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Comparative analysis of extraction methods for bioactive compounds in aromatic and medicinal plants

Análisis comparativo de los métodos de extracción de compuestos bioactivos en plantas aromáticas y medicinales

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ABSTRACT

The main extraction techniques for bioactive compounds from aromatic and medicinal plants include maceration, distillation, supercritical CO_2, and ultrasound. These methods can be differentiated based on their efficiency, sustainability, and their ability to extract and preserve compounds such as essential oils, which primarily contain flavonoids and terpenes. Traditional methods, such as maceration and distillation, are useful for extracting heat-sensitive and volatile compounds but have limitations in terms of time and energy consumption. In contrast, modern techniques, such as supercritical CO_2 and ultrasound, are more efficient and environmentally friendly, enhancing compound preservation and significantly reducing environmental impact; however, they are more costly than the other methods. Nevertheless, recent research has shown a significant increase in studies on supercritical CO_2 and ultrasound, along with their growing adoption in industries such as cosmetics, food, pharmaceuticals, and biotechnology.

Keywords: Bioactive compounds; maceration; distillation; supercritical CO_2; ultrasound.

RESUMEN

Las principales técnicas de extracción de compuestos bioactivos de plantas aromáticas y medicinales incluyen la maceración, la destilación, la extracción con CO_2 supercrítico y la aplicación de ultrasonido. Estos métodos se diferencian por su eficiencia, sostenibilidad y capacidad para extraer y preservar compuestos como los aceites esenciales, que contienen principalmente flavonoides y terpenos. Los métodos tradicionales, como la maceración y la destilación, son útiles para extraer compuestos volátiles y sensibles al calor, pero presentan limitaciones en cuanto a tiempo y consumo energético. En cambio, las técnicas modernas, como la extracción con CO_2 supercrítico y la aplicación de ultrasonido, son más eficientes y respetuosas con el medio ambiente, mejoran la preservación de los compuestos y reducen significativamente el impacto ambiental; sin embargo, son más costosas. No obstante, investigaciones recientes han mostrado un notable aumento en los estudios sobre la extracción con CO_2 supercrítico y la aplicación de ultrasonido, así como su creciente aplicación en industrias como la cosmética, la alimentaria, la farmacéutica y la biotecnológica.

Keywords: Bioactive compounds; maceration; distillation; supercritical CO_2; ultrasound.

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1. Introduction

In the last decade, the extraction of bioactive compounds from aromatic and medicinal plants has gained increasing relevance due to the growing interest in natural products for the pharmaceutical, cosmetic, food, and biotechnological industries. These compounds, among which flavonoids, terpenes, and phenols stand out, have been shown to possess highly important antimicrobial, antioxidant, and anti-inflammatory properties in the aforementioned industries (Azmir et al., 2013; Herrero et al., 2010). Traditional techniques, such as maceration and distillation, remain commonly used for the extraction of certain types of compounds; however, modern methods such as supercritical CO_2 and ultrasound have demonstrated significant advantages in terms of efficiency and sustainability, particularly due to their ability to preserve heat-sensitive compounds and reduce environmental impact (Wang & Weller, 2006). As efforts continue to improve extraction processes, these advanced techniques have been extensively investigated, with numerous recent scientific publications highlighting their potential.

2. Bioactive compounds

Currently, bioactive compounds are substances present in plants in small quantities; however, they hold great relevance for human health, as they possess biological properties that can be beneficial, such as antioxidant, antimicrobial, anti-inflammatory, and anticancer activities (Samtiya et al., 2021). These compounds can be found across various chemical classes, with essential oils, flavonoids, alkaloids, terpenes, phenols, and tannins being particularly abundant in aromatic and medicinal plants (Kapadia et al., 2022).

Essential oils are mixtures of volatile compounds mainly extracted from the leaves, flowers, or roots of aromatic plants. These oils are composed of terpenes, such as limonene, and aldehydes, such as citral, and are widely used in the cosmetic industry due to their antimicrobial and aromatic properties, as noted by Bakkali et al. (2008). Flavonoids, on the other hand, represent one of the most important classes of bioactive compounds; they are polyphenols well known for their antioxidant activity and their role in protecting against cardiovascular diseases as well as certain types of cancer (Panche et al., 2016). Alkaloids, such as morphine and caffeine, are nitrogen-containing compounds recognized for their biological activity, including analgesic and stimulant effects, and have historically been used as a basis for drug development (Yang & Stöckigt, 2010). Other important bioactive compounds include terpenes, which, in addition to being responsible for the aromatic characteristics of plants, also have applications in the production of pharmaceuticals, cosmetics, and food products (Ben Salha et al., 2021). Phenols and tannins, in turn, are known for their antioxidant capacity and are mainly found in leaves, barks, and fruits, where they play a role in protecting plants against oxidative stress (Gallego et al., 2013).

3. Overview of extraction techniques

The extraction of bioactive compounds from aromatic plants can be carried out using both conventional and modern techniques, each with its own specific characteristics. Traditional methods, such as maceration and steam distillation, have been widely used for centuries to obtain secondary metabolites of pharmaceutical and cosmetic importance (Seidel, 2005). Maceration involves immersing plant material in solvents at room temperature or slightly elevated temperatures, making it a useful method for extracting thermosensitive compounds such as flavonoids and phenols; however, its efficiency may be limited by the prolonged time required to achieve complete extraction (Martins et al., 2023). Steam distillation, on the other hand, is mainly used for the extraction of essential oils and other volatile compounds, being ideal for plants such as rosemary (*Rosmarinus officinalis*) and lavender (*Lavandula angustifolia*). Nevertheless, this method is not suitable for non-volatile compounds or for those sensitive to heat (Boateng et al., 2023).

Modern techniques, such as supercritical CO_2 extraction and ultrasound-assisted extraction, have been developed to overcome some of the limitations of traditional methods. Supercritical CO_2 extraction employs carbon dioxide in its supercritical state to dissolve and extract bioactive compounds with high purity and selectivity, without the use of toxic solvents; however, its high cost has limited its large-scale adoption (Arumugham et al., 2021; Del Valle, 2015). Ultrasound-assisted extraction, on the other hand, uses ultrasonic waves to disrupt plant cell walls, thereby accelerating the release of bioactive compounds and reducing solvent consumption, proving effective for the extraction of antioxidants and terpenes (Wen et al., 2018). These modern techniques, together with the combination of different approaches, such as the use of ultrasound followed by supercritical extraction, have demonstrated greater sustainability and efficiency in terms of energy and time, while also enabling the extraction of a broader range of bioactive compounds (Boateng et al., 2023).

3.1 Maceration

Maceration is considered a traditional extraction process and consists of immersing plant material in a solvent, generally ethanol, methanol, or water, at room temperature or slightly elevated temperatures, for a prolonged period of time. It is particularly used for the extraction of thermosensitive bioactive compounds (Figure 1), such as flavonoids, tannins, and phenolic compounds, which could degrade at higher temperatures (Lezoul et al., 2020). The solvent penetrates the plant cells, dissolving the bioactive compounds, which are subsequently recovered after solvent evaporation (Martins et al., 2023). Regarding the compounds extracted through this process, maceration is especially effective for obtaining flavonoids, phenols, and tannins, all of which are known for their antioxidant and anti-inflammatory activity, as reported by Mena et al. (2016) in the case of such compounds in leaves and flowers of rosemary (*Rosmarinus officinalis*). This method has also been used to extract alkaloids and glycosides from various plant species, although its efficiency may depend on the polarity of the solvent employed, as reported by Kaiser et al. (2013). In terms of operation, the duration of the process varies considerably, ranging from a few hours to several days or weeks, depending on the type of compound to be extracted and the nature of the plant material. Although it is a low-cost and easy-to-implement method, its main drawback lies in the long time required to complete extraction and the intensive use of solvents, which can increase costs in large-scale operations (Chen et al., 2016).

3.2 Steam distillation

Steam distillation is one of the most widely used methods for the extraction of bioactives such as essential oils, as it enables the efficient recovery of volatile compounds (Figure 2), including terpenes and alcohols, such as those found in plants like Origanum compactum (El Kharraf et al., 2021). This process allows the separation of volatile compounds, such as terpenes and alcohols, through steam, facilitating extraction without significant thermal degradation of active compounds (Chemat et al., 2012). Essential oils obtained by this method exhibit high purity, which is crucial for their use in the pharmaceutical, cosmetic, and food industries due to their antimicrobial and antioxidant properties (Bakkali et al., 2008).

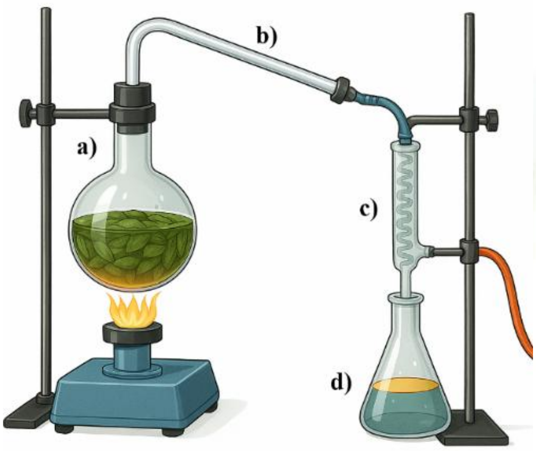

Figure 2. Steam distillation process: heating (a); conduction of steam with volatile compounds (b); condenser with coil and water circulation for cooling (c); phase separation of water and essential oil (d).

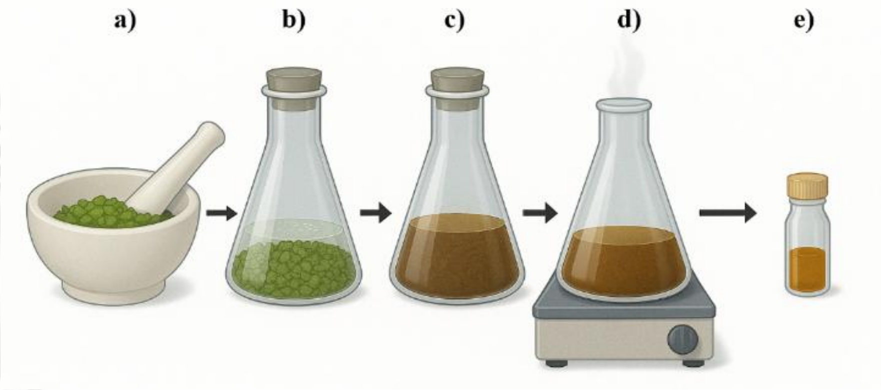

Figure 1. Maceration process of plant material: grinding of plant material in a mortar (a); immersion of the ground material in solvent (b); maceration stage evidenced by color change (c); concentration of the extract through heating with partial solvent evaporation (d); concentrated active compound (e).

Nevertheless, this method has limitations, as it is not suitable for the extraction of non-volatile or heat-sensitive compounds, such as flavonoids or phenolic compounds, thereby restricting its application to certain types of metabolites (Azmir et al., 2013). Moreover, steam distillation requires higher energy consumption compared to other methods, such as maceration, which can translate into higher costs and lower sustainability in industrial implementation (Raut & Karuppayil, 2014). Recent studies have shown that steam distillation is particularly efficient for obtaining essential oils with antimicrobial properties, as in the case of *R. officinalis* oil, which has demonstrated significant effects against pathogenic bacteria (Sharifi-Rad et al., 2017).

3.3 Supercritical CO_2

Supercritical carbon dioxide (CO_2) extraction is a modern technique that has gained relevance due to its efficiency and high selectivity in extracting bioactive compounds from aromatic plants. In this method, CO_2 in its supercritical state is used as a solvent capable of penetrating plant material (Figure 3) and dissolving compounds such as essential oils, flavonoids, and terpenes without the need for organic solvents (Pourmortazavi & Hajimirsadeghi, 2007). Furthermore, supercritical CO_2 extraction is particularly useful for obtaining compounds sensitive to heat and oxygen, as it operates at relatively low temperatures, thereby preserving the integrity of bioactive metabolites (Herrero et al., 2013). This method has been successfully applied in the extraction of essential oils from plants such as *Origanum vulgare* and *Salvia officinalis*, demonstrating high purity and efficiency (Fornari et al., 2012). Although this process is considered cleaner and more environmentally friendly compared to conventional methods, its main drawback lies in the high initial costs associated with the technology required to handle CO_2 in its supercritical state and the extreme pressures necessary for its operation (Chemat et al., 2012). Nevertheless, the high purity of the extracts and the possibility of adjusting pressure and temperature conditions to target specific compounds are significant advantages that have driven their adoption in the pharmaceutical and food industries, particularly for obtaining bioactive compounds with antimicrobial and antioxidant applications (Herrero et al., 2010).

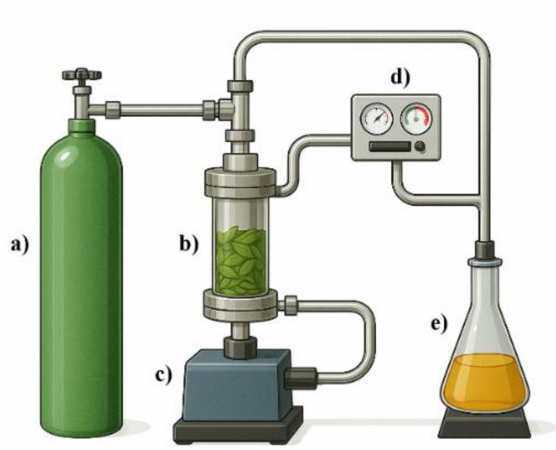

Figure 3. Supercritical CO_2 extraction: compressed CO_2 cylinder (a); extractor with plant material (b); high-pressure pump (c); pressure and temperature control system (d); collector with concentrated extract (e).

3.4 Ultrasound

Ultrasound-assisted extraction is an emerging technique used for obtaining bioactive compounds from aromatic and medicinal plants, based on the use of ultrasonic waves to generate cavitation in the solvent (Figure 4), thereby facilitating the release of metabolites from the plant matrix (Chemat & Khan, 2011). This technique is employed for the extraction of phenolic compounds, flavonoids, and essential oils, and has been applied to plants such as *R. officinalis* and *Thymus vulgaris*, showing high yields within a reduced time compared to conventional methods (Wang & Weller, 2006).

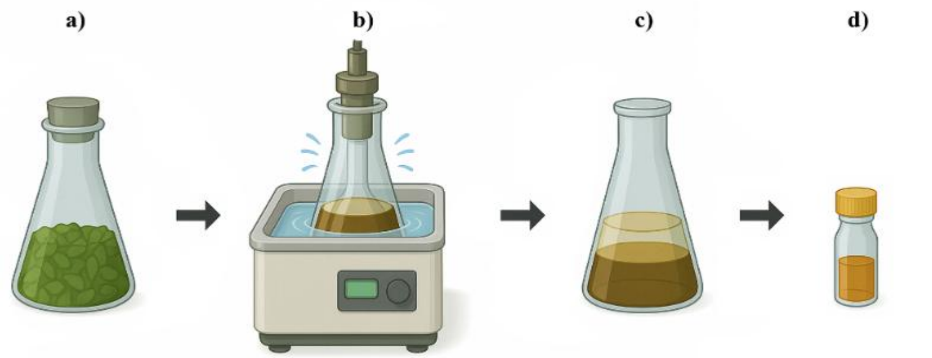

Figure 4. Ultrasound-assisted extraction process: plant material (a); treatment in ultrasonic bath (b); extract recovery with phase separation (c); concentrated active compound (d).

The cavitation generated by ultrasound disrupts plant cell walls, enabling greater release of active compounds even at low temperatures, thus preserving the integrity of heat-sensitive compounds (Zhang et al., 2018). One of the main advantages of this method is its low cost, operational simplicity, and reduced extraction time; however, its effectiveness may depend on variables such as ultrasonic wave intensity, treatment duration, and the type of solvent used, requiring proper optimization for each plant and compound (Chemat & Khan, 2011). This technique has been highlighted as a promising alternative for the extraction of essential oils in the cosmetic and pharmaceutical industries, where extract quality and purity are fundamental (Wang & Weller, 2006).

4. Importance of bioactive compound extraction methods

The efficiency and quality of compounds extracted from plants largely depend on the extraction method employed, as each technique varies in its ability to preserve the chemical integrity of the compounds (Table 1). Furthermore, the selection of an extraction technique must consider factors such as the thermolability and volatility of the target metabolites, as well as the nature of the solvent and the extraction conditions (Azmir et al., 2013; Jokić et al., 2018).

Over the years, methods such as maceration, distillation, supercritical CO_2 extraction, and ultrasound have been widely studied and applied due to their unique characteristics and their ability to extract different groups of bioactive compounds.

Table 1
Comparison of bioactive compound extraction techniques: principles, plants, and key bioactives

Technique	Principle	Processed plants and bioactives obtained	Sources
Maceration	The plant is immersed in a solvent for a prolonged period at room or slightly elevated temperature.	Lavender (*Lavandula angustifolia*): linalool, linalyl acetate, cineole, geraniol, borneol, and camphor. Chamomile (*Matricaria chamomilla*): apigenin, bisabolol, luteolin, quercetin, chamazulene, and various flavonoids. Peppermint (*Mentha piperita*): menthol, menthone, pulegone, cineole, limonene, and flavonoids.	Azmir et al., (2013); Uwineza & Waśkiewicz, (2020).
Steam distillation	Steam passes through the plant material, carrying volatile compounds, which are then condensed and separated.	Thyme (*Thymus vulgaris*): thymol, carvacrol, linalool, borneol, flavonoids, and rosmarinic acid. Eucalyptus (*Eucalyptus globulus*): 1,8-cineole, limonene, α-pinene, globulol, and citronellal. Camphor tree (*Cinnamomum camphora*): camphor, safrole, cineole, terpineol, and pinene. Star anise (*Illicium verum*): anethole, safrole, limonene, cineole, and terpineol. Cypress (*Cupressus sempervirens*): α-pinene, δ-3-carene, cedrol, cadinene, and germacrene.	Azzaz et al., (2019; Guo et al., (2016); Shiferaw et al., (2019).
Supercritical CO_2	CO_2 in its supercritical state acts as a solvent to extract bioactive compounds, operating at critical pressures and temperatures.	Basil (*Ocimum basilicum*): eugenol, linalool, cineole, methyl chavicol, and rosmarinic acid. Fennel (*Foeniculum vulgare*): anethole, fenchone, estragole, limonene, and α-pinene. Sage (*Salvia officinalis*): carnosic acid, carnosol, rosmarinic acid, cineole, and camphor. Clove (*Syzygium aromaticum*): eugenol.	Coelho et al., (2003); Filip et al., (2016); Jokić et al., (2018).
Ultrasound	Ultrasonic waves generate cavitation in the solvent, breaking cell walls and facilitating the release of compounds.	Green tea (*Camellia sinensis*): epigallocatechin, catechin. Cardamom (*Elettaria cardamomum*): γ-terpinyl acetate, 1,8-cineole, limonene, borneol. Turmeric (*Curcuma longa*): β-turmerone, ar-turmerone, zingiberene, curcumin.	Bindes et al., (2019); Sereshti et al., (2012); Hwang et al., (2016).

These methods differ not only in their operational principles but also in their environmental impact, operational costs, and capacity to extract compounds with medicinal and functional properties (Chemat et al., 2012; Herrero et al., 2010).

Research on these methods for extracting bioactive compounds has been extensive and diverse over the past decades, with each method being the subject of numerous studies due to its specific capacities to extract compounds with varied properties and industrial applications. According to Yıldırım et al. (2024), the use of supercritical CO_2 for obtaining bioactives has accounted for more than 7,800 studies in the Scopus database between 2000 and 2024, confirming its relevance in natural product research. Ultrasound, in turn, has also gained popularity in the last decade; as reported by Rahman & Lamsal (2021), approximately 5,000 publications had been registered up to 2024, focusing mainly on the extraction of phenolic compounds and flavonoids. Regarding distillation, this traditional method continues to be fundamental for the extraction of essential oils and volatile compounds, with around 4,000 studies published up to 2024, demonstrating its persistence in the scientific field (Yıldırım *et al*., 2024).

Finally, maceration, although slower and less efficient compared to modern methods, remains useful for the extraction of non-volatile and thermosensitive compounds such as flavonoids, with approximately 3,000 publications reported between 2000 and 2024 (Herrero et al., 2010), highlighting its continued application in research involving medicinal plants. This comparative analysis underscores the evolution of these extraction techniques and their impact across various industries. The most recent methods, such as supercritical CO_2 and ultrasound, have shown considerable growth in research, while traditional techniques such as distillation and maceration continue to hold an important place in the extraction of specific compounds.

5. Conclusions

The review of the main techniques for extracting bioactive compounds highlights the effectiveness of traditional methods such as maceration and steam distillation, which, although useful for heat-sensitive and volatile compounds, present various limitations in terms of efficiency and processing time. However, more modern techniques such as supercritical CO_2 extraction and ultrasound have proven to be more sustainable and efficient, offering high selectivity and lower environmental impacts. These techniques have experienced a significant increase in recent research, with publications reflecting their growing relevance in industries such as cosmetics, food, and pharmaceuticals. Current trends indicate that while traditional methods continue to play an important role in the extraction of certain compounds, advanced methods are leading the evolution towards faster and more efficient processes.

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