Trends in Horticulture (2023) Volume 6 Issue 2
doi: 10.24294/th.v6i2.3000

REVIEW ARTICLE

Innovative extraction technologies

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ABSTRACT

The enormous biological potential of herbal products is one of the main reasons for their frequent use in the production of dietary supplements and functional foods, which, in addition to their nutritional properties, have pharmacological and physiological effects. New scientific knowledge on the isolation of pharmacologically active compounds from complex matrices has led to significant advances in this field. Today, the process of extraction plays a significant scientific role, with "green" technologies occupying a special place in today's science. Herbal medicine is one of the oldest human skills, which has worn off with its centuries-old application in the path of modern medicine. Microwave-assisted extraction, or more simply, microwave extraction, is a new extraction technique that combines traditional extraction solvents and microwaves. The mentioned method takes less time, consumes less energy, and has strong penetration power into the plant matrix to obtain more oils, but it can also reduce production costs. This can eventually increase the quality of the final product and reduce the product price at the consumer level. Microwave-assisted extraction could be useful to the herbal industry for oil extraction as well as other pharmaceutically important plant components. Based on a comparison and study of published literature, this research examines the present state of extraction procedures. This review includes a detailed discussion of the most important extraction techniques.

Keywords: extraction techniques; conventional extraction; supercritical extraction; ultrasonic-assisted extraction; microwave-assisted extraction

ARTICLE INFO

Received: 9 October 2023
Accepted: 6 November 2023
Available online: 13 November 2023

1. Introduction

For centuries, medicinal herbs were widely used in folk medicine and nutrition. Herbal medicine is one of the oldest human skills, which has worn off with its centuries-old application in the path of modern medicine.

Natural remedies have been used for thousands of years for the prevention and treatment of human diseases[1].

In the development of new drugs, natural products are often used as the main source. They offer more drug-like properties than molecules from combinatorial chemistry in terms of functional groups, chirality, and structural complexity[2–5].

Medicinal and aromatic plants are an inexhaustible resource of raw materials for the pharmaceutical, cosmetics, and food industries, and recently also for agriculture for pest control[6–9].

A large number of active ingredients of medicinal herbs were isolated in pure form, their chemical structure was determined, and then they were synthesized[10]. However, despite the exceptional success of organic synthesis, a number of pharmacologically active substances have not been synthesized to this day, or their synthesis is only of academic importance[10]. It is undeniably and scientifically demonstrated that extraction and isolation from natural sources are required[11]. In order for the extraction process to be successful, samples and knowledge of the types of connections formed are necessary[11]. Matrix effects were among the least elucidated phenomena in extraction processes. These effects were often unpredictable, and they significantly affected the efficiency of the process. If the analytes were trapped in the matrix by various processes, the extraction efficiency could not be sufficient, even though the compounds were well soluble in the applied solvent.

These phenomena explain the different efficiencies of the same analyte/solvent extraction systems in different samples. Some overcome the extremely pronounced effects of the matrix, which also represents their most significant shortcoming[12].

Traditional extraction techniques include a variety of batch or semi-batch procedures, such as maceration, remaceration, digestion, and percolation, which are prescribed by Pharmacopoeia, or continuous extraction procedures, most often counter-current multistage or differential extractions[13–18].

2. Traditional extraction techniques

Conventional medicinal herb extraction was most often performed using a whole range of easily volatile organic solvents, such as ethyl ether, methylene chloride, chloroform, and benzene[13–19].

These organic solvents are not sufficiently selective because they also dissolve nonvolatile components of large molecular weights, such as resins, fatty components, pigments, and other accompanying components.

Conventional extraction processes are quite laborious and time-consuming, involving large amounts of solvents such as hydrocarbons, alcohols, and chloroalkanes, because most bioactive compounds are insoluble in water and, ultimately, can cause degradation of the target molecule and partial loss of volatile substances[20,21].

Above all, in spite of the high energy consumption and the large amounts of solvents, the yield was often very low[22]. So, it was important to be largely focused on finding solutions that minimize the use of solvents[22].

In summary, traditional extraction techniques require long process times, large amounts of samples, and organic solvents, rendering them uneconomical and unsuitable for sustainable development.

3. Supercritical fluid extraction—Supercritical extraction

3.1. Supercritical fluids

The most commonly used solvents in the traditional methods of extraction process were organic solvents, which have a number of disadvantages and above all, relate to their negative impact on health and the environment. Starting from the last decade of the 20th century until today, there have been more and more efforts to develop considerate technologies towards the environment. The most modern research focuses on the development and application of “clean” technologies.

Special attention was paid to the development of chemical processes that use non-polluting solvents. For that purpose, the use of sub- or supercritical fluids has become more popular[23–25]. Among the many contemporary extraction methods, those that use a fluid under high pressure to facilitate the extraction take a special place in the industry.

Fluids under pressure, or by other definitions, high-diffusion fluids, are actually fluids that are in a state of elevated temperature and pressure, or a state in which they become fluids of high diffuse power.

3.2. Extraction with supercritical fluids

Extraction with pressurized fluids was actually based on the fact that the mass transfer rate can change by changing values of the pressure and temperatures. As the temperature increases, so does the solubility of an analyte, weakening the relationship between the analyte and the matrix from which it was extracted and thus facilitating the diffusion of analytes[26].

An increase in temperature causes a decrease in fluid viscosity, which allows for better penetration into the pores of the matrix. It also leads to a reduction of the solvent's surface tension and better "wetting" of the material.

Such fluids have characteristic physico-chemical properties in relation to floor fluids' ambient conditions. Small changes in fluid density successfully regulate the yield and composition of the extract obtained, so this method of extraction provides an unusual range of possibilities for selective extraction, fractionation, and purification of natural products.

Due to these advantages, fluid extraction with elevated pressure is a good alternative to classical processes of extraction.

Nowadays, extraction methods are mainly focused on providing solutions that minimize usage of solvents[22].

The use of supercritical fluid extraction was an alternative and efficient method of polyphenol extraction. The critical point of a pure substance is defined as the highest temperature and pressure at which a substance can exist in a vapor-liquid equilibrium. When it reaches temperatures and pressures above the critical point, it forms a homogeneous liquid called a supercritical fluid (SCF), which is heavy like a liquid with gas penetrating capability. The reasons mentioned make SCF an efficient and selective solvent[27].

SCF can be efficiently induced by compressing the liquid above the critical pressure or by heating the gas above the critical temperature.

3.3. Supercritical CO_2 extraction

Rosemary essential oil (*Rosmarinus officinalis*) was successfully extracted by Conde-Hernandez et al., by extraction of S-CO_2, hydrodistillation, and steam distillation[28].

The most used SCF was supercritical CO_2, and many other SCFs were used, such as ethane, butane, pentane, nitrous oxide, ammonia, trifluoromethane, and water.

Supercritical CO_2 is a safe and non-toxic method, with a low critical temperature (T_c = 31.1 °C), and the absence of light and air can reduce the risk of decomposition reactions. The critical temperature of the CO_2 mixture increases by adding a co-solvent to the mixture[29].

The addition of a high concentration of ethanol requires extraction to be performed under subcritical conditions of 40–60 °C[30].

Supercritical CO_2 extraction with methanol or ethanol as a co-solvent was used for the extraction of grape seeds[31–33].

CO_2 is not a very good solvent for polar polyphenols as it is itself a polar solvent, but adding organic co-solvents, i.e., methanol, ethanol, and acetone, can increase the dissolving ability of CO_2 and the extraction yield of polyphenols[33–36].

Hydroxycinnamic acid derivatives and coumaric acid derivatives[33] were poorly soluble in supercritical extraction of CO_2 in the absence of a co-solvent, whereas quercetin, catechin, epicatechin, and resveratrol were soluble in supercritical extraction with 5%–30% ethanol[37,38], and anthocyanins were also poorly soluble in subcritical CO_2 + ethanol. Sarmento et al. developed a method of extraction with supercritical fluid, using ethanol or supercritical CO_2 ($scCO_2$) as pure solvent and $scCO_2$ with ethanol as co-solvent, to obtain polyphenols from cocoa beans, which were further concentrated by polymer membranes[39].

SCF was a common extraction method for phenolic compounds. SCF is easily removed from the extract as it evaporates rapidly, and as a non-toxic solvent, it leaves no harmful residues in the extract.

Compounds that are thermally stable as well as the high-boiling components can be extracted at low temperatures using the SCF method.

On the other hand, compounds that are thermally labile can also be extracted with minimal damage at low temperatures.

Even though it brings huge benefits by preserving the structural integrity of polyphenols, large capital investments are necessary to set up this method and equipment, and increased pressure is also required for equipment operation.

4. Ultrasonic assisted extraction

4.1. Ultrasonic waves—Cavitation

Ultrasonic-assisted extraction (UAE), also known as sonication, uses the energy of the ultrasonic wave in the extraction. Furthermore, solvent compression requires intensive recycling measures to reduce energy costs.

With its application, it was possible to achieve higher reproducibility in a shorter period of time compared to traditional extraction techniques[40].

Ultrasonic waves can cause disturbance in plant tissue by physical forces that develop during acoustic cavitation and help release components in a solvent in a very short time by increasing mass transfer[41]. Ultrasound, which creates the cavitation in the solvent, increases solute dissolution and diffusion as well as heat transfer, improving extraction efficiency.

Through cavitation, which is created by the propagation of ultrasound through a medium, microbubbles of air molecules are formed due to the alternating distance and approach of molecules. Rapid compression of air-filled bubbles releases a huge amount of energy, which is characterized by a dramatic increase in temperature and pressure[12]. The advantage of using ultrasound lies in the fact that ultrasonic waves propagate through any medium, and the choice of solvents that can be considered in this type of extraction is quite wide. It should be borne in mind that due to the action of ultrasound, drastic changes occur in the medium itself, and possible dissociation of molecules and the creation of free radicals at the expense of the decomposition of the desired analyte are present at low concentrations in the matrix[12].

What gives the UAE a special advantage is the low energy and solvent consumption, as well as the reduced temperature and extraction time. The UAE is used for the extraction of unstable and thermolabile compounds. Many different types of natural products were extracted by using the UAE[40,42,43].

Ultrasound is a mechanical wave whose frequency (>20 kHz) is greater than the frequency range that a human can hear (20 Hz to 20 kHz). Mentioned waves are composed of a series of compression cycles and dilutions that have the ability to spread through a solid, liquid, or gaseous medium, causing displacement of molecules from their starting points. In a high-intensity sound wave, the negative pressure during dilution transcends the attractive force that binds the molecules together, stretching them and creating cavitation bubbles. These bubbles grow by coalescence and later, in the compression phase, collapse, creating a hot spot and an extreme local condition. The temperature can increase up to 5000 K, and the pressure increase can be up to 1000 atm. These hot spots accelerate biochemical reactions in their vicinity[42,44–46].

The main mechanism involved in ultrasonic extraction is acoustic cavitation. Fragmentation, localized erosion, force and shear, pore formation, increased absorption, and swelling index in the plant matrix can be produced by collapsing cavitation bubbles and sound waves. Cavitation bubbles in the collapse create shock waves, and the accelerated collision between the particles causes fragmentation in the cell structure. Rapid fragmentation causes the solubilization of the bioactive component in the solvent due to reduced particle size, increased surface area, and high mass transfer rates at the interface of the solid matrix[47].

Ultrasound can induce localized impairments in the plant tissues in the process known as erosion. The implosion of cavitation bubbles on the surface of plant tissues can also cause the process of erosion, ultimately resulting in eroded parts that make solvent contact easier, thus increasing the extraction yield[48].

In the process of cavitation, pores can be formed, a phenomenon known as "sonoporation", in cell membranes, which leads to the release of bioactive compounds present in the cell[49–51].

In addition, the formation and collapse of cavitation bubbles lead to shear forces and turbulence in the fluid, resulting in the collapse of cell walls and contributing to the release of the bioactive substance[44,52].

The swelling index of the plant tissue matrix can be increased by ultrasound, which leads to the diffusion of dissolved substances and desorption, ultimately improving and increasing extraction[53].

Extraction yield increase in the UAE cannot be assigned to only one mechanism because of the total effect of all mechanisms. Ultrasonic extraction is broadly used to obtain plants' compounds using water, ethanol, ethanol/water mixture, and acetone[45,54]. The chemical properties needed to be extracted from the components greatly influence the choice of solvent.

4.2. Examples of UAE

In their paper, Audah et al.[55] showed that UAE with ethanol is an effective method, and the mangrove leaves of *Rhizophora mucronata* are a very powerful natural source of antioxidants. Solvent extraction has already been assisted by ultrasound, potentially making ultrasound a very useful tool in the phytopharmaceutical extraction industry. Ultrasonically assisted extraction can be used on both small and large scales[56].

The United Arab Emirates showed specific heed to the UAE. They used the UAE's reducing energy consumption in the context of green chemistry in the evaluation of seme lana (*Linum usitatissimum* L.) as a by-product of linseed oil production[50].

A substantial and fast extraction method has been developed from apple pomace using ultrasound for the extraction of polyphenols[57].

Ultrasonic extraction is also used to recover the active ingredients of plant material and is useful for applications for thermally unstable compounds because it can be performed at low temperatures[58].

The extraction of ginseng (saponin) using ultrasound was about three times faster than the traditional extraction method.

4.3. Advantages and disadvantages of UAE

Compared to other conventional techniques, the application of the ultrasonic bath in industry is cheaper and quite simpler[58].

The UAE method is an efficient, economically profitable, and environmentally friendly method.

The advantages of using UAE can be seen in the possibility of using it for the extraction of thermolabile compounds, increasing the efficiency of the extraction of phenolic compounds, and reducing the extraction time.

The disadvantages of applying UAE are a decline in power over time and a decline in uniformity in the distribution of ultrasonic energy[59].

The UAE method can be applied to aqueous extraction where generally recognized organic solvents can be replaced by organic solvents, which can reduce the use of solvents. Also, the UAE method can be used with existing equipment (ultrasonic bath) with minimal changes in its structure.

5. Microwave-assisted extraction

One of the most advanced techniques used to extract natural products from plant material is microwave-assisted extraction (MAE).

5.1. Advantages and disadvantages of MAE

The MAE method is a fast extraction method in which less solvent is used for the extraction of thermolabile ingredients[60].

Microwave energy is a non-ionizing electromagnetic wave. Non-ionizing electromagnetic wave has a frequency between 300 MHz and 300 GHz, so it produces dipole rotation and ion migration by molecular movement[61,62].

The MAE principle is based on the ionic conductivity of molecules and dipole rotation. Polyphenols and ionic solutions, since they have a dipole moment, absorb microwave energy, and thus there is a rapid increase in temperature, which leads to a rapid completion of the reaction[63–65].

The reason why solvent polarity is an important factor is that solvents with high dielectric constants absorb much more microwave energy. That's why polar solvents are usually better than non-polar solvents[66].

Microwave extraction of phenol is not efficient as compared to conventional methods with water. The reason for this is that the extraction also depends on the type of extracted plant material and solvents used for extraction. Solvents that have a high dissipation factor and a high solvent dielectric constant should be used. Considering that water, compared to other solvents, has a low dissipation, higher dielectric constant, and low dissipation factor, microwave extraction of phenol with water is not efficient compared to conventional methods.

Also, compared to methanol and acetone, methanol has a higher dissipation factor and a higher dielectric constant. That's why polyphenol microwave extraction was found to be more efficient with acetone than methanol[67].

Microwave extraction can be conducted at atmospheric pressure. The reason for this is that MAE, in the presence of ionic species or polar molecules, provides rapid warming, leading to collisions with surrounding molecules[68].

5.2. Examples of MAE

MAE was used to extract polyphenols from a variety of plant sources, thus at tea leaves, vanilla, flaxseed, radishes, and others[69–71].

To a large extent, the effect of microwave energy depends on the solid plant matrix and on the dielectric sensitivity of both solvents. By using MAE, the sample is immersed in a mixture of solvents or a solvent that firmly absorbs microwave energy, increasing the temperature expansion and penetration of the solvent into the matrix, which leads to the release of the ingredients into the surrounding hot solvent[72,73].

Using MAE for the extraction of polysaccharides, many activities in vivo and in vitro have been proven, for example, antiradical, antifungal, and antiviral[74].

By using MAE from raw *Calophyllum inophillum*, very purified triglycerides (TG) have been obtained. Biodiesel obtained by this method is of lower quality. However, since it is a green method that reduces the extraction time, this method has become the potential method for the production of biodiesel[75].

The economy and landfill reduction may be relevant in the future with a study on adding value to red and white pomace on an industrial scale to apply the MAE methodology, which is more energy efficient and time efficient and can restore phenols and colour to commercial value[76].

The use of MAE in industry is very significant. The reason for this is the reduction in the extraction time of polyphenolic compounds (ellagic acid and apigenin)[77]. For metal immobilization, MAE gave a high-efficiency metal extraction, e.g., for the extraction of Pb, Co, Cd, Ba, and Cr[78].

Microwave-assisted extraction has many advantages, such as reducing energy consumption, extraction time, and solvents.

6. Conclusion

Microwave-assisted extraction is a new method. MAE has many advantages over other extraction methods. Some of the advantages are reduced use of solvents, shorter time extraction, higher speed extraction, mixing during the process as well as higher yield extraction.

Disadvantages of the MAE extraction method (if fine particles are used for extraction) are the sample filtration and the high capital costs.

The main advantage of MAE lies in the performance of the heating source.

The advantages of the MAE method of extraction are the high temperatures achieved by microwave heating, as this reduces the number of solvents and the time of extraction.

Also, the advantage of the MAE method is its ability to rapidly heat a sample of a solvent mixture.

From an economic aspect as well as a practical aspect, the MAE method is a very good and strong competitor to newer techniques of sample preparation.

Author contributions

DPI: funding acquisition, project administration, conceptualization, resources, methodology, supervision, visualization, formal analysis, investigation, writing—original draft, writing—review & editing; DV: writing—review & editing.

Acknowledgments

The part of the research reported in the paper was realized according to the research co-financed to the Program for financing scientific research work, number 451-03-47/2023-01/200102 from the Republic of Serbia (Ministry of Education, Science and Technological Development).

Conflict of interest

The authors have no competing interests to declare that are relevant to the content of this article.

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