



## Review Article

# Recent updates on extraction techniques of bioactive compounds

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### ABSTRACT

Bioactive compounds obtained from different natural resources and showed valuable effects in the treatment of various diseases. Extraction processes for these compounds depend on various factors such as the organic solvent, technique that is used, and the raw material. This review focuses on the extraction of bioactive compounds from food by-products of plant origin by a number of novel methods. The various extraction techniques and their recent updates have been summarized to reduce the economic and ecological impact of these processes. In the present review, we tried to explore some novel things related to these techniques with their schematic presentation, which may be helpful for the researchers for selecting right path for extraction of bioactive compounds.

**Keywords:** Extraction methods, bioactive compounds, soxhlet extraction, enzyme-assisted extraction, ultrasonic extraction

## INTRODUCTION

Bioactive compounds are important nutritional factors that are found in small amounts in foods and food products, and imparting numerous health benefits beyond the essential nutritional value of the products.<sup>[1]</sup> Bioactive compounds have different activities such as antioxidant, anticarcinogenic, antimicrobial, and anti-inflammatory, which can be exploited using foods and pharmaceutical industries.<sup>[2]</sup> They are studied to evaluate their impact on health and found beneficial physiological, immunological, and behavioral effects.<sup>[3]</sup> Bioactive compounds are valuable components of plant products that decreased the risk of developing various diseases such as cancer, Alzheimer's, cataracts, and Parkinson's.<sup>[4]</sup> In recent times, several bioactive compounds have been discovered.<sup>[5]</sup> These compounds vary broadly in chemical form and characteristics and are grouped accordingly.<sup>[6]</sup> A few examples of bioactive compounds are flavonoids, carnitine, choline, coenzyme Q, dithiolthiones, phytosterols, phytoestrogens, glucosinolates, polyphenols, and taurine.<sup>[7]</sup> As bioactive compounds are found in all plants, almost all researches related to the extraction<sup>[8]</sup> of bioactive compounds focus on bioprospecting for new plant varieties to serve

as sources of these compounds.<sup>[9]</sup> However, the extraction of these bioactive compounds is challenging because they can be unstable and biological activity can be affected by both extraction process parameters and external factors such as the presence of oxygen and light.<sup>[10]</sup> In recent years, the bioactive compounds have been extracted using many conventional and non-conventional extraction methods, including maceration, decoction (DC), percolation, Soxhlet extraction, pulsed electric field extraction, enzyme-assisted extraction (EAE), pressurized liquid extraction (PLE), ultrasonication-assisted extraction (UAE), ultra high-pressure extraction, and supercritical fluid extraction (SFC).<sup>[11,12]</sup> Conventional extraction techniques generally require a long time, higher solvent volume consumption.<sup>[13]</sup> Non-conventional extraction techniques have higher, more selective product recovery, less time consuming.<sup>[14]</sup> For laboratory scales and industrial, achieved pure extraction yield using this method.<sup>[15]</sup> These processes are recognized as environmentally friendly and are associated with short extraction times and low solvent consumption rates.<sup>[16]</sup> A recent study updated by Lee *et al.*, 2017, given maceration and Soxhlet extraction of oil from leaves of agarwood consisting bioactive compounds squalene, n-hexadecanoic acid, phytol, and octadecatrienoic acid using different temperature and solvent systems showed different retention time. The result gives the highest oil yield with longer retention time using maceration.<sup>[17]</sup> Vitor *et al.*, 2019, reported extraction of monomeric anthocyanins and total phenolic compounds in dried grape marc by PLE extraction method with

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set a temperature 40–100°C using a mixture of ethanol and water. As a result of this extraction of phenolics compounds, monomeric anthocyanins in sequence have been discovered. The results were applicable for the recovery of two different extract fractions.<sup>[18]</sup> This review showed the updates of different extraction methods of bioactive compounds with their details in recent developments. It includes the characteristics, extraction of bioactive compounds, and parameters influencing different extraction methods [Table 1]. The uses of different solvents for the extraction of bioactive compounds are summarized in Table 2. Different extraction processes with their application, advantages, disadvantages with recent studies of bioactive compounds are described in Table 3.

## EXTRACTION OF BIOACTIVE COMPOUNDS

The numerous variations between bioactive compounds and a large number of plant species have been identified. We need to build up the quality of different extraction approaches with screen out compounds with significant human health benefits.<sup>[19]</sup> Different integrated approaches have been used in the plant study with its use in industry.<sup>[20]</sup> A specific sequence of works for the study of medicinal plants and the role of extraction procedures have been described in the present manuscript. It is only possible to conduct further separation, identification, and characterization of bioactive compounds followed by a suitable extraction process.<sup>[19,21]</sup> Different extraction methods

used various conditions to aware the extraction selectivity from a variety of natural sources. There are different types of extraction techniques which are available in which most of the techniques are used for hundreds of years for extracting bioactive compounds. These techniques are used with common objectives, that is, extraction of targeted bioactive compounds from plant samples,<sup>[19,21,22]</sup> to enhance the selectivity of analytical methods,<sup>[19,23]</sup> and enhance the bioassay sensitivity by increase the concentration of the targeted compounds, to convert<sup>[24]</sup> into a more suitable form of separation,<sup>[19,25]</sup> and detection of bioactive compounds, that are given a reproducible and effective method that freely differentiates of the sample matrix.<sup>[26]</sup>

## BIOACTIVE COMPOUNDS

The history of plants used for mankind is old as the start of humankind, people used plants for their nutritional purpose but after the invention of medicinal functions and properties,<sup>[27]</sup> this natural flora becomes a useful source of disease and health improvement across various peoples.<sup>[28]</sup> Egyptian papyruses showed that coriander was useful for cosmetics and thousands of recipes, secondary plant metabolites are produced as bioactive compounds.<sup>[19,29]</sup> All compounds are related to the biological system divided into two types, first one is primary metabolites and the second one is secondary metabolites.<sup>[30]</sup> In primary metabolites, chemical substances have goals and objectives to growth and development of proteins and carbohydrates,<sup>[31]</sup> whereas in secondary metabolites, a group of active compounds helps to

**Table 1: A summary of various extraction methods for active constituents**

Extraction methods	Choice of solvents	Temperature	Pressure	Extraction time	Consumed volume of organic solvent	Extracted bioactive compounds polarity
Maceration	Hexane, dichloromethane, acetone, ethanol, and water	High	High	Long	More	Non-polar compound
Percolation	Acetone, methanol, butanol, and water	Low	High	Long	More	Depend on extracting solvent
DC	Water	High	High	Short	None	Polar compounds
Soxhlet extraction	Hexane/dichloromethane, dichloromethane/light petroleum, cyclohexane/acetone or hexane/acetone, and methanol,	High	High	Long	Lower	Depend on extracting solvent
PLE	Water, aqueous, and non-aqueous solvents	High	High	Short	More	Depend on extracting solvent
SFC	Hexane, pentane, butane, nitrous oxide, sulfur hexafluoride, and fluorinated hydrocarbons	High	High	Short	None or lower	Non-polar to polar compounds
Ultrasound-assisted extraction	Ethanol, ethyl acetate, and butanone	Low	High/low	Short	More	Depend on extracting solvent
Accelerated assisted extraction	Methanol, ethanol, acetone, and water	Elevate	High	Short	Lower	Depend on extracting solvent
EAE	Hexane, dichloromethane	Low	High	Short	Lower	Depend on extracting solvent
Ultra high-pressure extraction	Ethanol, methanol	High	High	Long	Lower	Non-polar compounds

DC: Decoction, EAE: Enzyme-assisted extraction, PLE: Pressurized liquid extraction, SFC: Supercritical fluid extraction

**Table 2: Some solvents use in bioactive compounds extraction**

Solvents	Ether	Ethanol	Methanol	Water	Chloroform	Acetone	Dichloromethane
Plant constituents	Alkaloids Terpenoids	Tannins Polyphenols Flavonoids Alkaloids	Terpenoids Anthocyanins Tannins Saponins Flavonol Terpenoids Polyphenols	Anthocyanins Tannins Saponins Terpenoids	Terpenoids Flavonoids	Flavonoids	Terpenoids

**Table 3: Advantages and disadvantages of various extraction methods**

Model	Advantages	Disadvantages
Maceration	<ol style="list-style-type: none"> <li>Using non-complicated utensils and equipment, maceration is a simple procedure</li> <li>A trained operator is not required. Phase of energy saving</li> <li>It is suitable for those compounds that are much less soluble in the solvent and require only continuous solvent contact</li> <li>Effective technique for less potent and inexpensive drugs</li> </ol>	<ol style="list-style-type: none"> <li>The period of the extraction time is usually long and often takes up to weeks</li> <li>Not to remove the drug exhaustively</li> <li>It is a time consuming and very slow process</li> <li>Using more solvents</li> </ol>
Percolation	<ol style="list-style-type: none"> <li>It takes less time to macerate</li> <li>It may be necessary to remove thermolabile constituents</li> <li>An effective method for drugs that are potent and expensive</li> <li>Short time and more complete extraction</li> </ol>	<ol style="list-style-type: none"> <li>It takes more time than soxhalation</li> <li>Required more solvent</li> <li>A skilled person is required</li> <li>The particle size of the material and in the process should receive special attention</li> </ol>
DC	<ol style="list-style-type: none"> <li>Suitable for heat stable compound extraction</li> <li>This technique does not include the more and more costly equipment. It is straightforward to do</li> <li>No need for a trained operator</li> </ol>	<ol style="list-style-type: none"> <li>Unfortunately, the extraction of heat-sensitive constituents is not recommended</li> </ol>
Soxhlet extraction	<ol style="list-style-type: none"> <li>Significant quantity of plant material</li> <li>It can be extracted at a particular time</li> <li>Solvent can be used repeatedly</li> <li>After extraction, this process does not require filtration</li> <li>This process is not based on the matrix</li> <li>It is a process that is very simple</li> <li>Displacement of the shift equilibrium by bringing fresh solvent into contact with the solid matrix repeatedly</li> </ol>	<ol style="list-style-type: none"> <li>For a relatively long period of time, the samples are heated to a high temperature, so the risk of thermal destruction of certain compounds cannot be ignored if the plant material contains heat-labile compounds</li> <li>The time for extraction is long and the method is labor intensive</li> <li>Manipulations of specific variables are allowed in the process</li> <li>A wide evaluation of the Soxhlet extraction technique results in the time and requirement of a large amount of solvent</li> </ol>
PLE	<ol style="list-style-type: none"> <li>Using less solvent</li> <li>Less time of extraction</li> </ol>	<ol style="list-style-type: none"> <li>Not suitable for thermolabile components</li> </ol>
Sonication extraction	<ol style="list-style-type: none"> <li>Efficient large-scale commercial instrument</li> <li>Applications decreased working time and ease of use improved yield, reduced consumption of solvents, and high quality of extracts</li> </ol>	<ol style="list-style-type: none"> <li>Only the range of the ultrasonic emitter is the active component of the ultrasound</li> <li>The presence of a distributed phase leads to the attenuation of ultrasound waves</li> <li>Weak impact on oil extraction</li> </ol>

(Contd...)

**Table 3: (Continued)**

Model	Advantages	Disadvantages
Ultra high-pressure extraction	<ol style="list-style-type: none"> <li>Short extraction time</li> </ol>	<ol style="list-style-type: none"> <li>Compound impurity issues.</li> </ol>
SFC	<ol style="list-style-type: none"> <li>The pressure and/or temperature influence the dissolving capacity of the SCF</li> <li>Due to its instability, SCF is quickly recoverable from the extract</li> <li>Non-toxic solvents leave no residue that is harmful</li> <li>At relatively low temperatures, high boiling components are removed</li> <li>Sometimes, separations that are not achievable by more conventional methods may be affected</li> <li>Low temperatures can be used for extraction, thermally labile compounds can be extracted with minimal damage</li> </ol>	<ol style="list-style-type: none"> <li>High pressure is needed</li> <li>It requires solvent compression</li> <li>To reduce energy costs, elaborate recycling system</li> <li>Significant investment of resources in equipment</li> </ol>
Accelerated solvent extraction	<ol style="list-style-type: none"> <li>Potential SFC alternative technique for polar compound extraction</li> <li>Reduce the production and extraction time of solvents</li> </ol>	<ol style="list-style-type: none"> <li>Only suitable for the extraction of a high-temperature stable compound</li> </ol>
EAE	<ol style="list-style-type: none"> <li>High product yield</li> <li>Reduce by-product formation</li> <li>Avoid severe operational conditions</li> </ol>	<ol style="list-style-type: none"> <li>High capital cost of equipment</li> <li>Food enzymes and bacterial spores are very resistant to pressure and required very high pressure for their inactivation</li> <li>The residual enzyme activity and dissolved oxygen results in enzymatic and oxidative degradation of certain food components</li> <li>Most pressure processed foods need low-temperature storage and distribution to retain their sensory and nutritional qualities</li> </ol>

DC: Decoction, EAE: Enzyme-assisted extraction, PLE: Pressurized liquid extraction, SFC: Supercritical fluid extraction

increase<sup>[32]</sup> its capability to survive and to overcome all the challenges by interacting with their surroundings.<sup>[33]</sup> In other words, the secondary metabolites are often produced after growth which showed no function in growth and have unusual chemical structures closely related to the chemical family.<sup>[34]</sup> The production of secondary metabolites is based on the use of pharmaceutical industries.<sup>[35]</sup> This simple definition of bioactive compounds in plants is secondary plant metabolites eliciting toxicological<sup>[36]</sup> effects in animals and humans are divided into following main categories: <sup>[37]</sup> (a) Phenolic compound 8000 types, (b) alkaloids of 12,000 types, and (c) terpenes and terpenoids of 25,000 types.

Bioactive compounds belong to many families,<sup>[38]</sup> each has a different structural characteristic that depends on how they are built-in nature (biosynthesis).<sup>[39]</sup> There are four main pathways for the separation of bioactive compounds or secondary metabolites<sup>[19]</sup> such as shikimic acid pathway, malonic acid pathway, mevalonic acid pathway, and non-mevalonate (MEP) pathway. Through the malonic acid pathway and shikimic acid pathway, phenolic compounds are separated. Terpenes are produced through the MEP and mevalonic acid pathway.<sup>[40,41]</sup>

## FACTOR INFLUENCING DIFFERENT EXTRACTION PROCESSES

Various common factors affecting different extraction processes are included matrix properties of the plant part, choice of solvents, temperature, pressure, pH, moisture content, extraction time, foreign matters, solvent ratio, and particle size.<sup>[42]</sup>

## DIFFERENT EXTRACTION METHODS

### Maceration

For medicinal preparation, maceration is one of the oldest techniques. It is a widely used technique and cost-effective method to get natural products from plant material.<sup>[43]</sup> There are three different types of maceration processes popularly known extended maceration, cold soak, and carbonic maceration.<sup>[44]</sup> Carbonic maceration includes fermentation with carbon dioxide which makes it different from other maceration processes. The maceration is a solid-liquid extraction process which generally takes place before or during fermentation.<sup>[45]</sup> Maceration process completed in step-by-step processes where the first step includes grinding of plant materials, second proceeds with addition of solvent, and final includes strained off the liquid.<sup>[46-48]</sup> During the maceration process, occasional shaking facilitates extraction by increasing diffusion and removes the concentrated solution from the sample surface for increasing the yield of extraction.<sup>[49,50]</sup>

### Maceration process

In this process, powdered solid materials are put in a closed vessel and added a solvent allowed for a long time to stand at room temperature with regular agitation, till the soluble matter has dissolved.<sup>[51,52]</sup> After the combined liquid has been strained off, the liquid mixture is pressed to recover the solvent through filtration.<sup>[53,54]</sup>

### Recent updates

Cujic *et al.*, 2016, reported that a maceration extraction method was used for extraction of polyphenols from chokeberry (*Aronia melanocarpa*) dried fruit. Optimum condition includes maceration of 0.75 mm size berries using a 50% ethanol with 1:20 solid-solvent ratio. The result of maceration showed that it was the more effective and simple technique for extraction of bioactive compounds from chokeberry dried fruit.<sup>[55]</sup> Naima *et al.*, 2015, compared maceration and infusion for extraction of polyphenol and hydrolyzable tannins from Moroccan barks of *Acacia mollissima* with microwave-assisted extraction method. The highest polyphenols contents were obtained using methanol. For hydrolyzable and condensed tannins, the polyphenols contents were extracted using maceration.<sup>[56]</sup> Coelho *et al.*, 2019, reported two

maceration methods for extraction of liqueurs from mango peels by the method of alcoholic maceration and maceration with pectinase, and evaluated by reversed-phase high-performance liquid chromatography coupled to diode array detection and fluorescence-detection (reversed-phase high-performance liquid chromatography (HPLC)/DAD/FD). This study presented the produced liqueur allows the recovery of an important part of the bioactive content of mango peels, suggesting unusual recovery of antioxidant substances from this product. The main bioactive compounds were, flavonols (quercetin-3-O-glucopyranoside and rutin), flavanols (epicatechin-gallate, epigallocatechin-gallate), and phenolic acids (gallic acid, o-coumaric acid, and syringic acid).<sup>[57]</sup> Albuquerque *et al.*, 2018, showed the method for extraction of different bioactive compounds from *Arbutus unedo* L. fruits by maceration, microwave, and ultrasound-assisted extraction.<sup>[58]</sup>

### DC

It is a suitable method which constituents soluble components in solvent and cannot be destroyed by the effect of heat. It is generally divided into three different types, namely, simple maceration, double maceration, and triple maceration. It is a solvent-based preparation where the liquid preparation was prepared by boiling the plant material with water solvent.<sup>[59]</sup>

### DC process

In this process, the solvent including plant material is heated by boiling plate in a quantified volume of water for a specific time, then the combined solvent is cooled and strained, after that solvent is removed and the non-soluble part of the solid discarded. Its process allowed to replicates many times, hours, and days. The advantage of this method is that instead of many parts just one batch of solvent is reprocessed. The non-soluble component remains in the thimble after the concentrated solvent is removed by filtering.<sup>[59]</sup>

### Recent updates

Santos *et al.*, 2013, reported the extraction method of organic acids, tocopherols, and oligosaccharides from leaves of *Juglans regia* L. (walnut) using DC method. The bioactivity and phenolic composition of walnut leaves were examined in methanol extract and by DC process. Methanol extract gives a higher antitumor and antioxidant potential than a DC. This study resulted that phenolic compound of walnut leaves provides different types of compounds are taxifolin derivatives, procyanidins, and tocopherols.<sup>[60]</sup> Martins *et al.*, 2014, compared and evaluated the method of infusion, DC, and hydroalcoholic extract of essential oils and oregano methanolic extraction. The optimal result of DC showed the highest concentration of total phenolic compounds and flavonoids according to hydroalcoholic extract and infusion. This study describes that the DC can be used for the purposes of antioxidant, during the hydroalcoholic extraction and can be included in the preparation for antimicrobial features.<sup>[61]</sup>

### Percolation

Percolation is a continuous flow of solvent through a bed of plant material to get the extract. The preparation of tinctures and fluid extracts to make active ingredients is the most frequently used method. It is a narrow-based method that is generally used.<sup>[59]</sup>

### Percolation process

In this process, first, the powered plant material with sufficient menstruum to make a uniform solution, and allowed to stand about 4 h and then transfer to percolator which is in a v-shaped vessel and open at both ends. Then, definite menstruum is added to the material and then placed the lid on the top when the liquid starts dripping out from the outlet of the percolator the lower opening is closed. The plant material is allowed to macerate in the vessel for 24 h. The percolation is continued gradually using sufficient menstruum till completion.<sup>[59]</sup>

### Recent updates

This study compares two different refining processes using percolation. Acid/clay-percolation and solvent extraction/clay processes were established to refine used oil. The optimal work compares virgin base oil different product characteristics with established Egyptian transformation of quality lubricating oil characteristics. This work result shows that the feed oil flow point increased  $-15^{\circ}\text{C}$ , acid/clay-percolation process increased  $-2^{\circ}\text{C}$ , and solvent/clay process increased  $-6^{\circ}\text{C}$ . This all processes flow compared with virgin base oil flow  $-8^{\circ}\text{C}$ . 0.42 wt% sulfur content was found in acid/clay-percolation and 0.81 wt% sulfur was found insolvent/clay. In common, the using acid/clay percolation was obtained and nearly meets the Egyptian standards is the best standard of the refined base oil. The solvent extraction/clay process, on the other hand, yielded a higher yield of about 83 percent.<sup>[62]</sup> Hashemi *et al.*, 2014, compared extraction methods (Soxhlet, percolation, and ultrasonically assisted extraction). This method analyzed antioxidants from *Vicia faba* L. bean and hulls. Using four different tests for extracting and evaluating antioxidant activities, total flavonoid and phenolic contents were determined by Folin-Ciocalteu and aluminum chloride methods. The yield of extractions for ultrasonically assisted extraction was about half to one-fourth of that of other methods, the extraction ratio of total phenol (TP) was higher. Hull extracts had higher antioxidant activities and total flavonoid and phenolic contents and then extract beans. The best 2,2-diphenyl-1-picrylhydrazyl (DPPH) ( $\text{IC}_{50} = 56.9 \pm 2.5 \text{ mg/ml}$ ) showed by hull ultrasonic extract and NO radical scavenging ( $11.3 \pm 0.5 \text{ mg/ml}$ ). The best iron-chelating ability ( $171.8 \pm 6.8 \text{ mg/ml}$ ) and reducing power showed by hull percolation extract. The results show that all extraction methods can do successfully extract antioxidants from medicinal plants.<sup>[63]</sup>

### Soxhlet extraction

This method was described in 350 BC by William B. Jensen. It is also known as hot continuous extraction. It can compare the new extraction techniques with bioactive constituents. It involves the use of the Soxhlet apparatus for bioactive constituents. It is the process of continuous circulation with the same solvent several times. It also involves the evaporation of the solvent. This method is nothing but a series of short macerations.<sup>[59]</sup>

### Process

In this method, side tube and siphon tube are attached in extractor, the lower side of extractor attached to distillation flask and mouth is fixed to the condenser. The crude material powder is packed in Soxhlet

directly in a thimble. The diameter of the thimble has corresponded to the internal diameter. Extraction assembly is set up by fixing a condenser and a distillation flask with avoid bumping by adding fresh activated porcelain pieces to the flask. The vapors pass through the side tube and the condensed liquid gradually increases the level of liquid in the extractor and the siphon tube. A siphon was transferred to the flask. To get efficient extraction, we can do it as many times as possible without changing the solvent.<sup>[59]</sup>

### Recent updates

Dos Santos *et al.*, 2013, were examined the concentration of bioactive compounds which are squalene,  $\alpha$ -tocopherol, and various phyosterols in avocado oil by the Soxhlet method. Fortune variety avocados pulp part dried by lyophilization and set temperature 40 or  $70^{\circ}\text{C}$ . The optimal condition, petroleum ether using for extraction, the cold pressing process using for obtaining yielded oil and analyze the different oils by infrared spectroscopy and gas chromatography with FID and mass spectrometry detection, oil samples presented in  $\alpha$ -Tocopherol, cycloartenol acetate,  $\beta$ -sitosterol, campesterol, squalene, and stigmasterol. This study has resulted in the maximal oil yield with Soxhlet extraction and lyophilization, but cold pressing and lyophilization produced oils had high concentrations of bioactive compounds and antioxidants.<sup>[64]</sup> Mohamed *et al.*, 2016, performed determination and comparison of the constituent of bioactive compounds and check the activities of antioxidants in six different grape seed oils using two different methods supercritical carbon dioxide ( $\text{SC-CO}_2$ ) and Soxhlet extraction method. Identified the tocopherols, chlorophylls, carotenoids contents, and also hydrophilic and lipophilic antioxidant activities.  $\text{SC-CO}_2$  extraction shows higher TP contents and levels of carotenoids related to greater lipophilic antioxidant activity.<sup>[65-67]</sup>

### PLE

PLE was described in 1996 by Richter *et al.* which is also known by different names accelerated fluid extraction (ASE), PFE, high-pressure solvent extraction, and enhanced solvent extraction. PLE is a sample preparation process. This process associated elevated pressure and temperature with liquid solvents to reach fast and effective extraction of the ingredient from the solid matrix. The important development of PLE-based techniques results in automation techniques with time and solvent requirements. Nowadays, PLE is also considered as a potential alternative technique to SFC for the extraction of polar compounds.<sup>[68]</sup>

### PLE process

PLE was completed in step-by-step process. Its first step includes the packing of sample into extractor. To reach the desired temperature, the solvent pumped into the extractor using a liquid pump and passes through a heating system. For maintaining temperature, the extractor should have a heating jacket. PLE can be either in static or dynamic mode. Static extraction is a batch process in which the extractor is pressurized when the outlet valve remains closed. The valve is opened and the extract is collected. In dynamic mode, the outlet valve remains open and the solvent is pumped through the extractor continuously.<sup>[68]</sup>

### Recent updates

Barbosa *et al.*, 2019, have performed sequential PLE and examined their antibacterial and antioxidant activity to isolate phenolic compounds from *Hancornia speciosa* leaves in three steps. The extraction results increased with increase in temperature from 25 to 60°C, which provide remarkable results. Fractionated ethanol extract gives highest yield at 60°C.<sup>[69,70]</sup>

### SFC

In 1879, SFC is discovered by Hannay and Hogarth for extraction purposes but also Zosel is involved in this method presented a patent for decaffeination of coffee using SFC. In 1964, it is the most efficient and effective method too valuable constituents. It separates one extract from another matrix using supercritical fluids CO<sub>2</sub> extracting solvent. At the critical temperature, CO<sub>2</sub> is above 31°C and critical pressure of 74 bar. SFC is a highly compressed gas which have high properties, it consists of the following parts a tank of the mobile phase usually CO<sub>2</sub> a pump to a pressure in the gas. Usually, different types of meters such as flow meters and dry/wet gas attached to the system.<sup>[71]</sup>

### SFC process

This method is performed with a continuous flow of SCF. An extraction medium is stored through a feed tank and liquid SCF is pumped from a reservoir. It is heated and pressurized to obtain the supercritical conditions. SFC enters the chamber where contact with the material bed occurs and the more volatile substances are dissolved into the supercritical fluid. SCF and solute reach extractors and the sample becomes gaseous in SCF separation process. Gas is recycled by condensation before returning to the liquid reservoir.<sup>[71]</sup>

### Recent updates

Gallo *et al.*, 2016, have performed extraction of certain species of chrysanthemums and found some insecticidal properties in pyrethrum with the comparison between three extraction processes which include traditional maceration. The height of the dried flowers is lower. For the values of percent in this case, maceration is the cheapest method. For the extraction of compounds, all three techniques are valid in which supercritical CO<sub>2</sub> is less efficient.<sup>[72]</sup> Faber *et al.*, 2014, have been evaluated extracts obtained from peach palm fruit (*Bactris gasipaes*) using supercritical carbon dioxide, in terms of yield, total phenolic content, total flavonoids, total carotenoids, and antioxidant activity by carotene bleaching method. Soxhlet extraction was performed with methanol and petroleum ether extraction was managed. This study showed that supercritical CO<sub>2</sub> allows to get an extract rich in carotenoids and, although it presents the lowest yield than conventional extraction (SOX). The best operation situation for supercritical extraction was once given that the high amount of carotenoids was achieved, without the yield being suggestively different from that with extract had antioxidant activity comparable to that of commercial caffeic acid.<sup>[73]</sup>

### UAE

It includes sound waves of high intensity and frequency, and interacts with materials. This implies low costs and the hot, complex instrument

required, which is potentially useful technology. It is used on both small and large scales. It also involves ultrasonic effects of acoustic cavitation. In ultrasonication, both solid and liquid particles are vibrated because of the quick diffusion of solute.<sup>[74]</sup>

### UAE process

UAE consists of ultrasonic energy in the form of waves through a liquid containing solid particle. Waves hit the surface of the material with a force, which is the cause, parallel or perpendicular. Ultrasonic energy is converted into mechanical energy waves which are equivalent to a pressure of thousand atmospheres. The random increase in temperature and pressure is liable for the detection of cell membranes that facilitate the migration into the cell and also the desired portion.<sup>[74]</sup>

### Recent updates

Kumar *et al.*, 2021, have been explained the ultrasonic-assisted extraction method and discussed their advantages or disadvantages, parameters' influence on extraction time. In industries growing the extraction processing in fruit and vegetables, generate a large number of products in the form of seed, skin, pomace, and rind. These generated products having a significant quantity of bioactive compounds which are polyphenols, polysaccharides, carotenoids, and dietary fiber. These deals with wastes are measured selected small value compared to the treated fruit or vegetable due to a lack of viable extraction technique. Conventional extraction has reliable parameters conditions of energy, time, and required solvent. UAE method was extracted bioactive compounds in a very short time, with less energy, lower temperature, and requirement of solvent. This method was better for maintaining the role of bioactive compounds.<sup>[74-76]</sup>

### Ultra high-pressure extraction process

In a polyethylene bag, plant material and solvent were placed and sealed after bubbles remove then bag was placed in a pressure vessel with a temperature controller and pressure valve. This fluid was used to apply pressure to the vessel using a pump. Extraction was carried out at high pressure (100 Mpa–1000 Mpa) and room temperature for a specified duration (5–15 min).<sup>[76]</sup>

### Recent updates

Alexandre *et al.*, 2018, was described the extraction of phenolic content (TPC) and antioxidant activity in *Arbutus unedo* fruits (strawberry tree fruits) using a high-pressure CO<sub>2</sub> assisted extraction process (HPCDAE). Different parameters were optimized, such as high temperature, high pressure, and a less solid:liquid/CO<sub>2</sub> volume ratio. This HPCDAE method was used to recovery extract compared with a solid: liquid conventional extraction method and also use to increase the extraction of 5-O-galloylquinic acid and galloyl hexoside. The extraction of both compounds increases the activity of antioxidants in the extract. The results show that HPCDAE is a capable method to increase the extraction of bioactive ingredients from strawberry tree fruits.<sup>[77]</sup> Aguiar *et al.*, 2019, have been examined a high-pressure extraction of bioactive compounds from biquinho peppers. The optimized condition was maintained in different temperatures to the recovery of high polarity compound and chose solvent ethanol and water mixture for PLE extraction. The extraction of oleoresin by sc-CO<sub>2</sub> yield was 4.75%, with a concentration of 8.67 mg/g. In PLE,

the solvent mixture affects the extraction yield and standard. Theirs evaluate 16 phenolics in PLE extracts by UHPLC-MS/MS and were quantified the rutin isomer and vicenin-2. The highest amount of rutin isomer (441 g/g extract) was achieved with pure ethanol whereas, for vicenin-2, the 50% ethanol best solvent (299 g/g extract). For the purpose of total phenolic extraction, 75% ethanol is one of the most effective solvent. Sc-CO<sub>2</sub> extraction using PLE is a remarkable alternate to achieve bioactive from peppers.<sup>[78]</sup>

## ASE

It is a process for extracting several active compounds from a complex solid or semi-solid sample matrix that uses high-pressure temperature. It waded at elevated temperatures (50–200°C) and pressures between 10 and 15 min which maintains the solvent in liquid form. It is also called pressurized solvent extraction.<sup>[79]</sup>

### ASE process

In this method, a cell is a fill up with the solid sample to be examined and temperature controllable oven. The cell is heated at constant pressure after adding the solvent up to the maximum temperature of 200°C. In a sample tube, the extract is transferred. A sample will go through multiple cycles as well. The cell is fully rinsed with solvent, the rinsing valve is opened, and all lines are prepared for further extraction with nitrogen.<sup>[79]</sup>

### Recent updates

Hossain *et al.*, 2011, have optimized the ASE to maximize the antioxidant capacity of the extracts from three spices of the Lamiaceae family; rosemary, oregano, and marjoram. Here, the optimization conditions were maintained at temperature (66–129°C) using solvent methanol with a concentration of 32–88%. The characterization was performed by response surface methodology. The activity of antioxidant yields of the best ASE extracts was suggested to the higher than extracts of solid/liquid. The highly significant projected models existed for both ferric reducing antioxidant property and TP varying values in all the spices with high regression coefficients (R<sup>2</sup>) values 0.952–0.999.<sup>[80]</sup>

Rodríguez-Solana *et al.*, 2014, have performed an extraction of essential oils from the fennel using two techniques, accelerated solvent extraction and Soxhlet. Observed extract identified by GC–MS. The method was quantified extract showed good precision (RSD <5%) and linearity ( $r^2 = 0.998$ ) with quantification limits and small values of detection. Their suggested different parameters for extraction that as temperature, contact time sample – solvent, and extracted the quantity of estragole with various phases. ASE using for the extraction of estragole. The optimized conditions were 7 min, 125°C, and three phases. In other words, the step-by-step Soxhlet technique was studied and optimized the two variables: Solvents and time (4 and 8 h), according to compound polarity. Qualitatively and quantitatively both showed the best result using a 4 h of extraction and methanol. The Soxhlet technique provided a higher performance of extraction and greater amounts of compounds extracted compared to ASE, but a similar concentration of estragole. ASE used the lower amount of solvent and lower time of extraction and acceptable the ASE technique choice to characterize fennel essential oils.<sup>[81]</sup>

## EAE

Enzymes can be perfectly matched with catalysts to assist in the extraction of many bioactive compounds from natural origins. It is confirmed to be a high-quality, environmentally friendly, and selective approach for bioactive compounds extraction. It is solvent-based extractions. EAE growing alternatively more efficient methods for the extraction of phytochemicals from biological matrices. Its inherent ability to be possessed by enzymes and degrades or disrupts cell walls and mild processing conditions to produce EAE.<sup>[19]</sup>

### Accelerated Solvent Extraction process

This process followed to take each aliquot of 1 g homogenous plant material and the enzymes were added in each tube, then vortexed for 2 min and tubes were incubated at 40°C for 2 h, then add a solvent then filter all portion and partition in the separation of all active ingredients with solvents, the upper organic phase was the temperature at 30°C using a rotary evaporates the residue was revolved.<sup>[19]</sup>

### Recent updates

Boulila *et al.*, 2015, have been described the extraction of bay leaves (*Laurus nobilis* L.). The method involves the treatment with cellulase, hemicellulase, and xylanase to increase the efficiency of extraction of bioactive compounds. The cellulose treated samples showed improvement of essential oils extraction with a percent increment value of 243, 227, 240.54, and 0.48%. DPPH and amino-bis-(3-ethylbenzothiazolone 6-sulphonic acid) assays showed improvement of antioxidant properties. The prominent compounds in the final extract were 1,8-cineole, -terpinyl acetate, methyl eugenol, linalool, pinene, and sabinene. These results suggest that pre-treatment of enzymes may also be useful for extracting components of valuables and have great potential for use in the food, cosmetic, and pharmaceutical industries.<sup>[82]</sup> Vázquez *et al.*, 2018, have performed a study for the extraction of protein content from the red seaweed *Chondracanthus chamosoi* and brown seaweed *Macrocystis pyrifera* using EAE. The evaluation of protein content achieved by enzymatic and non-enzymatic methods recommended that the interruption of the cellulase-sensitive carbohydrate medium enhances the protein content on the extract. *M. pyrifera* and *chamosoi* extraction showed the presence of 74.6% and 36.1% of protein, consecutively which exhibited antioxidant and antihypertensive activities.<sup>[83]</sup>

## CONCLUSION

For convenient extraction methods, the ever-growing demand to extract plant bioactive compounds encourages continuously. Industry and consumers are aware that compounds derived from natural sources can prevent and treat certain illnesses. For the food and pharmaceutical industries, bioactive compounds are a promising option. Here, the key factor in all cases is the extraction processes because of the instability of the desired compounds extraction be challenging. A useful extraction processes integrity. Conventional and non-conventional extraction process such as maceration, DC, percolation, soxhalation, SFC, PLE, EAE, ultra high-pressure extraction, accelerated solvent extraction, and UAE offers an effective process for achieving extracts rich in bioactive compounds that preserve bioactivity, the solubility

of solute from plant materials into solvent conventional methods is base to extract the desired compound large quantity of solvent is required. The non-conventional process allows for the extraction of bioactive compounds using lower solvent consumption rates, shorter extraction time, and solvents. Both methods are influencing factors such as pressure, particle size, solvent choice, and different extraction temperature. To ensure all solvents are recycled, extraction processes should be used and guarantee the bioactivity of bioactive compounds. Near in the future, plants could be turned into a real source of natural products to substitute synthetic food additives. At present, the techniques and its scale-up are start-ups to develop the industrial scale to obtain food components based on a bioactive compound with all advantages. On the other side, increase in bioactive compounds and their significance and rich in commodities may lead to finding more extraction methods in the future.

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