

ULTRASONIC- AND MICROWAVE-ASSISTED EXTRACTION OF
CURCUMINOIDS AND CYCLODEXTRIN COMPLEXES OF CURCUMIN
FROM *C. domestica* Val.

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I dedicated this thesis to my parent and my family for their support, encouragement and understanding.

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ABSTRACT

This study investigates the isolation of curcuminoids from *Curcuma domestica* Val. using ultrasonic-assisted extraction (UAE), microwave-assisted extraction (MAE) compared with conventional cold solvent extraction method and the use of inclusion complexation of curcumin with methyl- β -cyclodextrin (M β -CD) for improving their solubility. The extractions were optimized by determining the content of three curcuminoid markers, namely curcumin (C), demethoxycurcumin (DMC) and bisdemethoxycurcumin (BDMC). The extraction efficiencies were compared in terms of extraction time, sample through-put and solvent consumption. The optimized parameters for UAE of curcuminoids were extraction amplitude of 100, particle size of 0.30-0.60 mm, extraction time of 20 min, extraction solvent volume of 10 mL and extraction temperature of 60°C. Meanwhile, the relative recoveries (RRs) for aqueous extraction were in the range of 91.59-98.99%, 89.79-94.95% and 89.33-94.77% for C, DMC and BDMC, respectively. Although UAE using methanol resulted in a slightly higher extraction yield and shorter extraction time compared to those using water, both methods showed similar pattern of results. Despite these, water is cost effective, safe and environmentally friendly. These advantages of aqueous solvent can be used as a yard stick to substitute organic solvents for UAE of curcuminoids from *C. domestica*. At maximum set energy, the MAE optimum extraction parameters were particle size of 0.30-0.60 mm, extraction time of 3 min, extraction solvent volume of 10 mL and extraction temperature of 60°C with RRs of 92.48-99.44%, 90.58-97.43% and 90.03-96.07% for C, DMC and BDMC, respectively. Both UAE and MAE applications showed remarkable improvements in terms of extraction time, solvent consumption, extraction yield and the quality of extracts compared to conventional cold solvent extractions method. However, as compared to UAE, the optimized MAE application was better in term of quantity of curcuminoids. MAE is also simpler, faster, more efficient approach and allows the possibility of simultaneous multiple extractions. The inclusion complex formed using M β -CD with the application of MAE was more stable than that with UAE based on the stability constant (K_C) values of 213.08 M⁻¹ and 515.19 M⁻¹, for UAE and MAE, respectively. Results from characterization of the inclusion complex with scanning electron microscope showed that co-precipitation method was best for UAE while all of the mixing methods can be used for the inclusion complexation with MAE application. The kneading and co-precipitation methods were found to be the best for the inclusion complexation between turmeric rhizome oleoresins and M β -CD in UAE, while all of the mixing methods were found to be suitable for inclusion complexation of turmeric rhizome oleoresins with M β -CD in MAE as indicated by Fourier transform infrared spectroscopy.

ABSTRAK

Kajian ini menyelidik pengasingan kurkumin daripada *Curcuma domestica* Val. menggunakan pengekstrakan berbantuan ultrasonik (UAE) dan pengekstrakan berbantuan gelombang mikro (MAE) berbanding dengan kaedah pengekstrakan pelarut sejuk konvensional dan penggunaan pengkompleksan rangkuman kurkumin dengan metil- β -siklodekstrin (M β -CD) bagi meningkatkan keterlarutan. Pengekstrakan telah dioptimumkan dengan menentukan kandungan tiga kurkuminoid penanda iaitu kurkumin (C), demetoksikurkumin (DMC) dan bisdemetoksikurkumin (BDMC). Kecekapan pengekstrakan telah dibandingkan daripada segi masa pengekstrakan, kadar pemindahan sampel dan penggunaan pelarut. Parameter optimum bagi UAE kurkuminoid ialah amplitud pengekstrakan 100, saiz partikel 0.30-0.60 mm, masa pengekstrakan 20 min, isipadu pelarut pengekstrak 10 mL dan suhu pengekstrakan 60°C. Sementara itu, pengembalian relatif (RR) bagi pengekstrakan akueus adalah dalam julat 91.59-98.99%, 89.79-94.95% and 89.33-94.77% bagi masing-masing C, DMC dan BDMC. Walaupun UAE yang menggunakan metanol menghasilkan pengembalian pengekstrakan yang lebih tinggi sedikit dan masa pengekstrakan lebih singkat berbanding dengan pengekstrakan yang menggunakan air, kedua-dua kaedah ini menunjukkan pola hasil yang sama. Di sebalik itu, air adalah efektif kos, selamat dan mesra alam. Kelebihan pelarut akueus ini boleh digunakan sebagai kayu pengukur untuk menggantikan pelarut organik bagi UAE kurkuminoid daripada *C. domestica*. Pada tenaga maksimum yang ditetapkan, parameter optimum MAE ialah saiz partikel 0.30-0.60 mm, masa pengekstrakan 3 min, isipadu pelarut pengekstrakan 10 mL dan suhu pengekstrakan 60°C dengan nilai RR 92.48-99.44%, 90.58-97.43% dan 90.03-96.07% masing-masing bagi C, DMC dan BDMC. Kedua-dua aplikasi UAE dan MAE menunjukkan penambahbaikan yang ketara daripada segi masa pengekstrakan, penggunaan pelarut, hasil pengekstrakan dan kualiti ekstrak berbanding dengan kaedah pengekstrakan pelarut sejuk konvensional. Walau bagaimanapun, berbanding UAE, aplikasi MAE yang optimum adalah lebih baik daripada segi kuantiti kurkuminoid. MAE juga merupakan pendekatan yang lebih ringkas, cepat, lebih cekap dan memungkinkan pengekstrakan berganda serentak. Kompleks rangkuman yang dihasilkan menggunakan M β -CD dengan MAE adalah lebih stabil berbanding dengan UAE berdasarkan nilai pemalar kestabilan (K_C) iaitu 213.08 M⁻¹ and 515.19 M⁻¹, bagi masing-masing UAE dan MAE. Hasil daripada pencirian kompleks rangkuman dengan mikroskopi elektron pengimbas menunjukkan kaedah ko-pemendakan adalah terbaik bagi UAE manakala semua ko-pemendakan didapati boleh digunakan bagi pengkompleksan rangkuman dengan penggunaan MAE. Kaedah ulian dan ko-pemendakan didapati terbaik bagi pengkompleksan rangkuman antara oleoresin rizom kunyit dengan M β -CD dalam UAE, manakala kaedah pencampuran yang lain didapati sesuai bagi pengkompleksan rangkuman oleoresin rizom kunyit dengan M β -CD dalam MAE seperti ditunjukkan oleh spektroskopi inframerah transformasi Fourier.

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LIST OF ABBREVIATIONS

| | | |
|----------------|---|--|
| α -CD | - | Alpha-cyclodextrin |
| ACN | - | Acetonitrile |
| ASE | - | Accelerated solvent extraction |
| AOAC | - | Association of analytical communities |
| ATR | - | Attenuated Total Reflectance |
| BDMC | - | Bisdemethoxycurcumin |
| β -CD | - | Beta-cyclodextrin |
| BP | - | Biphenyl |
| CD | - | Cyclodextrin |
| C | - | Curcumin |
| CP | - | Co-precipitation |
| DMC | - | Demethoxycurcumin |
| DMAE | - | Dynamic microwave assisted extraction |
| FTIR | - | Fourier transform infrared spectroscopy |
| γ -CD | - | Gamma-cyclodextrin |
| GC-MS | - | Gas Chromatography-Mass Spectrometry |
| HS-SPME | - | Head space-solid phase microextraction |
| HPLC | - | High performance liquid chromatography |
| HPLC-FD | - | High performance liquid chromatography Flourescence detection |
| HP β CD | - | Hydroxylpropyl β -cyclodextrin |
| HP γ CD | - | 2-hydroxypropyl- γ -cyclodextrin |
| IS | - | Internal standard |
| K | - | Kneading |
| LOD | - | Limit of detection |

| | | |
|-------------------|---|---|
| LOQ | - | Limit of quantification |
| M β -CD | - | Methyl- β -cyclodextrin |
| MAE | - | Microwave-assisted extraction |
| MAE-HS-SPME | - | Microwave-assisted extraction head space-solid phase microextraction |
| M β CD-K | - | Methyl Beta cyclodextrin-kneading |
| M β CD-CP | - | Methyl Beta cyclodextrin-co-precipitation |
| M β CD-PM | - | Methyl Beta cyclodextrin-physical mixture |
| PHWE | - | Pressurised hot water extraction |
| PLE | - | Pressurised liquid extraction |
| PSE | - | Pressurised solvent extraction |
| PAHs | - | Polyaromatic hydrocarbons |
| PCBs | - | Polychlorinated Biphenyls |
| PFP | - | Penta fluoro phenyl |
| PM | - | Physical mixture |
| RSD | - | Relative standard deviation |
| RP-HPLC | - | Reversed phase high performance liquid chromatography |
| RP-HPLC-UV | - | Reversed phase high performance liquid chromatography ultraviolet spectroscopy |
| RR | - | Relative Recovery |
| RT | - | Retention time |
| SFC | - | Supercritical fluid chromatography |
| SFE | - | Supercritical fluid extraction |
| SWE | - | Subcritical water extraction |
| SEM | - | Scanning electron microscope |
| SWE | - | Subcritical or superheated water extraction |
| SBE β CD | - | Sulfated butyl ethyl β -cyclodextrin sodium salt |
| SPME | - | Solid phase microextraction |
| TLC | - | Tin layer chromatography |
| TRO-M β -CD | - | Turmeric rhizomes oleoresin-methyl β -cyclodextrin |
| UV | - | Ultraviolet spectroscopy |
| UAE | - | Ultrasonic-assisted extraction |

LIST OF SYMBOLS

| | | |
|---------------------|---|-------------------------------|
| α | - | Alpha |
| β | - | Beta |
| r^2 | - | Coefficients of determination |
| CO ₂ | - | Carbon dioxide |
| °C | - | Degree celsius |
| γ | - | Gamma |
| g | - | Gram |
| g mol ⁻¹ | - | Gram per mole |
| h | - | Hour |
| μm | - | Micrometer |
| μL | - | Micro liter |
| μgL^{-1} | - | Microgram per liter |
| min | - | Minutes |
| mL | - | Milliliter |
| mm | - | Millimeter |
| mgL^{-1} | - | Milligram per liter |
| nm | - | Nanometer |
| % | - | Percent |
| pm | - | Picometer |
| rpm | - | Revolution per minutes |
| K _C | - | Stability constant |
| S _O | - | Intrinsic solubility |
| k | - | Slope |

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CHAPTER 1

INTRODUCTION

1.1 Research Background

Turmeric is a member of the Zingiberaceae family native to South Asia, which is a perennial herb with short and thick rhizomes with yellow flesh (Somchit *et al.*, 2002), grown in warm, rainy regions of the world such as India, China, Indonesia, Jamaica and Peru. Its rhizomes are oblong, ovate, perform and often short branched (Jayaprakasha *et al.*, 2002). The plant reaches up to 3 feet (0.9 m) tall and the leaves are dark and medium green in colour with about 1.5 feet (0.45 m) long by 8 inches (20.3 cm) wide (Jayaprakasha *et al.*, 2005). The dry rhizomes of *C. domestica* Val. have been reported to contain 3 - 5% of essential oil and 0.02 - 2.0% aromatic yellow curcuminoids (Began *et al.*, 2000). It exhibits poor to moderate stability in water, oxidized or changes in pH when exposed to light but, has good tinctorial strength. Turmeric oleoresin is the combination of flavours and colour principles obtained from turmeric, however, the principal colouring material in turmeric and its oleoresin are curcumin. Curcumin is orange yellow in colour, crystalline powder, insoluble in water and hexane. It is partially soluble in ether, dichloromethane and freely soluble in ethanol, methanol, acetone and glacial acetic acid (Cheng *et al.*, 1982).

It has been reported that the leguminous plant has a great commercial and medicinal value. *C. domestica* Val. consists of two constituents: phenolic pigment and essential oil. However, the major components of essential oil are ar-turmerone, zingiberene, turmerone and curlone, while that of phenolic pigments are C, DMC and BDMC (Taylor and McDowel, 1992). The yellow pigments are used as colouring agents and the mature rhizomes are ground to give an aromatic yellow powder which is used as spices (Kan, 1997; Anna *et al.*, 2003). Several phenolic compounds are flavonoids and curcuminoids as reported by Jayaprakasha *et al.* (2005). Health benefits of flavonoids are well known and they displayed a remarkable range of biomedical and pharmacological properties that may significantly affect the function of various mammalian cells (Middleton *et al.*, 2000).

Although several active phytochemicals, and high activity profile drugs have been discovered from plants, but the quality and safety related problems of herbal drugs have still been challenged for researchers. The main problems for these drawbacks are the lack of reliable extraction, methodologies and high performance for establishing the purity and standard for the herbal drugs (Huie, 2002). As a result of the above-mentioned factors, herbal medicines have yet to find their way in order to be accepted in the global market. An individual plant may consist of several active phytochemicals existing in abundance along with certain constituents of the low activity profile. There is thus a need in the development of efficient procedures of extraction and analytical techniques with high performance (Smith, 2003) for extracting the phenolic compounds (Beejmohun *et al.*, 2007).

Recent years have shown growing popularity and faith in the use of herbal medicine worldwide. This is attributed to the realisation that modern synthetic drugs have failed to provide curative and guarantee to most of the human diseases with sometime producing side effects and in the end then give more problems than the actual disease. The natural medicine provides a ray of hope through its phytochemicals, which are believed to act in a synergistic manner, providing healing without side effects (Vivekananda *et al.*, 2007).

There has been an increasing interest in newer extraction techniques, in the herbal drug (Nyiredy, 2004). These techniques are amenable to automation and provide shortened extraction times, organic solvent consumption reduction, prevention of pollution in analytical laboratories and reduced sample preparation costs (Poole and Poole, 1996; Wan and Wong, 1996). These conventional methods for the extraction of natural products from plant material for instance Soxhlet, has been widely used not only as a technique for extraction of natural products, but also as a comparison for newer extraction techniques (Luque-Garcia and Luke de Castro, 2004; Sanghi and Kannamkumarath, 2004) which are characterised by the consumption of large volumes of solvent and energy, lengthy extraction procedures, and the potentially deleterious degradation of labile compounds (Kerem *et al.*, 2005).

However, with the problem of consumption of solvent, often in large quantities, toxic and together with time consumption problem. This also resulted in consideration of more new extraction techniques such as microwave-assisted extraction (MAE) (Letellier and Budzinski, 1999; Lopez-Avila, 1999; Camel, 2000), supercritical fluid extraction (SFE) (Hawthorne, 1990; Bowadt and Hawthorne, 1995; Smith, 1999), subcritical water extraction (SWE) or superheated water extraction and accelerated solvent extraction (ASE) (Bjorklund *et al.*, 2000). In addition, ultrasonic-assisted extraction (UAE) as a novel technique for extraction of plant tissue has gained increasing attention (Djilani *et al.*, 2006). A variety of methods for extraction of plant materials have been reported (Ong *et al.*, 2000). The traditional solvent extraction techniques for natural products are mostly based on solvent type and required long extraction time and have low efficiency. Most of these techniques have advantages and disadvantages with regard to solvent volume, extraction time and extraction efficiency as well as working at a high elevated temperature and pressure which improves the extraction process.

Microwave energy has a greater potential for rapid heating of sample and have long appeared in analytical laboratories. Abu-Samra *et al.* (1975) were the first researchers to use a domestic microwave oven in the laboratory in metals analysis

from biological samples. Since then the application of microwave method has been developed for different applications (Sparr and Bjorklund, 2000). But in the last two decades, pharmaceutical and natural products have become interested in using MAE as an alternative to conventional methods of extraction. The use of MAE has created increasing interest in the last couple of years due to its rapid, safe, easy to use and cost effective. The microwave heating allows a better recovery and a better sensitivity than conventional methods and good linearity (Pare, 1991; Pare *et al.*, 1994). In comparison with pressurized solvent extraction or supercritical fluid extraction, MAE can be conducted at atmospheric pressure and therefore can be initiated very rapidly. Furthermore, it offers a significant improvement in terms of analysis time and solvent consumption. Microwaves find their applications not only in plant matrix extraction but also in pesticides, organic pollutants, metals and polymers (Tatke and Jaswal, 2011).

The possibility of the use of ultrasonication process was due to the fact that ultrasonic waves break the cells of the vegetal matrix and the cell's contents are released into the extraction medium (Vinatoru *et al.*, 1997). The enhancement of extraction efficiency of organic compounds by ultrasonic is due to the phenomenon called acoustic cavitations (Toma *et al.*, 2001). When ultrasonic is used in combination with conventional heating, the effect of ultrasonic treatment increased. Ultrasonic also offers a mechanical effect allowing greater penetration of solvents into the sample matrix, increasing the contact surface area between the solid and liquid phase, as a result the solute quickly diffuses from the solid phase to the solvent (Rostagno *et al.*, 2003). Thus, UAE proved to be an inexpensive, simple and efficient alternative to conventional extraction techniques. Ultrasonic has an important role in food engineering due to consumer interest in minimally processed foods and has a wide range of current and future applications in the food industry (Ertugay *et al.*, 2004).

Cyclodextrin (CD) is a well-known material used as the solubilising agent for hydrophobic drugs. The CD is a cyclic oligosaccharides of α -(1,4)-linked D-glucopyranose units arranged in a ring formation containing a hydrophilic outer

surface (Szejtli, 1982). The hydrophobic internal cavity provides the capability to form inclusion complexes with a variety of “guest” hydrophobic larger molecules. Such binding allows CD to increase the water solubility of the oleoresin, which is very hydrophobic and not soluble in water (Zaibunnisa *et al.*, 2009). CDs are thus often used to enhance the solubility of pesticides for agricultural and environmental application (Zhang *et al.*, 2005).

Among all the CDs, the β -CD (β -CD) and its derivatives are most widely used in research and manufacturing due to cost availability and suitable cavity size for most of the common guests (Loftsson and Brewster, 1996a). It has a molecular weight between 200-800 g/mol (Waleczek *et al.*, 2003). Substituent on the CD molecules is likely to influence the interactions between drug and carrier by changing the shape of the CD cavity or altering the charge-charge interactions (Tonnesen *et al.*, 2002).

Several methods have been developed for the determination of curcumin, including using TLC and spectrophotometry (Janssen and Gole, 1984). Reversed-phase HPLC (RP-HPLC) separated on a styrene-divinylbenzene copolymer column using a diode array detector has been reported by Taylor and McDowell (1992). Tonnesen and Karlsen (1983) and Smith and Witoska (1984) reported the use of RP-HPLC separations using ultraviolet spectroscopy and electrochemical detection. The research work was focused on the application of novel extraction methods of MAE and UAE in isolating three major components of phenolic pigments: curcumin, demethoxycurcumin and bisdemethoxycurcumin in *C. domestica* Val.. Methanol and water were used for the optimized with UAE application while water was only used for optimized MAE application. RP-HPLC coupled with UV was used because it offers a more convenient and accurate means of separating and estimating individual curcuminoids. Solubility optimization of aqueous extracts with CD was carried out with MAE and UAE methods.

1.2 Problem Statement

Curcuminoids are natural substances with a lot of biological activities, including antiinflammatory, antioxidant and antitumor. However, their usage in the pharmaceutical field is limited by their aqueous insolubility as well as their isolation with aqueous solvent. These shortcomings have led to the consideration of methods which enhance the aqueous solubility. Despite being well established, conventional techniques for natural products isolation suffer from a few drawbacks due to their high cost, time consuming, less environmentally friendly and less health promoting compatibility. The research explores unconventional MAE and UAE techniques of natural product isolation that are most promising, efficient, cost effective and environmentally friendly and improving the solubility of extracting compound by inclusion complexes with CD.

1.3 Objectives of Study

The research is aimed towards improved extraction of curcuminoids, a group of less water soluble compounds using UAE and MAE methods and the inclusion complexation of CD with curcumin. In line with the major aim the targeted objectives are as follows:

- i. To optimize UAE methods for turmeric compounds using water and methanol.
- ii. To optimize MAE methods for turmeric compounds using water
- iii. To compare the optimized MAE and UAE methods.

- iv. To investigate the application of CD for improving the solubility of curcumin in aqueous extract for both MAE and UAE.
- v. To characterize the inclusion complex of turmeric using Fourier transform infrared spectroscopy (FTIR) and Scanning Electron Microscope (SEM).

1.4 Scope of the Study

The work was centred on the extraction of the major compounds of phenolic pigments from *C. domestica* Val. using MAE and UAE and the analytes were analysed using HPLC with UV detection. Enhancement of the solubility of CD was studied with methyl beta-cyclodextrin (M β -CD) and the inclusion complex was analysed by HPLC-UV and characterized by FTIR and SEM.

1.5 Justification of the Research

Extraction techniques have been widely investigated to obtain such valuable natural compounds from plants for commercialization. However, the quality and safety related problems of natural drugs have still been challenged for researchers. The main reasons for this drawback are the lack of reliable high performance and extraction, and methodologies for establishing the purity and standard for the herbal drugs. As a result of the above mentioned factors, the herbal medicines have still to find their way in order to be accepted in the global market. Thus, there is a need arises for development of newer extraction techniques in the herbal drug which is amenable to automation, with shortened extraction times, reduced organic solvent

consumption, prevention of pollution in analytical laboratories and reducing sample preparation costs. The ultimate goal is total or partial replacement of organic solvent with aqueous one that is cost effective, environmentally friendly and safe. The issues of aqueous turmeric rhizomes oleoresin crude extract solubility are also an area of interest.

1.6 Framework of the Research

The research entails extraction of curcuminoids from turmeric, a member of the Zingiberaceae family. The sample (rhizomes) was chopped into smaller pieces and air dried for two weeks before ground into powder in a mill blender and finally, stored in a sealed plastic container for further analysis. Extraction experiments were carried out using water for both MAE and UAE applications. Methanol was used in UAE application. In UAE, the parameters optimized are irradiation time, particle size, amplitude, solvent volume and temperature for both aqueous and methanol. The irradiation time, solvent volume, particle size and temperature were optimized with MAE application. The crude extract was carefully decanted and rinsed with the solvents. The combined solutions were centrifuged at 3800 rpm for 15 min, and then evaporated to dryness in a water bath heater. The methanol crude was filtered and evaporated using a rotary evaporator. In both cases the concentration in form of percentage yield was estimated using HPLC.

Phase solubility studies were performed using the optimum 20 mg of evaporated turmeric rhizomes oleoresin crude extract. The crude extract were obtained by the optimized condition of UAE and MAE methods was added to a glass bottle each separately containing M β -CD in 5.0 mL of ethanol-water (20:80; v/v), solution at various concentration ranging from 0 – 200 mM. The apparent stability constant, K_C , of curcumin in turmeric oleoresin for the M β -CD inclusion complexes was calculated from the slope and intercepts of the linear segment of the phase

solubility line. The mixing methods in M β -CD-turmeric rhizomes oleoresin inclusion complex used include kneading method, co-precipitation method and physical mixture method. The complexes were characterized using FTIR and SEM.

1.7 Thesis Organization

An overview of related research works on curcumin, extraction methods, conventional and unconventional extraction methods, CD inclusion complexes were presented in Chapter 2. The review provides a commentary on the general significance of the curcumin. It then provides a summary of the key mechanisms involved and aims to provide some background information that can be utilized in subsequent extraction work. The review also summarizes developments of natural product isolation using unconventional methods.

The experimental program is presented in Chapter 3. The apparatus, laboratory equipment, stock solution preparation, HPLC parameter optimization, optimization of extraction parameters, methodology of validation, phase solubility, preparation of inclusion complexation and its characterisation are explained together with technicality in the sample preparation.

Chapter 4 presents UAE with methanol together with cold solvent extraction. The optimized effect of extraction parameters with methanol using both UAE and cold solvent extraction are also presented in this chapter.

Chapter 5 presents the extraction of CD inclusion complexes with turmeric oleoresin using UAE with water. The optimized extraction parameters with aqueous solvent coupled with CD and cold solvent extraction are also described.

Chapter 6 presents MAE with water coupled with CD in order to improve the solubility of curcumin. The optimized effect of extraction parameters with aqueous solvent coupled with CD are also discussed in this chapter.

The overall conclusions and suggestions for further research are presented in Chapter 7.

precise economic evaluation, an additional experiments for establishing large-scale units is necessary.

Although UAE can be used successfully for extraction purposes, it should be borne in mind that ultrasonic conditions, including amplitude used and time can lead to the destruction of bioactive compounds. It is also well known that ultrasonic can lead to the production of free radicals within the cavitation bubbles and in some circumstances, these free radicals can induce undesirable changes and/or destruction of the compounds extracted. This unfavourable reaction can be looked into further in order to guard against destruction of bioactive compounds and formation of free radical due to acoustic cavitations.

This research looked at the solubility of turmeric rhizomes oleoresin as a whole. However, if the main aim is to increase solubility in the individual curcuminoids, there is a need for purification after extraction using any available and suitable method in order to avoid interference of the other compounds before inclusion complexation is carried out. CD as solubilizing agent is an expensive material used for solubility improvement, a further research is needed to understand whether re-usage is possible as a spent material.

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