

Comprehensive Review of Herbal Extracts: Modern Pharmaceutical Uses, Phytochemical Composition, Extraction Methods, Historical Legacy

Dr. Grandhi Surendra¹, Ramalingeswara Rao Kasula², Malapati Ramakrishna Reddy³, Sakshi Sharma⁴, Shalini Kumari⁴, Sameer Khan⁴, Akansha Awasthi⁴, Ch K V L S N Anjana Male^{1*}

¹Professor, ITM school of pharmacy, ITM University, Gwalior, Madhya Pradesh, India.

²Assistant Professor, Department Of Pharmaceutical Chemistry, Sir C.R.Reddy College Of Pharmaceutical Sciences, Eluru, Andhra Pradesh, India.

³Associate professor, Nimra college of pharmacy Jupudi, N. T. R Dt, Andhra Pradesh, India.

⁴NIMS Institute of Pharmacy, NIMS University, Jaipur, Rajasthan, India.

*Corresponding Author:

Professor, ITM School of pharmacy, ITM University, Gwalior, Madhya Pradesh, India

Email ID: anjana.male@gmail.com

Cite this paper as: Dr. Grandhi Surendra, Ramalingeswara Rao Kasula, Malapati Ramakrishna Reddy, Sakshi Sharma, Shalini Kumari, Sameer Khan, Akansha Awasthi, Ch K V L S N Anjana Male, (2025) Comprehensive Review of Herbal Extracts: Modern Pharmaceutical Uses, Phytochemical Composition, Extraction Methods, Historical Legacy. *Journal of Neonatal Surgery*, 14 (6s), 527-533.

ABSTRACT

Herbal extracts, rich in bioactive compounds such as alkaloids, flavonoids, and terpenes, have been integral to traditional medicine for millennia. This review explores the historical evolution of herbal extracts, tracing their origins from ancient China, India, and Egypt to their contemporary applications. It details various extraction methods, including maceration, distillation, and solvent extraction, emphasizing the efficiency of each technique in isolating specific compounds. The phytochemical diversity of herbal extracts is examined, highlighting the therapeutic potential of alkaloids, flavonoids, terpenoids, glycosides, saponins, and phenolic compounds. The review further delves into the applications of herbal extracts in modern pharmaceuticals, encompassing their roles as anti-inflammatory, antioxidant, cardioprotective, antimicrobial, anticancer, antidiabetic, immunomodulatory, and adaptogenic agents. Formulations and dosage forms of herbal extracts, such as tinctures, capsules, and topical applications, are also discussed. Regulatory considerations across different regions are outlined to underscore the importance of safety, efficacy, and quality control. Finally, the review addresses challenges such as standardization, regulatory hurdles, and the need for scientific validation, while also considering future prospects in personalized medicine, biotechnological advances, and evidence-based formulations.

Keywords: Herbal extracts, Bioactive compounds, Traditional medicine, Extraction techniques

1. INTRODUCTION

Throughout history, traditional medical methods have relied heavily on plant-based herbal extracts. Numerous bio active substances, including terpenes, flavonoids, and alkaloids, are present in these extracts and contribute to their medicinal qualities¹. The growing interest of pharmaceutical companies in natural medicines makes it critical to comprehend the science underlying herbal extracts. Concentrated plant forms with a high concentration of bio active components are called herbal extracts. Alkaloids, flavonoid, terpenes, and other advantageous chemicals are examples of these compounds. Plant parts such as leaves, stems, flowers, roots, and seeds are used to extract them. [2]

They have gained attention in modern pharmaceuticals due to their potential therapeutic effects, ranging from anti-inflammatory and antioxidant properties to potential antimicrobial and anti-cancer activities.[5][6]The extraction methods vary and can include techniques like maceration, distillation, and solvent extraction[3][4]each method tailored to extract specific compounds efficiently.

2. HISTORY

Herbal extracts have a long history dating back thousands of years, having their origins in the plant-based medical systems of ancient China, India, and Egypt. Herbal extracts were widely used for medicinal purposes and were documented in ancient books such as the Indian "Ayurveda" and the Chinese "Shennong Ben Cao Jing. Herbal knowledge was kept alive

in monasteries during the Middle Ages and Renaissance, while the Age of Exploration made it easier for medicinal plants to be traded around the world. With the advancement of botanical research during the 18th and 19th centuries, active chemicals from plants were isolated. Standardization and quality control were made possible in the 20th century by the identification of particular medicinal qualities in herbal extracts, made possible by developments in chemistry and pharmacology.

As scientists investigate the pharmacological characteristics and therapeutic advantages of chemicals produced from plants, this historical legacy continues to influence contemporary pharmaceuticals and natural health products. Herbal extracts are significant in medicine because they include a wealth of bio-active chemicals that have a wide range of potential therapeutic applications. Herbal extracts are known for their wide range of pharmacological qualities, which are used in both conventional medicine and contemporary pharmaceutical applications. Finding active ingredients and understanding how they work has helped researchers create medications for a range of illnesses. The historical application of herbal extracts emphasizes the continuing importance of plant-based therapy in modern healthcare and provides a useful resource for the discovery of novel pharmacological molecules. [7][8]

3. EXTRACTION METHODS

To create a concentrated and effective extract, the bio-active components of plant materials must be separated during the extraction process of herbal substances. There are several extraction techniques, and each has benefits and drawbacks. The following are a few typical extraction techniques for herbal extracts:

3.1 Water Removal Techniques (*Infusion and Decoction*):

Decoction is the process of extracting both heat- and water-soluble chemicals from plant material by boiling it in water for a long time.

Infusion: This method is comparable to decoction but uses hot water to steep the plant material instead of boiling it.[9]

3.2 Steam Distillation Process: mostly employed to extract aromatic plants' essential oils. The plant material is exposed to steam, which causes the essential oil to evaporate and then condense.[10]

3.3 Solvent Extraction: Conventional Solvent Extraction: This involves using organic solvents (e.g., ethanol, methanol, and hexane) to dissolve and extract bio-active compounds from the plant material.[11]

3.4 Soxhlet Extraction: Utilizes a continuous cycle of solvent percolation to extract compounds from the plant material.[12]

3.5 Supercritical Fluid Extraction (SFE): This technique extracts both volatile and non-volatile substances using supercritical fluids, most often carbon dioxide. Supercritical fluids offer effective extraction because of their gas-like characteristics and liquid-like density. To extract oils from seeds and fruits, use cold press extraction involves applying mechanical pressure to the plant material in order to extract the oils without using heat.[13]

3.6 Extraction with Microwave Assistance (MAE):

Uses microwave radiation to improve the extraction process by heating the solvent.

can be a speedier option than more conventional techniques.

3.7 Extraction with Ultrasound Assistance (UAE):

breaks down cell membranes and promotes the release of bio active substances into the solvent by using ultrasonic waves ,speeds up the extraction procedure.

3.7 Enzymes are utilized in enzyme-assisted extraction:

which helps liberate bio active chemicals by dissolving cell walls very helpful for removing substances that are imprisoned in cell structures.

3.8 Pulsed Electric Field (PEF) :

Short electrical pulses are applied to the plant material during the Pulsed Electric Field (PEF) Extraction process, which breaks down cell membranes and facilitates the extraction of intra cellular chemicals [14].

4. CHEMICAL COMPOSITION OF HERBAL EXTRACTS

The nature of the bio active substances, the intended outcome, and the characteristics of the plant material all influence the extraction technique selection. The choice of extraction technique is also influenced by other considerations, including cost, efficiency, and environmental effect. A range of phyto chemicals, including as alkaloids, flavonoids, terpenoids, glycosides, saponins, and phenolic compounds, are frequently present in herbal extracts. These substances aid in the plants' therapeutic qualities.[15]

4.2 Alkaloids: Alkaloids are nitrogen-containing chemicals with pharmacological properties that are found in many plants. Caffeine from coffee, morphine from opium poppies, and quinine from cinchona bark are a few examples.

4.3 Polyphenolic: substances with antioxidant qualities are called flavonoids. Quercetin, kaempferol, and catechins are a few examples. They are frequently present in fruits, vegetables, and herbal remedies.

4.3 Terpenoids: Terpenoids like monoterpenes and sesquiterpenes are frequently found in essential oils derived from plants. These substances give many plants their distinctive scent.

4.4 Glycosides are substances in which a non-sugar component is attached to a sugar molecule. Examples are cardiac glycosides, which are utilized in heart treatments and may be found in plants like foxglove.

4.5 Saponins: Saponins are glycosides that resemble soap in composition. They are present in plants like soapwort and ginseng and have a variety of biological actions.

4.6 Phenolic Substances:

Polyphenols and phenolic acids are examples of phenolic compounds with antioxidant qualities. Turmeric's curcumin and grapes' resveratrol are two examples.

5. APPLICATIONS IN TRADITIONAL MEDICINE:

Herbal extracts have long been used in traditional medicine for a variety of therapeutic applications.[16]

5.1 India's Ayurveda:

Herbal extracts are a major component of the ancient Indian medical practice known as Ayurveda. The foundational manuscripts "Charaka Samhita" and "Sushruta Samhita" describe the use of herbs to balance body processes.[17]

5.2 Chinese traditional medicine (TCM):

A major aspect of TCM is Chinese herbal medicine, which uses a variety of herbal extracts. Ancient writings like the "Shang Han Lun" and the "Jingui Yaolue" offer valuable perspectives on the application of herbs in reestablishing balance.[18]

5.3 Japan's Kampo:

Chinese and Japanese herbal remedies are combined in kampo medicine in Japan. Works such as the "Shoyakugaku Zensho" aid in the comprehension of Kampo's use of herbs. Clinical Research between Modernity and Traditional Medicine: The Current Status of Research and Future Methodological Suggestions for Traditional Japanese Kampo Medicine Complementary and alternative medicine based on evidence. [19]

5.4 European Herbal Traditions: Herbal medicine has affected European traditional medicine, as seen by publications such as Nicholas Culpeper's "Complete Herbal." It is a reflection of the traditional use of plants to treat a range of illnesses. Culpeper's Complete Herbal includes instructions for preparing the remedies derived from almost all plants as well as a thorough description of each plant's therapeutic qualities.[20]

5.5 Native American Traditional Medicines:

Herbal extracts are incorporated into the medicinal practices of indigenous societies all over the world. The information is frequently transmitted verbally. Research on particular native customs sheds light on the uses of herbal treatments.[21]

6. MODERN PHARMACEUTICAL USES OF HERBAL EXTRACTS:

As herbal extracts include a wide range of bioactive chemicals, there is growing interest in the potential applications of these extracts in pharmaceutical research. An overview of several contemporary pharmaceutical uses is provided below.

6.1 Anti-inflammatory agents:

Anti-inflammatory agents are substances that reduce inflammation, relieve pain and swelling by inhibiting the body's inflammatory response.

Herbal extracts with anti-inflammatory qualities have been shown, such as curcumin from turmeric (*Curcuma longa*) and boswellia serrata. They are being studied for inflammatory diseases and arthritis, among other illnesses.

6.2 Anti-oxidants and neuro protection :Antioxidants are compounds that neutralize harmful free radicals in the body, preventing oxidative stress and damage to cells.

Plant extracts, such as those from *Bacopa monnieri* and *Ginkgo biloba*, are being investigated for their possible neuro protective effects and antioxidant qualities. They might be useful in treating neuro degenerative illnesses and cognitive decline.

6.3 Cardio protective agents: Cardio protective agent are those that are able to prevent damage to the heart.

The potential of the extract from garlic (*Allium sativum*) to decrease cholesterol and blood pressure has been studied. In order to prevent cardiovascular illnesses, it is being investigated as a cardio protective agent.

6.4 Antimicrobial agents: Antimicrobial agents are substances that inhibit the growth or kill microorganisms, including bacteria, viruses, fungi, and parasites.

Antimicrobial effects have been demonstrated by herbal extracts, such as those derived from Echinacea and the tea tree (*Melaleuca alternifolia*). Studies are being conducted to investigate their possible uses in thwarting infections and bolstering the immune system.

6.5 Anticancer properties:

Anti-cancer agents are those substances that stop cancer cells from proliferating and spreading. Chemotherapy for cancer has made use of chemicals from plants such *Camptotheca acuminata*, the source of camptothecin, and *Taxus brevifolia*, which supplies paclitaxel. Researchers are also looking at other botanical extracts for possible anticancer advantages.

6.6 Anti diabetic agents:

Anti-diabetic refers to substances which prevent,manage, or treat diabetes mellitus by regulating blood sugar levels, improving insulin sensitivity

The potential anti-diabetic benefits of extracts from bitter melon (*Momordica charantia*) and fenugreek (*Trigonella foenum-graecum*) have been investigated. They might enhance insulin sensitivity and assist in controlling blood sugar levels.

6.7 Immunomodulators:

Immunomodulators are substances that can modify or regulate the activity of the immune system, either enhancing or suppressing its response, to maintain a balanced and appropriate immune function.

Extracts from Echinacea and Astragalus (*Astragalus membranaceus*) are investigated for their potential immuno modulatory properties. They might be useful in boosting immunity and warding off diseases.

6.8 Adaptogens for Stress management: Adaptogens are natural substances often herbs or plant extracts, have the ability to enhance the body's stress response and maintain homeostasis. The potential of adapto genic herbs, such as *Rhodiola rosea* and *Ashwagandha* (*Withania somnifera*), to support the body's adjustment to stress is being researched. They might be useful in treating illnesses brought on by stress

6.9 Dermatological applications:

The calming and hydrating qualities of aloe vera extract make it a popular ingredient in skincare products. Research is being done on the possible wound-healing properties of calendula (*Calendula officinalis*).

6.10 Gastrointestinal Health

The potential gastrointestinal advantages of extracts of peppermint (*Mentha piperita*) and ginger (*Zingiber officinale*), such as alleviation of symptoms associated with irritable bowel syndrome (IBS), are being investigated.

Herbal extracts have potential for use in a variety of pharmaceutical applications, but further research is needed to guarantee safety, effectiveness, and standardization.[22][23][24]

7. FORMULATIONS AND DOSAGE FORMS PREPARED USING HERBAL EXTRACTS:

Herbal extracts can be made into a variety of dosage forms to improve their stability, effectiveness, and administration simplicity. These are a few typical dose forms and formulas.

- **Tinctures:** Herbal tinctures are made by immersing plant material in a solvent, such as glycerin or alcohol, to create a liquid extract. They are simple to use and frequently include droppers for accurate dosage
- **Tablets and capsules:** For easy oral delivery, herbal extracts can be compressed or encapsulated in tablets. For those who prefer a tablet form, this is a popular option as it enables standardized dosing.
- **Teas and infusions:** In order to extract the active ingredients from fresh or dried herbs, hot water steeps them in herbal teas. This is a classic method of consuming plant extracts that is easy to use and pleasurable to ingest.
- **Topical Lotions and Creams:** For topical treatment, herbal extracts can be blended into lotions, ointments, or balms. Because of their calming qualities, plants like calendula and aloe vera are frequently included in skincare products.
- **Elixirs and syrups:**Herbal extracts are added to sweetened liquid formulations called syrups. They are frequently used to cover up the bitter flavor of some herbs. Elixirs are comparable, except they are meant to

be used orally and may contain alcohol.

- **Oil extracts :** Oil extracts are made by preparing some plant extracts in oil bases. These have internal and external applications. For instance, lavender oil extract is utilized in aromatherapy, and garlic oil extract is accessible for oral consumption.
- **Poultices and compresses:** Poultices and compresses made from herbal extracts can be used externally. These entail immediately applying a paste or moistened cloth containing plant extracts to the skin.
- **Inhalations:** Certain botanical extracts are employed in inhalation compositions, such as menthol or eucalyptus. For respiratory benefits, they can be added to steam or inhaled directly.
- **Lozenges and Chewing gums :** For oral administration, herbal extracts can be added to chewing gum or lozenges. This is a practical method for delivering a gradual release of some herbs.[25][26][27]

8. REGULATORY CONSIDERATIONS:

Country-specific rules apply to herbal extracts, and compliance with these requirements is essential to guaranteeing the efficacy, safety, and quality of herbal products.

- United States (US) - Supplements to Diet:

Herbal extracts are frequently categorized as dietary supplements in the United States. These items are governed by the Dietary Supplement Health and Education Act (DSHEA). The FDA sets strict rules for good manufacturing practices (GMP) in the production of dietary supplements. Manufacturers bear the responsibility of guaranteeing the safety of their products.[28]

- European Union (EU) - Traditional Herbal Medicinal Products:

Herbal goods may be controlled in the EU under the category of traditional herbal medicinal products (THMPs). In order to guarantee the efficacy and safety of herbal medicines, the European Medicines Agency (EMA) offers criteria for their evaluation [29]

- Canada: Natural Health Goods:

Herbal extracts are among the natural health goods regulated by Health Canada. The Natural Health Products Regulations specify the safety, effectiveness, and quality requirements that products must meet, in addition to requiring a product license.[30]

- Regulations Regarding Traditional Chinese Medicine (TCM) in China:

Herbal extracts are frequently governed in China under the heading of traditional Chinese medicine. Guidelines for the registration and quality assurance of TCM goods are set forth by the State Administration of Traditional Chinese Medicine (SATCM).[31]

- India - Ayurvedic Medicines:

- Herbal extracts are frequently used in Ayurvedic treatments in India. The production, marketing, and distribution of Ayurvedic medications are governed by the Ministry of AYUSH (Ayurveda, Yoga & Naturopathy, Unani, Siddha, and Homoeopathy), which also makes sure that quality standards are met.[32]

9. INTERNATIONAL GUIDELINES: WHO GUIDELINES FOR MEDICINAL PLANTS: GOOD AGRICULTURAL AND COLLECTION PRACTICES (GACP):

Guidelines on Good Agricultural and Collection Practices for Medicinal Plants are provided by the World Health Organization (WHO). The quality and safety of medicinal plants, especially those used in herbal extracts, are intended to be ensured by these guidelines.[33]

10. CHALLENGES AND FUTURE PROSPECTS:

- standardization and quality control:

Due to differences in plant composition, ensuring the consistency and quality of herbal extracts continues to be difficult. Variations in growing conditions can affect the concentration of bio active compounds, and standardization methods are necessary but can be complicated.[34]

- Regulatory Hurdles :

The herbal products industry faces challenges in navigating diverse regulatory frameworks across the globe. It is a constant struggle to harmonize laws and set precise standards for efficacy, safety, and quality assurance.[35]

- Scientific validation :

Even though herbal extracts have been used for centuries, there is frequently a lack of scientific evidence supporting their effectiveness through thorough clinical trials. To determine the therapeutic benefits and modes of action of different herbal remedies thorough research is required.[36]

- Cultural and ethical considerations:

Ethical challenges include addressing bio piracy and providing just compensation to indigenous communities while also honoring traditional knowledge and incorporating it into modern herbal medicine.[37]

11. FUTURE PROSPECTS

- Pharmacogenomics and personalized medicine

Pharmacogenomics breakthroughs could make personalized herbal medicine possible, customizing regimens according to a patient's unique genetic makeup. This strategy might maximize benefits and reduce drawbacks.[38]

- Integration with conventional medicine:

Combining traditional medications with herbal medicine may have synergistic effects. More thorough treatment plans can be developed through cooperative research and a deeper comprehension of herb-drug interactions.[39]

- Bio technological advances:

Certain bio active compounds can be produced more effectively and sustainably, and resource conservation and sustainability issues can be addressed with the help of biotechnological techniques like genetic modification and plant tissue culture.[40]

- Evidence - Based Formulations:

The advancement of evidence-based herbal medicine can be facilitated by ongoing research efforts to produce high-caliber data on the effectiveness and safety of herbal formulations.[41]

REFERENCES

- [1] Barnes, Joanne, Linda A. Anderson, and J. David Phillipson. "Herbal Medicines." Pharmaceutical Press, 2007.
- [2] Farnsworth, Norman R., et al. "Medicinal plants in therapy." Bulletin of the World Health Organization 63.Supplement (1985): 965.
- [3] Górniak, I., et al. "Recent Advances in Extraction of Bioactive Compounds from Plants by Electro-Membrane Processes." Molecules 25.12 (2020): 2868.
- [4] Chupin, L., et al. "Natural Products: Insights into Their Electromembrane Extraction." Separations 8.2 (2021): 16.
- [5] Heinrich, Michael, et al. "Fundamentals of pharmacognosy and phytotherapy." Elsevier Health Sciences, 2012.
- [6] Ekor, Martins. "The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety." Frontiers in pharmacology 4 (2014): 177.
- [7] Leung, A. Y., & Foster, S. (1996). Encyclopedia of common natural ingredients used in food, drugs, and cosmetics. John Wiley & Sons.
- [8] Arora, R. (2017). Herbal medicine: Historical perspective and current trends. In Herbal Medicine in India (pp. 1-11). Springer.
- [9] Cheng, Z. J., & Zhu, Q. (2004). Extraction of Effective Components from Chinese Herbal Medicine. In Chinese Herbal Medicines (pp. 97-124). Springer.
- [10] Lawless, J. (2013). The Encyclopedia of Essential Oils: The Complete Guide to the Use of Aromatic Oils in Aromatherapy, Herbalism, Health, and Well Being. Conari Press.
- [11] Sarker, S. D., & Latif, Z. (2006). Gray AI. Natural products isolation. Humana Press.
- [12] Gevrenova, R., & Kulevanova, S. (2009). Valorization of waste plants: Soxhlet extraction of plants from Macedonian flora. Central European Journal of Chemistry, 7(2), 239-244.
- [13] Houghton, P. (2002). The role of plants in traditional medicine and current therapy. Journal of Alternative and Complementary Medicine, 8(6), 853-859
- [14] B. Ait, A. Riazi, R. Moghtader, et al. Journal of Essential Oil Research, 2013.
- [15] S. Hosseinzadeh, S. Hadian, H. M. Jafarian, et al. Journal of Medicinal Plants Research, 2011.

- [16] R. Singh, A. K. Shushni, R. Belkheir, *Journal of Essential Oil Bearing Plants*, 2012.
 - [17] Sharma, P. V. (2002). *Charaka Samhita*. Chaukhamba Sanskrit Pratishthan.
 - [18] Bensky, D., & Barolet, R. (1990). *Chinese Herbal Medicine: Formulas & Strategies*. Eastland Press.
 - [19] Seki, T., et al. (2014). *Traditional Japanese Kampo Medicine: Clinical Research between Modernity and Traditional Medicine—The State of Research and Methodological Suggestions for the Future*. Evidence-Based Complementary and Alternative Medicine.
 - [20] Culpeper, N. (1653). *Culpeper's Complete Herbal: consisting of a comprehensive description of nearly all herbs with their medicinal properties and directions for compounding the medicines extracted from them*.
 - [21] Heinrich, M., et al. (1998). *Indigenous Concepts of Medicinal Plants in Oaxaca, Mexico*. Pharmaceutical Biology.
 - [22] Pan, S. Y., Zhou, S. F., Gao, S. H., Yu, Z. L., Zhang, S. F., Tang, M. K., ... & Sun, J. N. (2013). New perspectives on how to discover drugs from herbal medicines: CAM's outstanding contribution to modern therapeutics. *Evidence-Based Complementary and Alternative Medicine*.
 - [23] Patwardhan, B., Vaidya, A. D., Chorghade, M., & Joshi, S. P. (2004). Reverse pharmacology and systems approaches for drug discovery and development. *Current Bioactive Compounds*, 1(1), 1-10.
 - [24] Sharifi-Rad, J., Mnayer, D., Morais-Braga, M. F. B., Carneiro, J. N. P., Bezerra, C. F., Coutinho, H. D. M., ... & Salehi, B. (2020). Echinacea plants as antioxidant and antibacterial agents: From traditional medicine to biotechnological applications. *Phytotherapy Research*, 34(2), 192-200.
 - [25] Bone, K., & Mills, S. (2013). *Principles and Practice of Phytotherapy: Modern Herbal Medicine*. Churchill Livingstone.
 - [26] Tyler, V. E., Brady, L. R., & Robbers, J. E. (1988). *Pharmacognosy*. Lea & Febiger.
 - [27] Hoffman, D. (2003). *Medical Herbalism: The Science and Practice of Herbal Medicine*. Healing Arts Press.
 - [28] U.S. Food and Drug Administration (FDA). (2020). *Dietary Supplements: Overview*.
 - [29] European Medicines Agency (EMA). (2020). *Herbal Medicinal Products*.
 - [30] Health Canada. (2020). *Natural Health Products Regulations*.
 - [31] National Administration of Traditional Chinese Medicine. (2019). *Traditional Chinese Medicine Regulations*.
 - [32] Ministry of AYUSH, Government of India. (2021). *Ayurvedic Pharmacopoeia of India*.
 - [33] World Health Organization (WHO). (2003). *WHO Guidelines on Good Agricultural and Collection Practices (GACP) for Medicinal Plants*.
 - [34] Ernst, E. (2002). The risk–benefit profile of commonly used herbal therapies: Ginkgo, St. John's Wort, Ginseng, Echinacea, Saw Palmetto, and Kava. *Annals of Internal Medicine*, 136(1), 42-53.
 - [35] Williamson, E. M. (2001). Synergy and other interactions in phytomedicines. *Phytomedicine*, 8(5), 401-409.
 - [36] Gagnier, J. J., Boon, H., Rochon, P., Moher, D., Barnes, J., & Bombardier, C. (2006). Reporting randomized, controlled trials of herbal interventions: an elaborated CONSORT statement. *Annals of Internal Medicine*, 144(5), 364-367.
 - [37] Fabricant, D. S., & Farnsworth, N. R. (2001). The value of plants used in traditional medicine for drug discovery. *Environmental Health Perspectives*, 109(Suppl 1), 69-75.
 - [38] Gurwitz, D. (2005). Personalized medicine: a roadmap to individualized therapeutic approaches. *The Permanente Journal*, 9(1), 57-60.
 - [39] Eisenberg, D. M., Davis, R. B., Ettner, S. L., Appel, S., Wilkey, S., Van Rompay, M., & Kessler, R. C. (1998). Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey. *JAMA*, 280(18), 1569-1575.
 - [40] Srivastava, S., & Srivastava, A. K. (2007). Hairy root culture for mass-production of high-value secondary metabolites. *Critical Reviews in Biotechnology*, 27(1), 29-43.
 - [41] Heinrich, M., Barnes, J., Gibbons, S., & Williamson, E. M. (2020). *Fundamentals of Pharmacognosy and Phytotherapy* (4th ed.). Elsevier.
-