EXPLORING NATURE'S PHARMACY: BREAKTHROUGHS IN HERBAL DRUG DEVELOPMENT AND TECHNOLOGY

Abstract

The trend towards different treatment includes herbal medications considerably. As more people look for natural remedies, herbal therapy is growing in popularity. Subsequently the beginning of civilization, herbal therapies have been used to support health and treat a wide range of ailments. More medicinally beneficial herbal medicines need to be used and scientifically verified in order to compete with the growing pharmaceutical industry. The chapter's goal is to help readers better grasp the therapeutic efficacy of diverse herbal medicines, standardisation methods, herbal medication development techniques, stability testing principles and pharmacovigilance of herbal products.

Keywords: Herbal medicine, Herbal drug Standardization, Computation advancement, Applications, nanotechnology

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I. INTRODUCTION

Herbal remedies, frequently referred to as the plant-based products or herbalism, use the entire plant or sections of the plant for healing wounds or ailments. In addition to treating and preventing diseases, herbal medicine has roles that include boosting health[1]. These are substances that are used to make medications or other preparations derived from a plant. The earliest known type of medical care is herbal medicine. There are a variety of herbal treatments available that advertise treating the symptoms and indications of various illnesses, everything from melancholy to the usual flu and cold symptoms. According to the World Health Organization (WHO), unique herbal medications are full-spectrum[2], labelled pharmaceuticals that contain active chemicals, aerial or secretive plant parts, or similar botanical matter as well.

The World Health Organization has set specific guidelines for the testing of the efficacy, safety, and purity of herbal medications. 80% of people worldwide already use herbal medications for their primary healthcare, according to WHO figures. By custom natural organic or inorganic active components that are sourced from sources other than plants, herbal remedies may on rare occasions also contain these compounds.

Ayurveda, homoeopathy, naturopathy, and other medical systems regularly use herbal medicine, which is an important part of traditional medicine[3]. Herbs are frequently seen as safe because they are made from organic materials. The manufacture of herbal drugs has dramatically increased as a result of the toxicity and negative effects of allopathic pharmaceuticals [4]. Over the past few decades, people without a prescription have grown more and more likely to use herbal drugs.

Herbal medicines have been prepared for thousands of years using roots, seeds, leaves, stems, bark, flowers, and extracts of these plants. Herbal products have progressed to the point where they can be used for therapeutic agents such as killing microbes, decreased blood glucose, anti-fertility, anti-aging, anti-arthritic, sedative, CNS depressant, antianxiety, antispasmodic, pain reliever, anti-inflammatory properties, anti-HIV, vasodilatory, hepatoprotective, and for treating liver disease, asthma, acne, and impotence.

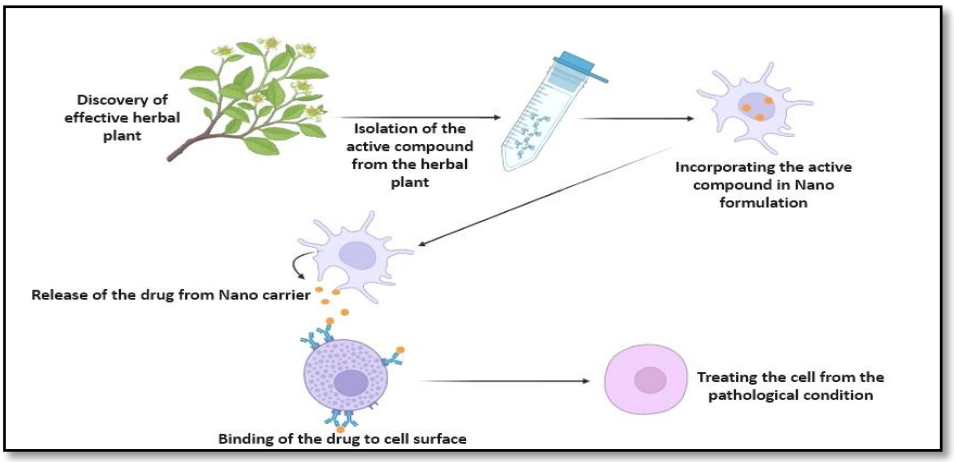

Figure 1: Represents the discovery, isolation, and incorporation of drugs into nanocarrier.

About 4,000 years ago, the use of herbal medicines was acknowledged. These medications have withstood extensive human testing over many centuries and in the real world[5]. Due to their toxicity, several medications have been ceased from use, while others have been altered or combined with Raw materials for herbal medications may come from well tended plants or be gathered from the wild. There are numerous varieties of herbal medications available, and many of them require preparation before use [6]. For herbal drinks and mixes, you may typically purchase them in bulk as dried plants, plant bits, or loosely packaged plants. To prepare decoctions, herbs are cooked in water, and the plant material is then filtered out. There are liquid extracts and hydro alcoholic tinctures available as more strong herbal medicine compositions [7,8]. Techniques for preparation of herbal products are differing depending on type of photochemical components present in plants.

II. PHARMACEUTICAL PREPARATION

This comprises the creation of numerous drug delivery systems, including tablets, capsules, injections, creams, and ointment. Lindberg et al., in 2023 proposed that pharmaceutical preparation includes selecting the proper excipients (inactive components), figuring out the proper dosage, and guaranteeing the product's stability and quality [1].

III. DRUG DELIVERY SYSTEMS

Drug delivery is the science of getting a pharmaceutical compound into the body to achieve a therapeutic effect. Some key areas in drug delivery include:

1. **Oral Drug Delivery:** This is the most common route for drug administration. It entails creating formulations that can resist the demanding circumstances of the digestive system and release the medication at the proper rate and place [2,3].

2. **Parenteral Drug Delivery:** This involves intravenous, intramuscular, and subcutaneous injections as well as implanted drug delivery methods.

3. **Transdermal Drug Delivery:** Delivering drugs through the skin using patches or creams.By applying herbal medications directly to the skin, transdermal herbal drug administration enables the delayed and regulated release of active ingredients. Monton et al., in 2022 discovered thatbypassing the digestive tract, this method increases bioavailability while minimizing systemic negative effects. Securing skin penetration, formulation stability, and safety are difficulties. The effectiveness and practicality of administering herbal medicines may be improved with further research and innovation in this area.

4. **Nanotechnology in Drug Delivery:** Enhancing drug delivery, increasing bioavailability, and targeting certain cells or tissues using nanoscale nanoparticles[4–6]. Habeeb et al., in 2022 found that nanotechnology expands the potential uses of herbal medicines by protecting sensitive chemicals, enabling combination therapy, and improving penetration across biological barriers.

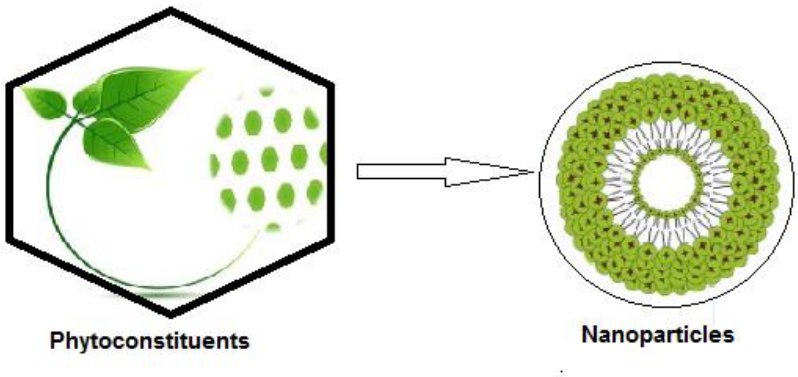

Figure 2: Nanotechnology in Herbal Drug

- ***Need for new "nano carriers" for delivery of drugs for "herbal remedies***
  Many of the herbal medications' contents will be damaged in the stomach's highly acidic pH before reaching the blood, and other constituents may be metabolised by the liver. As a result, the herbal medicines may not enter the blood in the proper amount [14]. There will be no way to demonstrate the therapeutic impact of the treatment if it is not delivered in the ideal quantity to the affected area at "minimum effective level." Bypassing obstacles like the stomach's acidic pH and liver metabolism, nanocarriers applied to herbal medicines will deliver the maximum quantity of the drug to its site of action. They will also prolong the drug's circulation into the body.

  Due to the following qualities, herbal medicines were chosen as a viable drug candidate for distribution via a nano delivery system:

  There are efficient extracts in acetone, chloroform, petrol, and methanol that may not be appropriate for distribution as such.

  - Since these medications are in bulk, a dose reduction is intended.
  - Target specificity is lacking in currently marketed formulations for a number of chronic illnesses.
  - With the formulations that are currently on the market are some additional adverse effects.
  - Large doses and lower effectiveness of the current formulations, which causes patient non-compliance.

IV. CONTROLLED RELEASE SYSTEMS

These systems are designed to release drugs at a predetermined rate, ensuring sustained therapeutic levels in the body. Both the patient's compliance and adverse effects may be improved [7,8].

V. HERBAL DRUG TECHNOLOGY AND HERBAL DRUG DEVELOPMENT

1. **Herbal Medicine:** Herbal medicine involves the use of plant-based materials (herbs, botanicals) for medicinal purposes. It has had a long tradition and is still prevalent throughout many cultures today[9,10].Jo et al., in the year 2022 said phytotherapy, a synonym for herbal medicine, is a branch of medicine that makes use of plants' therapeutic capabilities to treat and prevent disease. The therapeutic power of numerous plant components, including leaves, roots, and herbs, is harnessed in this age-old practice. Herbal remedies have been used extensively in healthcare throughout time and cultures, providing a wholistic approach to heath. They continue to be researched scientifically today and are commonly used in complementary and alternative medical methods due to their possible therapeutic benefits.

Table 1: Traditional Use and Scientific Use of Herbs

Traditional Use of Herbs	Scientific Use
Everyone routinely utilizes everyday plants or parts of them for a variety of reasons, such as in juices, decoctions, or tablets.	Making use of properly prepared extracts and medicines from plants.
Combinations of numerous plants, frequently more than ten at once, are typically used. Products frequently don't mention the chemical components or extraction method.	Typically used as symptomatic, for prevention or treatment, and is purified and standardised in the chemical ingredients that have pharmacological effect.
Generally regarded as risk-free and without any negative effects.	Potential adverse reactions, restrictions, medicine interactions, etc.
Pathophysiology and therapy (holism), which are often founded on philosophical in nature, theological, and cultural and socioeconomic theories, frequently allude to the personalities and feelings of emotions of the patients.	Diagnostic and therapeutic methodology abides by accepted medical practises because clinical administration is based solely on pharmacological activity as determined by standard laboratory procedures and clinical trials.

2. **Herbal Drug Technology:** Herbal technology combines the use of conventional herbal medicine with cutting-edge science and technology. It includes cutting-edge extraction, formulation, and quality control (QC) process to ensure the efficacy and consistency of herbal products. Rafi et al., in 2023 proposed that while strict regulatory compliance and research fuel innovation in the herbal medicine sector, biotechnology and nanotechnology improve the cultivation and distribution of herbal ingredients. It is encouraged by this multidisciplinary approach to use medicinal plants in healthcare in a safe and efficient manner.Here, natural medications are developed and produced using contemporary pharmaceutical and biotechnological methods[11,12].It includes:

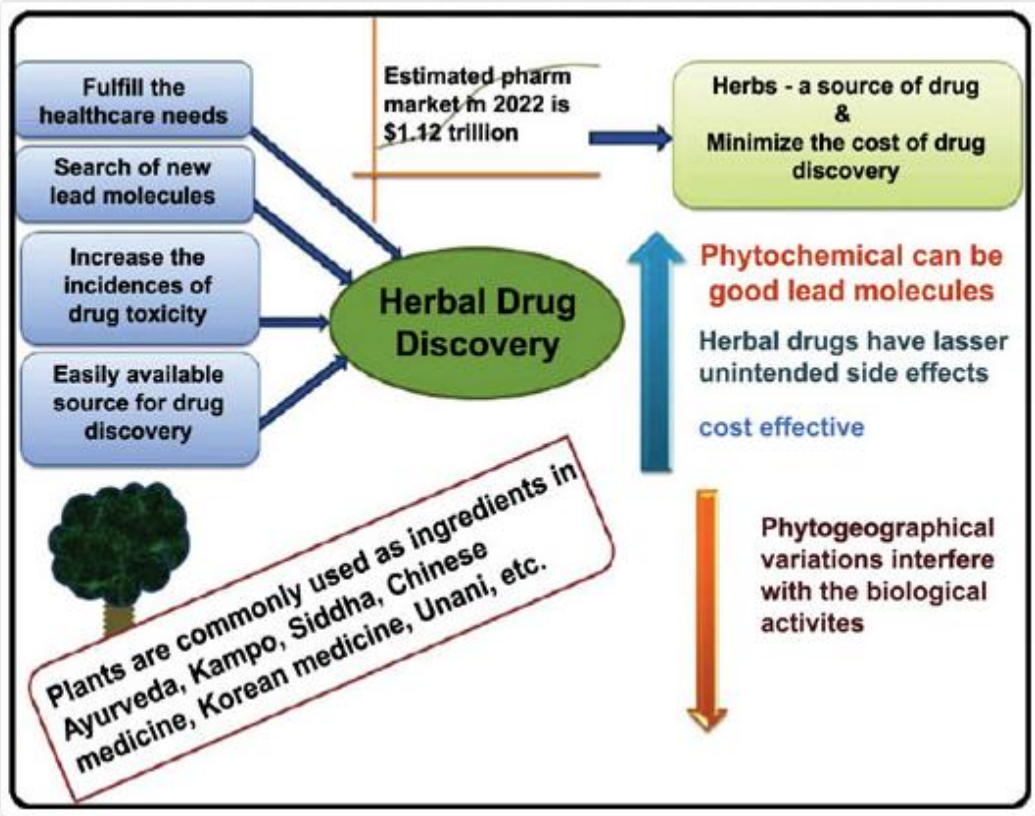

Figure 3: Herbal drug technology

- **Standardization:** Ensuring that herbal products contain consistent levels of active compounds.
  Analytical techniques used in herbal drug identification and auantification
  - TLC
  - HPLC
  - HPTLC
  - LCNMR
  - GC-MS
  - DNA FINGERPRINTING
  - GENETIC MARKER

    - Amplified fragment length polymorphism (AFLP)
    - Single nucleotide polymorphism (SNP)
    - Restriction fragment length polymorphism (RFLP)
    - Random amplification of polymorphic DNA(RAPD)
    - Variable number tandem repeat (VNTR)
    - Microsatellite polymorphism
    - Short tandem repeat (STR)
    - Single feature polymorphism (SFP)

- **Quality Control:** Testing for contaminants, purity, and consistency.

- **Formulation:** Developing herbal products in various forms like capsules, tablets, extracts, or topical creams [13].

- **Safety Assessment:** Evaluating the safety of herbal products through toxicological studies.

VI. HERBAL DRUG DEVELOPMENT

This entails the study and creation of novel herbal medications or the transformation of conventional herbal therapies for use in contemporary medicine [14,15]. It includes:

1. **Phytochemical Analysis:** Identifying and isolating active compounds in plants[16] .Rai et al.,in 2023 performed scientific examination of the bioactive substances contained in plants is known as phytochemical analysis. It entails locating, separating, and analyzing the numerous chemical elements that are present in plant materials. For this goal, methods like spectroscopy and chromatography are frequently employed. Drug discovery and the creation of herbal remedies are aided by phytochemical analysis, which offers insightful information on the therapeutic and potential health advantages of plants.

2. **Computation advancement of natural phytoconstituents:** The 30 % of land on the earth is covered with natural plants, which possess ‘n’ number of medicinally important molecules or leads. The evolving country data disclosed that up to 80 % of the public are hooked on herbal remedies for their prime healthcare, and over 25 % of given medicines are derived from wild plant class molecules [17]. The 60% of the FDA Natural materials and their derivatives are the source of FDA-approved medications. The major problem faced in herbal drug discovery is the categorizing, Identification, and separating of phytoconstituents from the herbal plants. As an example, *Tridax procumbens* contains more than 98 phytoconstituents in the leaves itself and similarly many herbal plants possess more than 50 phytoconstituents [18]. The recent advancement in a computational database of the MASS spectrum aids in screening and identifying the existing molecules from herbal medicines (**Figure 4**).

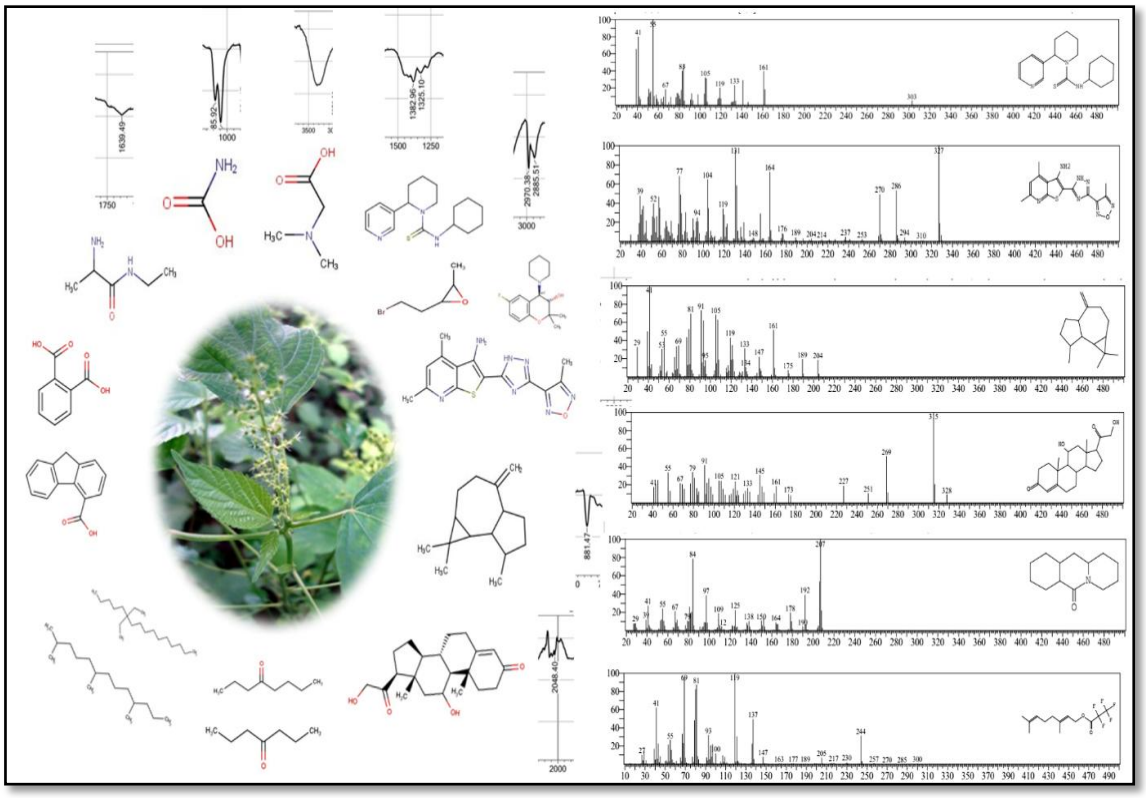

Figure 4: Identification of Phyto constitution from the MS database

The computational drug design (CADD) techniques are taken to the next level to screen and develop the natural product analogs. The docking protocol of CADD illustrates the natural molecule binding inside the binding cavity of the protein and exposes the atomic level insight of interaction between binding side amino acids and natural molecules. For example, Irfan et al., 2023 illustrated the binding of curcumin derivatives in the active site of the PCSK9 protein to treat cholesterol-related diseases [19] (**Figure 2**). Similarly, the same research group collected 98 phytoconstituents from 9 different herbal plants to identify the best lead natural fragment to inhibit the COVID-19 spike protein [18].

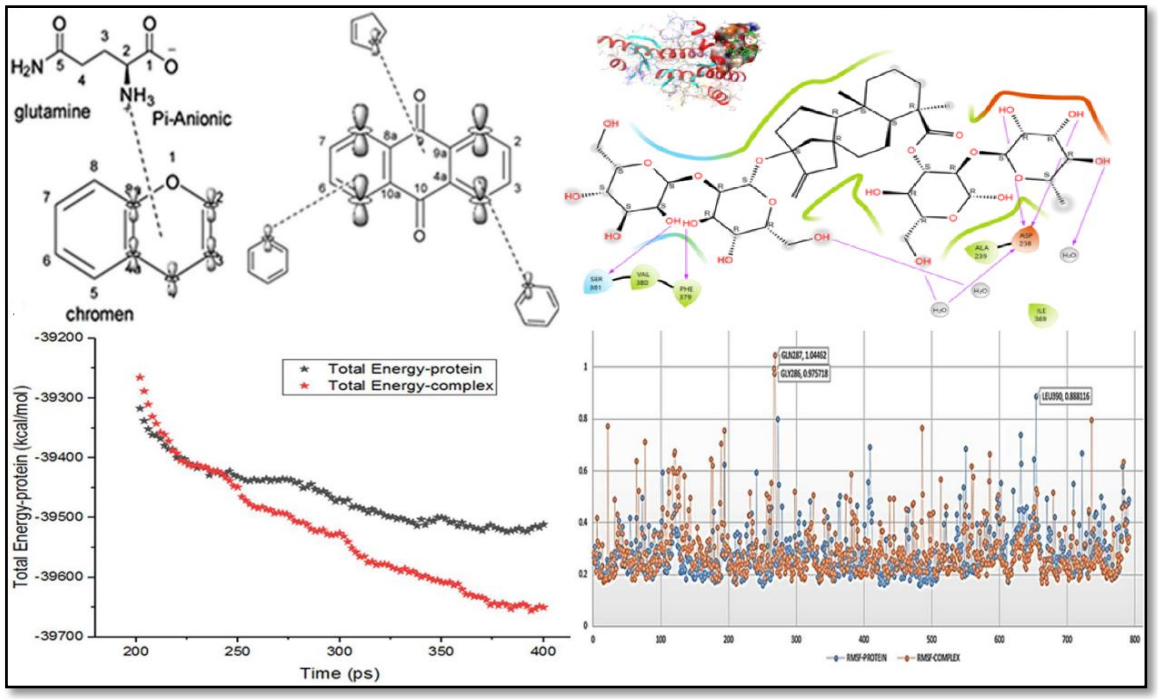

Figure 5: Best Binding Fragment Identification By Docking Pharmacophore and Dynamic Simulation Analysis.

The Ligand-based drug discovery modules such as pharmacophore and QSAR aid in predicting the fragments or functional groups responsible for the biological activity as well as in predicting the activity without sacrificing animals by the structure of the molecule [18]. Additional quantum mechanics-based molecular dynamic simulation studies mimic the stability of the protein-phytoconstituent complex in body conditions. This further strengthens and fastens the drug discovery process in small molecule discovery. The study performed by Sakthivel Balasubraminyan et al., (2021) designed and simulated the quinine derivative against the antimicrobial-resistant treatment [20]. These kinds of computational techniques advance and troubleshoot the problem faced in drug discovery and development from natural sources.

3. **Preclinical and Clinical Trials:** Examining the effectiveness and safety of herbal products in both humans and animals.

4. **Regulatory Approval:** Meeting regulatory requirements for herbal medicines in different countries.

The goal of both pharmaceutical and herbal drug development is to offer secure and efficient therapies for a range of medical diseases. While pharmaceuticals typically involve synthetic compounds, herbal drug development relies on natural plant-based ingredients. A greater range of therapeutic alternatives and all-encompassing healthcare solutions may result from integrating the two methodologies [21–23]. It's crucial to remember that, like pharmaceutical treatments, the efficacy and safety of herbal medicines should be thoroughly assessed through scientific research and clinical studies [24,25].

VII. APPLICATIONS OF HERBAL DRUG TECHNOLOGY AND DEVELOPMENT

Employing the medicinal potential of plants and natural substances to create safe and effective medications is the major goal of the pharmaceutical industry's critical sectors of herbal drug technology and herbal drug development [26,27]. Listed below are some important uses and components of the investigation and development of herbal medicines: Medicinal plant identification and screening: To find and screen plants with potential medicinal characteristics, researchers employ a variety of methods, including ethnobotany and phytochemical analyses. Finding the bioactive compounds in these plants is made easier by bioassays and high-throughput screening methods [28,29].

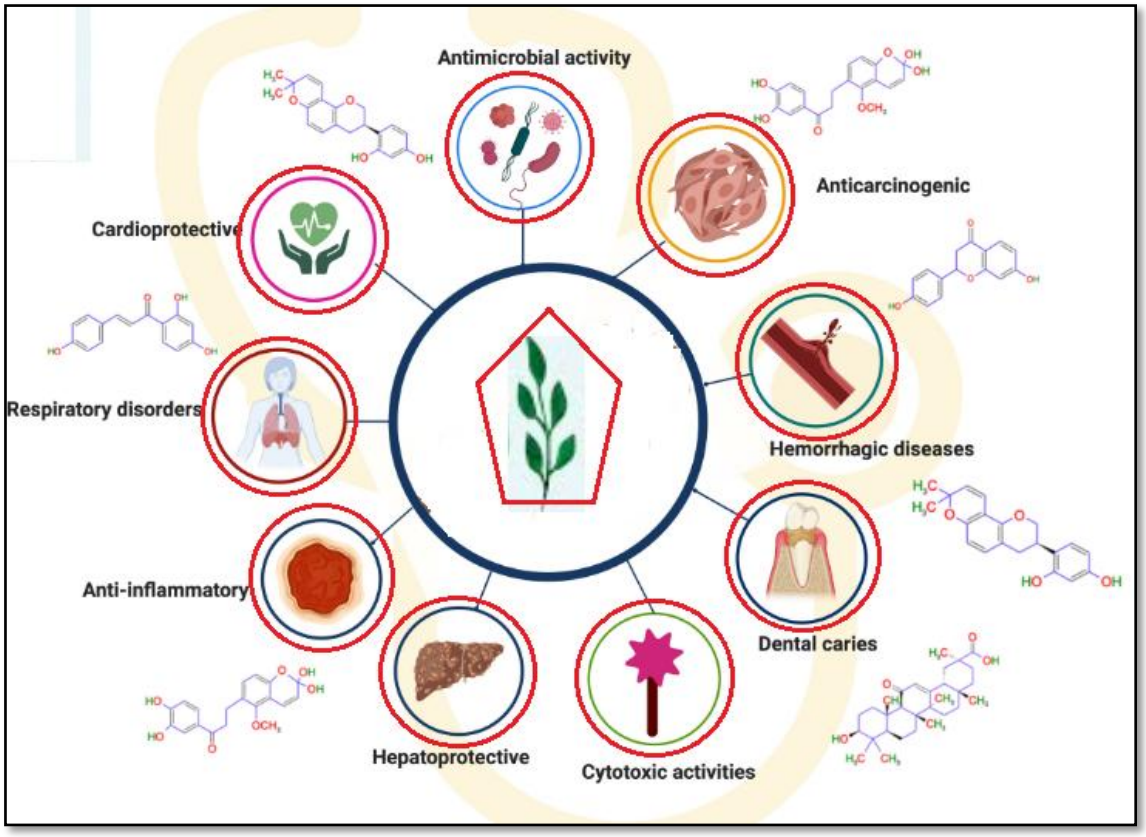

Figure 6: Application of herbal technology

1. **Extraction and Isolation of Active Compounds:** Herbal drug development involves extracting and isolating bioactive compounds from medicinal plants.Techniques like maceration, Soxhlet extraction, and supercritical fluid extraction are commonly used. To assure the safety and effectiveness of these chemicals, purification and characterisation are essential.

2. **Formulation Development:** Herbal medicines often require formulation development to improve stability, bioavailability, and patient compliance. The development of dosage forms such tablets, capsules, creams, and ointments are a research priority.

3. **Pharmacological and Toxicological Studies:** To understand their therapeutic benefits and safety profiles, herbal medications are subjected to extensive pharmacological and toxicological investigations. Efficacy and toxicity are evaluated using animal and cell culture models.

4. **Clinical Trials:** Clinical trials are conducted to evaluate the effectiveness and security of medicinal products made from herbs in humans. These tests are necessary for regulatory approval and adhere to defined norms. Herbal treatments are tested for safety and efficacy in clinical studies related to herbal technology. They employ exacting study methodologies, standardized herbal ingredients, and result metrics. Meta-analyses may provide results and ethical issues are essential. Due to the variances in herbal products, quality control and standardization are necessary.

5. **Standardization and Quality Control:** Developing standardized herbal manufactured products is crucial to ensure consistent quality and therapeutic effects. Assessing the presence of active substances, pollutants, and compliance with regulatory criteria are all part of quality control processes [30,31].

VIII. GENETIC MARKERS' FUNCTION IN HERBAL DRUG TECHNOLOGY

1. **Gene Typing and Genetic Variation:** It is generally known that geographic circumstances affect the active components of medicinal plants and, as a result, their activity profiles. Numerous researchers have looked into genetic variations due to geography. Estimates of genetic diversity are useful for developing agricultural improvement projects, managing germplasm, and creating conservation strategies[30]. It has been found that unique neem accessions collected from various geographical sites may be distinguished using RAPD-based molecular markers. To better understand genetic diversity, a lot of work has been done in the critical field of germplasm analysis. Numerous crops are being fingerprinted, including rice, wheat, chickpeas, pigeon peas, pearl millet, etc.

2. **Validation of Medicinal Plant Species:** DNA-based methods have been used frequently to confirm the authenticity of plant species with medicinal benefit. This is especially beneficial for individuals who frequently have other genera or varieties that are identical in terms of morphology and/or phytochemistry replaced or adulterated with them. RAPD markers were used to differentiate dried fruit samples obtained from Lycium barbarum and those of related species.

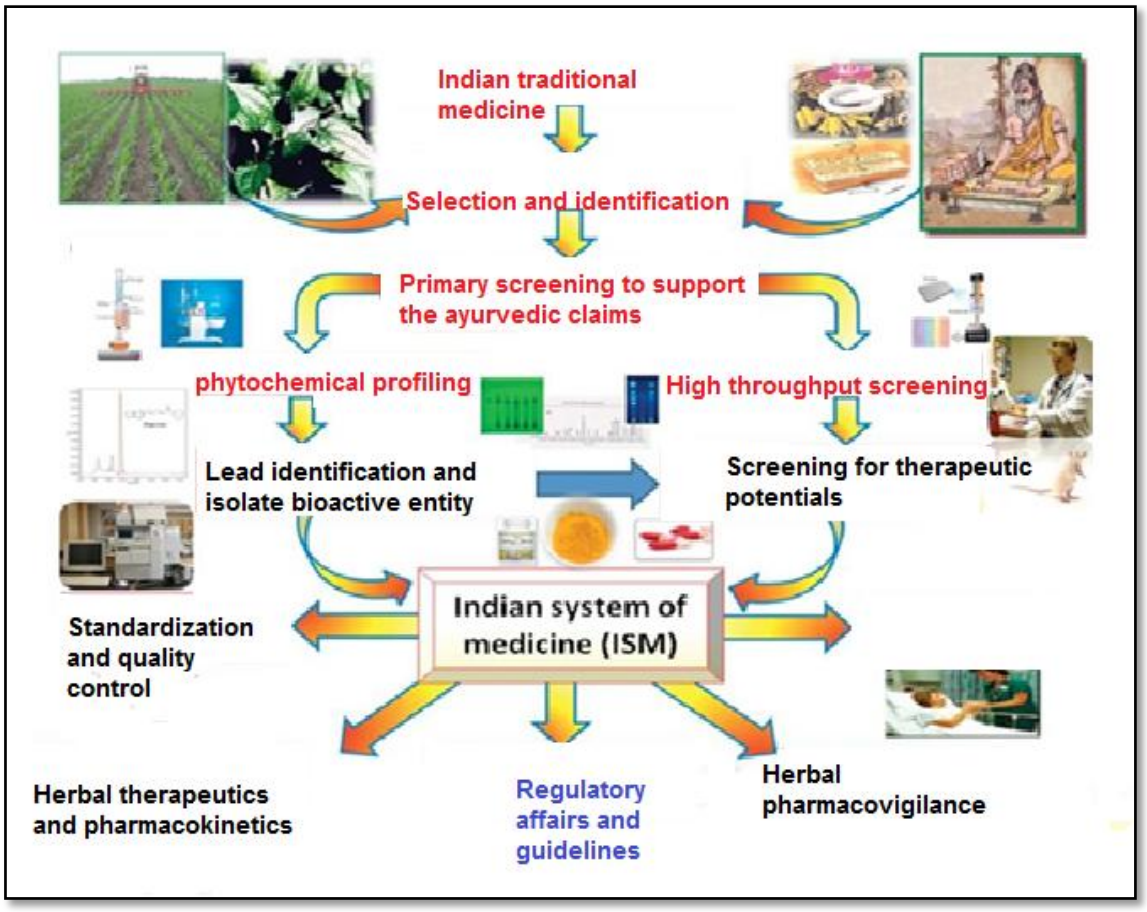

Figure 7: Validation of Herbal Medicine

3. **Regulatory Compliance:** The development of herbal drugs must follow regionally unique regulatory criteria and recommendations for herbal medications. This comprises supporting materials, safety evaluations, and evidence of effectiveness.

4. **Pharmacovigilance of Herbal Drugs:** The aim of pharmacovigilance is to recognize, assess, and comprehend any potential side effects which are connected towards conventional, complementary, and herbal medicines used for treatments. Both industrialised and developing nations employ a variety of herbal medications [31], however there has been an increase in several prominent herbal safety issues which have an impact on the well-being of the general population in recent years. Although traditionally believed to be risk-free, medicinal plants must be handled carefully to identify any potential risks. The hazard is brought on by either a contaminant or a medicine that was added, according to published evidence [32].

5. **Stability testing of Herbal Drugs:** The quality of a herbal product changes with time due to environmental elements such as humidity, light, temperature, oxygen other components or excipients in its dosage appearance, size of the particles, contamination from microbes, and possible metal trace contaminants. A stability test aims to establish suggested conditions for storage and a shelf-life by demonstrating how these changes occur [32]. To

make sure the product is of sufficient quality for the duration of its storage period, stability testing is required.

6. **Herbal Supplements and Nutraceuticals:** Apart from traditional herbal medicines, herbal drug technology is also applied to develop herbal supplements and nutraceuticals for health promotion and disease prevention [33,34].

IX. FUTURE OF HERBAL MEDICINE

Taking into account the rapidly expanding global market for herbal medicines along with additional healthcare products in developed as well as developing nations; the legislators and policymaker's health care providers, and consumers in general are concerned about the safety, effectiveness, performance, accessibility, storage, and a variety of other research development issues that are impeding the availability of herbal products [35]. Public need for information about the caliber, security, and efficacy of herbal products and TM/CAM practices has also increased. In order to calm these concerns and satisfy public demand, extensive research on herbal medicines is needed. This is true not only for their high therapeutic worth but also for the financial advantages.

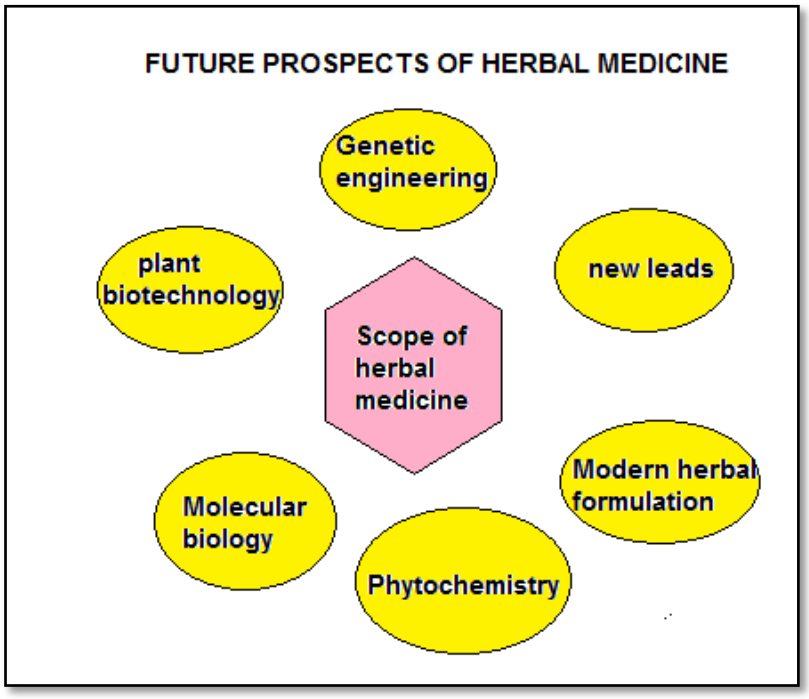

Figure 8: Herbal Medicine future prospects

Fortunately, quite a few in-depth phytochemical and pharmacological studies on medicinal plants and herbal treatments have previously been conducted all over the world. To support the efficacy and safety claims made for these treatments, efforts are being conducted to isolate and identify the active chemical components used in these investigations. It has been established that herbal treatments do not wholly lack scientific evidence because the majority of them have the requisite chemical components and manifest the indicated benefits. Additionally, reliable scientific data from randomised clinical trials supports the use of several herbal medicines [36].

X. CONCLUSION AND FUTURE ASPECTS

In conclusion, the symbiosis of the development of herbal drugs and technology offers hope for safer and more potent treatments. Looking to the future, personalized medicine, AI-driven discoveries, sustainability, combination therapies, regulatory clarity, and raised public awareness are key elements that will shape the evolving field of herbal medicine, enhancing our healthcare options and advancing the fusion of traditional knowledge with contemporary science.

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