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Importance Of Herbal Medicine In Modern Drug Therapy

[1]Prachi Hawale, [2]Aishwarya Patane, [3]Prachi Kamble, [4]Dr.Shital Dange, [5]Dr.Dhanraj Jadge

[1,2,3]Student, [4]Associate Professor, [5]Principal

Womens College of Pharmacy, Peth-Vadgaon

Abstract –

Natural products and traditional medicines hold significant importance. Various forms of medicine, including traditional Chinese medicine(69), Ayurveda, Kampo, traditional Korean medicine, and Unani, have been practiced in certain regions of the world and have evolved into systematically regulated medical frameworks. This study aims to review the literature on the interplay between natural products, traditional medicines, and modern medicine, as well as to investigate potential concepts and methodologies derived from natural products and traditional medicines to enhance drug discovery.(69) The unique characteristics regarding the theory, application, current status, and contemporary research of eight traditional medicine systems are summarized in this study. Although only a small fraction of existing plant species has been scientifically investigated for bioactivities since 1805,(69) when the first pharmacologically active compound, morphine, was isolated from opium, natural products and traditional medicines have already made significant contributions to modern medicine. When utilized for the development of new drugs, natural products and traditional medicines offer unparalleled advantages, including extensive clinical experience and a unique diversity of chemical structures and biological activities.(69)

***Index Terms*:- Medicine , Plant, herbal , traditional medicine ,modern drug therapy**

I. Introduction :-

Herbal medicine, often referred to as botanical medicine or phytotherapy, harnesses the healing properties of various plant parts, such as leaves, roots, and flowers(1). Across the globe, diverse tribal communities thrive in harmony with their surroundings, embodying the wisdom of nature in their practices(2)The incorporation of traditional herbal remedies into contemporary medicine is gaining traction, fueled by scientific advancements that allow us to identify and isolate bioactive compounds.(3)

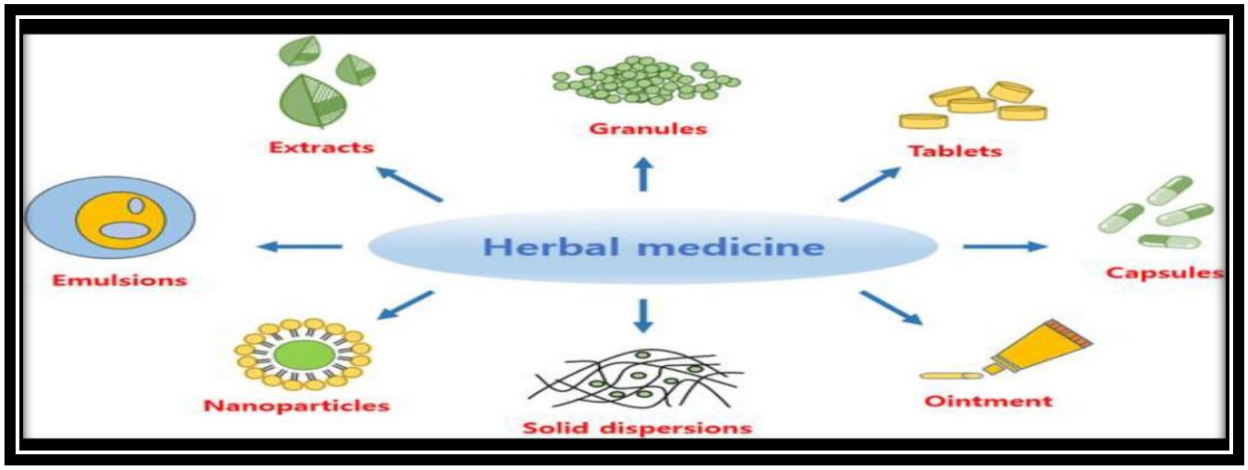

Fig 1:- Formulations that can be made from herbal drugs

Fig 2:-Herbs

For centuries, herbal medicines have served as powerful remedies for the prevention and treatment of various health conditions, embraced by nearly every known culture. The earliest documented use of herbal medicine dates back 5,000 years, showcasing its enduring legacy.(20)Today, many populations around the world still rely on herbal medicines to meet their healthcare needs. In the United States, the use of herbal remedies is on the rise, following the groundbreaking national study on complementary and alternative medicine conducted by Eisenberg and his team(5).Nanotechnology opens up a world of possibilities in contemporary research, encompassing theranostic agents,(68) innovative ocular drug delivery methods, advanced nano-enabled drug delivery systems, and transformative applications in agriculture(6).Nanoparticles play a vital role in various industries, including food, water treatment, textiles, and electronics. Indigenous and tribal communities depend profoundly on forest resources for their(68) survival, drawing on them for food, medicine, and building materials(7,8),.

Tribal communities frequently hold their knowledge close, emphasizing the importance of building genuine relationships for anthropologists seeking to gather valuable insights9,10.The potential for interactions between herbs and diseases, as well as between herbs and drugs, grows within older adult populations. Currently, there is a significant lack of research assessing the use of herbal medicines, particularly in clinical trials. This challenge, combined with the continuous advancement of new conventional drug therapies,(20) amplifies the uncertainty surrounding the combined use of these two treatment methods. .Globalization has significantly enhanced the accessibility of herbal medicines from around the world to individual consumers. There is a pressing need for coordinated efforts to conduct essential clinical trials to evaluate the efficacy and safety of herbal medicines, both independently and in combination with conventional drug therapies(20). Silver, recognized for its antimicrobial properties, was utilized by ancient civilizations including the Greeks, Romans, and Egyptians(68) as a preservative for food and water. In traditional Ayurvedic medicine, silver has been employed for over 2000 years in the forms of silver ash, both suspended and colloidal(68), to aid in restoring the body(11,12).

The tribal population cultivates millets that have unique nutritional and toxicological characteristics. It is essential to gather and digitize tribal knowledge while conducting laboratory research with the expertise of scientists(13,14,15).

II. Regulations of herbal medicines:-

One of the fundamental challenges in the use of herbs lies in the inconsistent terminology used to categorize them. For instance, a single product might be regarded as a food item by some and as a dietary supplement by others. As a result, this product(20) could be subject to various regulations based on its classification. In the United States, the 1994 Dietary Supplement Act plays a crucial role in this context(16). The manufacturing, provision, and use of herbal medicines are subject to varying regulations across the globe. In certain countries, efforts to demonstrate the efficacy and safety of herbal medicines are regarded as more advanced than those in the U.S. The Commission E monographs in Germany exemplify a more scientific methodology for assessing the efficacy and safety of herbs within Western medicine(17).

China boasts a long and rich history of traditional medicine, prominently featuring the use of herbs. Traditional Chinese Medicine (TCM) stands as an established medical system, operating alongside conventional medicine in China since 2004(20).

2.1.Culture and traditional medicine:

Culture significantly influences how communities utilize herbs. Acknowledging this, in 2009, the World Health Assembly adopted Resolution 62.13, urging national governments to honor, safeguard, and actively share the knowledge of traditional medicine(19). Many patients who consume herbal teas often do not consider them as herbal medicine. Our research with Mexican Americans reveals that individuals who utilize herbs in this manner typically do not recognize them as herbal medicine unless explicitly prompted in surveys (Rivera)(20.)

The journey to uncover new medicinal drugs derived from plants is a complex and dynamic process that often embraces a variety of methodologies.(68) One widely embraced approach is the ethnobotanical method, which explores the traditional healing practices of indigenous cultures and their relationship with plants.(68) Ethnobotanical studies offer valuable insights into the potential therapeutic properties of plants and assist in the selection of plants for further investigation. An alternative approach is the phytochemical method, which focuses on isolating and identifying the bioactive compounds found in plants. This method typically employs techniques such as chromatography and spectroscopy to separate and analyze the chemical constituents of plants.(68)
Once bioactive compounds are identified, they can be further evaluated through in vitro and in vivo assays to ascertain their pharmacological properties and potential therapeutic applications. Furthermore, computational techniques such as molecular modeling and virtual screening may be employed to predict the bioactivity of plant-derived compounds and to inform the selection of candidates for additional investigation.(23) This research identified herbs as the most commonly utilized plants, accounting for 46% of the total, followed by shrubs at 26%, trees at 14%, and climbers at 14%. Families such as Euphorbiaceae, Fabaceae, Solanaceae, and Asteraceae were frequently employed, with the first two families facilitating ten distinct treatments.(24) Traditional healers addressed stomach issues using nine plant species, whereas the Paliyar community utilized 21 medicinal plants for gastrointestinal complaints. Jaundice was treated with 13 plant species, toothache was alleviated with Spilanthesacmella, and diabetes was managed with Syzygiumcumini, Santalum album, and Ficus retusa.(25) Respiratory issues were treated with ten distinct remedies, including Ocimum basilicu and Adhatodavasica.(26) Topical and internal applications of various plant pastes, juices, and powders have been reported for the treatment of paralysis, poisonous bites, asthma, leucorrhea, headaches, snakebites, arthritis, and other ailments.(27,28) A notable illustration of the drug discovery process is the development of artemisinin derivatives from *Artemisia annua*, commonly referred to as Qing-hao in Chinese.(68) This plant produces a highly oxygenated sesquiterpene known as artemisinin, which is highly effective against malaria; however, its oral bioavailability is limited. Another example is *Datura stramonium*, or thornapple, which contains the alkaloid atropine and has been utilized for asthma treatment, although it is also a powerful hallucinogen. Additionally, Bicyclol, a synthetic second-generation derivative derived from the fruit of the Chinese magnolia vine, is employed in the treatment of hepatitis, a serious condition caused by the hepatitis B virus. In summary, the discovery of new

plant-derived medicinal drugs is a multifaceted process involving various methodologies to identify and develop treatments for a range of diseases.(68)

- **Herbal Medicine-**

The World Health Organization (WHO) has recently defined traditional medicine, including herbal remedies, as encompassing therapeutic practices that have existed for centuries prior to the emergence and dissemination of modern medicine.Traditional medicine represents the accumulated therapeutic knowledge of generations of

Exploring diverse methodologies to uncover new medicinal drugs derived from plants:

practitioners within indigenous medical systems. Traditional preparations include medicinal plants, minerals, and organic substances. Herbal medicines specifically refer to those traditional remedies that primarily utilize medicinal plant formulations for therapeutic purposes. The earliest documented use of these remedies can be traced back approximately 5,000 years in texts from Indian, Chinese, Egyptian, Greek, Roman, and Syrian cultures. Notable classical Indian texts such as the Rigveda, Atharvaveda, Charak Samhita, and Sushruta Samhita contribute to this rich legacy. Consequently, herbal medicines and traditional remedies are rooted in the extensive traditions of ancient civilizations and their scientific heritage.(29)A frequently referenced reason is the "sense of control, a mental comfort derived from taking action," which helps elucidate why many individuals using herbal remedies are dealing with chronic or incurable conditions such as diabetes, cancer, arthritis, or AIDS. In these circumstances, they often perceive that conventional medicine has not met their needs. When patients resort to home remedies for acute, typically self-limiting conditions like colds, sore throats, or bee stings, it is often due to the unavailability of professional care, or because it is deemed too inconvenient, expensive, or time-consuming.In rural areas, various cultural factors promote the use of botanicals, including the environment and cultural beliefs surrounding a "man-earth relationship." It is commonly held that if a region is associated with a specific disease, it will also yield plants that can be utilized for its treatment. (30)

- **Differences Between Herbal and Conventional Medications-**

Despite appearing similar on the surface, herbal medicine and conventional pharmacotherapy exhibit three significant differences:

Utilization of Whole Plants- Herbalists typically utilize unrefined plant extracts that contain multiple constituents. It is asserted that these components can interact synergistically, resulting in an overall effect of the whole herb that surpasses the cumulative effects of its individual components. Additionally, it is suggested that the use of whole herbs may diminish toxicity compared to isolated active ingredients, a phenomenon referred to as "buffering." Although two samples of a specific herbal remedy may exhibit varying proportions of constituent compounds, practitioners maintain that this variability usually does not lead to clinical issues. While there is some experimental evidence supporting synergy and buffering in certain whole plant preparations, the extent to which this applies to all herbal products remains uncertain.(31)

Diagnosis: Herbal practitioners employ diagnostic principles that differ from those of conventional practitioners. For instance, when addressing arthritis, they may note “underfunctioning of a patient’s elimination symptoms” and conclude that the condition stems from “an accumulation of metabolic waste products.” Consequently, a combination of diuretic, cholerectic, or laxative herbs may be recommended, in addition to herbs possessing anti-inflammatory properties. (31)

- The active principles are often unidentified.
- Standardization, stability, and quality control are achievable, although they present challenges.
- The availability and quality of raw materials are often challenging.
- Thoroughly conducted double-blind clinical and toxicological studies demonstrating their efficacy and safety are indeed uncommon.
- The practical application of folk medicine is a vital and significant aspect.
- They offer a diverse array of therapeutic benefits and are well-suited for long-term treatment.
- While undesirable side effects appear to be less common with herbal medicines, well-controlled randomized clinical trials have shown that they can still occur.
- They often come at a more affordable price than synthetic medications.(58)

- **Reasons for Utilizing Herbal Medicine-**

The earliest evidence of human use of plants for healing dates back to the Neanderthal period.(31)An increasing number of patients are now utilizing herbal medicine, often without informing their clinicians about this concurrent use.(32)Hundreds of primary health centers designed to serve rural areas are lacking in staff, diagnostic facilities, and sufficient supplies of medication. The rural

population relies significantly on traditional medical systems.(33)Natural plant products are regarded as healthier alternatives to manufactured medicines.(34)Additionally, reports of adverse effects associated with conventional medications appear in popular media at a significantly higher rate than reports of herbal toxicities. This discrepancy is partly due to the established mechanisms for tracking adverse effects of conventional medicines, while data regarding self-treatment is more challenging to obtain. Furthermore, many physicians often regard herbal remedies as harmless placebos.(30)

- **Regulation of Herbal Medicines-**

Herbal remedies encompass a diverse array of products, ranging from plants that individuals gather for personal health purposes to officially approved medical products. A significant portion of herbal products, estimated to constitute over 80 percent of herbal sales, falls within the regulatory gray area. European Union legislation mandates that herbal products must obtain marketing authorization if they are produced industrially and if their presentation or function, or both, categorize them as medicinal products. However, establishing clear boundaries in this regard proves challenging. Numerous medicine-like products within the British herbal market remain unregistered due to two primary factors: the lack of acceptable data on efficacy, safety, and quality, as well as the high cost of licensing fees.(35)The primary registering and regulatory organization for Western herbal practitioners is the National Institute of Medical Herbalists, located in Exeter, U.K. Only graduates from accredited programs are eligible for inclusion on the register, and a stringent code of ethics is upheld. The European Herbal Practitioner Association, which serves as an umbrella organization with approximately 1,000 members, has been established to promote greater cohesion among herbalists. However, it currently lacks formal criteria for membership screening and has not yet published a code of ethics.(31)The principal registering and regulatory body for Western herbal practitioners is the National Institute of Medical Herbalists, based in Exeter, U.K. Only graduates from accredited programs may be included in the register, and a rigorous code of ethics is maintained. The European Herbal Practitioner Association, which functions as an umbrella organization with approximately 1,000 members, has been created to foster greater unity among herbalists. However, it currently does not have formal membership screening criteria and has yet to publish a code of ethics.(35)

- **Safety Concerns Regarding Herbal Medicines-**

Traditional herbal products exhibit a heterogeneous nature. They present several challenges regarding quality control, quality assurance, and regulatory processes. The majority of herbal products available on the market today have not undergone the drug approval process to verify their safety and efficacy. Certain products may contain hazardous substances such as mercury, lead, and arsenic.(36)There have been reports of hepatic failure and even death following the ingestion of herbal medicine.(37)A prospective study indicates that 25% of corneal ulcers in Tanzania and 26% of childhood blindness in Nigeria and Malawi are associated with the use of traditional eye medicine.(38)When patients are using conventional medications, herbal preparations should be employed with great caution and only under the guidance of a herbalist knowledgeable in the relevant conventional pharmacology. There have been case reports of significant adverse events following the use of herbal products. In many instances, the herbs involved were self-prescribed and purchased over the counter or sourced from providers other than registered practitioners. Recently, several women experienced rapidly progressive interstitial renal fibrosis after consuming Chinese herbs prescribed by a slimming clinic.(31)Medicinal plant materials and herbal tea, if not stored correctly, can promote the growth of Aspergillus flavus, which is known to produce aflatoxin, a harmful mycotoxin.(39)Many of the Ayurvedic products available on the market may unfortunately be ineffective, compromised, or incorrectly labeled.(40)Many commercially available preparations do not align with ancient Ayurvedic texts. The medicinal properties of the herb diminish within a year after collection, while powders retain their effectiveness for only six months, and pastes last for about a year. Unfortunately, these formulations often do not include an expiry date or information on potential side effects.

It's concerning that herbal medicines are sometimes mixed with allopathic medications. For instance, at Leicester Royal Infirmary, a sample of traditional Chinese medicine provided to a woman for her eczema was discovered to contain a steroid.(41)Several undeclared substances, including phenylbutazone, diazepam, and corticosteroids, have been found in a traditional Chinese remedy for arthritis.(42)Without quality control, there is no guarantee that the herb in the bottle matches what is claimed on the label. The health food industry’s frequent neglect of quality control has harmed the reputation of many valuable medicinal herbs. For instance, it has been estimated that due to supplier mistakes in collection, over 50% of the Echinacea sold in the U.S. from 1980 to 1991 was actually Parthenium integrifolium. This underscores the importance of using Latin scientific names, as both

herbs are referred to as 'Missouri snakeroot,' and emphasizes the necessity of accurate plant identification through organoleptic, microscopic, and technological analysis.(43)Plant materials are utilized in both developed and developing countries as home remedies, over-the-counter products, and raw materials for the pharmaceutical industry, making up a significant portion of the global drug market. Therefore, it is crucial to establish internationally recognized guidelines to assess their quality.The World Health Assembly, through resolutions WHA31.33 (1978), WHA40.30 (1987), and WHA42.43 (1989), has highlighted the importance of ensuring the quality of medicinal plant products by utilizing modern control techniques and implementing appropriate standards. (44)

- **The importance of clinical trials :-**

To build public trust and integrate herbal products into today's healthcare system, it's essential for researchers, manufacturers, and regulatory agencies to employ rigorous scientific methodologies and clinical trials. This will help ensure the quality and consistency of traditional herbal products from batch to batch. Given that the identities of these final products are often not clearly defined and that there are typically no purification steps in their production, the quality and consistency largely depend on the control of the source materials and their transformation into the final products.Modern technologies enable us to monitor the quality and consistency of diverse herbal products. A well-designed clinical trial is essential for demonstrating the safety and effectiveness of therapeutic products. It is important for manufacturers of herbal products to follow good manufacturing practices (GMPs) and conduct preclinical testing before these products can be tested on humans. The basic principles and design of clinical trials for herbal products are similar to those for single-component chemical products. Numerous randomized double-blind controlled studies have been conducted using herbal formulations, and these studies have shown their effectiveness with minimal side effects. The extensive history of traditional use offers valuable insights into the selection, preparation, and application of herbal formulations. To be recognized as viable alternatives to Western medicine, it is crucial that the same rigorous scientific and clinical validation methods are applied.(45)While anecdotal reports of herbal utility can provide valuable insights and suggest areas for future research, they should never replace comprehensive clinical trials. The financial challenges associated with such evaluations can be daunting, yet they are not insurmountable for organizations that genuinely prioritize public health over mere profit from product sales. Several herbal marketers have already made significant investments in clinical studies and continue to do so. For instance, Indena from Italy has sponsored various trials on herbal remedies, including grape seed extract. Pharmaton in Switzerland has supported clinical trials on ginseng, while Schwabe from Germany has conducted numerous studies on St. John's wort. Madaus, also based in Germany, has financed countless research on ginkgo. Lichtwer is recognized for its studies on garlic. Additionally, Nutrilite and Pharmanex in the United States have promoted research on saw palmetto and red yeast, respectively.(46)A study on the oral absorption of cinnabar in mice revealed a notable rise in mercury levels in the liver and kidneys. Additionally, using cinnabar alongside medications that contain bromides, sulfates, sulfides, nitrates, and iodine could potentially heighten its toxicity by increasing how much is absorbed in the gastrointestinal tract.(47)

- **The Current Status of Herbal Medicine in India-**

India possesses a rich tradition of herbal medicine, as exemplified by Ayurveda, which has thrived for over two thousand years without any scientific foundation. The term Ayurveda, which translates to "knowledge (Veda) of life (Ayur)," originated in the Atharvaveda (circa 1500-1000 BC). The Charak Samhita and Sushruta Samhita are the two most renowned texts of Ayurveda, alongside several others compiled over the centuries, including the Bela Samhita, Kashyap Samhita, Agnivesh Tantra, Vagbhata's Ashtanga Hridaya (600 AD), and Madhava Nidan (700 AD).(48)Vegetable products played a significant role in Indian Materia Medica, which extensively utilized bark, leaves, flowers, fruits, roots, tubers, and juices. The principles of rasa, vipaka, virya, and prabhava constituted the foundation of Ayurvedic pharmacology, which did not clearly differentiate between diet and medicine, as both were essential components of treatment.(49)Charak, Sushruta, and Vagbhata documented 700 herbal drugs along with their properties and clinical effects. Based on these clinical effects, 50 categories of drugs have been identified, including appetizers, digestive stimulants, laxatives, anti-diarrheals, anti-haemorrhoids, anti-emetics, anti-pyretics, anti-inflammatories, anti-pruritics, anti-asthmatics, anti-epileptics, anti-helminthics, haemoptytics, haemostatics, analgesics, sedatives, and promoters of life (Rasyana), strength, complexion, voice, semen and sperm, breast milk secretion, fracture and wound healing, as well as agents for the dissolution of kidney stones, among others.(48)The introduction of

Western medicine in the eighteenth century posed a setback to the practice of Ayurveda, which experienced significant neglect under colonial administration. Following the initial success of reserpine, extensive characterization of medicinal plants was conducted in various laboratories and university departments; however, the results were disappointing due to the disorganized, widely spread, and unfocused nature of the efforts. Molecular pharmacology now offers a new interface between Ayurveda and modern medicine.(49)

➢ **Challenges to Address Before Herbal Medicine Achieves Mainstream Acceptance-**

To achieve the integration of high-quality and effective herbal products into mainstream medical treatment, several challenges must be addressed. One significant barrier is the bias among current healthcare professionals who did not study phytomedicines during their academic training, leading them to view these products as ineffective.(46)Utilizing folk beliefs and the expertise of traditional healers can expedite the discovery and isolation of pharmacologically active compounds.(49)Intellectual property rights should safeguard tribal and traditional knowledge to help eliminate the 'piracy' perpetrated by both Indian and foreign pharmaceutical companies.(50)Another issue is that clinicians working with herbal products are often relatively unfamiliar with them and may not recognize the importance of adequate dosage as defined in published literature. Numerous erroneous and unreproducible results have emerged in the medical literature because clinicians tend to accept the quality of an herb at face value, even when it has been adulterated or misidentified. Furthermore, they frequently do not specify the scientific names of the botanicals in the tested products, nor do they indicate the precise dosages administered.(51)

➢ **Medications Developed from Traditional Remedies that Adhere to Traditional Applications-**

1.Traditional Medicine (TM) is an invaluable aspect of research and development in modern pharmaceuticals. Despite its complex nature, there are extensive applications for TM within the realm of non-Western medical practices. In TM, a single herb or formulation may encompass numerous phytochemical constituents, including alkaloids, terpenoids, and flavonoids. Typically, these compounds operate independently or synergistically to achieve the intended pharmacological effect.(69)

2.It is noteworthy that many plant-derived medications used in clinical medicine today have their origins in traditional medicine.(53)

3.Furthermore, it has been shown that numerous valuable pharmaceuticals derived from plants were identified through their use in traditional medicine.(69)

4.A comprehensive investigation of the pharmacopoeias from both developed and developing nations, along with relevant global scientific literature, was undertaken as part of the World Health Organization's Traditional Medicine Program. The objective of this study was to assess whether Traditional Medicine had indeed influenced modern drug discoveries and to explore any correlations between the contemporary use of various compounds and their applications in Traditional Medicine.

5.The study examined various compounds utilized in plant-derived drugs across different countries, confirming that traditional medicine has significantly contributed to the development of effective new pharmaceuticals. It analyzed 122 compounds, with 80% demonstrating pharmaceutical effects as identified in folk medicine, and established that these compounds were derived from 94 plant species.(54)

6.The acceptability, convenience, and accessibility of therapeutic modalities have proven to be beneficial for new drug research and will continue to do so.(69)

7.Artemisinin, known as qinghaosu in Chinese, has undergone significant advancements in research, including the synthesis of new analogs and derivatives, as well as investigations into its biological activities and associated mechanisms(69).

8.Consequently, artemisinin and its effective derivatives are widely utilized globally as novel anti-malarial medications.(56)

9.As part of the phytochemical and pharmacological research(69) initiative, numerous Chinese herbal medicines were screened and examined for their toxicity and efficacy. Ultimately, artemisinin was derived from Artemisia annua L. in 1972.(56)

10.Notably, one of these scientists, Youyou Tu, was awarded the 2015 Nobel Prize in Medicine for her significant contributions to the discovery of artemisinin.

11.The discovery of artemisinin exemplifies the extensive knowledge embedded in Traditional Chinese Medicine (TCM) regarding natural products, including Chinese herbs, and suggests significant potential for future advancements. The development of effective new medications can benefit from this wealth of knowledge.(57)

Interactions between herbal products and pharmaceutical medications.-

Numerous medicinal herbs and pharmaceutical drugs can be therapeutic at one dosage while becoming toxic at another.Interactions between herbs and pharmaceuticals can enhance or diminish the pharmacological or toxicological effects of either substance. Synergistic therapeutic effects may complicate the dosing of long-term medications.Herbs that are traditionally used to lower glucose levels in diabetes could potentially lead to hypoglycemia if used in conjunction with conventional medications.(59)The potential for herb-drug interactions is a significant and under-researched concern. This matter is poised to become increasingly relevant in discussions regarding the safety of phytomedicines.(60)

The most significant risk associated with herbal medicines is the potential for interactions with pharmaceutical drugs. Although this area remains significantly under-researched, there exists a lengthy list of herbal medicines that may interact with synthetic medications.Experimental data regarding herb-drug interactions are limited, with few case reports and rare case series. This scarcity of data extends to drug-drug interactions as well; published clinical studies predominantly consist of case reports, as controlled trials are infrequently conducted due to ethical concerns surrounding the random assignment of patients to trials investigating unintended effects.The actual prevalence of drug interactions is significant yet not fully understood. A study involving 1,000 elderly individuals admitted to a hospital from the emergency department revealed that 538 patients were exposed to 1,087 drug-drug interactions, with 30 patients experiencing adverse effects as a result of these interactions.(61)The treatment of depression accounts for 15% of all herbal medicine usage, with St. John's Wort being the most frequently purchased herbal product for this condition. Initial case reports highlighting adverse effects associated with this popular product drew public attention to the clinical significance of herb-drug interactions. St. John's Wort was found to reduce blood concentrations of cyclosporine to a level that could lead to acute rejection of heart transplants. As measuring cyclosporine levels is a standard part of clinical practice, the pharmacokinetic basis for this adverse effect quickly became evident. Numerous cases of interactions between St. John's Wort and cyclosporine following organ transplantation were reported in the subsequent two years. Additionally, St. John's Wort was shown to decrease plasma concentrations of indinavir, resulting in an increased HIV viral load. In both instances, the interaction mechanism involved the activation of the pregnane X receptor, leading to the induction of the drug-metabolizing enzyme CYP3A4 and the efflux drug transporter P-glycoprotein, which are both crucial for the oxidative metabolism of approximately 50% of all medications.(62)Many patients are likely to contemplate the use of herbal medications. Consequently, it is essential for healthcare professionals to be informed about the associated issues and potential therapeutic management options. There is often a deficiency in the effective regulation of the manufacturing, sale, or composition of herbal products. As a result, these products may occasionally be adulterated with potent chemicals. Furthermore, they have generally not been evaluated for potential drug interactions.

- **Intellectual Property Rights (IPR)**

Traditional medicine, which is largely based on natural remedies derived from natural products, serves as a significant primary healthcare system in developing countries, especially in rural areas where access to Western biomedicine is limited or prohibitively expensive. Medicinal and aromatic plants (MAPs) play a crucial role in these traditional healthcare systems, providing an accessible, affordable, and culturally appropriate source of primary healthcare for over 80 percent of Asia's population.(63)Traditional knowledge (TK) related to medicinal herbs, along with their cultivation, innovation, and preservation, is predominantly a gendered activity in many countries. In various cultures, women and men assume complementary roles and responsibilities in traditional medicinal knowledge, yet these roles are not adequately represented in mainstream policy discussions. There is ongoing debate regarding the inclusion of intellectual property rights (IPRs) within the World Trade Organization (WTO).(64)Currently, members are required, in accordance with their commitments to the Trade-Related Aspects of Intellectual Property Rights (TRIPS), to establish minimum standards of protection for intellectual property rights either by enacting new legislation or by amending existing national laws. Consequently, the governance of rights related to knowledge and resources traditionally managed by rural and indigenous populations has shifted from local communities to multilateral trade forums, and increasingly, to regional and bilateral trade agreements. Traditional medicine is widely utilized in India, particularly in rural regions, with Ayurveda, Unani, Siddha, naturopathy, homeopathy, and yoga being recognized by the Government of India under the Central Council of Indian Medicine Act of 1970.(65)There exists a substantial and varied body of literature concerning intellectual property rights (IPRs) and traditional knowledge, highlighting the numerous discussions about the potential role

of IPRs in the preservation or commercial exploitation of traditional knowledge, the conservation of biodiversity, the protection of indigenous peoples' rights, and the efficacy of public health systems. The unauthorized exploitation of traditional medical knowledge for drug development is not permissible under international law. State parties must respect, preserve, and maintain the knowledge, innovations, and practices of indigenous and local communities that embody traditional lifestyles. Furthermore, they should promote the involvement of knowledge holders and encourage the equitable sharing of benefits arising from the utilization of such knowledge, innovations, and practices. Contracting parties should foster and develop cooperative models for the development and use of technologies, including those that are traditional and indigenous.(66)Until recently, the Convention on Biological Diversity contended for influence alongside the more dominant Trade-Related Aspects of Intellectual Property Rights (TRIPS) established by the World Trade Organization. TRIPS does not address the protection of traditional knowledge and fails to differentiate between indigenous, community-based knowledge and that of the industry. In early 2002, the World Trade Organization initiated a process to harmonize TRIPS with the Convention on Biological Diversity to ensure sufficient protection for indigenous intellectual and cultural property rights.(67)

Conclusion-Herbal medicine has acquired considerable significance in contemporary therapy due to its natural origins, therapeutic efficacy, and widespread acceptance among global populations. Historically, medicinal plants have been utilized in traditional systems such as Ayurveda, Traditional Chinese Medicine, and Unani for the treatment of various ailments. Recent scientific research has substantiated the medicinal properties of numerous herbs by identifying their active phytochemical constituents and pharmacological activities. Herbal medicines are frequently employed in the management of chronic conditions, including diabetes, cancer, cardiovascular diseases, arthritis, and infections, owing to their antioxidant, anti-inflammatory, antimicrobial, and immune-boosting properties. When used appropriately, herbal drugs are often perceived as safer and associated with fewer side effects compared to conventional medicines. Modern technologies and advanced analytical techniques have enhanced the standardization, quality control, and formulation of herbal products, rendering them more reliable for therapeutic applications. Clinical trials and pharmacological studies are also crucial in validating the safety and efficacy of herbal medicines. Nevertheless, challenges such as lack of standardization, improper dosing, herb–drug interactions, and regulatory concerns require further attention. Despite these challenges, the global demand for herbal medicine continues to rise due to increasing awareness of natural healthcare and preventive medicine. Consequently, herbal medicine has become a vital component of modern healthcare systems and continues to play a significant role in the discovery and development of new therapeutic agents.

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