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Review Article

Driving/Critical Factors Considered During Extraction to Obtain Bioactive Enriched Extracts

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ABSTRACT

Extraction is the process of separating desired compounds from a mixture using a solvent. The efficiency of extraction is influenced by several factors. This review delves into the intricate realm of extracting bioactive compounds from medicinal plants, examining the driving factors critical for obtaining enriched extracts with enhanced medicinal efficacy. The exploration begins with the strategic selection of medicinal plants, incorporating insights from ethnopharmacology and chemo taxonomy. Further considerations include understanding the influence of plant components, secondary metabolites and the impact of plant states (fresh or dried) on the extraction process. Processing techniques, such as various drying methods, are pivotal in shaping the chemical composition and bioactivity of the final extracts. Particle size optimisation, extraction duration and matrix characteristics of phytoconstituents within the inert solid matrix emerge as integral factors. Solvent diffusion is explored for its influence on mass transfer, extraction kinetics and solute accessibility. The choice of solvent, considering its polarity, boiling point and compatibility with extraction methods, plays a crucial role in shaping the bioactive profile of the extract. The review addresses the solvent-to-solid ratio's impact on extraction efficiency, yield and solvent consumption, emphasizing the delicate balance needed for optimisation. Physical treatments during extraction, including methods like Soxhlet, maceration, ultrasound-assisted extraction, supercritical fluid extraction and microwave-assisted extraction, are examined for their distinct advantages and critical parameter. In essence, a comprehensive understanding and strategic manipulation of these driving factors determine the success of obtaining bioactive enriched extracts. Researchers, practitioners and industries engaged in medicinal plant extraction can leverage this knowledge to unlock the full therapeutic potential of nature's Pharmacopoeia. This review definitely serves as a valuable guide, ensuring not only the efficiency of the extraction process but also the quality and richness of the bioactive extracts obtained.

Keywords: Medicinal plants, Extraction duration, Solid to solvent ratio, Physical treatment, Extraction parameters, Solvent influence, Phytoenrichment, Phytoconstituents.

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INTRODUCTION

Plants have been used in traditional medicine for as far back as human records exist. Plants and humans are interdependent in terms of their growth, development as well as for their survival and existence. Huge number of different disease and illness prevention measures come from our knowledge of medicinal materials, with many people all over the world learning how to maintain their health based on this form of information. Medicinal herb uses are deeply integrated into cultural forms and tradition; people continue to learn about them from generation after generation.[1] These natural remedies or cures can enhance health and wellness of human beings. In terms of producing new drugs or healthcare systems, medicinal plants have an outstanding significance. Many contemporary semi-synthetic and synthetic drugs are derived from lead molecules isolated from plants. A wide range of health issues starting from simple to complex syndromes has been relieved by employing herbal drugs or their derived products. In fact, quite a large amount of medications available in today's market have some direct connection to old-fashioned medicine. Traditional medicine's peculiar expertise and knowledge about the medicinal properties of plants, have facilitated the exploration and development of new drugs. Research conducted around the globe demonstrates that a significant part of drugs now come under the heading natural medicine.[2]

Use of medicinal plants can increase the quality of our life and give alternative kinds of therapy which are especially useful in areas where modern medical care is not available.[3] Additionally, the usage of medicinal plants can support the sustainability of healthcare systems by offering accessible and cheap healthcare

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alternatives.[1] Due to their pharmacological properties and the need for herbal treatments, they are highly valuable economically.[4] But their risk of becoming extinct has also grown due to the rise in habitat damage and human usage of medicinal herbs. In order to protect biodiversity and guarantee their availability for future generations, it is crucial to conserve and sustainably use medicinal plants. The world's healthcare systems rely heavily on medicinal plants as therapeutical resources.[5] They have long been a part of conventional medicine and have given researchers important information on the development of new drugs. Utilizing medicinal plants can lead to better health outcomes, alternate forms of therapy and the sustainability of healthcare systems. To guarantee that medicinal herbs are available for future generations, however, conservation and sustainable usage are essential.[6]

Many countries of Asian continent are blessed with a huge number of therapeutic and aromatic plant species. Fragrant and medicinal plants are found abundant throughout the Himalayas of India, Nepal, Bhutan and Tibet. The region's high heights and variable weather may favours the cultivation of a variety of medicinal plant species. Till today many Himalayan countries use Ayurveda and Tibetan medicine that are mainly composed of medicinal herbs.[7] The Western Ghats are a biodiversity hotspot in India as this region is known for its aromatic and medicinal flora. For generations, indigenous culture has practiced traditional medicine and the Western Ghats are home to many healing plants. Yunnan Province in China has a rich source of many medicinal plant species that grow in the province's mountains, woodlands and rivers. The ethnic diversity of Yunnan Province is well-known and each ethnic group has its own medicinal plant wisdom. Aromatic and therapeutic plants are also found abundant in Thailand, Vietnam and Indonesia. Tropical climate and diverse habitats allow many medicinal plant species to thrive and hence are used in Thai and Chinese traditional medicine.[8]

Huge researches are conducted around the globe with respect to the pharmacological screening, isolation of bioactive compounds, preparation of herbal formulations and standardization of herbal extracts and their formulations. These researches help in providing scientific evidences for the traditional claims. It is well known fact that the therapeutic efficacy of the herbal formulation mainly depends on the method employed for the formulation, administration and dosage of various herbal medicines can undergo changes, offering diverse methods for absorption. Raw materials used in the herbal formulation may includes unaltered plant parts like leaves, roots, stems, or flowers for poultices, infusions, or teas. Decoctions entail boiling plant components in water to create a liquid consumed for its active ingredients. Infusions, akin to teas, extract constituents by steeping plant materials. Tinctures, concentrated liquid extracts, are made by soaking plant parts in alcohol, known for extended shelf life. Capsules and tablets provide regulated doses, often containing concentrated herbal medicines. Ointments and creams are topical preparations for localized issues.[8]

Traditional medicine heavily relies on plant extracts that are concentrated herbal remedies with increased biologically active ingredient concentrations. These extracts are prepared through various traditional methods like distillation, percolation, or maceration as well as advanced methods like sonication, microwave assisted extraction, supercritical fluid extractions, etc. Compared to crude herbal remedies, extracts offer regulated dosage and simplicity, frequently used in ancient medical systems like Ayurveda and Traditional Chinese Medicine (TCM). Extracts play a crucial role in maintaining therapeutic benefits, ensuring consistent efficacy in conventional medical practices.[9,10] This review aims to comprehensively explore the term 'Extract,' elucidating its significance as a concentrated form of active substances derived from plants through various extraction methods. The objective is to analyze the critical factors influencing successful extraction, including plant material selection, processing, particle size, extraction duration, matrix characteristics and the role of extraction solvents. The review further investigates the impact of extraction parameters, such as temperature, constituents and methods, solid-to-solvent ratio and physical treatments. Emphasizing the importance of these factors, the study delves into the methodologies employed by researchers, focusing on experimental optimization techniques and statistical methodologies like Response Surface Methodology (RSM). By systematically manipulating extraction parameters, the aim is to discern optimal conditions for maximizing the extraction of specific bioactive compounds. Ultimately, this review emphasize the pivotal role of these critical factors in driving successful extraction strategies, leading to the production of bioactive-enriched extracts with diverse potential applications.

DEFINITION OF EXTRACT AND IMPORTANCE OF EXTRACT OF HERBS

The term "Extract" pertains to concentrated forms of active substances that have been extracted from plants. During the process of extraction, mass transfer of chemical constituents will take place from the insoluble plant matrices into the soluble solvent in which the plant material is treated. The essential components are extracted and concentrated from plant materials through the implementation of various techniques, including maceration, percolation and distillation. Traditional medicine relies heavily on extracts due to their potency, utility and controlled dosage.[11-13]

The process of extraction facilitates the standardization of herbal medicines. There may be variations in the chemical composition and potency of different plant species or even specific parts of the same plant. Through the process of extraction, specific components of herbal medicines can be targeted and standardized, thereby ensuring consistent quantities of the active constituents.

This standardization ensures the quality control, safety and repeatability of botanical medications.In an effort to enhance the efficacy, durability and safety of herbal extraction processes, there has been a growing inclination towards the development of novel extraction methodologies and technologies in recent times. Green extraction methods have become increasingly prevalent in the field of herbal medicine due to their ability to decrease energy and organic solvent consumption. These techniques prioritize the preservation of bioactive substances during the extraction process, in addition to considering environmental friendliness and sustainability.[13] One may employ various perspectives in order to grasp the significance of extraction in herbal therapy. To begin with, the process of extraction enables the concentration of active constituents present in plants, thereby augmenting their efficacy and appropriateness for the treatment of specific medical conditions. Extracts contain medicinal compounds in greater concentrations than crude formulations of herbal medications, as the active components are transformed from the insoluble plant matrix into the extraction solvent and concentrated during extraction. The enhanced bioavailability and effectiveness of the active constituents are consequences of this concentration, leading to more consistent and reliable therapeutic outcomes. Extraction methods may also have an effect on the selectivity of active compounds. Herbal extracts can be customized to achieve specific therapeutic effects by employing diverse solvents and extraction methods that are capable of extracting various chemical groups. For example, through the use of heat-refluxed and heat-pressurized extraction methods, unique profiles of bioactive chemicals can be obtained, enabling practitioners and researchers to examine the varied chemical composition of plants and their possible health advantages.[14] For a number of reasons, extraction is regarded as a vital step in producing bioactive enhanced extracts in herbal medicine.

Bioactive component concentration

The concentration of bioactive substances present in plants is made possible through extraction. Numerous medicinal plants contain a diverse array of chemical constituents, including terpenoids, flavonoids, alkaloids, resins, tannins, essential oils and polyphenols, which are reported to exhibit therapeutic properties.[15] By extracting these components, their concentration can be increased, thereby augmenting the potency and utility of the resulting extract in the treatment of specific medical conditions.

Standardisation of herbal medicines

The extraction procedure is critical to the standardization of herbal remedies. There may be variations in the chemical composition and potency of different plant species or even specific parts of the same plant due to the accumulation of significant amount of the active constituents in that part of the plant. By enabling the targeting and standardization of specific components, extraction ensures that herbal remedies contain constant quantities of active constituents. In order to ensure the safety, quality and reproducibility of botanical medicines, the standardization process is very crucial.

Customisation of extracts

Different extraction techniques and solvents can be used to extract various kinds of biologically active chemicals from plants. As a result, plant extracts can be tailored to provide the desired medicinal effects. For instance, various solvents like ethanol, methanol or hydroalcohol for polyphenols, may be more efficient in extracting particular bioactive components. The content and bioactivity of the extract may be customised to fit individual demands by choosing the best extraction technique and solvent.[16]

Synergic effects

Effects that exist due to the ability of the bioactive compounds work together: Herbal extracts frequently include a diverse blend of bioactive substances. Compared to isolated molecules, these substances can combine synergistically to increase their therapeutic benefits. Multiple bioactive components combined in an extract can increase effectiveness, boost bioavailability and lessen negative effects.[17] This emphasizes how crucial it is to preserve and extract the inherent complexity of plant materials in order to fully use their bioactive components.

Facilitating research and development

Isolation, purification and identification of bioactive compounds from medicinal plants require extraction. To separate pure substances from extracts, a number of procedures are employed, including column chromatography, Thin-Layer Chromatography (TLC) and preparative High-Performance Liquid Chromatography (HPLC). The pharmacological effects, mechanisms of action and possible therapeutic uses of these isolated compounds may then be further investigated.[18] Researchers may study the enormous chemical variety of plants through extraction and find novel useful chemicals.

The World Health Organization (WHO) advises using "reverse pharmacology," where current herbal medicines are validated scientifically based on their traditional claims. With this strategy, the effectiveness and security of historically used herbal medications are supported scientifically. The WHO seeks to demonstrate a cause-and-effect link and validate the conventional claims made about herbal medicines by carrying out scientific research and clinical studies.[19] The WHO also stresses the significance of pharmacovigilance, or the monitoring of drug safety, in relation to herbal medicines. The WHO acknowledges the necessity for active engagement of health professionals in monitoring and reporting adverse effects or interactions associated to herbal medications given the growing use of herbal medicines globally. This aids in risk assessment and guarantees the security of using herbal medicinal products.[20] The

WHO also supports the incorporation of conventional medicine, including herbal medicine, into national healthcare systems. In order to encourage the safe and efficient use of herbal medicines, laws and regulations must be developed. Guidelines and research frameworks are provided by the WHO to aid in the creation and application of conventional medical practices. In order to guarantee the safety, effectiveness and quality of herbal products, the WHO highlights the necessity for scientific evidence in herbal medicine research.[19] The WHO has created recommendations and methods to encourage evidence-based practices because it acknowledges the value of conventional medicine, including herbal medicine, in healthcare systems. The necessity to guarantee the quality, safety and efficacy of herbal products motivates the WHO to place a strong focus on scientific evidence in its research on herbal medicine. The WHO seeks to increase the legitimacy and acceptability of herbal therapy within the medical profession and among the general public by supporting evidence-based methods.[21,22]

FACTORS INFLUENCING THE EXTRACTION YIELD AND QUALITY

Selection of Medicinal Plant

In herbal medicine research, information obtained from chemotaxonomy and ethnopharmacology are used for the preparation of extract. Ethnopharmacology is the study of customs and knowledge relating to the application of herbal remedies by various societies and civilizations. Identification and comprehension of the medicinal characteristics of plants that have been traditionally utilised to treat particular medical ailments are the goals of ethnopharmacological study.[23] As it offers insights into the possible therapeutic characteristics of particular plant species, this information is useful in directing the selection of plants for extraction. On the other hand, chemotaxonomy is the study of the chemical makeup and categorisation of plants according to their chemical components and taxonomical status. In order to determine whether particular chemicals or groups of compounds are responsible for a plant's medicinal characteristics, it is necessary to analyse the chemical profiles of the plant.[24-26] Chemotaxonomy aids in comprehending the variety of chemicals present in plants and can direct the selection of plants with certain bioactive components for extraction. Researchers can find plants that have a history of traditional use for particular health issues and contain chemical components that may contribute to their medicinal benefits by combining ethnopharmacology with chemotaxonomy. Researchers can choose which plants to prioritise for extraction and use by taking into account both the traditional knowledge and the chemical makeup of plants.[27]

The kind and quantity of secondary metabolites like alkaloids, glycosides, tannins, resins and, essential oils in the extract can be greatly influenced by various factors that are used for extraction. Secondary metabolites are chemical substances that plants make but they do not directly contribute to their growth and development but are crucial for disease defense, pollinator attraction and other ecological tasks.[28] The metabolic profiles and secondary metabolite concentrations of various plant sections might differ from parts to part of the plants. For instance, various kinds and quantities of secondary metabolites may be present in leaves, stems, roots, flowers, fruits and seeds. The plant's development stage, the environment and the particular function of the metabolite may all have an impact on how secondary metabolites are distributed inside a plant.[29]

Processing of medicinal plants

Plant state

The quality of the final extract and the extraction procedure can both be strongly impacted by the plant's state (fresh or dry). The following are some crucial considerations about how plant health affects extraction and extract quality:

Chemical composition

Due to metabolic changes that take place during drying, fresh and dried plants might have distinct chemical compositions. Fresh plants may have larger quantities of volatile chemicals, but drying may cause some molecules to degrade or disappear.[30] However, presence of high amount of moisture in the fresh plant material may interfere in the yield and isolation process of secondary metabolites. In most of incidences, traditional herbal healer's employs fresh plant materials to prepare the herbal remedies that cannot be mimicked by modern method of preparation of extracts. The types and amounts of secondary metabolites found in the extract might therefore vary depending on whether fresh or dried plant material is used.

Extraction efficiency

This term refers to the capability of the extraction process extracting the necessary components from the plant material. The state of the plant might have an impact on extraction efficiency. Fresh plants frequently contain more water, which can make it easier to extract chemicals that are water soluble. On the other hand, due to the loss of water during the drying process, dried plants may have a greater concentration of desired chemicals. The target chemicals' solubility and the chosen extraction technique should be taken into account while choosing the plant conditions.[31]

Compound stability

Depending on the state of the plant, bioactive chemicals might be more or less stable during the extraction process. During the drying process, some substances may be more vulnerable to deterioration or oxidation when exposed to air or heat.[33] Therefore, the stability of the target components and the intended shelf life of the extract should be taken into account when choosing fresh or dried plant material.

Antioxidant activity

Plant health can have an impact on antioxidant activity, which is frequently linked to the amount of phenolic chemicals. Fresh plant material may have a stronger antioxidant activity than frozen or dried material, according to studies.[32] The variation in antioxidant activity can be ascribed to phenolic molecules losing their potency or degrading after freezing or drying.

Allelopathic potential

The state of the plant can have an impact on a plant's allelopathic potential, or its capacity to prevent the growth of other plants. Fresh and dried plant extracts have different allelopathic effects, according to studies.[34] The inhibitory effects on seed germination and seedling growth of the target plants might vary depending on the plant condition chosen.

Processing and drying techniques

The selection of plant material processing and drying techniques can have a big influence on the extraction procedure and the caliber of the extracted product. The following are some crucial points about how various processing and drying techniques affect extraction:

Dry ashing and wet ashing

In order to prepare plant materials for elemental analysis, dry ashing and moist ashing are frequently employed. Through the application of elevated temperatures to plant matter, these methodologies eradicate organic substances. For material degradation, wet ashing utilizes acid solutions, whereas dry ashing employs direct heating.[35] The selection of the ashing technique can influence the composition and accessibility of components in the plant material, which in turn can impact the extraction procedure and analysis of the target material.

Air drying

Frequently, plant matter is desiccated by the air method, which entails allowing the object to dry naturally at room temperature. Drying can lead to modifications in the composition of the plant material, such as the degradation or loss of specific components.[36] The concentration and presence of the target chemicals may be affected by the choice to air dry the plant material, which in turn could potentially affect the extraction procedure and the grade of the extract. Shade drying helps in retaining most of the volatile bioactive compounds as well as anthocyanins that may degrade at higher temperature in addition to retaining the color of the plant materials.

Freeze drying

Freeze drying, also known as lyophilisation, involves the sublimation of frozen plant material under vacuum conditions in order to extract the water. By preventing the decomposition and loss of volatile substances that can occur during conventional drying methods, freeze drying aids in the preservation of the plant material's structure and thermosensitive bioactive components.[37] By opting to freeze-dry the botanical material, its quality and integrity can be maintained, thereby enhancing the extraction process and the composition of the extract's bioactive compounds.

Drying in an oven

Drying in an oven includes warming or heating the plant material to certain temperature. The content and stability of bioactive chemicals in the plant material might be affected by the oven drying temperature selection. Low drying temperatures typically around 40-60°C, may assist maintain the integrity of the plant material and its bioactive components, whereas high drying temperatures may cause the loss of volatile compounds and the breakdown of heat-sensitive phytoconstituents. Many parameters to be considered while submitting the plant materials for oven drying method.

Alternatives techniques

Plant material may also be dried via convection drying, microwave vacuum drying, enzymatic processes and fermentation.[38] The selection of a method should be based on the unique properties of the plant material, nature of the chemical constituents present and the intended results, since each process has its own benefits and considerations.[39]

The final extract's quality and the extraction process can be greatly affected by the choice of processing and drying techniques for plant material. The content, stability and availability of bioactive chemicals in plant material can be impacted by various ways, which can therefore have an impact on the effectiveness of the extraction process and the bioactivity of the extract. The individual traits of the plant material and the desired attributes of the final extract should be taken into account while choosing the best method of drying procedure.

Particle Size (Coarse Powder or Fine Powder)

Several factors, including the extraction procedure, yield and the bioactive composition can be impacted by the plant material's particle size.

Cell disruption

In order to extract substances from within plant cells, disruption of the cell is vital. The fragmentation of plant cells by smaller particles may facilitate the release of internal compounds, thereby increasing the accessibility of target components for extraction.[40]

Solvent penetration

Reducing the particle size results in an increased surface area, which facilitates exposure of plant constituents to the solvent along with the enhanced solvent penetration and interaction with the plant material.[40] Potential benefits of enhanced solvent penetration include a simplified extraction process and a higher extraction yield of the desired compounds.

Mass transfer

Reducing the particle size of the plant material can enhance the efficiency of target chemical transfer to the solvent. Due to the shorter diffusion channels of smaller particulates of powdered drug, extraction will be more efficient along with the augmented extraction yield.[41]

Surface area-to-volume ratio

Smaller particle sizes produce bigger surface areas per unit volume, which can enhance interaction between the plant material and the solvent.[41] This enhanced and greater contact may improve target chemical extraction effectiveness and yield.

Extraction Kinetics

The extraction kinetics, which determines the pace at which target chemicals are extracted, can be influenced by the particle size of plant material. Since mass transfer is enhanced and surface area is increased, smaller particle sizes might result in quicker extraction rates.[42] Although additional particle reduction may not considerably increase extraction efficiency after a certain particle size (specify the size), as it may clog the solvent penetration through the fine powder particles. In such cases, extraction with occasional or continuous stirring is preferred to prevent the clogging.[43]

It is significant to note that depending on the individual plant material, target chemicals and extraction technique used, the effect of particle size on extraction yield might change. To achieve the required extraction efficiency and yield, particle size optimisation should be taken into account together with other extraction parameters. In summary, through regulating solvent penetration, mass transfer, cell disruption, surface area-to-volume ratio and extraction kinetics, the particle size of plant material can affect the extraction process and yield. There may be an ideal particle size beyond which further reduction does not appreciably increase extraction. However, smaller particle sizes often result in greater extraction efficiency and higher yields. It is crucial to remember that the individual traits of the plant material, target chemicals, extraction strategy and intended results of the extraction process should all be taken into account when deciding between coarse powder and fine powder. In order to obtain the necessary extraction efficiency and yield, particle size optimisation is essential.[44-50]

Duration of extraction for different types of constituents and methods of extraction

The quantity and makeup of bioactive chemicals in the extract can be significantly influenced by the length of the extraction process. The optimal extraction time provide ample of time for the powder crude drug to be in contact with the solvent leading to the optimum mass transfer of bioactive compounds. The following are some crucial details about the impact of extraction duration:

Bioactive compound yield

The amount of bioactive compounds in the extract might vary depending on how long the extraction process takes. Longer extraction durations can occasionally result in larger yields of the desired chemicals since more time allows for better compound extraction and diffusion from the plant material into the solvent. There could be an ideal extraction period, though, after which additional extraction has no effect on yield.

Composition of bioactive compounds

Additionally, the duration of the extraction procedure can influence the composition of the extract's bioactive components. Diverse substances may manifest distinct kinetics of extraction and their solubility and stability may undergo temporal variations. Given this, it is possible that the duration of the extraction procedure could influence the proportional amounts of different bioactive constituents present in the extract.[51]

Degradation of bioactive compounds

Prolonged extraction periods may, on occasion, lead to the degradation or depletion of bioactive compounds as a consequence of factors such as light, heat, physical treatment or enzymatic activity. Consequently, minimizing the annihilation of sensitive compounds with maximizing the extraction of desirable bioactive chemicals is of the utmost importance.

Efficiency of extraction

Length of extraction may have an effect on the overall efficacy of the extraction. Extended extraction durations have the potential to enhance extraction efficacy by facilitating more comprehensive extraction of the desired chemicals. Conversely, prolonged extraction durations might not yield a significant enhancement in extraction efficiency and could potentially lead to increased energy and time requirements.

Extraction kinetics

Depending on variables including chemical solubility, particle size and extraction technique the extraction kinetics of bioactive substances can change. In case, extraction technique involves heating then shorter duration of extraction is employed to avoid the degradation of extracted bioactive compounds. To establish a balance between extraction efficiency and extraction time, the extraction period should be tuned.[52-56]

The quantity and makeup of bioactive chemicals in the extract are greatly influenced by the duration of the extraction process. To enhance extraction efficiency, yield and final extract quality, the extraction period must be optimized. While choosing the ideal extraction time, variables such chemical solubility, stability, degradation kinetics and method of extraction process should be taken into account.

Matrix Characteristics of Phytoconstituents and the Inert Solid Matrix

The extraction procedure heavily depends on the solute's position inside the solid matrix. Generally, phytoconstituents are embedded in the insoluble solid matrix of the powdered crude drugs. Here are some crucial details about its importance:

Solute accessibility

The location of the solute within the solid matrix influences its accessibility to the extraction solvent. Placing the solute on the surface or in the outermost layers of the solid matrix facilitates the solvent's access to it, thereby enhancing and expediting the extraction procedure. Conversely, should the solute be firmly embedded within the solid matrix, the solvent may encounter greater difficulty in accessing it, thereby impeding the extraction procedure and diminishing its efficacy.[57]

Diffusion and mass transfer

The diffusion and mass transfer of the solute from the solid matrix to the solvent are affected by the position of the solute inside the solid matrix. Diffusion and mass transfer are promoted by the solute's proximity to the surface or in areas with greater porosity, which speeds up extraction. However, diffusion and mass transfer may be hampered if the solute is situated in areas with lesser porosity or deeper into the solid matrix, leading to slower extraction kinetics.[58]

Release and desorption

During the extraction process, the solute's release and desorption can be influenced by the solute's position inside the solid matrix. Loosely bonded or on the surface of the solid matrix placed solute molecules are more readily released and desorbed into the solvent. Contrarily, solute molecules that are well bonded or dispersed throughout the solid matrix can need more effort and time to release and desorb.[59]

Efficiency of extraction

The total extraction efficiency can be impacted by the solute's position inside the solid matrix. The extraction efficiency is often better if the solute is dispersed uniformly throughout the solid matrix or is located in easily accessible areas. However, the extraction efficiency could be reduced if the solute is dispersed unevenly or is situated in inaccessible areas.[57,58]

Optimisation of extraction conditions

Knowing where the solute is located inside the solid matrix can aid with temperature, time, solvent composition, particle size optimization and physical treatment.[59] The extraction conditions may be changed to optimise solute accessibility, diffusion and release by taking the solute's position into account. This increases extraction efficiency and yield.

State of the plant material

If the plant material is derived from soft tissues like leaves, flowers and pulp then the bioactives present might be extracted easily without the application of heat or physical treatments. However, if it is the stem, roots and barks then the powder must be softened by soaking prior to extraction like sonication, stirring or heat is employed to enhance the extraction efficiency as well as the yield.[60]

Key Aspects of Solvent Diffusion

The process by which the solvent molecules penetrate the solid matrix and make contact with the solute is known as solvent diffusion. The solute's solubility, position within the solid matrix and the solvent's characteristics are only a few examples of the variables that affect the pace and depth of solvent penetration.

Mass transfer

The mass transfer of phytoconstituents from the solid matrix to the solvent is greatly aided by solvent diffusion. The solute is dissolved as the solvent molecules infiltrate into the solid matrix and are carried back into the solvent phase. The position of the solute inside the solid matrix and the solvent's diffusion coefficient both has an impact on the rate of mass transfer.

Extraction kinetics

The pace at which phytoconstituents are removed from the solid matrix is known as extraction kinetics and it is influenced by solvent diffusion. The rate of extraction is determined by the solvent's diffusion into the solid matrix and the phytoconstituents' subsequent dissolution.[61] The solvent-to-solid ratio, temperature and particle size are only a few examples of the variables that might affect the extraction kinetics.[61]

Solute accessibility

The solute's accessibility inside the solid matrix is determined by solvent diffusion. Faster extraction results from enhanced solvent diffusion, which is made possible by the solute's proximity to the surface or in areas with higher porosity. However, solvent diffusion may be impeded if the solute is deeply entrenched in the solid matrix or in areas with lesser porosity, that result in slower extraction process.[62]

Understanding the role of solvent diffusion can assist in the optimisation of extraction conditions, which will improve the yield and extraction efficiency of phytoconstituents. To encourage solvent diffusion and enhance the extraction procedure, variables such solvent choice, solvent-to-solid ratio, temperature and extraction duration can be changed.[63]

Choice of solvent used in the extraction process

The choice of solvent used in the extraction process plays an important role in extraction. It can influence the extraction temperature, constituents and method of extraction and here are the few points regarding the influence of extraction solvents:

Extraction temperature

Various solvents have different boiling points and vapour pressure, it determine the extraction temperature. The selection of a suitable solvents allows for the extraction at temperatures that avoid the degradation or variation of phytoconstituents.[64] Solvents with lower boiling points can be used for the extraction at lower temperatures, it minimise the risk of thermal degradation.[65]

Constituent's extraction

Different solvents are having varying affinities for specific phytoconstituents, leading to differences in the extraction efficiency and selectivity of various compounds. The polarity, solubility and chemical properties of the solvent influence the ability to dissolve and extract specific constituents. Therefore, the choice of solvent impact the composition and concentration of the phytoconstituents to be extracted.[66]

The choice of an appropriate solvent is closely tied to the extraction method used. Different extraction methods, like Soxhlet extraction, maceration, percolation, or Pulsed Electric Field (PEF)-assisted extraction, may require specific solvents to achieve the best extraction efficiency. It's crucial to pick a solvent that works well with the chosen extraction method to ensure effective extraction of the target compounds.[64]

The polarity of the solvent plays a significant role in its ability to dissolve various types of compounds. Polar solvents like water or ethanol are great for extracting polar compounds like phenolics, while non-polar or organic solvents like hexane, petroleum ether, ethylacetate or chloroform are better for extracting non-polar compounds like lipids or essential oils. While selecting a solvent, it's important to consider its polarity based on the desired phytoconstituents for extraction.

Selection of right solvent involves consideration of several factors such as safety, cost, availability, environmental impact and how well it aligns with the intended use of the extract. It's vital to choose solvents that are safe, non-toxic and suitable for the specific phytoconstituents needed for the intended application.[66]

Influence of Extraction Solvents Based on Extraction Temperature, Constituents and Methods

The choice of the right solvent is crucial for extracting specific phytoconstituents. Different solvents have different affinities for various types of compounds.[67] Some solvents are better at extracting polar compounds like phenolics, while others are more effective for non-polar compounds like lipids or essential oils. So, selecting the appropriate solvent significantly impacts the extraction efficiency and the types of phytoconstituents obtained.[68] The polarity, boiling point and compatibility of solvents play important roles in the extraction process:

Polarity

A solvent's polarity affects its ability to dissolve polar or non-polar compounds. Polar solvents work well for polar compounds, while non-polar solvents are better for non-polar compounds. It's crucial to use a solvent that matches the polarity of the target phytoconstituents for efficient extraction.[67,69]

Boiling point

The boiling point of a solvent determines the extraction temperature needed. Lower boiling point solvents allow extraction at lower temperatures, which helps protect thermolabile phytoconstituents like flavonoids and essential oils. However, some compounds may require solvents with higher boiling points for extraction and they can be used for the extraction of thermostable phytoconstituents like alkaloids and tannins.[69]

Compatibility

Solvents must be compatible with the extraction method and the phytoconstituents being targeted. Some extraction methods may require specific solvents for optimal efficiency and must not form artefact after reacting with the phytoconstituents present in the extracts.[70] Additionally, the chosen solvent should meet safety, toxicity and regulatory requirements along with the environment friendly nature for the intended extract application.[69]

By considering these factors, researchers can optimise the extraction process and obtain extracts with the specific phytoconstituents we desire. It's essential to choose the right solvent based on the types of compounds we want to extract, their solubility and the extraction method we use Figure 1. Emphasizes the importance of optimizing extraction periods to avoid unintended chemical extraction or degradation. It highlights the need for preservation of bioactive compounds, ensuring they retain their therapeutic properties. Optimized extraction allows for selective extraction of desired substances, improving purity and quality. It also helps avoid extracting undesirable compounds, ensuring safety and efficacy.[70]

Solid to solvent Ratio Used for Extraction

The amount of solvent and the solid powder particles used in the extraction process, called the solid-to-solvent ratio, plays a crucial role. Here are some key points about its influence:

Extraction efficiency

The solid-to-solvent ratio determines how well the extraction happens by affecting the interaction between the solid material and the solvent. A higher ratio can make the extraction more

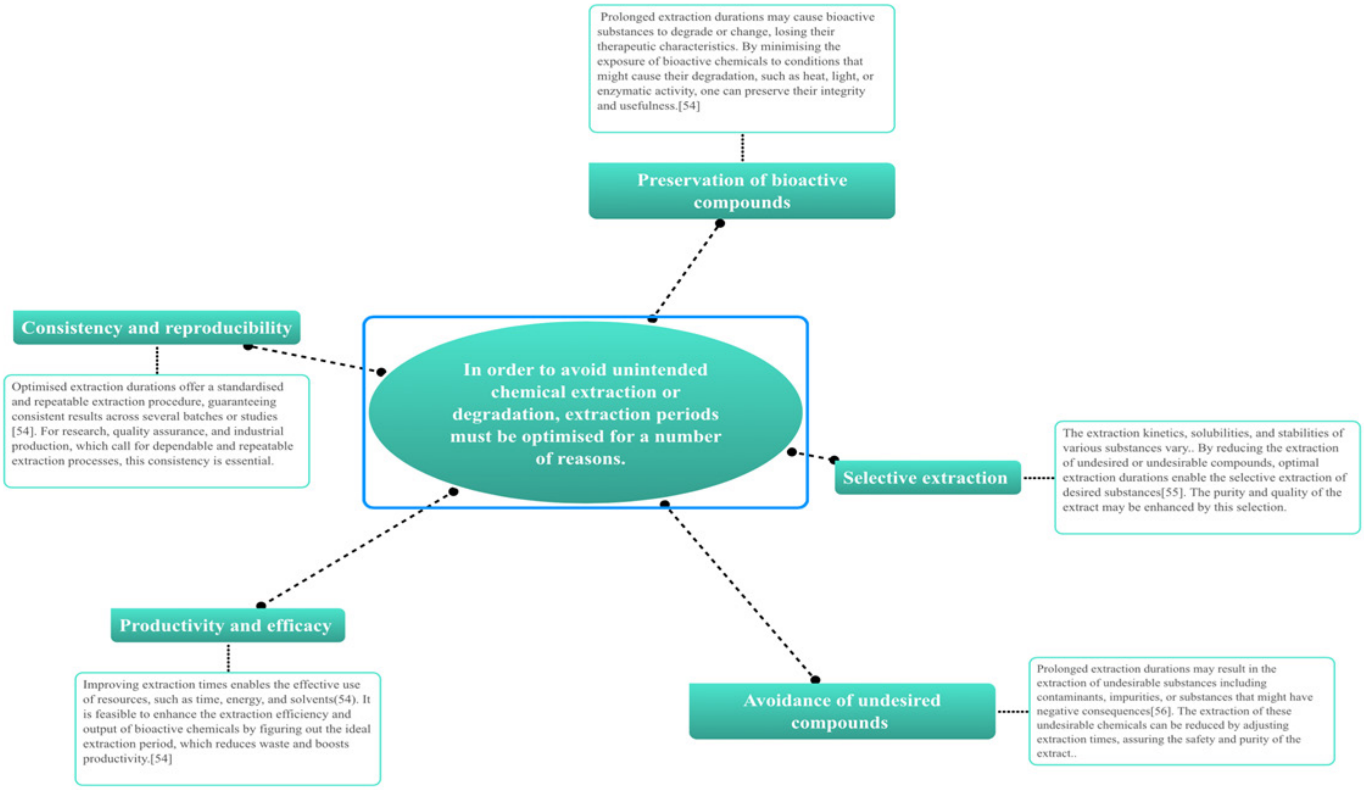

Figure 1: Precision in Extraction: Optimizing Time to Safeguard Against Unintended Chemical Extraction or Degradation.[54-56]

efficient as it provides more surface area for interaction. However, using too much solvent may not significantly improve efficiency, as it could have difficulty reaching the target compounds.[71-74]

Extraction yield

The solid-to-solvent ratio can also impact how much of the target compounds are extracted from the solid material. Generally, a higher ratio leads to extracting more compounds due to the increased solvent available for dissolving and extracting them. However, there may be a point where further increasing the ratio won't significantly boost the yield.

Solvent consumption

The solid-to-solvent ratio affects the amount of solvent needed for the extraction. A higher ratio means using more solvent, which could have cost and environmental implications.[73] The Figure 2 outlines methods to determine the optimal solid-to-solvent ratio for extraction. It includes preliminary experiments to test different ratios, Response Surface Methodology (RSM) for statistical optimization, cost and practical considerations to ensure feasibility and literature review to leverage existing research insights. These methods help identify the most efficient and cost-effective ratio for maximum extraction yield.

Physical Treatment Applied during Extraction

There are various methods available to extract phytoconstituents from plant materials. This may include traditional extract methods that are holds still good for the extraction and advanced extraction techniques. Let's take a look at some examples:

Soxhlet extraction

This is a traditional method also known as continuous hot percolation where the plant material is continuously extracted using a solvent.[75] The material is placed in a thimble and the hot solvent circulates through it, making the extraction process more efficient. To maximize the extraction process, it is essential to comprehend the fundamental parameters influencing Soxhlet extraction tools. Numerous research works have emphasized important elements that are crucial to Soxhlet extraction. The extraction of total phenolics required a certain ethanol concentration and solid-solvent ratio, whereas the extraction of anthocyanins was dependent on the solid-solvent ratio.[76] Furthermore, the water bath is a novel critical component of Soxhlet extraction, influencing reflux and siphon periods that are associated with the concentrations of specific chemicals compared to conventional extraction techniques.[77] The study showed that Soxhlet extraction offered higher efficiency in the recovery of hydrophilic chemicals because of the combination of water and heating for longer periods of time promoted more

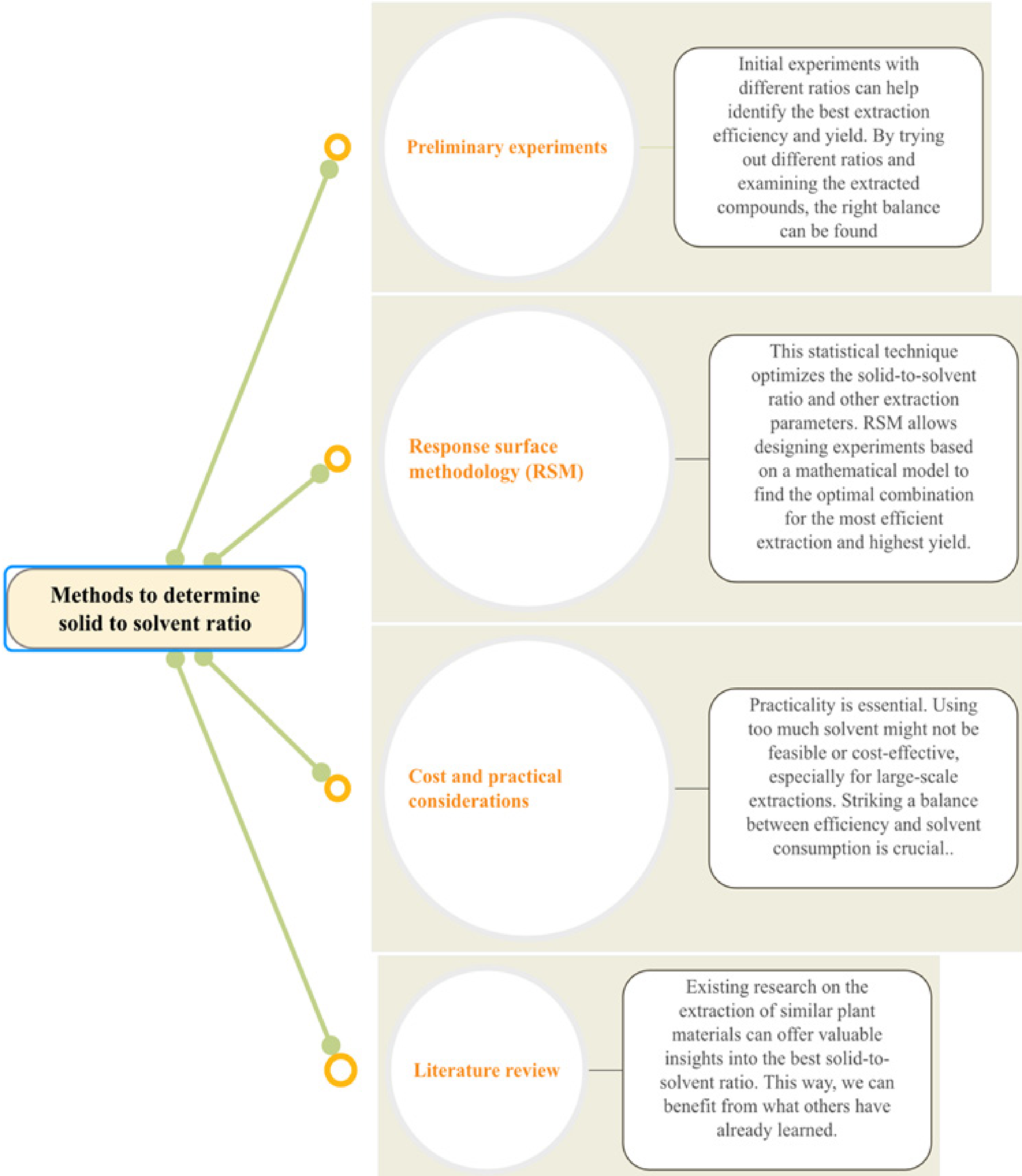

Figure 2: Methods to determine solid to solvent ratio.[73]

effective cell disruption.[78]Additionally, various studies have emphasized the importance of solvent polarity, the proportionate vapor pressure of the marginal solvent to the Soxhlet extraction speed and the impact of solvent selection on the extraction procedure. A number of other parameters, including solvent type and concentration, solvent-to-solid ratio, extraction temperature and time, were also found to have an impact on the extraction efficiency and antioxidant capacity. Additionally, the application of ultrasound-assisted extraction was also found to affect the extraction procedure. Lastly, some studies highlighted the drawbacks of traditional Soxhlet extraction techniques, such as their high energy, time and solvent consumption and comparatively low yields, suggesting the necessity of optimizing the Soxhlet extraction procedure.[79-84]

Maceration

In this method, the plant material is soaked in a solvent for a certain time to allow the phytoconstituents to be extracted with occasional stirring in a dark place to avoid photolysis of phytoconstituents. After that, the solvent is separated from the insoluble solid material followed by the evaporation of the solvent to obtain the extract. Important variables impacting the extraction process include the composition of the target chemicals, the way the analyte bonds with the extraction solvent and the moisture content and particle size distribution of botanical samples. Additionally, the amount of leftover unextracted coffee husk and the tannin content produced were significantly influenced by the kind of organic solvent and maceration length. Comparing the effects of several extraction techniques demonstrated that maceration produced lower polyphenolic concentrations than other extraction techniques. Furthermore, the maceration procedure affected the oxidative stability of the extracted components by producing higher levels of peroxides and free fatty acids in comparison to the control oil.[85-89]

Ultrasound-assisted extraction

In case of ultrasound extraction, ultrasound waves produced by the instrument are used to boost the extraction process. The plant material is mixed with a solvent, kept in the ultrasound bath and the ultrasound helps to break cell walls, enhancing the extraction efficiency. A number of critical parameters impact the effectiveness and result of Ultrasound-Assisted Extraction (UAE) in the extraction of bioenriched plants. These variables include the target compound's nature, temperature, extraction time and kind of solvent employed for extraction. By enhancing mass transfer and breaking down biological cell walls, the application of ultrasound encourages the solvent to penetrate cellular materials more deeply, which facilitates the release of contents.[90] Furthermore, the temperature, kind of solvent and duration of the extraction process all have a significant impact on the biological activity of phenolic compounds extracted using UAE.[91] UAE is a good choice for bioenriched plant extraction because it is also recognized for its efficacy in increasing extraction yield, cutting down on extraction time and offering excellent extraction efficiency.[92] The method's great extraction capabilities and efficiency have drawn a lot of attention. Furthermore, a study's findings showed that the flavonoid extraction process with ultrasound assistance is straightforward, environmentally friendly, effective and repeatable.[93]

Supercritical fluid extraction

This method uses supercritical fluids like carbon dioxide as solvents. The solvent is brought to a supercritical state, acting like both a liquid and a gas, making it great for efficient extraction. Several crucial criteria and aspects have a substantial impact on the effectiveness and performance of supercritical extraction techniques. Because carbon dioxide is non-toxic, non-flammable, non-polluting and recoverable, it is an excellent supercritical fluid for solubilizing lipophilic compounds without harming the environment.[94] High-intensity ultrasound is a useful tool for inducing small-scale agitation because it improves mass transfer in supercritical fluid extraction operations.[95] Additionally, the optimization of supercritical Carbon Dioxide (SC-CO_2) extraction procedures is greatly impacted by the choice of co-solvents, including ethanol, water, methanol and aqueous solutions of ethanol-water and methanol-water to extract polar phytoconstituents.[96] Additionally, in order to achieve more efficient extraction and purification techniques that satisfy the demands of industrial production, the supercritical fluid technology for the extraction of natural essential oils and terpenoids from plants should be integrated with other extraction technologies.[97] The study investigated the impact of various process parameters, including temperature, pressure and extraction time, on the supercritical CO_2 extraction method used to extract steroidal sapogenins from fenugreek. To achieve effective and successful supercritical extraction operations, it is crucial to comprehend and optimize these crucial elements and aspects.

Microwave-assisted extraction

In this method, the plant material and solvent are mixed and microwave energy is applied that heats up solvent rapidly, leading to better extraction efficiency. Many parameters have a substantial impact on the effectiveness of Microwave-Assisted Extraction (MAE) for plant materials. Important factors in the extraction process are the choice of solvent, extraction duration and microwave power. Target compound solubility is influenced by the solvent used, while extraction efficiency is influenced by extraction time and microwave power. It has been demonstrated that MAE techniques yield better products at lower prices by requiring shorter extraction times, using less solvent and providing higher extraction rates.[98] Furthermore, important variables that greatly affect the efficiency of MAE include the extraction temperature, microwave power and the ratio of solvent to material. Although excessive temperature and microwave power can cause thermal degradation and contaminant leakage into the solvent, high temperature and a lengthy extraction period can boost heat/mass transfer with microwave power, leading to fast plant cell wall rupture and enhanced target active yields.[99] Critical criteria that have been discovered as determining the extraction efficiency of certain chemicals from plant materials include the type and concentration of the extraction solvent, the ratio of liquid to material, the extraction temperature and the microwave duration.[100] In MAE, optimizing parameters including extraction duration, microwave irradiation power and water volume to plant mass ratio is crucial to attaining optimal essential oil production and quality. Enhancing the efficiency of MAE for plant material extraction requires a thorough understanding of and optimization of these aspects.[101]

The choice of extraction method depends on factors like the type of plant material, the target phytoconstituents and yield of the extract. By optimizing conditions like temperature, time and solvent ratio, we can further improve the extraction process and get a higher yield of phytoconstituents.

CONCLUSION

In conclusion, the present review explains the process of extracting bioactive chemicals from medicinal plants is a complex and multi-faceted procedure that is influenced by a wide variety of important aspects. The intricate topography of extraction procedures is navigated by means of a rigorous examination of these crucial considerations, which allows us to generate bioactive enhanced extracts that have increased medical efficacy. The success of the extraction process is cumulatively influenced by the numerous driving elements that are covered in this article. These variables include the selection of medicinal plants based on ethnopharmacology and chemotaxonomy, as well as the optimization of parameters in a variety of extraction methods. The earliest steps entail the careful selection of medicinal plants, taking into account ethnopharmacological insights and chemotaxonomy in order to discover plants that contain particular bioactive components. It is possible to further improve the selection process by gaining an understanding of the impact of plant parts, the secondary metabolites that they produce and the influence of the plant condition (fresh or dried). The chemical composition and bioactivity of the final extract are significantly influenced by the processes that are utilized, which include a variety of drying methods. As integral factors, the optimization of particle size, the period of extraction and the matrix properties of phytoconstituents inside the inert solid matrix are all important in the process. Both the kinetics and the efficiency of extraction are greatly influenced by these parameters, which include the accessibility of the solute, diffusion and mass transfer. Mass transfer, extraction kinetics and solute accessibility are all impacted by solvent diffusion, which is another essential component. In addition, the bioactive profile of the extract is further shaped by the selection of the solvent, the properties of the solvent and the influence that the solvent has on the extraction temperature and components. To achieve the necessary level of extraction efficiency and selectivity, it is essential to choose an appropriate solvent that is compatible with the extraction method that is being utilized. This selection should be based on the solvent's polarity, boiling point, cost, environment friendliness and compatibility levels. The efficiency, yield and solvent consumption of an extraction process are all determined by the ratio of the solvent to the solid. In order to maximize these aspects, it is necessary to strike a precise balance. The physical treatments that are done throughout the extraction process, which include a variety of techniques such as Soxhlet, maceration, ultrasound-assisted extraction, supercritical fluid extraction and microwave-assisted extraction, each have their own unique set of benefits and disadvantages. In order to get the desired extraction result, it is of the utmost importance to have a thorough understanding of the crucial parameters for each method and to optimize the conditions.

Furthermore, the achievement of the goal of creating bioactive enriched extracts is contingent upon having a full understanding of these driving elements and manipulating them strategically. It is possible for researchers, practitioners and industries that are involved in the extraction of bioactive substances from medicinal plants to make use of this information in order to unleash the full therapeutic potential of nature's Pharmacopoeia. Furthermore, the present review also continues to dive deeper into the complex science of extraction, the incorporation of these essential elements guarantees not only the effectiveness of the process, but also the quality and richness of the bioactive extracts that are obtained.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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