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REVIEW ON GREEN CHEMISTRY APPROACHES IN HERBAL DRUG EXTRACTION AND FORMULATION

[1]*Prof. Shriniwas R. Mane, [2]Dr. Sanjay K. Bais, [3]Aditi. A. Patale

[1]Assistant Professor at Fabtech College of Pharmacy, Maharashtra – 413307.
[2]Principle and Professor at Fabtech College of Pharmacy, Sangola, Maharashtra – 413307.
[3]Student at Fabtech College of Pharmacy, Sangola, Maharashtra – 413307.

***Corresponding Author: Prof. Shriniwas R. Mane**

Assistant Professor at Fabtech College of Pharmacy, Maharashtra - 413307.

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ABSTRACT

Green chemistry aims to make chemical processes More secure and longer-lasting Safer and more environmentally friendly by minimizing the use of hazardous substances, energy consumption, and waste generation. In herbal drug development, green extraction techniques provide alternatives to conventional methods through suitable solvents and efficient technologies such as ultrasound-assisted extraction, microwave-assisted extraction, enzyme-assisted extraction, and pressurized liquid extraction. This review discusses the use of water, ethanol, bio-based solvents, and natural deep eutectic solvents to extract valuable phytoconstituents, including polyphenols, flavonoids, alkaloids, and terpenoids.[4,6] It also highlights the influence of their chemical properties on solubility, stability, and extraction efficiency. The application of herbal extracts in pharmaceutical formulations such as gels, creams, tablets, capsules, films, and hydrogels is explored, along with the benefits and challenges of sustainable formulation development. Optimizing extraction conditions may improve extract quality and consistency while supporting the development of cost-effective and environmentally responsible pharmaceutical products.

KEYWORDS: Herbal drug extraction, green extraction technologies, phytoconstituents, green solvents, sustainable extraction.

INTRODUCTION

Green chemistry is about developing chemical processes that reduce or prevent the use and the generation of hazardous substances and also serve to minimize their environmental impact. The twelve principles of green chemistry stress waste prevention, energy efficiency, the use of safer chemicals, and the use of renewable resources. It is pertinent to pharmaceutical development since they promote safer and more sustainable methods of manufacturing.[1,2]

Medicinal plants contain a variety of bioactive phytoconstituents, such as alkaloids, flavonoids, phenolic acids, terpenoids, glycosides, saponins, and tannins. Extraction of these compounds is a key stage in the development of herbal drugs.[3,10] Traditional extraction methods, such as maceration, Soxhlet extraction, and reflux extraction, are commonly used to obtain compounds from plant materials. However, the efficiency of these methods depends on the plant matrix, the chemical characteristics of the target compounds, and the extraction conditions Some conventional techniques may require prolonged processing times and large quantities of solvents Therefore, selecting an appropriate extraction method is important for improving extraction efficiency and reducing environmental impact.[9,10]

Green chemistry principles can also guide the development of herbal formulations by encouraging the selection of suitable excipients and the reduction of material waste during manufacturing. Herbal extracts may be incorporated into dosage forms such as gels, creams, tablets, capsules, and hydrogels. The use of appropriate renewable or biodegradable materials may help reduce the environmental impact of pharmaceutical products, although their suitability must be evaluated in

terms of safety, stability, compatibility, and performance. Assessing the environmental properties of pharmaceutical excipients can help guide more sustainable formulation choices.[2,14,15]

GREEN CHEMISTRY: CONCEPTS IN HERBAL DRUG DEVELOPMENT

Green chemistry aims prevent the use and generation of hazardous substances during the development and manufacture of products. It focuses on designing safer chemical processes, reducing waste, conserving energy, and selecting eco-friendly materials. Green chemistry offers opportunities to improve the extraction and processing of therapeutic compounds recovered from medicinal plants. Conventional extraction methods may require large quantities of organic solvents, prolonged heating, and considerable energy consumption. These factors can increase environmental pollution and may affect the stability of sensitive phytoconstituents.[2,3,9]

The selection of appropriate extraction solvents is an important application of green chemistry. Water, ethanol, and certain bio-based solvents can serve as alternatives to some conventional organic solvents, depending on the compounds and the intended application. The selection of solvent relies on factors such as polarity, solubility, toxicity, and the chemical stability of phytoconstituents, including phenolic compounds flavonoids and alkaloids. Choosing a solvent which is suitable can improve extraction efficiency.[12,16,17]

SIGNIFICANCE OF GREEN CHEMISTRY IN HERBAL DRUG DEVELOPMENT

Green chemistry is important for the sustainable development of herbal medicines because it encourages environmentally responsible approaches to extraction, processing, and formulation. Medicinal plants contain a variety of bioactive compounds that are examined for their capability of pharmaceutical applications. However, obtaining these compounds through conventional methods can involve use of hazardous organic solvents, intensive energy requirement and the formation of chemical waste. Green chemistry provides alternatives to reduce these environmental concerns while maintaining the nature of obtained components.[2,3,9]

Appropriate alternatives, such as water, ethanol, and certain bio-based solvents, can reduce some of the environmental and dangers caused by conventional organic solvents. The choice of solvent depends on the chemical characteristics of the desired phytoconstituents, particularly their polarity, solubility, and stability. Understanding the relationship between solvent properties and the chemical structures of plant compounds is essential for developing beneficial and sustainable extraction processes.[7,12]

Green chemistry also contributes to the sustainable development of herbal formulations, including gels, creams, tablets, and capsules. The selection of suitable excipients, renewable raw materials, and biodegradable polymers may aid to minimize the pharmaceutical manufacturing. However, the selected ingredients must be evaluated for compatibility, stability, safety, and efficacy to ensure the quality of resulting product.[12,14,15]

FUNDAMENTALS AND CHALLENGES OF HERBAL DRUG EXTRACTION

1. Significance of Extraction in Herbal Medicine

Extraction plays a crucible role in herbal medicine because it helps isolate important therapeutic compounds present in medicinal plants. Extraction facilitates the separation of compounds from plant tissues. The extraction performance relies on the plant species, the plant part used, and the processing conditions employed. Appropriate extraction is therefore necessary to obtain extracts with suitable quality, consistency, and concentrations of the desired constituents.[3,10,11]

2. Challenges in Conventional Herbal Drug Extraction

Conventional separation processes such as maceration, infusion, decoction, and Soxhlet extraction, are used to obtain compounds from medicinal plants. Some of techniques requires high temperature which leads to degradation of heat-sensitive constituents. These drawbacks have driven researcher into alternative methods that improve extraction performance while addressing environmental and safety concerns.[9,10]

3. Need for Green Approaches in Herbal Drug Extraction

Choosing safer solvents and optimizing processing conditions can help lower the environmental impact of producing herbal extracts. Furthermore, modern extraction process allows for correct control over processing parameters, helping for improving the recovery of desired bioactive compounds. The suitability of any approach depends on the plant material, the target constituents, the required extract quality, and the practical conditions of production. Thus, green approaches provide an opportunity to develop herbal extraction processes that consider both product quality and environmental performance.[3,8,10]

4. Factors Influencing the Extraction of Phytoconstituents

The extraction of phytoconstituents is influenced by several physical and chemical factors. Solvent polarity affects the ability of a solvent to dissolve different plant compounds, while particle size influences the part which is interacted with solvent. Temperature can increase the rate of mass transfer, but excessive heating may damage sensitive constituents.[3,8,10]

PRINCIPLES GOVERNING GREEN EXTRACTION AND SUSTAINABLE FORMULATIONS

Green extraction and sustainable formulation are important approaches in the development of herbal

medicines. These approaches aim to obtain high value bioactive molecules while reducing environmental pollution. They also focus on developing pharmaceutical formulations that are safe, effective, and environmentally friendly.[2,3]

1. Selection of Environmentally Friendly Solvents
Conventional organic solvents may be toxic, flammable, and harmful to the environment. Therefore, greener alternatives such as water, ethanol, and certain bio-based solvents are preferred wherever suitable. These solvents can help reduce environmental risks while extracting useful phytoconstituents from medicinal plants.[7,12]

2. Reduction of Energy Consumption
Technology like an ultrasound-assisted extraction can enhances extraction effectiveness and shorten processing duration when optimal conditions are employed. Decreased energy utilization can help make herbal extraction more sustainable, depending on the method and operating conditions.[13,22]

3. Reduction of waste generation
An important principle of eco conscious extraction is to minimize waste during extraction and formulation. Appropriate selection of plant materials, suitable extraction conditions, and efficient use of solvents can help reduce unnecessary waste. Plant residues may also be evaluated for further use when safe and technically suitable.[2,3,4]

4. Efficient Use of Natural Resources
Sustainable formulation encourages the responsible use of medicinal plants, water, solvents, and other raw materials. Plants should be collected or cultivated using practices that protect biodiversity and prevent the decline in natural resources. Renewable and responsibly sourced materials can support the long-term availability of herbal ingredients.[2,4]

5. Protection of Active Phytoconstituents
Extraction conditions such as temperature, pressure, pH, and extraction time can influence the stability and recovery of phytoconstituents. Suitable conditions should be selected to limit the degradation of sensitive compounds, such as polyphenols and flavonoids. Maintaining the quality and biological activity of these compounds is important for preparing herbal formulations with consistent properties.[3,10,12]

6. Development of Sustainable Pharmaceutical Formulations
Sustainable formulation involves selecting suitable excipients, packaging materials, and manufacturing process that does not give impact on the environment and does not compromise the product quality. Biodegradable or renewable materials may be considered when they meet the required safety, stability, and performance standards. The final formulation should maintain its quality, effectiveness, and patient acceptability throughout its intended shelf life.[2,4,15]

7. Safety and Environmental Compatibility
The selected solvents, excipients, and processing methods must be evaluated for their safety and environmental impact therefore, quality control and appropriate toxicity assessment remain important in herbal medicine development.[2,12]



GREEN SOLVENTS AND THEIR ROLE IN SUSTAINABLE HERBAL DRUG DEVELOPMENT
GREEN SOLVENTS USED IN HERBAL DRUG EXTRACTION
Green solvents are considered alternatives because, when appropriately selected, they can reduce certain environmental and safety risks. Their suitability influenced by variables such as toxicity, biodegradability, renewability, and compatibility with the target phytoconstituents. In herbal drug extraction, solvents help dissolve and recover valuable plant constituents. The choice of solvent depends on the chemical structure, polarity, solubility, and stability of compounds.[7,12]

Water

Water is commonly used solvents in herbal extraction as it is readily available, economical, and generally presents fewer environmental and safety concerns than many conventional organic solvents. It is particularly useful for extracting polar compounds, including certain glycosides, tannins, and phenolic compounds. Water is used traditional aqueous extraction methods and in modern techniques such as ultrasound-assisted extraction. However, it may be less effective for extracting certain non-polar compounds. Furthermore, water-based extracts may require careful processing and storage because their moisture content can encourage microbial growth.[7]

Ethanol

Ethanol is widely used in herbal drug extraction because it can dissolve a range of plant constituents and is compatible with many pharmaceutical applications. Ethanol produced through the fermentation of renewable biomass may offer advantages in terms of renewable sourcing. Ethanol can be mixed with water in different proportions to modify solvent polarity of selected phytoconstituents. Aqueous ethanol solutions are used for extracting certain flavonoids, phenolic compounds, and other plant constituents.[12]

Bio-Based Solvents

Bio-based solvents are obtained wholly or partly from renewable biological resources, such as plant biomass and agricultural materials. Examples include ethyl lactate and certain bio-derived alcohols. These solvents are being investigated as alternatives to some petroleum-derived organic solvents. Depending on their chemical properties, bio-based solvents may be suitable for extracting selected phytoconstituents from medicinal plants.[12]

Natural Deep Eutectic Solvents (NADES)

These are mixtures of chemical components or the substances which are naturally obtained like organic acids, sugars, and other hydrogen-bond donors and acceptors. When combined in suitable proportions, these substances can form the solution with the lower melting point of their individual components. However, even when they contain naturally occurring substances, NADES should not automatically be considered harmless. Their toxicity, biodegradability, suitability for pharmaceutical use, and removal from or retention in the final extract require appropriate evaluation.[5,17,18]

Supercritical fluid extraction

This is carbon dioxide, which exhibits properties of both gas and liquid. It can act as an extraction medium for selected compounds, particularly relatively non-polar substances such as certain essential-oil constituents and terpenes. Supercritical carbon dioxide offers advantages such as relatively low solvent residue after depressurization and the possibility of adjusting extraction selectivity. However, the equipment requires a specialized high-pressure system, which can increase initial costs.[3,4,19]

TYPES OF HERBAL DRUG EXTRACTION METHODS: CONVENTIONAL AND MODERN APPROACHES

The extraction process is essential in herbal medicine research, as it helps recover therapeutic constituents from medicinal plants. These substances include various phytochemicals, such as alkaloids, flavonoids, phenolics, terpenoids, glycosides, tannins, and saponins. Extraction efficiency depends on several factors, including the type of plant material, the choice of solvent, temperature, extraction time, and the chemical characteristics of the target phytoconstituents.[9,10]

Herbal drug extraction methods can generally be divided into conventional and modern techniques. Conventional methods are well-established processes that usually involve soaking, heating, boiling, or the circulation of a solvent. Modern methods, on the other hand, use technologies designed to improve extraction efficiency and, under suitable conditions, reduce processing time, solvent consumption, or energy requirements. These techniques use different physical or biochemical mechanisms to release and recovery of phytoconstituents.[8,10]

Conventional Extraction Methods

Traditional extraction techniques have been employed for several decades to obtain medicinally important compounds from plants. These techniques generally involve transferring soluble components from plant tissues into solvent. The selection of an appropriate technique depends on the plant material, the solubility of the desired compounds, and their stability under the extraction conditions.[9,10]

1. Maceration

Maceration is a simple extraction method that involves soaking powdered plant material in an appropriate solvent for a specified period, generally at room temperature. During this process, the solvent penetrates the plant tissues and dissolves the soluble phytoconstituents. Occasional stirring helps improve the interaction between the solvent and the plant material. The mixture is then filtered to separate the liquid extract from the solid plant residues.

2. Percolation

Percolation involves the slow passage of a solvent through a bed of prepared plant material. The powdered material is first moistened with water and allowed to stand before being kept in a percolator. As the solution flows through the plant material, soluble constituents dissolve and are collected as a liquid extract. Percolation allows the solvent to pass through the plant material and is commonly used to prepare liquid extracts and tinctures. However, careful control of solvent flow and the packing of plant material is necessary. Channel

formation may reduce extraction efficiency, and the process may consume considerable amounts of solvent.

3. Infusion

Infusion is a traditional extraction method in which plant material is soaked in a suitable liquid, usually hot water, for a specified period. Water-soluble constituents pass from the plant material into the liquid, after which the solution is filtered. This is commonly applied to relatively soft plant parts, such as leaves and flowers. Some compounds may degrade under excessive heat, and the resulting aqueous extract may have limited storage stability.

4. Decoction

In decoction the plant material is boiled in water for a specific duration to obtain water-soluble compounds. It is generally used for relatively tough plant parts, such as roots, bark, and other woody materials, because heating can help release certain constituents into the water. The mixture is then cooled, when appropriate, and filtered to obtain the extract.

Decoction is a simple and economical method that uses water as the solvent. It is suitable for extracting compounds that remain stable under the selected heating conditions. However, prolonged heating may degrade heat-sensitive substances, and the method may be unsuitable for compounds with low water solubility.

5. Soxhlet Extraction

Soxhlet extraction is a technique that uses a heated solvent to recover soluble compounds from solid plant material. The powdered plant material is placed in a porous thimble, while a suitable solvent is heated in a flask. The solvent evaporates, condenses, and passes over the plant material, dissolving the desired components. When the extraction chamber reaches a certain level, the solvent returns to the flask through a siphon. This cycle is repeated to facilitate extraction.

One advantage of Soxhlet extraction is the repeated contact of the plant material with fresh portions of condensed solvent, which can support efficient recovery of suitable compounds. However, the method may require prolonged heating, substantial energy, and considerable solvent consumption. It may also be unsuitable for phytoconstituents that degrade during prolonged exposure to heat.[9,10]

6. Steam Distillation

Steam distillation is a conventional technique primarily used to obtain volatile compounds, especially essential oils, from aromatic medicinal plants. Steam passes through the plant material and carries volatile components into a condenser, where the vapour is cooled and converted into liquid. The essential oil is then separated.

This method is useful for recovering suitable volatile constituents from aromatic plants. However, it is not appropriate for all phytoconstituents, particularly non-volatile compounds or substances that may degrade under the temperature conditions used during distillation.[9,20]

MODERN EXTRACTION METHODS

1. Ultrasound-Assisted Extraction (UAE)

Ultrasound-assisted extraction (UAE) works on the principle of acoustic cavitation. When ultrasonic waves pass through a solvent, they produce microscopic bubbles that grow and collapse, generating mechanical forces that can damage plant cell walls and improve solvent penetration into the plant material. UAE helps reduce extraction time and the amount of solvent used while improving the extraction of active compounds. It is especially useful for obtaining phenolic compounds and flavonoids from medicinal plants.[13,22]

2. Microwave-Assisted Extraction (MAE)

Microwave-assisted extraction (MAE) uses microwave energy to heat the solvent and plant material. Polar molecules absorb this energy and convert it into heat, which helps in the extraction process. These molecules absorb microwave energy and convert it into heat through dipole rotation and ionic conduction. The resulting rapid heating can increase internal pressure within plant cells, causing cell disruption and facilitating the release of phytoconstituents into the surrounding solvent. MAE can provide faster extraction and lower solvent consumption than some conventional extraction methods. However, temperature and extraction time must be controlled to prevent the degradation of heat-sensitive compounds.[23]

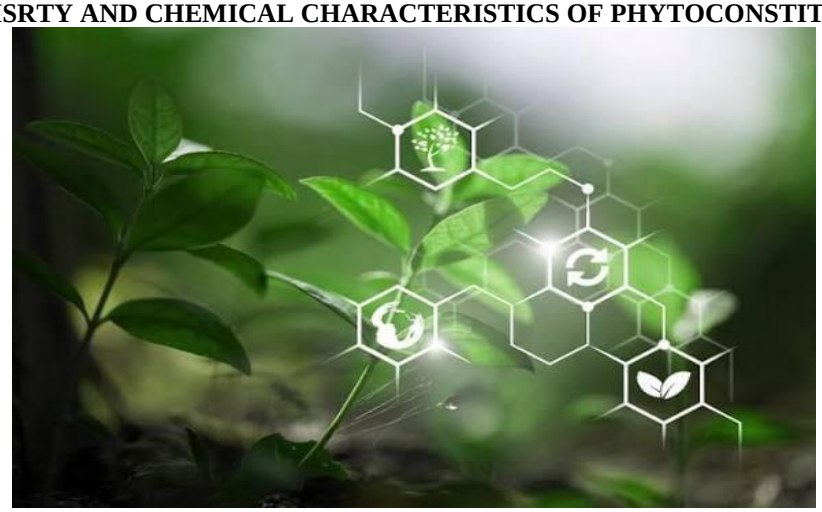
3. Enzyme assisted extraction

Enzyme-assisted extraction (EAE) uses specific enzymes to break down structural components of plant cell walls. Enzymes such as cellulase, pectinase, and hemicellulase act on cellulose, pectin, and hemicellulose, respectively. The breakdown of these structural materials increases cell-wall permeability and facilitates the release of intracellular bioactive compounds. EAE generally operates under suitable, often relatively mild, temperature and pH conditions, which can help preserve sensitive phytoconstituents.[24]

4. Pressurized Liquid Extraction (PLE)

Pressurized liquid extraction (PLE) uses a solvent maintained at elevated temperature and sufficient pressure to keep it in the liquid state during extraction. The increased temperature can improve solubility, and reduce solvent viscosity. Pressure helps maintain the liquid state of the solvent under the selected operating conditions. These combined effects can improve mass transfer and shorten extraction time. PLE may consume less solvent than the conventional methods, although its environmental performance depends on the solvent used, energy requirements, and operating conditions.[8,10]

ORGANIC CHEMISRTY AND CHEMICAL CHARACTERISTICS OF PHYTOCONSTITUENTS



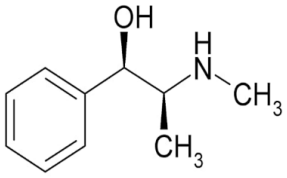
ORGANIC CHEMISTRY AND CHEMICAL CHARACTERIZATION OF PHYTOCONSTITUENTS

Phytoconstituents are those compounds which are found in plants as a result of their metabolic activities. They are obtained by different metabolic processes and contribute to various properties of medicinal plants, including colour, taste, aroma, and biological activity. From an organic chemistry perspective, phytoconstituents do not belong to a single group of compounds. Instead, they possess diverse carbon skeletons and distinct functional groups. Phytoconstituents are structurally diverse molecules containing different carbon frameworks and functional groups, such as hydroxyl (–OH), carbonyl (C=O), carboxyl (–COOH), amino ($–NH_2$), methoxy ($–OCH_3$), and glycosidic groups.[10,25]

3.1 Alkaloids

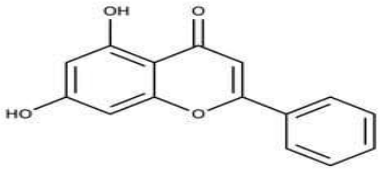
Nitrogen-containing natural compounds are natural and present in plants that contain nitrogen. Many of them show basic properties and are available in plants in form of salt. In numerous alkaloids, the nitrogen atom forms part of a heterocyclic ring, although some alkaloids contain nitrogen in non-heterocyclic structures. Their diverse carbon skeletons contribute to most of the biological activities. Examples of naturally occurring alkaloids include morphine, quinine, atropine, caffeine, and berberine.

The nitrogen atom and the presence of other functional groups influence the basicity, polarity, and solubility of individual alkaloids. Consequently, different alkaloids may behave differently during extraction, even when obtained from the same plant material. Understanding these structural characteristics helps in selecting suitable extraction conditions and solvents.



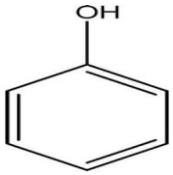
3.2 Flavonoids

Flavonoids are an important compound which are found in medicinal plants. Their basic structure consists of a $C_6–C_3–C_6$ carbon skeleton, containing three carbon bridge connected to a two aromatic ring. Differences in ring arrangement, oxidation state, and substitution patterns gives several subclasses, including flavones, flavanones, flavan-3-ols, and anthocyanidins. Flavonoids involve quercetin, kaempferol, catechin, rutin, and apigenin. Hydroxyl groups present on the aromatic rings facilitate hydrogen bonding. The existence of sugar groups can modify their polarity and solubility. Therefore, flavonoid glycosides and their corresponding aglycones may exhibit different solubility and extraction profiles.



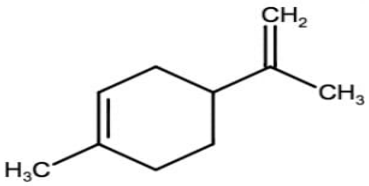
3.3 Phenolic Compounds

These compounds contain an aromatic ring which is attached to one or more hydroxyl groups. The hydroxyl and carboxyl groups present in many phenolic compounds influence their polarity and interactions with solvents. The number and position can affect their solubility and antioxidant properties. Phenolic compounds may occur in plants in either free or bound forms, which can influence their availability during extraction.



3.4 Terpenoids

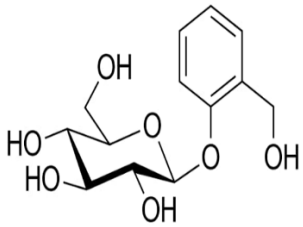
Terpenoids form a large class of plant metabolites. Their carbon skeletons are mainly derived from five-carbon isoprene units, and classified into diterpenes, tetraterpenes, sesquiterpenes, triterpenes, and monoterpenes. Examples include limonene, menthol, phytol, beta-carotene, and various triterpenoids. The oxygen-containing functional groups, such as hydroxyl, carbonyl, and ester groups, can influence the polarity of terpenoids. Some terpenoids are relatively non-polar, whereas oxygenated derivatives may show greater polarity and different solvent behavior.



3.5 Glycosides

Glycosides are compounds consisting of a sugar component, known as the glycone, chemically linked to a non-sugar component called the aglycone or genin. This linkage is generally called as glycosidic bond. Glycosides are commonly found in plants and include cardiac glycosides, saponin glycosides, flavonoid glycosides and anthraquinone glycosides.

The sugar moiety generally increases the hydrophilic character of a molecule compared with its corresponding aglycone. Glycosylation can alter the solubility, polarity, and stability, of plant compounds. The difference in the structure is also vital while selecting suitable extraction conditions for specific phytoconstituents.

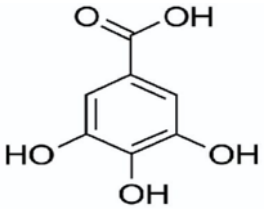


3.6 Saponins

These compounds are glycosidic consisting of a hydrophobic aglycone, usually with triterpenoid and steroidal structure, attached with sugar chains as they are both hydrophobic and hydrophilic. They exhibit amphiphilic properties and can interact with aqueous systems. These properties help to form a foam when it is shaken with solvent.[10,25]

3.7 Tannins

Tannins are high-molecular-weight polyphenolic compounds, they are broadly classified into hydrolysable tannins and condensed tannins. The phenolic groups enable tannins to interact strongly with macromolecule and protein.[10,16]



3.7 Chemical Characteristics Influencing Phytoconstituent Behaviour

The characteristics and structure of phytoconstituent directly influence its behaviour during extraction. Important properties include polarity, molecular size, hydrogen-bonding capacity, functional groups, ionization, and solubility. Among these factors, polarity is particularly important because it influences how strongly a compound interacts with a particular solvent.

Phytoconstituents containing several polar groups, such as hydroxyl or carboxyl groups, generally show greater affinity for polar solvents. In contrast, compounds whose structures mainly consist of hydrocarbon groups generally shows more affinity to less polar solvents. However, the extraction behaviour of a phytoconstituent cannot always be predicted from a single functional group.

Understanding these chemical characteristics is important for selecting an appropriate solvent and extraction technique. Knowledge of the organic structures of phytoconstituents is useful for designing selective and suitable green extraction process.[3,10,12,25]

DISCUSSION

Green chemistry achieves sustainable extraction and formulation of herbal drugs by cutting down the hazardous solvents, waste, and energy consumption. Since medicinal plants has bioactive components like terpenoids, glycosides flavonoids, and alkaloids, the process of extracting these compounds depends on their chemical properties and the methods employed.

Solvents that are green—such as water, ethanol, and certain bio-based solvents—have the potential to lower environmental risks. Nowadays, methods like ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), and enzyme-assisted extraction (EAE) can increase extraction efficiency whilst at the same time cutting down on processing time and the amount of solvent used. Yet the advantages of these techniques depend on the type of plant material, the extraction conditions, and the energy requirements.

Understanding the chemical structure and stability of phytoconstituents enables the choice of appropriate solvents and the optimization of the extraction conditions. Green chemistry promotes the development

of sustainable formulations by using the right excipients and biodegradable materials.

The problems such as plant variability, standardization, equipment costs, and industrial scale-up still exist. In general, integrating green chemistry with phytochemical characterization and process optimization is able to promote development of herbal products to be safer, more effective, and environmentally sustainable.

CONCLUSION

Green chemistry offers a sustainable method for the extraction and formulation of herbal drugs by encouraging the incorporation of safer solvents, increasing energy efficiency, and reducing waste. The implementation of modern extraction methods together with appropriate green solvents can enhance the recovery of the bioactive phytoconstituents while at the same time lowering the environmental impact. It is necessary to understand the chemical properties and stability of these compounds if suitable extraction conditions are to be chosen and high-quality herbal formulations are to be developed. Despite challenges associated with standardization, production costs, and industrial implementation, applying green chemistry principles to herbal drug development can support the production of safer, more effective, and environmentally sustainable herbal products.

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