AUSTRALIAN HERBAL INSIGHT
REVIEW

Optimizing Extraction Techniques for Maximized Bioactive Compound Yield in Medicinal Herbs

Md Shamsuddin Sultan Khan [1*], Marjan Ganjali Dashti [2]

Abstract

The goal of this review is to advance the field of herbal medicine through the creation and refinement of novel extraction methods. The main objective is to discuss increasing the yield and extracting bioactive components from medicinal plants to maximize their therapeutic value. Since ancient times, medicinal herbs have been prized for their many health advantages. One of the most important aspects of utilizing these benefits is extracting bioactive components from the herbs. Conventional extraction techniques frequently fail to properly extract the range of bioactive chemicals found in medicinal plants. This study investigates and improves on state-of-the-art extraction methods to overcome this constraint. The review analyzes how to overcome current limitations and improve the extraction process's efficiency by utilizing advances in science and technology. Optimizing extraction techniques is essential for maintaining the integrity of bioactive chemicals and maximizing production. In order to achieve the best possible balance between compound stability and extraction process efficiency, the review explores variables like temperature, pressure, and solvent choice. The research aims to create procedures that may be used with a variety of therapeutic herbs by methodical trial and analysis, guaranteeing a wide-ranging influence on herbal medicine.

Moreover, maximizing bioactive substances' therapeutic potential aligns with the general goal of achieving better health outcomes. Potential uses include pharmaceuticals, nutraceuticals, complementary and alternative medicine, and other medical domains. In conclusion, this review discusses the further practical advances in herbal medicine and the scientific understanding of extraction methods, potentially leading to innovations that favor global health.

Keywords: Extraction techniques, Medicinal herbs, Bioactive compounds, Optimization, Therapeutic potential.

Significance | This review discusses the optimizing extraction methods, enhancing bioactive compound yield, and advancing therapeutic potential of herbal medicine.

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Introduction

Bioactive substances are widely found in fruits, nuts, roots, vegetables, herbs, and spices, particularly polyphenols and non-starch polysaccharides (Saeed at all,2012). Because bioactive compounds are so important, the manufacturing sector is searching for environmentally innovative solutions to reduce bioactive compound loss (Gomes et al,2021). These substances possess antioxidant, anti-inflammatory, anti-tumor, anti-diabetic, anti-lipidemic, and antidepressant qualities(Saeed at all,2012). Bioactive substances have been isolated by numerous researchers utilizing various contemporary techniques. These important bioactive chemicals are extracted or recovered from various sources using a variety of extraction techniques. The kind, preparation process, and energy usage all influence the extraction method selection (Azmir et al,2013). It must be selected to maximize the extraction yield of the required chemicals while minimizing loss and energy

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consumption. Numerous researchers have noted that the sample preparation stage takes up about 60% of the entire time, notably Koçak and Pazir (Koçak & Pazır,2018). The spectroscopic or chromatographic approach, which is the final analysis, requires around 7% of the entire time(Sasidharan et al,2011).In addition to this incorrect interpretation of the conclusion or results, improper extraction technique selection may result in the loss of the intended component. The current review focused on distinct extraction methods that might be classified as conventional or environmentally friendly.For extraction purposes, a variety of conventional procedures are employed, including liquid-liquid extraction (LLE), solid-phase microextraction (SPME), and solid-liquid extraction (SLE). These antiquated, conventional techniques have numerous disadvantages, including nutrient loss, lengthy extraction times, poor extraction yields, increased energy costs, and poor economics. In earlier research, Sasidharan et al.(2011) detailed a variety of extraction methods and covered their benefits, which included lower solvent use, shorter processing times, reduced energy consumption, and increased extraction yields. Nowadays, the majority of novel and environmentally friendly methods are employed to extract bioactive substances from various natural sources. These extraction methods include surfactant-mediated extraction, enzymatic extraction with high yield and efficiency, membrane ultra-filtration extraction, instant-controlled pressure drop (DIC) extraction, pressurized liquid extraction (PLE), ultrasound-assisted extraction (UAE), supercritical fluid extraction (SFE), microwave-assisted extraction (MAE), and membrane ultra-filtration extraction.Moreover, some food businesses have employed high-pressure, microwave, and ultrasonic technologies to extend the shelf life of their products (Zhang et al,2021).

Role of food bioactive compounds in human health

Plants, fruits, vegetables, cereals, meat, and seafood are major sources of bioactive compounds.Bioactive substances like polysaccharides, polyphenols, carotenoids, alkaloids, etc. are widely found in the natural sources listed above.Others, such as triterpenes and triterpenoids (a functional form of triterpenes), comprise roughly eighteen distinct subclasses, the most well-known of which are saponins and squalene derivatives.According to research, ursane, lupine, and oleanane are the most potent anti-cancer substances(Hill, & Connolly,2018)Furthermore, Saeed et al (2021) reported that non-starch polysaccharides, particularly arabinoxylans, function as anti-inflammatory, anti-oxidant, and anti-diabetic agents.The main bioactive ingredient in plant cells is phytosterol (Gomes et al,2021).Numerous studies have shown that dietary consumption of phytosterols, such as sitosterol, campesterol, and stigmasterol, can reduce the body's reaction to low-density lipoprotein cholesterol (Moreau et al,2018). Another term for terpenoids, isoprenoid refers to a broad class of chemicals that make up the largest group of secondary metabolites.- Citrus fruits include limonene, since terpenoids are specifically present in copious concentrations in a variety of fruits and plants, and their volatility at room temperature is what gives them their distinct aroma.-Tocopherols, which include α and γ tocopherols, and carotenoids, which include β-carotene, are sources of vital nutrients, including vitamin A and E. For this reason, they are known as bioactive food molecules (Multari et al,2020) Mostly found in tea and coffee, caffeine is one of the most widely ingested alkaloids in the human diet.- Glucosinolates are mostly found in cruciferous plants, which are often a type of Mediterranean diet with distinct flavors and odors including cauliflower, broccoli, Brussels sprouts, and cabbage (Câmara et al,2020). These substances have also been shown to have a number of beneficial effects on the body, including anti-inflammatory and chemotherapy-preventive ones.The component found in broccoli, sulforaphane, functions as a preferred anti-cancerous agent.The most frequent polysaccharides linked to human health are cellulose, which provides the structural foundation for plant cells, and glucose and starch, which give animals and plants energy reserves. These polysaccharides are referred to as bioactive dietary components (Porter & Martens, 2017). Dietary fibers like inulin and its derivative fructooligosaccharides are shown to support the microbiota symbiosis of the human gut, which in turn benefits human health, infant nutrition, lipid metabolism, blood sugar regulation, and lowers the risk of obesity and colon cancer.(Porter & Martens, 2017) Polyunsaturated fatty acids, which include docosahexaenoic acid, linoleic acid, and eicosapentaenoic acid, are important food bioactive chemicals that have positive impacts on health (Saini & Keum, 2018). Excessive intake of these bioactive substances may exacerbate oxidative stress-related damage, mostly to the blood vessel walls, and may result in a fatal cardiovascular disease(Calder et al,2006)Because mammals cannot synthesize polyunsaturated fatty acids, they must be consumed through diet.Oils and seeds from soybean, flax, sunflower, corn, walnut, and fish, such as herring, salmon, and mackerel, are common sources of polyunsaturated fatty acids.Peptides are important bioactive substances that are found naturally in meat, including fish, poultry, cattle, and chicken, as well as other sea foods.These important substances also have the ability to prevent or lower the risk of numerous illnesses, including metabolic syndrome, functional intestinal environment, blood pressure homeostasis, and muscle wasting disease (also known as sarcopenia) (Ferreira et al,2009). Polyphenols are bioactive substances found in a range of therapeutic plants.-The quantity ingested and the bioavailability of polyphenols influence their health benefits.- Thus, according to current investigations, polyphenols have been found to be effective in the treatment of cancer, osteoporosis, neurological illness, diabetes mellitus, and cardiovascular disease (Abbas et al ,2017).

Factors affect the extraction of bioactive compounds

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The mass transfer and solubility of polyphenol are influenced by various factors such as pressure, sample particle size, temperature, pH of the solution, ultrasonic power and frequency in the case of (UAE), microwave power in the case of (MAE), electric field strength, and pulse duration in the case of (PEF), among others.-Numerous tests have been conducted to assess the effects of these significant variables.One of the best applications for determining the ideal circumstances for maximum recovery is the response surface method.According to Azmir et al.(2013) that exceptional efforts made on contemporary procedures could be employed by taking into account studies devoted to these issues.-Choosing a solvent for polyphenol extraction from various sources, particularly plants, is an essential step in selecting an appropriate solvent. This includes taking an extraction technique into account. Bart & PilzIn (2011) reported that the choice of solvent is influenced by the characteristics of particular bioactive substances.According to Altemimi et al. (2017), in order for the selected solvent to be completely dissolved in extraction procedures, it must have the same polarity as the intended solvent.-This means that various extraction techniques are needed for various solvents, and that these solvents can have polar, nonpolar, or even thermally labile chemical compositions (Leaky et al.2017) To extract polar solvents (ethanol, methanol, or ethyl acetate) and hydrophilic bioactive compounds. However, polar solvents with lower boiling points, such as ethanol, acetone, methanol, and acetone and water mixed together, would be the ideal option for the isolation of phenolic compounds. Leaky et al.(2017) revealed that the majority of products that need to be extracted with water are metals, hydrophobic chemicals, peptides, sugars, ions, nucleotides, and water-soluble amino acids.-It was also reported by Tomsone et al (2012) and ovarian cancer.Products requiring ethanol extraction are made up of extremely polar, basic, acidic, and neutral molecules, according to Bouchard et al (2007). Several studies have found that ethyl acetate extraction is required for compounds that are low to moderately polar, neutral, or somewhat hydrophobic(Cañadas et al,2020). Different- traditional- and- novel- extraction- methods-used- to- extract- bioactive- compounds-fromnatural-sources-are-shown-in-Figure-1.

Traditional extraction methods

Liquid-liquid extraction

It is also commonly referred to as solvent extraction, and it consists of two phases of immiscible liquid.There are two phases: the aqueous phase and the organic phase.The extraction process is contingent upon the analytic's dissolution in the organic phase.The organic and aqueous phases are combined in a separator funnel with a plant or other substance that the desired compound wishes to be extracted.Two separate liquid layers are produced as a result of shaking.- As stated by Wells (well et al,2003). After the intended analytical component is extracted liquid-to-liquid, the analyte is divided between the two immiscible liquids based on how soluble it is in each solvent(Yahya et al,2018). The liquid-liquid extraction method eliminates the requirement for a distillation process and is best suited for temperature-sensitive materials and azeotropic mixtures(Cond et al,2021). Idari et al. (2011) noted that this method has a number of limitations, including the high volume of organic solvents needed, the production of emulsions, automation-related challenges, labor-intensive nature, etc.

Solid-phase extraction (SPE)

The complete elimination of the chemical composition is guaranteed in this extraction method from a flowing liquid.The desired constituent is eventually extracted from the sorbent by the elution after the chemical constituent is retained on the solid absorbent(Murakami et al, 2020). The most crucial prerequisite for a successful solid-phase extraction is that the maximum amount of analytical solvent required for the process must be reproducible.The whole solute must elute from solid particles.In addition to this analyte disruption, Poole (2003) states that the limitation in the ability of sorbent sorption is caused by the inadequacy of solid-phase extraction.To remove small particles from solid phase extraction, a filtration process is required. Because solid-phase extraction uses solvent efficiently and affordably, it is a more advantageous technique than liquid-liquid extraction (Tan et al,2020).

Solid-phase microextraction (SPME)

A straightforward extraction procedure is used, which entails dispersing the solid phase in a small amount of extracting phase and exposing the sample to it for a predetermined amount of time.-It is documented by Merkle et al(2015)There are two basic processes in the SPME process: first, the target chemical or sample is exposed to externally coated fibers or absorbent, and then the absorbent is transported for gas chromatography or HPLC.As stated by Merkle et al.(2015)Because of their automation potential and simplicity, the SPME methods offer numerous advantages.-Moreover, SPME is a useful technique for examining bioactive compounds that are present in varying amounts in different foods.It can lessen issues with solvent clearance. Wells(2003) listed the ways in which SPME enables unique research, including the extraction of information from extremely small samples (single cells).For many years, phenolic chemicals have been extracted by the use of traditional techniques such maceration, infusion, digestion, and Soxhlet(Osorio et al,2020) Of these techniques, maceration and Soxhlet's et al. Are the most crucial(Caldas et al,2018) employed both standard and unconventional techniques to extract various phenolic components from the grape skin. Alara et al (2017) Utilizing the peel of feijoa and the leaves of Vernonia cinerea, also found that the total phenolic compound ranges between 48.6 and 71 mg of GAE (gallic acid equivalent) per gram. In soxhlet extraction and maceration, a high solvent to feed ratio roughly more than 20 is typically employed.Raw material is extracted when macerated in a particular solvent for a specified amount of time.-Formaceration requires little to no agitation.- Maceration can be carried out at a lower temperature than soxhlet extraction.-It was documented by Ji et al.(2017) that under ideal circumstances and room temperature, phenolic components were removed from an oil mixture via maceration.Somaceration is advantageous because to its low temperature needs and inexpensive procedures.Furthermore, the necessary equipment is user-friendly.UTMaceration produces lower yields and requires more time for extraction.

Novel techniques

Ultrasound-assisted extraction (UAE)

A unique kind of sound wave that is inaudible to humans is ultrasound. In chemistry, it is typically between 20 kHz and 100 MHz. It travels through a material by compressing and expanding, just like other waves do. The result of this process is a phenomena known as cavitation, which is the formation, expansion, and collapse of bubbles. When motion's kinetic energy is converted to heat and the contents of the bubble are heated, a significant amount of energy is produced. Suslick and Doktycz (1990) reported that bubbles have a temperature of around 5000 K, a pressure of 1000 atm, and a heating and cooling rate of more than 1010 K/s. UAE was established based on this idea. The cavitation effect is only present in liquids and liquids containing solid components.According to Herrera and Luque de Castro (2005), the primary advantage of UAE is seen in solid plant samples where organic and inorganic chemicals are easier to leach from the plant matrix. The acceleration of solvent access to plant cell components and the amplification of mass transfer via ultrasound are the likely mechanisms. According to Mason et al. (1996), the two primary physical processes involved in the ultrasonic extraction mechanism are (a) diffusion across the cell wall and (b) rinsing the contents of the cell once the walls are broken. Moreover, the controlling parameters for the action of ultrasound are temperature, pressure, frequency, and sonication time. Due to reports that they increase a conventional system's efficiency, UAE have also been included in addition to other traditional procedures. An ultrasonic device is positioned appropriately in a solvent extraction machine to improve extraction efficiency (Vinatoru et al., 1998). UAE appears to be a useful extraction method for removing bioactive compounds from medicinal plants. Four isoflavone derivatives—daidzin, genistin, glycitin, and malonyl genistin—were successfully extracted from soybeans using the mix-stirring process in 2003, according to Rostagno et al. Depending on the solvent used, the authors discovered that ultrasonic can increase the extraction yield. Herrera and Luque de Castro (2004) developed a semiautomatic approach based on ultrasounds to extract phenolic components from strawberries, including rutin, naringin, naringenin, quercetin, ellagic acid, and kaempferol, utilizing a 0.8 s duty cycle for 30 s. Li et al. (2005) discovered that when UAE operated under ideal conditions (80% methanol, 20:1 solvent, sample ratio), there was a greater recovery of chlorogenic acid from fresh leaves, fresh bark, and dried bark of Eucommia ulmodies Oliv.

Pulsed electric field (PEF)

Over the past ten years, it has been established that the pulsed electric field (PEF) treatment is beneficial for enhancing the pressing, drying, extraction, and diffusion processes (Barsotti and Cheftel, 1998; Angersbach et al., 2000; Vorobiev et al., 2005; Vorobiev and Lebovka, 2006). The idea of PEF is to break down the structure of the cell membrane in order to increase extraction. A living cell's membrane experiences an electric potential when it is suspended in an electric field. Electric potential divides molecules based on their charge in the cell membrane due to the dipole nature of membrane molecules. Charge-carrying molecules repel one another after surpassing a critical transmembrane potential of roughly 1 V. This results in holes forming in weak regions of the membrane and a sharp rise in permeability (Bryant and Wolfe, 1987). For PEF treatment of plant materials, a straightforward circuit with exponential decay pulses is typically utilized. Plant materials are placed in a treatment chamber that has two electrodes. The PEF process can run in batch or continuous mode, depending on how the treatment chamber is designed (Puértolas et al., 2010). The process parameters, such as field strength, specific energy input, pulse number, treatment temperature, and qualities of the materials to be treated, are what determine how effective PEF treatment is (Heinz et al., 2003).By breaking down the plant materials' membrane structure to improve extraction and shorten extraction times, PEF can boost mass transfer during extraction. PEF has been used to increase cell membrane permeability, which enhances the release of intracellular chemicals from plant tissue (Toepfl et al., 2006). Plant tissue's cell membrane is reported to be damaged by PEF treatment at a modest electric field (500 and 1000 V/cm; for 10 4 –10 2 s) with just a slight temperature increase (Fincan and Dejmek, 2002; Lebovka et al., 2002). PEF can thereby reduce the rate at which heat-sensitive chemicals degrade (Ade-Omowaye et al., 2001). In order to reduce the amount of work required for extraction, PEF can also be used on plant materials as a pretreatment step before traditional extraction (López et al., 2009). When betanin was extracted from beetroots using a solid liquid extraction procedure, PEF treatment (at 1 kV/cm with low energy consumption of 7 kJ/kg) demonstrated the highest degree of extraction when compared to freezing and mechanical pressing (Fincan et al., 2004). According to Guderjan et al. (2005), using PEF as a pretreatment procedure enhanced the recovery of phytosterols from maize by 32.4% and isoflavonoids (genistein and daidzein) from soybeans by 20–21%. Using a variety of methods, Corralesa et al. (2008) recovered bioactive compounds such anthocyanins from grape by-products and discovered that PEF produced a higher-quality extraction of anthocyanin monoglucosides. Before the maceration step, applying a PEF treatment to the grape skin can shorten the maceration period and increase the stability of the bioactives (polyphenols and anthocyanins) during the vinification process (López et al., 2008).

Enzyme-assisted extraction (EAE)

Enzyme-assisted Extraction (EAE) is a more recent approach where enzymes are added to the extraction medium to enhance the recovery method.(Nadar et al,2018). The main job of enzymes when they are taken from plant materials is to weaken or dissolve the cell walls.-This gives the active compounds access to the solvent.It is difficult to extract buried phytochemicals (found inside cells or on cell walls) using a standard solvent extraction method.Enzymes broke down the surrounding elements to assist bring these components out in a unique way.- Nonetheless, EAE is thought to be advantageous for the extraction of polyphenols attached to proteins or carbohydrates (within or on cell walls). Commonly used enzymes for enzymatic extraction include lipase, α-amylase, pectinase, amyloglucosidase, laccase, and protease(Gligor et al,2019).]The key control variables for optimizing the polyphenol yield are the particle size and the enzyme percentage to the sample.A sample (enzyme and solvent mixture) is incubated at low temperatures (35–50°C) and with apH adjustment in the enzymatic hydrolysis extraction process. At temperatures between 80 and 90°C, deactivating enzymes stops hydrolysis, and low-temperature extraction requires less energy to avoid deterioration.-The EAE is well-known for being an environmentally friendly procedure.- The ideal conditions for the enzyme to function are acidic media, and water is either utilized as an organic solvent or as a chemical substitute.The main drawback of EAE is its prolonged extraction time, which can range from three to 48 hours(Malik & Mandal, 2022).

Pressurized liquid extraction (PLE)

Methods of high pressure extraction are useful for handling polyphenols that are resistant to high temperatures.-These techniques also improve the polyphenol’s recuperation.- The theory behind pressurized liquid extraction (PLE) is the ratio of the boiling point temperature to the pressure. The solution stays liquid when the extraction system’s pressure is raised before the temperature is raised.The PLE’s temperature fluctuates between 50°C and 200°C(Hossain et al,2015). Nonetheless, the solvent and the polyphenols both affect the maximal extraction temperature. Several researchers have found that PLE has greater chemical solubility (polyphenols in liquids)(Alves et al,2021). Higher polyphenol concentrations are seen when the temperature is raised.The method is energy-saving because a liquid's sensible heat is smaller than that of vaporization, meaning that less heat is required to raise the temperature than is required to form vapor(Hossain et al,2015). The main solvents in PLE are water and aqueous alcohols.Because of this, a sizable portion of solvents are water. Additionally, solvents are inexpensive, safe, and environmentally benign.-The apparatus used for extraction is crucial, especially the extractor and its accompanying setup.

Principle supercritical fluids (SCF)

It is among the most sophisticated methods available for replacing organic solvents used in a variety of processes.The physical characteristics of SCFs determine their specificity, which can be altered by raising the temperature or/and pressure parameters above their critical values.-In contrast to conventional techniques, SCF exhibits a liquid-like density that results in a liquid-like solvating power.- The use of SCF has numerous primary benefits.When a fluid is treated (that is, heated and pressured) above its critical pressure (Pc) and critical temperature (Tc) values, it is said to be in its critical state.When solvents are used sparingly or not at all, solvent-free extract is developed (when using co-solvents).This process eliminates the need for purifying or separation steps by reducing the number of unit operations through the depressurization step.-SCFs are designed to process heat-sensitive biomolecules by running their entire mechanism at lower temperatures.The extraction efficiency has been improved by examining supercritical fluids with combined mechanisms. Recently, an extraction yield-boosting technique called Gas Assisted Mechanical Expression (GAME) has been developed. This technique combines pressing and supercritical gas use.This method has been extensively used with a variety of seeds, including sesame, cocoa, and lentils. According to Andarra et al. (2000), densegases or supercritical fluids are highly preferred for pressing, and a mechanical pressure reduction of about 10 Mpa is required to increase the yield of oil extracted from 10 to 20.-Current filtering technologies, such as SC-CO2, when combined with extraction techniques, have been tested to purify substances with lower molecular weights, like 1500 g mol−1.- This method has been used to remove triglycerides from fish oil and beta-carotene from carrot oil.-Temelli provided evidence that the combination of membrane and SCF technologies for refining edible oils is still undergoing development.

Microwave extraction

According to Paré et al. (1994), microwave-assisted extraction is regarded as a unique technique for utilizing microwave radiation to extract soluble compounds into a fluid from a variety of materials. Electromagnetic energies with frequencies between 300 MHz and 300 GHz are known as microwaves. They consist of two perpendicular oscillating fields, such as the magnetic and electric fields.The direct effects of microwave radiation on polar materials provide the basis of the microwave heating principle (Letellier and Budzinski, 1999). Ionic conduction and dipole rotation processes are the ways by which electromagnetic energy is transformed into heat (Jain, 2009). The resistance of the medium to ion passage causes heat to be produced during the ionic conduction mechanism. Ions, on the other hand, maintain their orientation along constantly shifting field indications. According to Alupului (2012), the extraction mechanism of microwave-assisted extraction consists of three sequential steps: the first is the separation of solutes from sample matrix active sites under increased pressure and temperature; the second is the diffusion of solvent across sample matrix; and the third is the release of solutes from sample matrix to solvent. Cravottoa et al. (2008) have detailed a number of benefits of MAE, including faster heating for the extraction of bioactive compounds from plant materials, less temperature gradients, smaller equipment, and higher extract yield (Figure 2). Compared to traditional extraction methods, MAE can extract bioactive chemicals more quickly and potentially achieve a greater recovery. It is a methodical approach to the extraction of more complete organic and organometallic compounds.Because MAE uses less organic solvent, it is also regarded as a green technology (Alupului, 2012). When extracting polyphenols and caffeine from green tea leaves, MAE produced a greater extraction yield after 4 minutes compared to all other extraction techniques used for 20 hours at room temperature (Pan et al., 2003). According to Shu et al. (2003), the yield of ginsenosides extracted from ginseng root in 15 minutes utilizing a targeted MAE approach was superior to that of a 10-hour traditional solvent extraction. When Dhobi et al. (2009) extracted the flavolignin silybinin from Silybum marianum instead of using traditional extraction methods such Soxhlet maceration, they were able to demonstrate enhanced extraction efficiency of MAE.Asghari et al. (2011) demonstrated that, as compared to traditional extraction methods, MAE is a quicker and simpler approach for extracting some bioactive chemicals (E- and Z-guggolsterone, cinnamaldehyde, and tannin) from a variety of plants under ideal conditions. Chiremba et al. (2012) used MAE to extract bound phenolic acids from bran and flour fractions of sorghum and maize of varying hardness. Using planned experiments, the MAE method from Chinese quince (Chaenomeles sinensis) was optimized for solvent concentration, extraction time, and microwave power to maximize flavonoid and phenolic recoveries and to improve the extracts' capacity to donate electrons (Hui et al., 2009).

Supercritical fluid extraction (SFE)

Supercritical fluid was first used for extraction purposes by Hannay and Hogarth in 1879, but Zosel deserves recognition as well as she submitted a patent for the use of SFE to decaffeinate coffee (Zosel, 1964). Since its inception, the supercritical fluid technology has garnered significant attention from scientists and has been effectively used to food analysis, pharmaceutical, environmental, and polymer applications (Zougagh et al., 2004). This method has been used for many years by a number of enterprises, most notably those that prepare decaffeinated coffee (Ndiomu and Simpson, 1988).There are three fundamental states for all substances on Earth: solid, liquid, and gas. Only when a substance is exposed to pressure and temperature over its critical point can it reach the unique supercritical state. According to Inczedy et al. (1998), the critical point is the characteristic temperature (Tc) and pressure (Pc) above which discrete gas and liquid phases do not exist. The unique characteristics of a gas or liquid vanish in a supercritical state, therefore changing the temperature or pressure will not cause the supercritical fluid to liquefy. Supercritical fluid has liquid-like density and solvation power along with gas-like diffusion, viscosity, and surface tension. Because of these characteristics, it can extract chemicals quickly and with better yields (Sihvonen et al., 1999). A mobile phase tank (often CO2), a pump to pressurize the gas, a co-solvent vessel and pump, an extraction vessel housed in an oven, a controller to keep the system's internal pressure at a high level, and a trapping vessel make up a basic SFE system. Various types of meters, such as flow meters and dry/wet gas meters, can often be connected to the system. Figure 3 shows a symmetric diagram of common SFE instrumentation.

Potential applications of bioactive compounds

Bioactive compounds are extensively employed as therapeutic agents and possess numerous health-promoting attributes.These substances have the ability to enhance the technological features of novel products.- Its primary application is in the creation of healthy, natural products that are also less harmful to the environment (Table 1). It has been demonstrated that polyphenols, a bioactive component, function as a preservative in food products.- The 1.5% lychee pericarp extract in sheep meat nuggets, similar to a typical synthetic antioxidant (hydroxytoluene, HT, 100 ppm), shows clear protection rather than lipidoxidation.(Das et al,2016). The antibacterial quality of polyphenol additions stops the growth of mold and yeast as well as some bacteria as mesophyll, Staphylococcus aureus, and coliforms(Martillanes et al,2020). Furthermore, the food manufacturing industry frequently uses anthocyanin polyphenols as coloring additives (additive number: E163).Albuquerque, et al.(2020) outlined how anthocyanin pigments, which are extracted from berries, can be used to create stable reddish-purple colors and natural colorants in a variety of food matrices.(Baldin et al,2016).

Additionally, polyphenol compounds, or phytochemicals, demonstrate their value in the cosmetics sector.The potential of polyphenols is essential for skin protection and anti-aging (vivo-ad in vitro skin)(Martillanes et al,2020). Owing to its anti-inflammatory qualities, it finds extensive application in cream bases. Additionally, because it inhibits UV radiation, it finds employment in sunblock creams.-Epigallocatechin-3-gallate, which is derived from green tea, stimulates hair growth during chemotherapy treatment(Albuquerque et al,2021), while a polyphenol-rich balm lessens nail damage. Therefore, it is now known that bioactive chemicals have significant positive impacts on

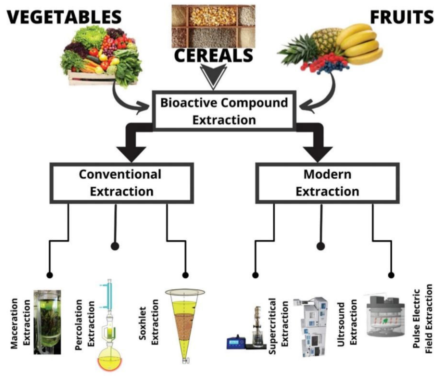

Figure 1. Traditional/Conventional and novel extraction methods used to extract bioactive compounds from different natural Sources.

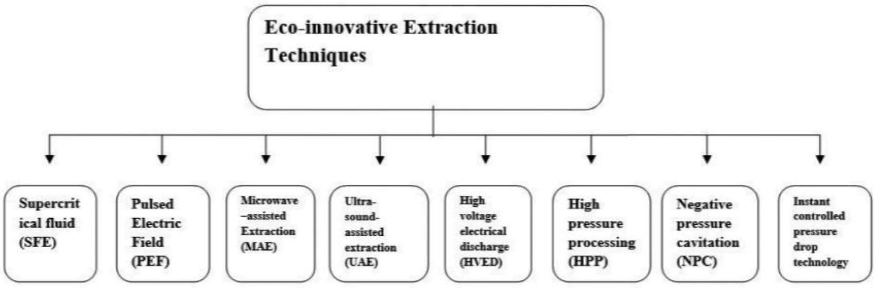

Figure 2. Modern extraction techniques

Table 1. Effect of different extraction techniques on extraction yield of bioactive compounds

Food Products	**Extraction Techniques**	**Process Conditions**	**Extraction Yield of Bioactive Compounds**
Green tea leaves	HHP, UAE	HHP: at 5000 bar, solvent ethanol 50% v/v UAE: 250 W, 20–40°C, 50 Hz for 90 minutes	HHP polyphenol extraction yield 30%, UAE polyphenol extraction yield 29%
Sesame cake	Pulse electric field	13.3 kV/cm, 60°C	Sesame cake Pulse electric field 13.3 kV/cm, 60°C Protein content 30.0–40.0%
Potato peel	SFE	65oC, ethanol 5% v/v as co-solvent	Maximum anthocyanin yield obtained at 65Oc
Carrot	SFE	27.6–55.1MPa, 313–343 K 5% canola oil co-solvent	Beta-carotene extracted 171.7–899.97 μg/g feed
Peach, Apple pomace, sour Che	SFE and HPP	For 10–25-40 minutes SFE: 20–40-60 MPa HHP: For 10–25-40 minute MPa	For cherry pomace optimum conditions, HPP: phenolics: O 3.8 mg GAE/g at

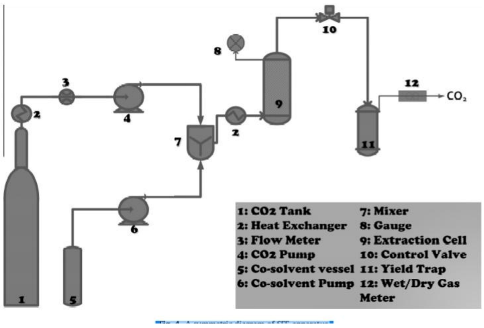

Figure 3. A symmetric diagram of SFE apparatus.

human health, such as antibacterial, antioxidant, anti-inflammatory, anti-cancer, antidiabetic, and wound-healing properties.

Challenges and Future Recommendation

The search for novel extraction methods is a daunting task in the rapidly changing field of medicinal plant science. The limited efficiency and probable destruction of bioactive components associated with existing approaches highlight the need for a paradigm shift in the way we extract therapeutic ingredients from medicinal herbs. To maintain the longevity of medicinal plant research, this challenge calls for interdisciplinary cooperation, ethical sourcing, and sustainable practices in addition to science.Developing extraction techniques beyond the limitations of existing processes is one of the main challenges. Even though they can be somewhat successful, traditional methods frequently lack efficiency and selectivity. Recent research (Smith et al., 2022) has shown that these constraints call for an all-encompassing strategy that takes into account aspects such as selectivity, scalability, and environmental effect. Developing extraction techniques that maintain the sensitive bioactive components that add to the medical potential of medicinal herbs while optimizing yield is crucial.Researchers are looking to novel extraction strategies to overcome these issues, and the incorporation of green extraction techniques is one approach that shows promise. Green extraction techniques like microwave-assisted extraction and supercritical fluid extraction have drawn interest because of their promise to lessen the environmental impact of conventional solvent-based techniques. By using physical procedures or ecologically friendly solvents, these techniques reduce the amount of dangerous chemicals used and encourage sustainability in the extraction process.Future study in this sector must include green extraction as a crucial component, as highlighted by Smith et al. (2022) who highlight the significance of taking the environmental impact of extraction methods into account.Another essential component of the proposals for the future is precision extraction technologies. According to recent research (Jones et al., 2021), focused extraction of particular bioactive chemicals is crucial, which emphasizes the importance of precision in extraction methods. Through the integration of technology that facilitate accurate regulation of extraction parameters, scientists can augment the process' selectivity, guaranteeing the separation of pivotal constituents accountable for the remedial impacts of therapeutic herbs. This accuracy enhances the extraction's effectiveness while also adding to the end product's overall potency and quality.Future methods must include real-time monitoring and control systems during the extraction process. Brown and White (2020) emphasize how crucial it is to make modifications in real-time to optimize crucial factors including temperature, pressure, and extraction time. By putting in place cutting-edge monitoring systems, researchers can respond quickly to changes in the raw materials, guaranteeing uniformity and repeatability in the extraction procedure. To overcome the inherent unpredictability in natural sources and preserve the quality of extracted substances across batches, this adaptability is essential.Furthermore, combining several extraction methods shows to be a strong strategy for optimizing the therapeutic potential of medicinal herbs. Chen and colleagues (2023) highlight the potential for synergistic benefits when combining conventional extraction techniques with contemporary technologies. By combining the best features of several extraction methods, this hybrid strategy seeks to produce an extensive extraction profile that includes a wider range of bioactive substances. Through an awareness of how different techniques complement one another, scientists can create extraction processes that provide a more complete and powerful end product.Scalability is a crucial factor to take into account when creating novel extraction methods. While early research and development must be conducted using laboratory-scale methods, scalability is crucial to fulfilling the growing demand for bioactive chemicals. The creation of extraction techniques that can smoothly go from small-scale laboratory settings to large-scale industrial production must be a part of future initiatives. This scalability makes novel extraction techniques viable for both commercial and academic applications by guaranteeing that their advantages may be realized on a larger scale.To guarantee uniformity and reproducibility, extraction methods must be standardized by the establishment of protocols. The need for meticulous characterisation of extracted chemicals stems from the diversity of therapeutic herbs and plant sources. Addressing the complex issues in the creation of novel extraction processes requires interdisciplinary cooperation. Fostering a comprehensive approach requires collaboration between researchers from several disciplines, including biology, engineering, and chemistry. By integrating knowledge from several disciplines, researchers can develop a more thorough grasp of the intricacies of the extraction procedure. Because of this interdisciplinary synergy, extraction processes that are both technologically and physiologically relevant can be developed, which is in line with the complex nature of medicinal plants and their bioactive components.The direction that medicinal plant research will take in the future will undoubtedly include ethical and sustainable sourcing methods.With the growing demand for bioactive ingredients, it is critical to make sure that medicinal herb sourcing practices support ecological and ethical norms. This entails taking into account how extraction methods affect nearby populations and ecosystems. Researchers help ensure that natural resources are used responsibly by adopting ethical and sustainable sourcing practices. This benefits the communities that grow and gather medicinal herbs as well as the environment.

In conclusion, the challenges and future recommendations in the realm of innovative extraction techniques for medicinal herbs encompass a multidimensional approach. Overcoming the limitations of current methods requires a concerted effort to integrate green extraction techniques, embrace precision technologies, implement real-time monitoring, and explore the synergies between different extraction methods. Scalability, standardization, and the exploration of untapped resources are crucial considerations for the future. Interdisciplinary collaboration, ethical sourcing practices, and a commitment to continuous learning are fundamental principles that guide the development of extraction techniques with enhanced therapeutic potential. By navigating these challenges and adopting forward-thinking strategies, researchers can unlock the full spectrum of bioactive compounds from medicinal herbs, paving the way for advancements in healthcare and pharmaceutical applications.

Author contributions

M.S.S.K. and M.G.D. contributed equally to this work. M.S.S.K. conceived the study and designed the experiment. M.G.D. conducted the data analysis and interpretation. M.S.S.K. provided critical revisions to the manuscript and ensured the accuracy of the final draft. M.G.D. assisted with data collection. All authors reviewed and approved the final version of the manuscript.

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