ALTERNATIVE EXTRACTION TECHNIQUES OF CURCUMINOIDS FROM TURMERIC*

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ABSTRACT

Curcumin, demethoxycurcumin, and bisdemethoxycurcumin have recently been the focus of attention on food science due to their growing popularity among health-conscious consumers. Traditionally, curcumin has been used as a colorant, a sweetener, and a food preservative. Natural plants contain various bioactive components such as lipids, phytochemicals, compounds used in pharmacology, flavors, odors, and pigments, so extracts of these plants are often used in industries such as pharmaceuticals, food, and cosmetics. Some traditional and mechanical processes are used to achieve maximum benefit in the commercial use of these high-cost compounds. Alternative techniques are used to overcome the disadvantages of traditional extraction methods. These techniques have been developed to overcome these disadvantages and, most importantly, maintain the

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integrity of the compounds and achieve an environmentally friendly process Developed as an alternative to traditional methods to extract chemicals from plant sources, ultrasound-assisted extraction (UAE), accelerated solvent extraction (ASE), supercritical fluid extraction (SFE), subcritical water extraction (SWE), microwave assisted extraction and enzyme-assisted extraction (EAE) methods, such as fast, effective, and relatively environmentally friendly compared to the organic solvents used are considered.

Keywords: Curcumin, *Curcuma longa* L., Extraction, Alternative techniques, Green extraction

INTRODUCTION

Turmeric (*Curcuma longa* L.) belongs to the genus *Curcuma*, which is in the family *Zingiberaceae*, where ginger and cardamom are also present, and consists of hundreds of plant species **[1].** Turmeric is widely grown in countries and regions with tropical and subtropical climates, especially in China, India, and Indonesia, as well as in some Latin American countries such as Brazil and Peru **[2].**

A group of phenolic components responsible for the yellow color in the roots of turmeric was isolated in the 19th century and named after curcumin. Curcuminoids found in turmeric, the main component of which is curcumin [1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione], consist of three main active components: curcumin, demethoxycurcumin and bis-demethoxycurcumin (Figure 1.) **[1, 3, 4].** Commercially available curcumin contains 77% of curcumin as well as other curcuminoids. Commercial curcumin contains about 75% of the total curcuminoids, while demethoxycurcumin contains 10-20% and bisdemethoxycurcumin usually contains <5% **[5].** These compounds are included in the group called diarileptanoids **[6].**

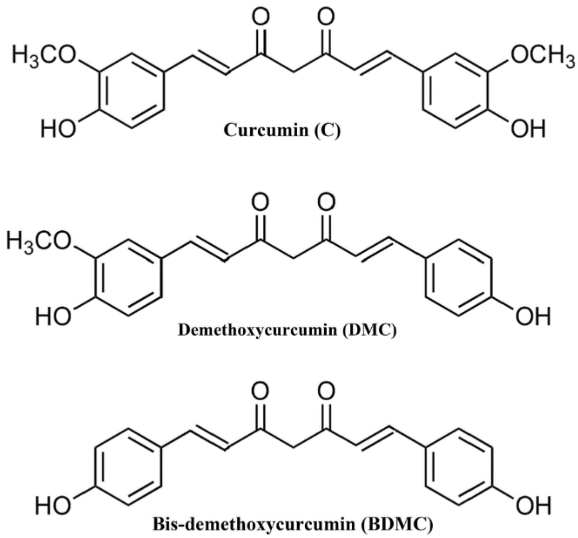

Figure 1. Chemical structure of curcuminoids **[7].**

Curcumin is the most active ingredient in turmeric, making up 2-5% of turmeric and is a water-insoluble compound. It was first isolated from curcuminoids in the form of a yellow-orange crystalline powder by Vogel in 1815 **[8].** The first chemical formula of curcumin ($C_{21}H_{20}O_6$) was described as diferulomethane by Lampe and Milobedeska in 1910 **[9].** The yellow color of turmeric's rhizomes is due to the presence of a group of phenolic compounds called curcuminoids **[2].** Curcumin has two methoxy groups and has a reddish orange color; demethoxycurcumin has a single methoxy group and has an orange-yellow color, and bisdemethoxycurcumin can be distinguished by its yellow color, while it does not contain methoxy groups **[1, 10].**

Figure 2. Representation of curcuminoids health benefits **[11].**

Importance of curcumin

Curcumin is a natural food dye of yellow-orange color that has the code E100 according to the European Food Safety Authority food dye numbering **[3].** In addition, it is also widely used as a preservative and aroma/flavoring agent **[2].** Curcuminoids belonging to the diferuloylmethane group have been used in Asia for centuries as spices, natural colorants, and traditional medical materials **[12].** The acceptable daily intake limit of curcumin has been determined by the World Health Organization (WHO) as 0-3 mg/kg. Products containing curcuminoids and turmeric have been described as safe by the Food and Drug Administration (FDA) in the United States **[11].**

Due to its wide range of biological activity, turmeric, and the curcumin, have been the subject of many studies. Curcuminoids have been used to treat a wide range of diseases such as cancer, inflammation, hepatic diseases, and diabetes (Figure 3) **[2, 13, 14, 15].** In 1949 they were discovered to have antibacterial properties **[16].**

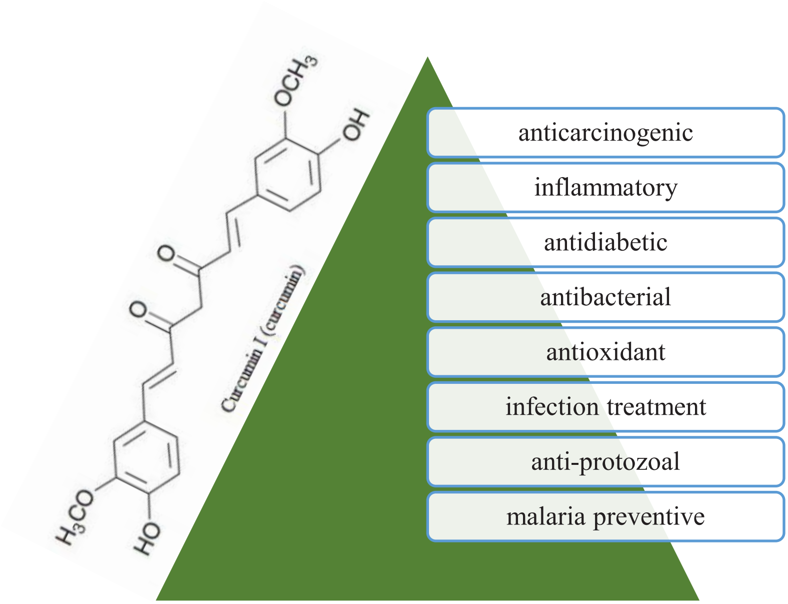

Figure 3. Chemical structure of curcumin and health benefits of curcuminoids

These compounds also have free radical cleansing antioxidant properties **[17, 18, 19]** are inhibitors of the human immunodeficiency virus Type 1 (HIV-1) integrase and are used to treat infection **[20, 21].** Many studies have shown that demethoxycurcumin and bisdemethoxycurcumin have as strong biological activity as curcumins in terms of anti-inflammatory and anti-protozoal properties **[22, 23, 24].** In addition, it has been noted in some studies that these compounds exhibit anti-malaria activity in vitro and in vivo **[25].** Although it is known that 3 compounds have a different effect, it has been observed that mixtures of these compounds prepared in certain proportions have more than the effect created by a single compound, creating a synergistic effect **[26].**

Extraction

Traditional extraction techniques such as traditional solid-liquid extraction, sonication, soxhlet extraction have been used to extract curcuminoids **[27].**

Curcuminoids are sensitive to light in the solution state and in the solid state, and if the pH of the solution is high, they undergo hydrolytic degradation **[28].** As a result of the application of traditional extraction methods of these active compounds, degradation of the extracted curcuminoids occurs due to their exposure to light, oxygen, and high temperatures. Because of this, extraction efficiency and application of the obtained compounds in food products may become limited **[29].** As a result of traditional methods used in mechanical processes, low extraction efficiency is achieved, as well as organic solvents that are harmful to the environment and human beings are used in traditional extraction methods **[30, 31].** Furthermore, because many natural products are thermally unstable during thermal extraction, degradation can be experienced **[30, 31, 32, 33].** Based on literature, traditional techniques usually have low extraction efficiency, high temperature processes, and longer extraction times **[34, 35].** The biggest disadvantage of traditional extraction methods is high energy consumption **[36].**

As a result of traditional techniques, low extraction efficiency is encountered despite high operating costs. Alternative techniques have been developed to overcome these disadvantages and, most importantly, maintain the integrity of the compounds and achieve an environmentally friendly process. Strict guidelines reported by the authorities on the use of organic solvents have encouraged researchers to develop cleaner/environmentally friendly extraction technologies **[37].** Demand for new extraction techniques is increasing due to short extraction time, low consumption of organic solvents and the desire to avoid increased pollution **[38].** Developed as an alternative to traditional methods to extract chemicals from plant sources, ultrasound-assisted extraction (UAE), accelerated solvent extraction (ASE), supercritical fluid extraction (SFE), subcritical water extraction (SWE), microwave assisted extraction (MAE) and enzyme-assisted extraction (EAE) methods, such as fast, effective, and relatively environmentally friendly compared to the organic solvents used are considered. Alternative extraction techniques of curcuminoids from turmeric is shown in Table 1.

Ultrasound-Assisted Extraction

Ultrasonic-assisted extraction (UAE) as a new technique for the extraction of plant tissues has received increasing attention and has also been the subject of many studies **[49, 50, 51].** Ultrasound has been noted to be effective in increasing the extraction rate by increasing mass transfer rates and cell wall breakdown due to the formation of microcavities leading to higher product yields with shorter extraction time and less solvent consumption **[52].** In other words, combining solvent extraction applied to the material with ultrasound has been reported to increase mass transfer and solvent penetration into the plant material by destroying the cell walls due to the mechanical effects of acoustic cavitations **[31, 35].** It is essential to optimize ultrasound extraction system parameters such as solvent, polarity, duration, pH to increase high extraction efficiency when obtaining desired compounds from plant materials **[5].**

A study by Rouhani et al. **[5]** compared traditional methods with ultrasound-assisted extraction of curcuminoids from turmeric samples. Extraction was performed in ultrasonic bath at 35 KHz and 25 °C and optimization was performed with independent variables. 3 different levels of 3 different factors were used in the optimization extraction process (pH-3/6/9; ethanol - 70/80/90%;

Table 1. Alternative extraction techniques of curcuminoids from turmeric

Method	Material	Extraction Medium	Reference
UAE, CE, SE	*Curcuma longa* L.	Ethanol	**[5]**
UAE, CE, SE	*Curcuma amada*	Acetone, ethanol, methanol, ethyl acetate and water	**[36]**
PLE, UAE	*Curcuma longa* L.	Methanol	**[28]**
PLE, UAE, MAE, SE	*Curcuma wenyujin Y.H.chen et C.Ling*	Methanol	**[39]**
SCFE, UAE, MAE, SE	*Curcuma longa* L.	CO_2, ethanol, acetone, water,	**[40]**
SCFE	*Curcuma longa* L.	Millii-Q water	**[41]**
USC-CO_2E, SC-CO_2E	*Curcuma longa* L.	CO_2, ethanol	**[42]**
SWE, SE	*Curcuma longa* L.	Acetone, ethanol, isopropanol, water	**[3]**
SWE	*Curcuma longa* L.	Water	**[43]**
MAE	*Curcuma longa* L.	Ethanol	**[44]**
MAE, CE	*Curcuma longa* L.	Ethanol, methanol	**[45]**
MAE	*Curcuma longa* L.	Acetone, acetic acid, ethanol, methanol, water	**[46]**
UAE, MAE, EAE, CE	*Curcuma longa* L.	Acetone, α-amylase, amyloglocosidase	**[47]**
CLAE, EAE, CE	*Curcuma longa* L.	*Acetone*, α-amylase, amyloglocosidase, *N*, *N*-Dipropyl ammonium *N′*, *N′*-dipropylcarbamate (DPCARB)	**[48]**

Ultrasound-assissted extraction (UAE), Conventional extraction (CE), Soxhelet extraction (SE), Pressurized liquid extraction (PLE), Supercritical fluid extraction (SCFE), Supercritical carbon dioxide extraction (SC-CO_2E), Ultrasound-assisted supercritical carbon dioxide extraction (USC-CO_2E), Subcritical water extraction (SWE), Microwave-assisted extraction (MAE), Enzyme-assisted extraction (EAE), Carbamate ionic liquid assisted extraction (CLAE) time-5/10/15min). The optimal combination of the factors of the parameters was determined as ethanol/water 70:30 v/v, pH 3 and 15 minutes. The ultrasound-assisted extraction yield was found to be about 3 times higher compared to the traditional method.

A study by Shirsath et al. **[36]** compared ultrasound-assisted extraction of curcumin from *Curcuma amada* (mango ginger) with traditional method extraction. In extraction, the effect of different parameters such as solvent (ethanol, methanol, acetone, ethyl acetate and water), solvent/solid ratio (1:15-1:55), particle size (0.09-0.85 mm), temperature (25- 55°C) and ultrasound power (22 kHz frequency 130-250 W) on extraction efficiency was studied. As a result of the study, ethanol was selected as the best extraction solvent. Curcumin extraction yield; increased with the increase of temperature, increased with increase of input power and increased with the decrease of particle size. According to the data obtained, curcumin extraction was performed optimally with 72% efficiency (9.18 mg/g) at 35°C, 1 hour, 1:25 solid/solvent ratio, 0.09 mm particle size and 250 W ultrasound power at 22 kHz frequency. The most important benefit of ultrasound-assisted extraction has been seen to shorten the extraction time. It has been stated that the extraction of thermally unstable components from plant materials can be carried out at low temperatures and the degradation of the components can be prevented.

Accelerated Solvent Extraction

Pressurized liquid extraction (PLE) or accelerated solvent extraction (ASE), as we can see in other sources, is a more attractive alternative than traditional extraction methods due to the need for fewer solvents and being more efficient **[53].** Today, it is widely known that PLE is a common green approach for the extraction of target compounds found in plant plants **[54].** PLE overcomes the disadvantages of traditional extraction methods and has often been used for analytical purposes in the preparation of samples. In addition to being a technique that can be easily automated and characterized, the main reason it is used as an alternative method is that it has a low cost and positive environmental impact due to low solvent use **[55].** PLE can be used over a wide temperature range (313-473 K) and at medium to high pressures (3.5-35 MPa) (Figure 4.). The main reason it is used in these values is to shorten the extraction time and keep the solvent in the compressed liquid region **[56].** The most important features that increase the extraction efficiency in this method are increased temperatures, increased mass transfer rate and diffusion rates **[53].**

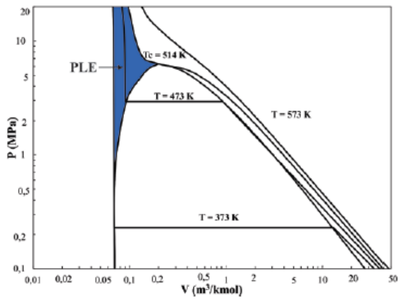

Figure 4. Pressure-volume diagram for ethanol calculated using Peng-Robinson equation **[57].**

A study by Schieffer **[28]** compared the extraction of curcuminoids from Curcuma longa with pressurized liquid extraction and ultrasound-assisted extraction. At a temperature of 373 K, under a pressure of 10 MPa, statically pressurized liquid extraction was performed for 5 minutes using methanol as a solvent. According to the study, higher performance was observed in pressurized liquid extraction in terms of curcuminoid extraction.

In a study by Shen et al. **[39]**, pressurized liquid extraction of curcuminoids from *Curcuma wenyujin Y.H.chen et C.Ling* (*Curcuma aromatica* Salisb.) using methanol as a solvent at a temperature of 100 °C under a pressure of 1500 psi was carried out. Compared to other extraction methods (soxhelet, ultrasound-assisted, microwave-assisted extraction), it was observed that it required a shorter extraction time and less solvents.

Supercritical Fluid Extraction

Another method that can be described as an alternative is supercritical fluid extraction (SFE). In SFE, the solvent used in extraction is in a critical state. A substance or mixture that is pressurized above the critical pressure and heated above the critical temperature that is unique to the fluid is called a supercritical fluid (Figure 5). Supercritical fluids carry the properties of the intermediate form of deciduous gas or liquid matter. They cannot be liquefied or evaporated by increasing pressure or temperature, so they exist in a single phase. Its most important features are higher diffusion coefficients and lower viscosity. Its dissolving and spreading properties are higher than those of liquids, and its reaction kinetics are fast. Because of these properties, supercritical fluids have a high ability to penetrate solid porous materials **[58, 59].** The higher the density of supercritical fluids, the higher the ability to dissolve. Because density and other properties can be easily changed by adjusting temperature and pressure, these fluids are seen as ideal solvents **[60].**

Carbon dioxide (CO_2) is the most used and preferred supercritical solvent in food applications due to its cheap, high purity, easy availability, reliability, and many properties **[61].** Supercritical CO_2 (SC-CO_2) is slightly polar or non-polar compounds can solve; low-molecular-weight compounds can solve; for it is a low resolution free fatty acids and glycerides; high molecular weight and/or pressure with an increase in more polar compounds can separate; solvent property for pigments is low, it cannot dissolve proteins, polysaccharides, sugars, and mineral salts **[62, 63].**

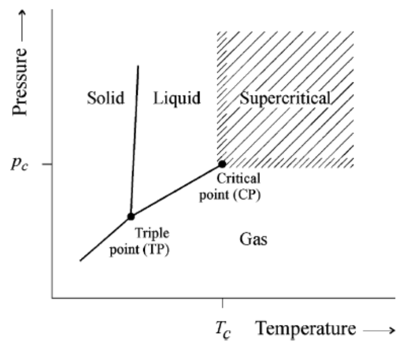

Figure 5. Diagram of supercritical state for a pure component **[65].**

In a study conducted by Kimthet et al. **[42]**, ultrasound-assisted supercritical carbon dioxide extraction (USC-CO_2) method was used to obtain curcumin from *Curcuma longa* L. Extraction was carried out at 50°C, under pressure of 25 MPa, CO_2 as solvent and 10% ethanol (flow rate 3 mL/min) as cosolvent. As a result of the study, it was determined that USC-CO_2 requires less extraction time compared to SC-CO_2 and a higher percentage of curcumin is obtained as a result of extraction. It has been reported that the reason for this is that ultrasound power breaks down the cell wall and therefore increases the release of target components.

In a study conducted by Kwon & Chung **[41]**, subcritic solvent extraction of curcuminoids in turmeric was performed. Different parameters (temperature as 110-150 °C; time as 1-10 min; pressure as 5-100 atm; solid-to-solvent ratio and mixing ratio of solvent) were examined in the study. The maximum extraction yield of the study was 13.58% (curcumin, demethoxycurcumin and bisdemethoxycurcumin; 4.94%, 4.73% and 3.91% in dried extracts, respectfully) in pilot-scale assembly (water/ethanol mixture at 135 °C in 5 minutes and solvent (50:50, v/v)). When using ethanol (50%, 95% and 100%) in different proportions for 120 minutes at 60 °C under atmospheric conditions, extraction yields of

10.49%, 13.71% and 13.96% were obtained, respectively. According to the data obtained from the study, supercritical solvent extraction has been suggested as a potential alternative to the extraction of curcuminoids as a fast and efficient extraction technique.

Subcritical Water Extraction

Subcritical Water Extraction (SWE); also known as Pressurized hot water extraction (PHWE), hot water extraction (HWE), high-temperature water extraction (HTWE), superheated water extraction or hot liquid water extraction, due to the use of organic solvents, is considered to be an environmentally friendly extraction method that can be a potential alternative to the traditional extraction method **[3, 64].** The use of pure water as a solvent at high temperatures for nonpolar analytes was first proposed by Hawthorne **[65].** This extraction method has been put forward as a promising green technique, based solely on the use of subcritical water solvent **[66, 67, 68].** The term "pressurized hot water" or "subcritical water" usually describes liquid water with the temperature of 647.096 K (374 °C) and the pressure of critical point 22.064 MPa **[3].** It has been suggested that subcritical water is more effective than SC-CO_2 for modifying sample matrices, rearranging analyte binding sites, and organic matter extraction **[69].**

A study by Euterpio et al. **[3]** shows that curcumin increases temperature to improve pressurized hot water extraction due to its low solubility in water used as a solvent. In the experiment, it was observed that at temperatures above 473 K, both the turmeric matrix and curcumin deteriorated, as well as the color of the extracted ginger rhizome particles turned dark brown. In the dynamic extraction process with a solvent speed of 0.5 mL/min under a pressure of 5 MPa at 370 K, the solubility of curcumin was increased by improving the solvent water with a buffer solution with a pH of 1.6 and using a phosphate buffer of 62 g/L.

In a study by Kiamahalleh et al. **[43],** subcritical water extraction of curcumin from turmeric root with different parameters such as pressure and time on the extraction efficiency was investigated. Optimum conditions are achieved with a temperature of 150 ◦C, a pressure of 10 bar, a particle size of 0.71 mm and time of 14 min, and the maximum extraction efficiency obtained under these conditions is 3.8%.

Microwave-Assisted Extraction

Microwave systems are systems where heat is generated through interaction between ions as well as the dipole rotation resulting from the high-frequency electromagnetic waves **[60].** They possess significant advantages over other common methodologies such as performing the extraction with high efficiency, making it possible to use less solvent and reducing the extraction time by some margin **[70].** Extraction is characterized by microwave radiation penetrating the cell walls and membranes, breaking down the cell structure, which makes it easier for solvent to permeate into the cells **[71].** It is also possible to influence the permeating capability of the solvent by changing its temperature **[70].** With the effect of the electric field created by the microwave energy, the transmission of electrons in the material structure is disrupted and the dipoles rotate around their own axis **[72].** The greater the resistance of electrons to motion and the continuous change of direction of ions or the dipole oscillation of the molecule, the higher the heat generated **[72, 73].**

The heating profiles of the materials depend on their dielectric properties, mainly dielectric constants, and dielectric losses **[74].** The resistance of the material against the passage of microwave energy is defined as the dielectric constant, and this energy turning into heat and dissipating in the material is defined as dielectric loss. Differences in dielectric properties of solvents such as ethanol, methanol, acetone, and water, which are frequently used in studies where microwave-assisted curcuminoid extraction is performed, affect the extraction properties of curcuminoids substantially **[44, 45, 46, 47, 75].** For example, while ethanol has lower dielectric constant than water, its dielectric loss is higher **[76].** In this case, ethanol is less resistant to the passage of microwave energy, while its ability to convert this energy into heat is higher and needs less energy, i.e., shorter times, to reach a certain temperature.

The most frequently used solvents are ethanol and acetone, which are not remarkably similar in terms of dielectric characteristics **[77].** While the dielectric constants of these two solvents are similar, it has been observed that the dielectric loss of ethanol is much higher **[76].**

Rezaei et al. **[46]** examined different solvents for curcumin extraction in their study and stated that acetone is the solvent that provides the extraction with the highest efficiency. A relationship could not be established between the dielectric constant of the solvents and the amount of extractable curcumin; however, it was stated that there was a direct relationship with the deterioration of the cell structure. This also makes the use of microwave systems for pre-application in curcumin extraction a possible approach.

Wakte et al. **[40]** investigated microwave application to ginger powders soaked with ethanol or water as a pre-treatment. It was observed that the extraction efficiency of the samples that were applied microwave pre-treatment with water with higher dielectric constant than ethanol was higher. In addition, microwave pre-treatment was found to be much more efficient at breaking down cell structure than ultrasound-assisted approach.

Sahne et al. **[47]** examined the extraction of curcumin from ginger using enzyme, ultrasound and microwave-assisted methods. Although the extraction efficiency was 3.72% in microwave-assisted extraction and 4.1% in enzyme-assisted extraction, extraction times of 2 minutes and 4 hours, respectively, created a significant advantage for microwave-assisted extraction.

Enzyme-Assisted Extraction

Nowadays, with the increase of consumer awareness, interest in organically produced foods has increased, while recent studies have focused on examining green alternatives to existing extraction techniques **[78].** Therefore, enzyme-assisted extraction (EAE), which is known to be organic and environmentally friendly, has been one of the most popular methods and numerous studies have shown that enzyme-assisted applications have high efficiency in the extraction of bioactive components such as lipids, polyphenols, oils, and aroma elements **[79, 80, 81, 82].** It is important to determine an enzyme suitable for the subject food, since the enzymes used show significant differences in extraction efficiency depending on the activity, the amount of substrate and the molecular composition of bioactive components **[80].** α-amylase, glucoamylase and amyloglucosidase were generally used in studies due to approximately 65% of curcumin consisting of carbohydrates and curcumin residing in the polysaccharide-lignin structure **[47, 48, 83, 84].** With enzymatic applications, the structure of the ginger cell wall is disrupted, and the solvent transition is facilitated, thus ensuring high efficiency extraction without the need for very high temperatures **[83].**

Kurmudle et al. **[84]** showed that the α-amylase and glucoamylase-assisted extraction system was 26.04% and 31.83% more efficient, respectively, compared to the system without enzyme assistance.

Sahne et al. **[47]** have compared ultrasound, microwave, and enzyme-assisted extraction of bioactive compounds in ginger and determined that enzyme-assisted extraction was performed with the highest efficiency among the three methods examined. It has been reported that with enzyme-assisted application, cell walls can be broken down more effectively and enable solvent to permeate far more effectively.

CONCLUSION

Curcumin, which has many positive health effects, is used as a natural color pigment, and is usually derived from turmeric, has an important place in the industrial sense as a multidisciplinary. Traditional methods for the extraction of curcumin from turmeric are still used today. But extraction methods such as UAE, ASE, SFE, SWE, MAE and EAE, which can be described as alternative methods, are known to overcome the disadvantages of traditional methods, achieving better extraction yields, and using solvents that are less harmful to nature. Each Extraction method has advantages and disadvantages compared to each other. Alternative and environmentally friendly extraction methods can be used for recovery instead of conventional (traditional) methods that can be applied in every laboratory with a low budget but require low extraction efficiency and high solvent use. After selecting the method, parameters such as the appropriate solvent type, solvent quantity and extraction temperature should be considered, and extraction should be supported by experimental design and optimization for maximum extraction efficiency and optimal conditions should be determined. Of course, determining the most appropriate extraction method in which maximum efficiency is achieved by using environmentally friendly and low-cost solvents at temperatures that will prevent curcumin from becoming degraded should be the first step. Developing technology will bring with it different alternative techniques. The goal of curcumin extraction techniques to be developed should be to require environmentally friendly solvent use (or reduction of solvent use), high extraction efficiency, low process costs and a short extraction time.

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