cultures infected with HSV-1. Receptor binding assays are used to study the mechanism of action of herbal extracts. These assays involve the study of the interaction of ligands with their receptors. These include radioligand displacement studies, e.g., the binding of morphine from Papaver somniferum to μ-opioid receptors, or valepotriates from Valeriana officinalis to benzoddiazepine receptor sites. Antiviral activity can be measured using virus yield reduction assays, where treated cells, such as Vero cells treated with Vernonia amygdalina extracts, are examined for reduced plaque-forming units after infection with viruses. High-end omics technologies, including transcriptomics, offer greater insights into mode of action. For instance, transcriptomic studies of Artemisia annua have shown gene expression profiles associated with bioactive compounds, thus providing a molecular understanding of pharmacological effects, including those that cannot be observed phenotypically (53).

5.3 In Vivo Pharmacological Models

In vivo validation is an evaluation of the entire organism's reaction to bioactive compounds, where the results obtained from in vitro studies are translated, and the experiments are carried out while adhering to the ethics of the experiments, as mentioned in the ARRIVE guidelines for animal experiments. Acute toxicity studies are performed using the OECD 423 guideline, fixed-dose method, usually on rodents, and the dose levels are between 5 and 2000 mg/kg (curcumin from Curcuma longa). The animals are kept under observation for 14 days for the appearance of acute toxicity, death, convulsions, and gastrointestinal upsets, and the LD_{50} levels are determined. Sub-chronic toxicity studies are performed using the OECD 407 guideline, where the animals are exposed to the test compound, usually by the oral route. These studies involve the measurement of various biochemical and hematologic parameters, such as liver function (ALT, AST) to detect hepatotoxicity, kidney function (creatinine, BUN) to detect nephrotoxicity, and a complete blood count to detect potential myelosuppression, as seen with taxanes from Taxus brevifolia (54). The antimalarial activity is also often measured by the Peter's 4-day suppressive test, performed on mice infected with Plasmodium berghei. Administration of extracts such as those found in Artemisia annua results in decreased parasitemia, measured by Giemsa-stained smears, as well as recrudescence. Antidiabetic activity is tested in streptozotocin-nicotinamide induced diabetic rat models. The administration of antidiabetic extracts like Momordica charantia decreases the levels of fastingblood glucose levels, measured using glucometers, and glycated hemoglobin levels, measured using HPLC. Anti-inflammatory activity is tested using carrageenan induced paw edema and cotton pellet granuloma models. In this model, Boswellia serrata extract decreases inflammation, indicated by reduced paw edema and decreased myeloperoxidase activity (55). Neuropharmacological studies use behavioral models like the forced swim test (for

antidepressant potential), the elevated plus maze (for anxiolytic potential), and the Morris water maze (for memory and learning). *Withania somnifera* and *Bacopa monnieri* extracts have shown potential in these models. Cardiovascular effects are studied by using models of hypertension and arrhythmias and testing compounds like Rauwolfia serpentina extracts, which are known to affect blood pressure and heart rhythm. These in vivo models establish initial safety margins and therapeutic efficacy, but they also allow for the assessment of pharmacokinetics, bioavailability, and plasma concentration-time profiles, such as area under the curve (AUC), determined using LC-MS analysis. These approaches offer invaluable information regarding dose–response relationships.

VI. CLINICAL EVIDENCE AND THERAPEUTICS

6.1 Evidence Synthesis and Human Clinical Trials

Clinical validation of plant-based therapeutics can be achieved through the development of appropriate protocols in the phases of clinical trials. Phase I trials are mainly focused on the evaluation of the safety, tolerability, and pharmacokinetics of the drug in healthy human volunteers. An example is the dose escalation studies conducted on curcuminoids derived from *Curcuma longa*, in which the dose was escalated up to 12 g/day to evaluate the safety profile, no-observed-adverse-effect levels (NOAEL), and pharmacokinetics, including absorption and biliary excretion. Phase II trials are focused on the evaluation of proof-of-concept and preliminary efficacy in the treatment of specific conditions. For example, randomized, double-blind studies using standardized extracts of the plant Ginkgo biloba, such as EGb 761, have shown positive effects on cognition using computerized cognitive assessment techniques. Similarly, studies using boswellic acids from the plant *Boswellia serrata* have shown significant improvement in the symptoms of knee osteoarthritis, as measured by the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) score, compared to placebo over 12 weeks. Phase III studies are designed to confirm the therapeutic efficacy and safety of the compound, using increased statistical power. Artemisinin-based combination therapies (ACTs) of Artemisia annua origin have shown parasitological cure rates of more than 95% in multicenter clinical trials of Plasmodium falciparum malaria in Africa and Asia. Similarly, clinical trials of Valeriana officinalis root extracts have shown improvements in sleep latency and quality using polysomnography in patients with insomnia. Systematic reviews and meta-analyses of heterogeneous clinical trial data can be performed using tools like PRISMA. Evidence of the efficacy of Panax ginseng and the role of cranberry proanthocyanidins in the prevention of recurrent urinary tract infections can be obtained from the Cochrane Library of systematic reviews. The GRADE system is often employed to grade the strength of evidence, from high (such as artemisinin-based treatments) to low, such as those for some adaptogenic herbal remedies. Efforts to improve the efficiency of clinical trials are increasingly using adaptive clinical trial designs, such as those with features such as interim analysis and futility boundary, such as those used for Echinacea in treating common cold (57).

6.2. Successful Examples of Cases

A notable instance of translational medicine is the transition from ethnomedicinal knowledge to the commercial development of drugs. The case of Paclitaxel or Taxol, which is derived from the bark of the Taxus brevifolia plant, can be cited as an instance of translational medicine. Paclitaxel, which originated from ethnobotanical knowledge of Native American ethnomedicine, has been the outcome of ethnobotanical knowledge, which led to the development of the drug through the National Cancer Institute's screening programs, eventually being approved by the Food and Drug Administration for the treatment of refractory ovarian cancer. The drug currently generates huge revenue in the global market, in addition to the development of other drugs in the same class, including docetaxel, which are used in the treatment of cancer. Artemisinin, which is derived from the plant Artemisia annua, has become integral in the treatment of malaria, as advocated by the World Health Organization. Their discovery was based on traditional Chinese medicine, which traditionally uses the herb to cure fever. Tu Youyou's research in the 1970s on the use of low-temperature methods to extract the herb resulted in the discovery of artemisinin and the consequent revolution in the treatment of malarial diseases (58). Metformin, which is the most widely prescribed medication for type 2 diabetes and is taken by more than 150 million patients worldwide, has its origin in the traditional use of *Galega officinalis*, French goat's rue. This herb's guanidine derivatives are the basis of the development of biguanides (59). Silybum marianum or milk thistle, is a source of the liver-protecting agent silymarin. It has received orphan drug designation for the treatment of certain diseases such as Amanita mushroom poisoning and has undergone clinical trials in the treatment of chronic liver diseases. In Ayurvedic medicine, *Semecarpus anacardium* (marking nut) has undergone evaluation of its therapeutic potential in the treatment of various diseases such as inflammatory conditions and cancer. Reverse pharmacology has shown significant success in the evaluation of polyherbal formulations. For instance, the Ayush-64 formula, which is an indigenous formula of India has shown efficacy in the treatment of febrile conditions such as malaria with evidence of parasite clearance. Padma 28, a multi-herbal formula of Tibetan medicine, has undergone a randomized clinical trial and shown efficacy in the treatment of patients with PAD, especially intermittent claudication (60).

6.3 Regulatory Frameworks and Pharmacovigilance

Regulatory guidelines on botanical products are necessary to ensure the quality, safety, and efficacy of the product. The World Health Organization Traditional Medicine Strategy is focused on developing pharmacopoeial monographs to establish the identity, purity, and quantitative standards. For instance, standardized extracts of Hypericum perforatum (St. John's Wort) need to have specific amounts of marker compounds, such as hypericin (e.g., ≥0.5%), and must comply with GMP guidelines and post-marketing surveillance programs. In the USA, the Botanical Drug Development pathway under the US Food and Drug Administration has resulted in approval for plant-based medicine such as Veregen® (Sinecatechins, derived from Camellia sinensis), approved under New Drug Application 021888 for the treatment of external genital warts. Similarly, In Europe, approval has been granted under the European Medicines Agency, through its Committee on Herbal Medicinal Products for herbal medicine such as Valeriana officinalis, also

known as Valerianae radix for use in sleep disorders. In the case of India, the Central Drugs Standard Control Organization (CDSCO), with the help of AYUSH, follows guidelines such as Schedule T, which regulates the manufacturing practices for herbal products (61). Pharmacovigilance is an important tool for monitoring adverse effects and ensuring the long-term safety of herbal products. Global sources such as WHO UMC VigiBase help to analyze adverse reaction reports. Hypericum perforatum is known to activate the CYP3A4 enzyme, resulting in significant herb-drug interactions and potential risks such as decreased drug efficacy or serotonin syndrome, especially when used with other medications. Safety concerns have also led to the regulation and ban of various herbal products. Species of the Aristolochia genus have shown nephrotoxicity and carcinogenicity after the administration of aristolochic acid. Similarly, cases of hepatotoxicity with black cohosh (Actaea racemosa) have been assessed using various causality assessment tools, such as the Naranjo algorithm. The United States Pharmacopeia general chapter <561> on articles of botanical origin outlines limits for contaminants, e.g., pesticides and heavy metals. Moreover, risk management plans are also developed to evaluate herb-drug interactions, e.g., CYP enzyme inhibition with furanocoumarins in grapefruit and piperine in Piper nigrum. Overall, the regulatory and pharmacovigilance tools provide an extensive framework to ensure the quality, safety, and efficacy of botanical drug products.

6.4 Meta-Analyses and Systematic Reviews

Evidence-based approach in phytotherapy policy-making involves a synthesis of clinical data through the use of robust methodologies. Systematic reviews under the PRISMA approach have pooled randomized controlled trials (RCTs) assessing the efficacy of Curcuma longa, showing substantial pain relief (weighted mean difference, WMD, −15.36 mm on the visual analog scale, VAS), with low levels of heterogeneity ($I^2 < 25\%$). Likewise, meta-analyses have established that Aloe vera gel is beneficial for the healing of burns, with a relative risk (RR) of 1.42 for re-epithelialization. Prospective registration of systematic reviews using PROSPERO facilitates transparency and minimizes bias. Publication bias is usually evaluated using funnel plots, especially in studies on adaptogenic herbal medicine. Network meta-analyses are used to evaluate the effectiveness of multiple interventions. These interventions are ranked according to their effectiveness. Panax ginseng has been found to be superior to placebo in managing erectile dysfunction with a Surface Under the Cumulative Ranking (SUCRA) value of 0.89. Living systematic reviews, where reviews are continuously updated as more evidence becomes available, have been particularly useful during the pandemic. For example, studies using Andrographis paniculata have shown symptom reduction in duration. The GRADEpro system has been widely used to evaluate the certainty of evidence. It supports grading down evidence based on indirectness, such as animal studies being applied to human studies, and imprecision, such as underpowered studies, while grading up evidence if results are strong and consistent. High certainty has been established for some interventions, such as artemisinin-based treatments, while others, such as some adaptogens and immunomodulators such as Echinacea, should be interpreted with caution (63).

6.5 Gaps in Clinical Evidence and Translational Challenges

However, there are many gaps in the evidence base for phytotherapeutics and many studies are underpowered and narrow in scope, such as studies on Passiflora incarnata for use in anxiety disorders, with sample sizes less than 100 participants. Ethnopharmacogenomic differences also present gaps in knowledge, such as differences in metabolic pathways e.g., CYP2D6 polymorphism in Asians, which may affect response to phytochemicals, such as susceptibility to psychotropic effects of tetrahydrocannabinol from Cannabis sativa. Bioavailability also remains a problem for many phytochemicals, such as curcumin from Curcuma longa, which has a bioavailability of less than 1% when given alone, although bioavailability can be improved when co-administered with piperine from Piper nigrum. These challenges of standardization are more apparent in polyherbal formulations. Differences in the composition and proportion of the herbs present in the formulations, as observed in traditional formulations like Triphala, pose challenges in standardization and replication of results. Large-scale RCTs on chronic diseases are still lacking and significant evidence gaps exist in special populations like the pediatric and geriatric populations. Conservative safety approaches are reflected in the presence of contraindications in pregnant women due to inadequate evidence. In the regulatory and economic arena, several barriers are currently impeding the progress of translational research. Among these barriers are the lack of incentives due to the low cost of current treatment options, such as metformin, intellectual property issues and legal hurdles, including the Association for Molecular Pathology Myriad Genetics case, which limits the patent protection of natural products. In addition, the need to incorporate new evidence from patient registries and pragmatic platform trials. In addition to traditional clinical trials, has become an emerging requirement in the field. Phase IV studies, conducted on a global level are critical in building the evidence base to support the integration of ethnopharmacognosy into modern medicine (64,65).

VII. CONTEMPORARY ADVANCES AND TECHNOLOGIES

7.1 Omics Technologies in Metabolomics and Genomics

The development of omics technologies has revolutionized the classification and understanding of phytochemicals by integrating genetic, metabolic and environmental information. These technologies have provided a complete “molecular snapshot” between genotype and metabolomic profiles, thereby deciphering biosynthetic pathways and environmental effects on medicinal activity. Metabolomics, based on untapped approaches such as liquid chromatography-mass spectrometry (LC-MS) and nuclear magnetic resonance (NMR) spectroscopy, allows for simultaneous investigation of thousands of metabolites. Multivariate statistical methods such as Principal Component Analysis (PCA) are used for differentiation between chemotypes, for example, differentiation between distinct Artemisia annua chemotypes based on artemisinin yield. This variation is associated with the differential expression of biosynthetic genes like amorpha-4,11-diene synthase, which might be upregulated during environmental stress like drought. It has also been proposed that metabolomics can be used in conjunction with transcriptomics for a holistic view of metabolic regulation (66).

Genomics has also contributed to the understanding of secondary metabolism. With advancements in next-generation sequencing (NGS) technology, plant genomes like Salvia miltiorrhiza (Danshen) have been assembled, aiding in the identification of genes involved in the biosynthesis of pharmacologically active molecules like tanshinones. Gene editing tools like CRISPR-Cas9 have also been used for validating these pathways. Furthermore, single-cell RNA sequencing has been utilized for the characterization of specific structures like glandular trichomes, which are important for the biosynthesis of essential oil in plants of the Lamiaceae family (67). Finally, proteomics can be used for the identification of proteins involved in the pathway of secondary metabolism. In plants like Catharanthus roseus, proteomic techniques like iTRAQ (isobaric tags for relative and absolute quantification) have been used for the characterization of enzymes like cytochrome P450, which are involved in the biosynthesis of alkaloids. Metabolomics can be used for optimizing harvesting techniques. For example, spatial variation in the content of withanolides in the roots of Withania somnifera can be used for optimizing harvesting techniques. The integration of multi-omics has facilitated advances in synthetic biology. For instance, engineered microbial systems have been developed for the production of key intermediate taxadiene from Taxus species, including yeast chassis expressing plant biosynthetic genes. This reduces the demand for Taxus species and offers a sustainable and cost-effective alternative for the production of paclitaxel and similar compounds (68).

7.2 Machine Learning and Artificial Intelligence

Artificial intelligence (AI) has been recognized as a promising driving force in the field of pharmacognosy, allowing for the automation of data analysis and the prediction of bioactivity using complex molecular and biological information. For instance, deep neural networks (DNNs) using convolutional neural networks (CNNs) have been found to offer high accuracy in image-based data analysis. For instance, the automated classification of powder micrographs has been able to distinguish sclereids and starch adulterants with accuracies close to 98%. These accuracies often surpass the capabilities of human expertise, which stand at 69 (69). Chemoinformatics tools like SwissADME have also been used to predict the drug-likeness and pharmacokinetics of a wide range of phytochemicals. Such tools allow for the rapid screening of thousands of plant-derived compounds. Furthermore, graph convolutional networks (GCNs) have been used to model the molecular structures and prioritize bioactive compounds such as sesquiterpenes derived from the Asteraceae family, which have the potential to act against the NF-κB pathway (70). Natural language processing (NLP) methods facilitate the large-scale mining of biomedical literature, including millions of abstracts from sources like PubMed. NLP methods also facilitate the extraction of ethnomedicinal information and the creation of linked knowledge graphs, like the connection between Curcuma longa and thousands of clinical studies on curcumin. Generative methods, including GANs, facilitate the creation of new phytochemical structures by learning from existing pharmacophores like limonoids from Citrus species. Advancements in protein structure prediction, like those in AlphaFold also improve drug discovery by simulating protein-ligand interactions and validating targets in silico, like those between ginsenosides and PPARγ receptors. Emerging computational approaches such as federated learning enable the integration of global pharmacovigilance and clinical data while maintaining data privacy and proprietary formulations. Additionally, real-time process optimization has been achieved by using reinforcement learning algorithms, such as the optimization of HPLC parameters to enhance the efficiency of separation and gradients (71).

7.3 Nanotechnology for Enhanced Delivery and Bioavailability

Nanotechnology has greatly influenced the delivery of phytotherapeutics, especially in the case of phytotherapeutic agents with low bioavailability. Encapsulation techniques have been developed to circumvent the main challenges, such as P-glycoprotein-mediated efflux, first-pass metabolism, and poor aqueous solubility. For instance, liposomes encapsulate curcumin in a phospholipid bilayer, thereby enhancing stability and bioavailability. PEG of liposomes (“stealth” liposomes) increases the systemic circulation time by evading the reticuloendothelial system, thus prolonging the plasma half-life to several days. Solid lipid nanoparticles (SLNs) loaded with Andrographis paniculata, when coated with biopolymers such as chitosan, allow sustained release in the intestine and exhibit potential in the management of inflammatory bowel diseases (IBD). Polymeric micelles are used for the delivery of hydrophobic drugs such as paclitaxel. These micelles are based on self-assembling amphiphilic block copolymers. These micelles are based on the enhanced permeability and retention effect. This allows for preferential tumor accumulation and increases therapeutic efficiency while reducing toxicity due to solubilizing agents such as Cremophor. Nanoemulsions are also used for enhancing drug delivery. For example, nanoemulsions containing 1,8-cineole from Eucalyptus have droplet sizes of 100 nm. These have shown enhanced transdermal permeation and therapeutic effects on respiration similar to oral administration (72). Metal-based nanocarriers have many therapeutic applications. Gold nanoparticles conjugated with lactones from Vernonia amygdalina have been investigated for their potential to be employed in plasmonic photothermal therapy to improve antimalarial activity. Dendrimers, including polyamidoamine (PAMAM) dendrimers, have been shown to be useful in the development of agents with the ability to deliver agents for gene silencing and phytochemicals, including agents that target Plasmodium falciparum resistance mechanisms and deliver artemisinin. New technologies include 3D printed phytosomal tablets, which have the potential to be useful in the development of personalized medicine with the ability to modulate drug release kinetics based upon pharmacogenomics, including CYP2D6. From a regulatory perspective, pathways such as the FDA 505(b)(2) pathway have facilitated the approval of botanical formulations like Veregen, and may similarly support the advancement of nano-enabled herbal therapeutics (73).

7.4 High-Throughput Screening and Automation

High-throughput screening (HTS) systems have revolutionized phytopharmaceutical research by enabling the rapid evaluation of large compound libraries. Miniaturized assays conducted in microplate formats (e.g., 384- and 1536-well plates) can screen up to 1,00,000 samples per day. For instance, 1536-well DPPH assays have been miniaturized for the rapid antioxidant profiling and comparative analysis of Traditional Chinese Medicine (TCM) formulations, while

fluorescence polarization assays have found application in the determination of the binding affinity of Ginkgo biloba flavonoids with target proteins (74). Automation is an important component of the HTS process. For instance, liquid handling robots have greatly facilitated bioassay-guided fractionation with high degrees of precision and reproducibility, while quadrupole time-of-flight mass spectrometry (QTOF-MS) has greatly enabled real-time dereplication by comparing mass spectral information against large libraries of reference compounds, including hundreds of thousands of entries. Other emerging technologies include digital microfluidics, which utilizes electrowetting-on-dielectric (EWOD) for the manipulation and analysis of nanoliter droplets for the rapid execution of assays, for instance, for the determination of the anti-diabetic enzyme inhibition potential of Momordica charantia, up to 1,000 assays per hour. Functional genomics tools can further improve target identification. CRISPR-based screening libraries, which can modulate thousands of genes at once, were employed to identify off-target effects and molecular pathways linked with phytochemicals such as boswellic acids from Boswellia serrata. Sophisticated in vitro systems, such as organ-on-chip technologies, mimic physiological environments such as the gut-liver axis, allowing for more predictive models for pharmacokinetics and toxicity. Lab-on-chip technologies, which include phytochemicals such as piperine from Piper nigrum, enable precise investigation of bioavailability-related bottlenecks and absorption-related dynamics. Multiplexed analytical strategies, such as quantum dot barcoding, enable simultaneous tracking and evaluation of various phytochemical constituents present in polyherbal formulations. Additionally, closed-loop systems, which integrate machine learning with robotic synthesis platforms, enable optimization of various phytochemical formulations, such as traditional formulations like Triphala to improve biological activities, such as Nrf2 pathway activation (75).

7.5 Sustainable Sourcing and Innovations in Pharmacovigilance

New innovations in sustainability have increasingly focused on biodiversity conservation and technology-based development in phytopharmacology. Modern technology allows for the real-time assessment of medicinal plant resources, such as tracking Hoodia gordonii plantation development and health condition. This can be accomplished via drone technology for hyperspectral imaging. Concurrently, phenotyping models based on artificial intelligence can be used to determine the most appropriate time for harvesting to obtain maximum phytochemicals. Biotechnology can be used for the sustainable development of phytochemicals. Hairy root cultures for Rauvolfia serpentina have shown significant increases in yield for reserpine, as much as 100-fold compared to traditional methods for harvesting from the wild. Satellite technology can be used for remote sensing for biodiversity conservation. This can be used for tracking species such as Commiphora wightii, which are affected by climate change. This can be used for ex-situ conservation and cryobanking. Pharmacovigilance 2.0 is a new technology for pharmacovigilance based on digital health technology for the real-time assessment of therapeutic outcomes. Wearable biosensors can be employed for measuring physiological responses to herbal drugs such as Hypericum perforatum, whereas large-scale surveillance systems such as the FDA Sentinel System can be employed for detecting potential adverse interactions. Digital twin technologies can also play an important role in promoting precision medicine. For instance, pharmacogenomics can be employed for identifying patient populations that respond best to Valeriana officinalis, thereby promoting more personalized therapeutic strategies. Thus, these technologies are transforming pharmacognosy from an empirical science to a more data-driven approach, thereby aligning it with Industry 4.0. The approaches discussed here can be employed for addressing some of the key challenges facing phytotherapeutics, such as validation, standardization, and scalability, thereby promoting evidence-based phytotherapeutics.

VIII. CHALLENGES AND FUTURE DIRECTIONS

8.1 Adulteration, Substitution, and Quality Variability

The integrity of medicinal plant materials is still marred by adulteration and substitution both intentional and unintentional. For example, ginseng powder is adulterated with rice starch and Valeriana officinalis roots are fraudulently replaced with morphologically similar Valerianella species. Such adulterations often go undetected by analysis through their organoleptic properties. Intentional substitution with morphological mimics is another problem. For example, florets of Sophora japonica are sold as leaves of the more valuable species Ginkgo biloba. Similarly, difficulty in species identification due to taxonomic confusion in the Cinnamomum species leads to considerable variation in the chemical content. Post-harvest factors contribute to the quality deterioration. Poor storage conditions allow the growth of aflatoxigenic species, enzymatic degradation, and loss of volatile compounds. For example, catechin present in Camellia sinensis is known to undergo enzymatic browning, whereas essential oil present in Mentha piperita is known to evaporate, thereby affecting its therapeutic activity. Environmental factors, such as variability, also play an important role in phytochemical composition. Soil, climate, and altitude are known to affect phytochemical composition. For example, drought stress is known to elevate artemisinin levels in Artemisia annua, whereas flavonoids are reduced. Similarly, altitude is known to affect withanolides in *Withania somnifera*. The problem of standardization is clearly evident in polyherbal formulations, as shown by variations in the formulation of Triphala, which is traditionally used. To combat these challenges, advanced technologies are now being employed. Metabolomics, along with high-resolution technologies such as LC-QTOF-MS has now enabled the development of certificates of analysis, thereby ensuring chemical consistency. DNA barcoding, specifically the use of ITS2 regions can offer reliable authentication of species, which is better than traditional approaches based on morphological features. Moreover, new technologies like blockchain technology for the supply chain and smart packaging through QR codes can offer traceability and transparency in the entire production process. These complex authentication mechanisms can be complemented by metabolomics profiling for better regulatory compliance, ensuring the quality, safety, and efficacy of herbal medicines.

8.2 Loss of Biodiversity and Sustainable Sourcing

Medicinal plant resources are under serious threat of depletion due to climate change, habitat loss and overexploitation. To exemplify the point, the reduction in glaciers and climatic belts has resulted in the reduction of the natural habitat of

the medicinal plant Swertia chirayita in the Himalayan belt. Similarly, the deforestation in the Amazonian region poses serious threats to the natural habitat of the medicinal plant Uncaria tomentosa. The overexploited medicinal plant Panax quinquefolius or American ginseng is threatened with severe depletion in its population, which is close to commercial endangerment. Similarly, overexploitation of the medicinal plant Commiphora wightii or guggul in the dry scrubland habitats of the Indian desert is causing serious degradation of the ecosystem. The medicinal plant is being over-exploited for its resin. Fungal diseases, introduction of alien species and loss of genetic diversity in the medicinal plant population due to the cultivation of pure cultures in plantations are the other serious threats. Despite international regulations such as the Nagoya Protocol, which aim to regulate access and benefit-sharing in bioprospecting, there is inequality in sharing as shown in the case of Hoodia gordonii, where there is limited sharing with indigenous peoples such as the San. Sustainable solutions promote cultivation, conservation, and innovation. The Good Agricultural Practices (GAP) for Curcuma longa (Turmeric) involve the use of certified planting materials and optimized irrigation systems. In vitro propagation methods for the conservation and cultivation of elite chemotypes are also employed as shown in the case of Taxus brevifolia. Biotechnological methods, such as hairy root cultures in bioreactors can be employed for the production of bioactive compounds such as reserpine from Rauvolfia serpentina without any negative impact on wild populations. Agroforestry systems play an important role in community-based conservation and resource utilization. The cultivation of Trichopus zeylanicus in Kerala is an example of how traditional knowledge is linked with resource utilization. Cryopreservation and germplasm banking strategies are also employed for the conservation of genetic resources and for mitigating the effects of climate change on medicinal plant species.

8.3 Intellectual Property Rights and Biopiracy

The issue of biopiracy still fuels mistrust between indigenous groups and business/research organizations. Some notable cases include the patent on Neem (Azadirachta indica) based fungicides in the USA and the patent on Hoodia gordonii for appetite suppression in South Africa both of which have led to questions regarding the exploitation of indigenous knowledge without adequate recognition and benefit-sharing. Some of the steps being taken against this include defensive documentation, for instance, the Traditional Knowledge Digital Library, which holds records of indigenous traditional medicinal knowledge so that it does not fall into the wrong hands and lead to false patent claims. Although these have successfully challenged false patents, problems like “patent thickets” still exist, which hinder development because of restricted access to secondary research. For instance, patents on modified compounds of Artemisia annua despite its traditional use being in the public domain. The indigenous data sovereignty principle has highlighted the importance of fair ownership of traditional knowledge. In this regard, the development of benefit-sharing approaches, like those established between the San people and Hoodia gordonii commercialization initiatives has resulted in the development of trust funds for the redistribution of royalties among indigenous peoples. Other approaches have promoted the collective ownership of ethnomedicinal knowledge and fair compensation for indigenous knowledge holders. In addition, emerging innovations, like blockchain technology for smart contracts, have provided the potential for transparent approaches in the fair redistribution of revenues where a set percentage (e.g., 10%) can be allocated for traditional knowledge custodians. Nevertheless, there have been ethical concerns regarding patent “evergreening”, like the development of nanoformulations for patent extensions. It is crucial to maintain a fair balance between intellectual property rights and public health interests. In this regard open access approaches, like PubChem have provided an essential tool for promoting fair access to scientific information for the development of innovations while addressing public health interests.

8.4 Regulatory Harmonization and Standardization Gaps

Regulatory fragmentation in the Global South continues to be a major impediment to the internationalization and standardization of herbal medicine. Differences in regulatory approaches lead to inconsistencies such as the stringent botanical drug standards mandated by the US FDA and the more lenient approval process by India’s Central Drugs Standard Control Organization AYUSH, where some products (e.g., Piper longum-based products) can be approved without extensive Phase III clinical validation. These inconsistencies are compounded by the absence of adequate post-marketing surveillance. For instance, the lack of adequate surveillance and regulatory control was exemplified by the case of herbal “detox” products containing the nephrotoxic aristolochic acid. While international guidelines have been developed via the WHO Traditional Medicine Strategy 2025-2034 implementation in the Global South and in low- and middle-income countries in particular, remains a challenge. Harmonization efforts in addressing the above challenges increasingly involve the concept of adaptive regulatory approaches. These approaches include the use of real-world evidence (RWE) to support or in some instances, replace the requirement for traditional large-scale RCTs, particularly in the case of low-risk herbal products. Further support for standardization and worldwide acceptability of botanical medicines can be obtained by adhering to international standards, like those advocated by the International Council for Harmonisation. Digital pharmacovigilance systems have also shown promise. Software like “HerbTrack” can be utilized for the collection and analysis of adverse event data in real time from diverse populations, enhancing the post-marketing surveillance capabilities in resource-limited countries. In summary, filling the regulatory gaps by harmonization, enhancing surveillance, and utilizing technology for monitoring is crucial for the safety, efficacy, and worldwide integration of phytotherapeutic agents.

8.5 Future Directions and Integrated Approaches

The future of pharmacognosy will involve the seamless integration of different scientific fields in translational science which will include ethnobotany, pharmacognosy, omics technologies and drug delivery technologies. Artificial intelligence will also be used to identify high informant consensus factor plants for targeted research and genetic engineering using the CRISPR technology. New technologies in computer science such as quantum computing have the potential to speed up the process of virtual screening by exploring vast chemical spaces. Meanwhile, new biological technologies such as organoid biobanks derived from induced pluripotent stem cells (iPSCs) will allow for the

personalized study of phytotherapeutics such as the optimization of the dose of the phytotherapeutic agent Hypericum perforatum based on the responses of different individuals. The concept of "Reverse Pharmacology 2.0" was developed to highlight the importance of microdosing and the subsequent conduct of large clinical trials. Decentralized clinical trials, with wearable technologies, enable the collection of real-world data, including the measurement of cognitive functions related to Ginkgo biloba extracts in various patient groups. Global collaborative initiatives, like the WHO Global Centre for Traditional Medicine are connecting clinical data platforms with biodiversity information and ethnomedicinal knowledge platforms to enable evidence-based policymaking and innovation. New equity-based and decolonized research frameworks are being promoted, including the involvement of indigenous principal investigators, community-based governance structures (e.g., veto rights) and tiered benefit-sharing arrangements. This ensures the active involvement and ownership of traditional knowledge holders in research and development. These integrated research and development frameworks have positioned pharmacognosy to address critical health issues including AMR, neurodegenerative diseases, and chronic diseases. These frameworks have successfully merged visionary research frameworks with cutting-edge technologies and responsible research practices to transform the traditional realm of ethnomedicinal knowledge to a futuristic and evidence-based pharmacopoeia.

CONCLUSION

The development of ethnomedicinal information into evidence-based therapeutics marks a major milestone in the development of modern pharmaceutical science, characterized by a paradigm shift from empirical medicine to scientifically supported phytopharmaceutical development. Although indigenous medicine systems have contributed immensely to the development of therapeutic information, there is a need for rigorous authentication, standardization, pharmacological validation and regulatory compliance for the development of modern medicine. Modern pharmacognosy has bridged this gap by applying sophisticated technology in the form of DNA-based identification, chromatographic fingerprinting by HPTLC and HPLC, metabolomics, spectroscopy and bioassay-guided isolation which ensures accurate botanical identification, chemical standardization and reproducible therapeutic efficacy. In addition, rigorous safety assessments involving toxicological profiling, heavy metal and pesticide residue analysis and microbial quality control have ensured herbal medicine compliance with international safety standards. Regulatory frameworks set up by organizations such as the World Health Organization, the European Medicines Agency, and the U.S. Food and Drug Administration serve to further reinforce the significance of quality control, validation and batch-to-batch reproducibility. The newly evolving fields of network pharmacology, nanophytomedicine, artificial intelligence-assisted drug discovery and cutting-edge methods in bioavailability enhancement are redefining the therapeutic potential of medicinal plants by embracing the philosophy of multiple targets and systems biology. All these scientific, technological and regulatory milestones point towards the fact that the traditional practice of herbal medicine is maturing into an internationally recognized form of therapeutics with the potential to continue making significant contributions towards modern healthcare systems in a safe, effective and sustainable manner.

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