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Extraction of curcumin from turmeric residue (*Curcuma longa* L.) using deep eutectic solvents and surfactant solvents

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Using waste materials to extract biologically active ingredients with green solvents is a new trend for sustainable development. Herein, different types of deep eutectic solvents (DESs) and surfactant solvents (SSs) were used to extract curcumin from turmeric residues (TRs), among which choline chloride–propylene glycol (ChCl–Pro) showed the highest yield. The optimized extraction conditions included a ChCl : Pro ratio of 1 : 2, water content in the DESs of 20%, solid : liquid ratio of 1 : 40 maintained for 60 min at 50 °C, and a TR particle size of 0.18 mm. The extraction yield was 54.2 mg g^{-1}, which was 1.31 times higher than when methanol was used as a solvent. Distilled water was used to recover curcumin from the DES extract with a recovery yield of 99.7%. Furthermore, the antioxidant and acetylcholinesterase (AChE) inhibitory activities of the recovered curcumin were evaluated, with IC_{50} values of 25.58 ± 0.51 and 19.12 ± 0.83 μg mL^{-1}, respectively. This study highlights the promising potential of using green solvents to extract bioactive compounds from waste materials.

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1. Introduction

Green chemistry is also known as sustainable chemistry. It is defined as the design of chemical products and processes that reduce or eliminate the use or generation of hazardous substances.[1] Organic solvents are commonly used to extract active ingredients from medicinal herbs.[2] However, organic solvents are toxic to human health, and they also contribute to environmental pollution, volatility, and explosion. Therefore, organic solvents are a significant obstacle to green chemistry.[1] In recent years, several new types of solvents have been developed for the extraction of bioactive compounds due to their green efficiency and the low cost of extraction methods.[3]

DESs are a new generation of solvents[4] made up of inexpensive and available solvents,[5] including a hydrogen-bond acceptor (HBA), *i.e.*, choline chloride, and a hydrogen-bond donor (HBD), *i.e.*, sugars, alcohols, carboxylic acids, vitamins, and amines.[6] When DESs are the primary metabolites in plants, they are called natural deep eutectic solvents (NADESs). The melting point of DESs is much lower than that of HBAs and HBDs.[7] DESs are used in many different applications, such as biocatalysis, electrochemistry, and extraction.[8] In spite of them emerging since 2003,[9] the application of DESs as extraction solvents has only appeared in the last few years. According to the statistics of Milena *et al.* reported in 2020,[10] there were about 100 research papers in which DESs/NADESs were used to extract natural bioactive compounds from plants within 3 years from 2017 to 2019. The studies focused on evaluating the extraction efficiency of compounds such as phenolics, flavonoids, terpenoids, and alkaloids.[11–13] DESs are safe, non-toxic, environmentally friendly,[14] and enable high extraction yields, so DESs are often called solvents of the 21st century, which could soon replace organic solvents.[8,12]

Surfactants are amphoteric molecules consisting of a hydrophilic head and a hydrophobic tail. Surfactants can form micelles in aqueous solutions when their concentrations are above the critical micellar concentration (CMC). The micelles have a hydrophilic shell and hydrophobic core. This structure allows micelles to interact with target compounds to increase their solubility, so that surfactants improve the extraction yields of aqueous solutions.[15] Furthermore, increasing the temperature to the cloud point can favor the formation of two liquid phases: one rich in surfactants containing high concentrations of the hydrophobic compounds in a small volume and the other containing hydrophilic constituents.[16] Therefore, the substances dissolved in the micelles can be easily concentrated by changing the temperature. This process is called cloud point

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extraction (CPE).[15] CPE has the advantages of eco-friendliness, fast, and economic efficiency.[17] Several studies have applied CPE to extract compounds from plants and food waste.[17,18]

Food loss and food waste are becoming a serious problem worldwide, with negative nutritional, economical, and environmental consequences.[19] According to the Food and Agriculture Organization of the United Nations, about 1.3 billion tons of food are wasted and lost every year, among which there are 0.5 billion tons of plant-derived wastes.[20] However, plant-derived wastes are known to be a rich source of potentially valuable components, including proteins, polysaccharides, and different phytochemicals. The bioactive compounds from wastes possess antimicrobial, antioxidant, anti-inflammatory, anti-cancer, and other valuable properties.[21] These phytochemicals have potential to be used in the food industry, medicines, and pharmaceuticals, and cosmetics. Consequently, useful components from waste are extracted using various techniques and solvents. However, along with the development of green chemistry, recent trends have focused on finding and using green solvents to replace traditional organic solvents in the extraction process.[20] The use of waste materials to extract biologically active ingredients with green solvents is a potential trend in sustainable development.[22]

Curcuma longa L. (*C. longa*), commonly known as turmeric, is a member of the ginger family (Zingiberaceae). This species is cultivated in Asian countries and is used extensively as a spice for coloring and flavoring foods.[23] In traditional medicine, turmeric has been used for thousands of years as a drug to treat many diseases, such as skin diseases, wounds, infectious diseases, digestive disorders, and liver ailments.[24] Curcumin, also called diferuloylmethane, is a major polyphenol found in turmeric. Curcumin displays a wide range of biological activities beneficial to human health, including antioxidant, anti-inflammatory, antineoplastic, antidiabetic, anticholinergic, immuno-modulatory, and hepatoprotective activities.[23–25] Depending on the geographical origin, variety, harvest season, curcumin can be found in turmeric at a content ranging from 2% to 8%.[26] Turmeric starch can be isolated from the fresh rhizome by performing several washes with water.[27,28] This process has produced commercially valuable turmeric starch and turmeric residue (TR), which is discarded with no value. Nevertheless, curcumin is very poorly soluble in water, so a large amount of curcumin is wasted in the TR.[29]

In this study, for the first time, an efficient choline chloride-based DES method was used to extract curcumin in TR. A series of DESs and SSs were prepared, and the extraction yields of curcumin were evaluated. Furthermore, the major factors affecting the extraction efficiency were optimized. In addition, the recovery of curcumin from the DES extract was performed using distilled water. Finally, the antioxidant and AChE inhibitory activities of the curcumin extracts were evaluated.

2. Materials and methods

2.1. Chemicals and materials

Turmeric, the rhizome of *C. longa*, was collected from Thua Thien Hue province, Vietnam, in May 2021, and was identified by Dr Tuan Anh Le and Dr Tien Chinh Vu, Vietnam National Museum of Nature. A voucher specimen was deposited at the Faculty of Pharmacy, University of Medicine and Pharmacy, Hue University, Vietnam.

Curcumin (98%, HPLC) was purchased from AK Scientific, Inc. (California, USA). Choline chloride (99%) was purchased from Thermo Fisher Scientific, Co. (Massachusetts, USA). Tween-85, Tween-80, Tween-40, Tween-20, Triton-X-100, Triton-X-114, LAE-7, LAE-9, ethylene glycol, glycerol, propylene glycol, citric acid, lactic acid, acetic acid, formic acid, oxalic acid, glucose, sorbitol, sucrose, maltose, xylose, fructose, acetamide, and tartaric acid were purchased from Xilong Scientific Co., Ltd. (Guangdong, China). 2,2-Diphenyl-1-picrylhydrazyl (DPPH), quercetin, AChE, acetylthiocholine iodide (ATCI), 5,5-dithiobis(2-nitrobenzoic acid) (DTNB), and galantamine were purchased from Sigma-Aldrich Co. (Missouri, USA).

2.2. HPLC analysis

Samples were filtered through 0.45 μm polytetrafluoroethylene filters (Whatman plc., Buckinghamshire, United Kingdom) prior to injection. Curcumin was quantitated by a reversed-phase HPLC system (Agilent Technologies Co. Ltd., California, USA) equipped with an auto-sampler, a pump, a UV detector, and an automatic column temperature control oven. The chromatographic separation of curcumin was performed with an eclipse XBD-C18 reversed-phase column (4.6 × 150 mm i.d., 5 μm, Agilent Technologies, USA). The mobile phase was 0.2% acetic acid aqueous solution (A) and acetonitrile (B) with a ratio of 55 : 45, respectively. The flow rate was 1.0 mL min^{-1}. The detection wavelength was 420 nm. The retention time of standard curcumin was 10.725 min and for curcumin in the sample, it was 10.724 min (Fig. 1).

2.3. Preparation of DESs and surfactant solvents

2.3.1. Preparation of DESs. All DESs were prepared by mixing ChCl and HBD substances at a specified molar ratio (Table 1) and heating at 80 °C from 2–6 h, with constant stirring

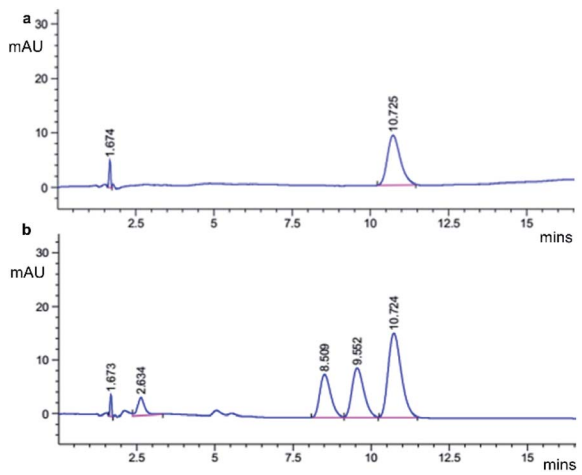

Fig. 1 HPLC chromatograms of curcumin at 420 nm, (a) reference compounds, (b) sample.

to obtain a stable homogeneous liquid. Then, the DESs were cooled down at room temperature for 24 h. The solvents were stored in sealed vials and kept in a desiccator for later use.[30]

2.3.2. Preparation of surfactant solvents (SSs). The SSs were prepared at a concentration of 5 mM in distilled water to ensure that this concentration value was greater than the CMC value of the surfactants (Table 2). The CMC values of surfactants were taken from the manufacturer's catalogs.

2.4. Separation of starch and TR from fresh turmeric

The process of separating the starch and TR from fresh turmeric was performed as follows: fresh turmeric (10.0 kg) was washed and minced, and then mixed with 50 L of distilled water; the whole mixture was filtered through a 0.25 mm sieve; this process was repeated two more times to separate the TR and filtrate. The obtained starch from the filtrate was washed with distilled water to remove impurities. The purified starch and TR were dried at 60 °C in an oven (humidity 8–10%). The starch and TR were preserved in desiccators to conduct further experiments.

2.5. Extraction of curcumin from TR

TR (1.0 g) was extracted with each 20 mL of the DESs containing 20% water and the SSs prepared in Section 2.3. The reference solvents used were distilled water, ethanol, and methanol. TR was extracted with solvents at room temperature under continuous stirring for 60 min. Then, the extracts were centrifuged for 15 min at 5000 rpm to remove any solids. The extract was diluted, filtered through a 0.45 μm filter, and the curcumin present in the extract was quantified by HPLC.

The ratio of components in the solvents, the water content in DESs, the liquid–solid ratio, extraction time, extractive temperature, and TR particle size were investigated to optimize the extraction process. Each experiment was repeated three times to ensure accuracy, and the results were reported as the mean with the standard deviation.

Table 1 List of the DESs used in this study

No.	Abbreviation	Combination	Mole ratio
1	ChCl–Eth	Choline chloride–ethylene glycol	1 : 2
2	ChCl–Gly	Choline chloride–glycerol	1 : 2
3	ChCl–Pro	Choline chloride–propylene glycol	1 : 2
4	ChCl–Cit–H_2O	Choline chloride–citric acid–water	1 : 2 : 2
5	ChCl–Lac	Choline chloride–lactic acid	1 : 2
6	ChCl–Ace	Choline chloride–acetic acid	1 : 2
7	ChCl–For	Choline chloride–formic acid	1 : 2
8	ChCl–Oxa–H_2O	Choline chloride–oxalic acid–water	1 : 2 : 2
9	ChCl–Glu–H_2O	Choline chloride–glucose–water	1 : 2 : 2
10	ChCl–Sor–H_2O	Choline chloride–sorbitol–water	1 : 2
11	ChCl–Suc–H_2O	Choline chloride–sucrose–water	1 : 2 : 2
12	ChCl–Mal–H_2O	Choline chloride–maltose–water	1 : 2 : 2
13	ChCl–Xyl–H_2O	Choline chloride–xylose–water	1 : 2 : 2
14	ChCl–Lac–H_2O	Choline chloride–lactose–water	1 : 2 : 2
15	ChCl–Fru–H_2O	Choline chloride–fructose–water	1 : 2 : 2
16	ChCl–Ace–H_2O	Choline chloride–acetamide–water	1 : 2 : 2
17	ChCl–Tar–H_2O	Choline chloride–tartaric acid–water	1 : 2 : 2
18	ChCl–H_2O	Choline chloride–water	1 : 2

Table 2 List of the surfactant solvents used in this study

No.	Surfactant	CMC values (mM)
1	Tween-85	0.06
2	Tween-80	0.01
3	Tween-40	0.03
4	Tween-20	0.06
5	Triton-X-100	0.23
6	Triton-X-114	0.20
7	LAE-7	0.02
8	LAE-9	0.11

2.6. Recovery of curcumin from the DESs

After curcumin was extracted from the optimized process, the extract was dissolved in distilled water, and precipitation was carried out at room temperature within 24 h. The precipitate was filtered through a filter paper and dried at 50 °C, and the recovery of curcumin was calculated. Different volume ratios of the ChCl–Pro extract and distilled water (1 : 10, 1 : 20, 1 : 40, 1 : 80, and 1 : 100, v/v) were investigated to find the optimal ratio for the process recovery of curcumin from the extract. The above experiments were carried out in triplicate.

2.7. Antioxidant activity

The antioxidant activity was determined by the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical neutralization assay, according to the method described by Masuda *et al.* with small modifications.[31] The DPPH and samples were dissolved in methanol. Then, 2.0 mL DPPH (0.135 μM) was added to 2.0 mL each sample. The mixture was shaken well with a vortex machine and incubated at room temperature for 30 min in dark. The absorbance of the mixture was measured at 517 nm using a UV/VIS spectrophotometer (UV-1800, Shimadzu USA Manufacturing, Inc., Oregon, USA). Quercetin was used as a positive control. The percentage of DPPH radical inhibition was calculated using the following formula:

$$\%\ \text{DPPH scavenging effect} = [(A_{\text{blank}} - A_{\text{sample}})/A_{\text{blank}}] \times 100$$

where A_{blank} is the absorbance of DPPH; A_{sample} is the absorbance of DPPH + sample.

2.8. AChE inhibitory activity

The AChE inhibitory assay was assessed according to the Ellman's method,[32] with slight modifications. The reaction mixture, consisting of phosphate buffer (pH = 8), the test sample solutions, and AChE solution (0.25 units per mL) was added to each well of a 96-well plate and incubated for 15 min at room temperature. Then, DTNB solution (2.4 mM) and ATCI solution (2.4 mM) were added to the reaction mixture, which produced a yellow 5-thio-2-nitrobenzoate anion. The mixture was incubated further for 15 min at room temperature. The absorbance of the solution was recorded at 405 nm using an ELISA microplate reader (EMR-500, Labomed Inc., California, USA). Galanthamine was used as a positive control. All the

tested samples and the positive control were dissolved in 10% DMSO (analytical grade). The inhibition percentage was calculated using the following equation:

$$I\% = (1 - A_{sample}/A_{control}) \times 100$$

where A_{sample} and $A_{control}$ are the respective enzymatic activities with and without the sample being tested.

2.9. Data analysis

Data processing was performed by the analysis of variance (ANOVA) using the software MSTAT-C, and the mean separation was assessed using the least significant difference (LSD) test at the $p \leq 0.05$ level of significance.

Data were expressed as the mean ± standard deviation (SD). Concentrations inducing 50% inhibition (IC_{50}) were identified by linear regression analysis.

3. Results and discussion

3.1. Curcumin content in the starch and TR

The starch and TR were separated from 10.0 kg of fresh turmeric (equivalent to 1.0 kg of dried turmeric). The amounts of curcumin present in the TR and starch were 20.57 ± 0.58, 5.29 ± 0.17 g, respectively. This result showed that TR contained four times more curcumin than turmeric starch. Therefore, extracting curcumin from TR is meaningful for taking advantage of the discarded materials.

3.2. Solvent selection for the extraction of curcumin from TR

Here, 18 DESs and 8 SSs were tested to investigate the ability to extract curcumin from TR, and the extraction yields of curcumin with different solvents are shown in Fig. 2 and 3. Methanol and ethanol were used as the reference solvents. The extraction yields of curcumin from the TR when using DESs and SSs were 0.3–22.3 and 5.0–11.3 mg g^{-1}, respectively. In general, the DESs formed from the HBD of alcohols and acids, such as ethylene glycol, propylene glycol, lactic acid, acetic acid, and formic acid, had better curcumin extraction efficiencies in the TR, and the extraction yields ranged from 17.1 to 22.3 mg g^{-1}. Moreover, the sugar-based DESs were the most ineffective extraction solvents with yields of less than 2.0 mg g^{-1}.

The extraction process of compounds in DES was based on the hydrogen bonding and π–π interactions between the target molecules and the DESs.[11] In this experiment, the difference in extraction yields using various DESs types may be explained by the different hydrogen-bonding interactions of curcumin with individual DESs. A recent report by Khadija *et al.*[33] showed that several DESs, including sucrose–choline chloride–water, fructose–lactic acid–water, sucrose–lactic acid–water, and lactic acid–choline chloride–water, exhibited a higher efficiency extraction for curcumin from *C. longa* than those in an 80% methanolic aqueous solution. According to Sujata *et al.*,[34] choline chloride : lactic acid (1 : 1) showed the best extraction yields of curcuminoids from *C. longa* using ultrasound-assisted DES-based extraction. Furthermore, Foozie *et al.*[26] used an ionic liquid of *N*,*N*-dipropyl ammonium *N*′,*N*′-dipropylcarbamate to extract curcumin from *C. longa* under enzyme assistance. Choline chloride : glycerol (1 : 1) can also be used to extract curcuminoids, as reported by Jeliński *et al.*[35] In the present study, the ChCl–Pro solvent resulted in the highest curcumin yields (22.3 ± 0.8 mg g^{-1}). In comparison, water, methanol, and ethanol showed curcumin yields of 2.4 ± 0.4, 0.5 ± 0.1, 22.7 ± 0.8, and 21.6 ± 1.3 mg g^{-1}, respectively. Therefore, ChCl–Pro was selected as the solvent to optimize the extraction process.

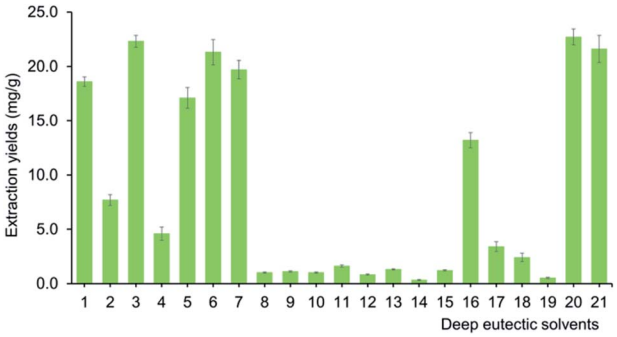

Fig. 2 Curcumin extraction yields of DESs, and the reference solvents water, methanol, ethanol for comparison (solid–liquid ratio of 1 : 20; extraction time of 60 min; extraction temperature of 25 °C). (1) ChCl–Eth; (2) ChCl–Gly; (3) ChCl–Pro; (4) ChCl–Cit–H_2O; (5) ChCl–Lac; (6) ChCl–Ace; (7) ChCl–For; (8) ChCl–Oxa–H_2O; (9) ChCl–Glu–H_2O; (10) ChCl–Sor–H_2O; (11) ChCl–Suc–H_2O; (12) ChCl–Mal–H_2O; (13) ChCl–Xyl–H_2O; (14) ChCl–Lac–H_2O; (15) ChCl–Fru–H_2O; (16) ChCl–Ace–H_2O; (17) ChCl–Tar–H_2O; (18) ChCl–H_2O; (19) H_2O; (20) MeOH; (21) EtOH.

3.3. Optimization of the curcumin extraction process in TR with the ChCl–Pro solvent

To optimize the extraction conditions of curcumin from TR, factors affecting the extraction yield were investigated,

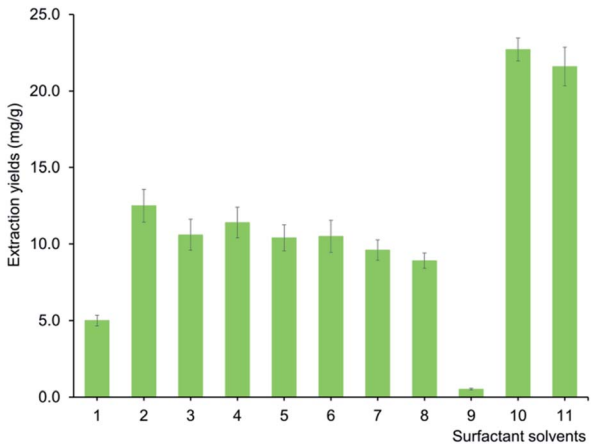

Fig. 3 Curcumin extraction yields of SSs, and the reference solvents water, methanol, ethanol for comparison (solid–liquid ratio of 1 : 20; extraction time of 60 min; extraction temperature of 25 °C). (1) Tween-85; (2) Tween-80; (3) Tween-40; (4) Tween-20; (5) Triton-X-100; (6) Triton-X-114; (7) LAE-7; (8) LAE-9; (9) H_2O; (10) MeOH; (11) EtOH.

including the ratio of ChCl and Pro, the water content in DESs, the liquid : solid ratio, extraction time, extractive temperature, and TR particle size.

3.3.1. Effect of salt on the HBD ratio. In order to find the most effective ratio of ChCl and Pro for the extraction process, the solvents were prepared with different ratios of ChCl and Pro (1 : 1, 1 : 2, 1 : 3, 1 : 4, 1 : 5, mol mol^{-1}) (Fig. 4A). The curcumin efficiency extraction increased with an increase in the Pro content in DESs. Specifically, the yields increased from 18.2 ± 0.9 to 25.8 ± 0.9 with the ChCl–Pro ratio increasing from 1 : 1 to 1 : 2. Viscosity is a major property that affects the extractability of DESs.[12] Pro is a liquid, therefore, increasing the Pro content reduced the viscosity of DESs, leading to the improved extraction yields of this solvent. However, an excessive increase of Pro resulted in a decreased concentration of ChCl in DESs. This result can be explained by the reduced interaction of the target compound with the chloride anion, thereby reducing the extraction yields.[36] In this study, the ChCl–Pro mole ratio of 1 : 2 was the highest yield. Hence, this ratio was selected for further experiments.

3.3.2. Effect of water content in DESs. To examine the effect of the water content in the DESs on the extraction efficiency, DESs with different water contents (0%, 20%, 40%, and 60%) were investigated (Fig. 4B). When 20% water was added into the DESs of ChCl–Pro, the average curcumin contents were the highest (25.8 ± 1.4 mg g^{-1}). When the water content in the DESs was increased to 40% and 60%, the extraction efficiency decreased significantly. A decrease in solvent viscosity was observed with increasing water content in the DESs, and the extraction performances were improved. However, excess water can rupture the hydrogen-bond interactions between HBA and HBD in DESs.[37] Dai *et al.* reported that DESs could still possess supramolecular characteristics with a water content of less than 50%.[38] In conclusion, the extraction capacity of DESs was most effective with a proper water percentage. Therefore, 20% water content in DESs of ChCl–Pro was selected for the subsequent experiments.

3.3.3. Effect of the solid–liquid ratio. The solid–liquid ratio is an essential factor affecting the extraction yields. The target compounds were not completely extracted with a low amount of solvent compared to the medicinal material. However, increasing the liquid volume will cause unnecessary solvent waste. In the present experiment, the tested ratios of TR and solvent were 1 : 10, 1 : 20, 1 : 40, and 1 : 80 g mL^{-1}. As shown in Fig. 4C, the extraction yields of curcumin increased along with the solid–liquid ratio from 1 : 10 to 1 : 80. The results of this experiment were consistent with the mass-transfer phenomenon. A large amount of solvent volume contributed to the formidable concentration gradient of compounds inside and outside the plant cells, promoting the target molecules to transfer from the cell–matrix into the solvents. When a small amount of solvent is compared to the solid, the cavitation of solvents into the cells is more complicated, resulting in an incomplete mass transfer.[34] Consequently, to achieve the best cost and environmental benefits, a solid–liquid ratio of 1 : 40 was selected for the subsequent experiments.

3.3.4. Effect of the extraction time. The extraction time of curcumin from TR was investigated at a 30, 40, 50, 60, 90, and 120 min (Fig. 4D). The extraction yields increased from 18.1 ± 1.3 to 25.9 ± 1.1 mg g^{-1} at the increased extraction time from 30 to 60 min. Moreover, the curcumin content obtained at 90 and 120 min extraction was 25.8 ± 0.9 and 25.9 ± 0.6 mg g^{-1}, respectively. Many studies have indicated that the extraction time significantly affects the yields of the extracted products.[39] Compounds in the plant's cell are dissolved and released within a certain period. This process depends on several factors, such

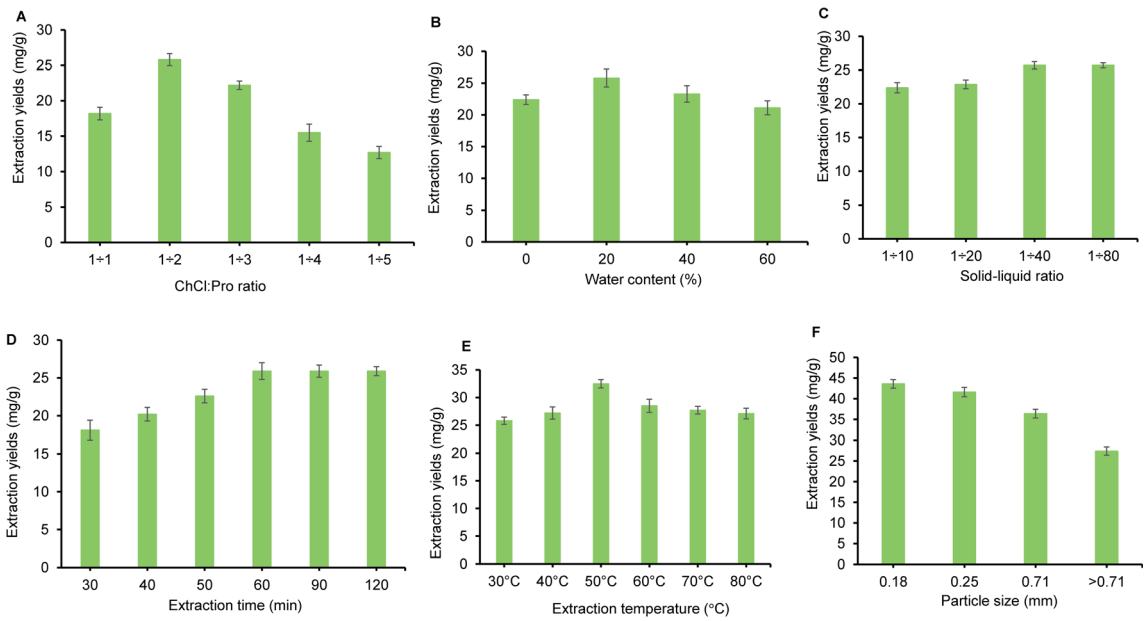

Fig. 4 Effect of the ChCl–Pro ratio (A), water content (B), solid–liquid ratio (C), extraction time (D), extraction temperature (E), and particle size (F) on the extraction yields of curcumin from TR.

as the physicochemical properties of solvents and target compounds, the structure of the extract material, and the extraction methods.[40] In general, the extraction yields increased with the increase in the extraction time. However, some extraction methods using high temperature and long extraction times, such as Soxhlet, will degrade many biologically active components.[33] In this study, to target the best economic benefits, the extraction time of 60 min was selected.

3.3.5. Effect of the extraction temperature. The extraction temperature is one of the most critical factors affecting the extraction process, so determining the optimal extraction temperature is very important.[33] The temperatures for curcumin extraction from TR were investigated at 30 °C, 40 °C, 50 °C, 60 °C, 70 °C, and 80 °C (Fig. 4E). The extraction yields increased from 30 °C to 50 °C while they decreased as the temperatures changed from 50 °C to 70 °C. The optimum temperature used to extract curcumin from TR was 50 °C with a yield of 32.5 ± 0.8 mg g^{-1}. In general, increasing the extraction temperature can increase the dispersion of the solvents into the cells, thereby increasing the ability of the soluble components from the cell and increasing the extraction efficiency.[41] Moreover, increasing the temperature reduced the surface tension and viscosity of the solvents, which are of great importance to improving the extraction yields of DESs.[33] However, excessive temperature increases can reduce the interaction between ChCl and Pro. This weakens the complex formed between the components in the solvent, thereby reducing the ability to extract curcumin from TR.

3.3.6. Effect of the TR particle size. DESs have high viscosity, so the size of the TR greatly affects the extraction process. In this study, the tested TR particle sizes included 0.18, 0.25, 0.71, and >0.71 mm. Along with the reduction in the particle size from >0.71 to 0.18 mm, the extraction yield of curcumin was improved from 27.4 ± 1.0 to 43.6 ± 1.1 mg g^{-1} (Fig. 4F). This result can be explained by the fact that the smaller the TR particle size, the easier it was for the solvent to contact and enter the cell, thereby increasing the extraction efficiency.[34]

Similar observations were reported in previous publications. For instance, Foozie *et al.*[26] indicated that the extraction efficiency of curcumin from *C. longa* increased from 2.64% to 3.84% along with the reduction of the turmeric particle size from 0.425 mm to 0.18 mm. In another report by Sujata *et al.*, the number of curcuminoids in ChCl–lactic acid DESs was significantly improved; however, an excessive particle size reduction of turmeric powder reduced the extraction yield.[34]

3.4. Comparison of extraction solvents

To evaluate the efficient extraction of the ChCl–Pro solvent and organic solvent, the reactions proceeded in parallel under the same conditions: a solid–liquid ratio of 1 : 40, extraction time of 60 min, extraction temperature of 50 °C, and TR particle size of 0.18 mm, with extracting three times in a row with newly added solvents. The extraction yields of curcumin from TR by ChCl–Pro and methanol are shown in Fig. 5. The total yield with ChCl–Pro DESs was 54.2 mg g^{-1}, while the first time extraction involved 80.6% curcumin. Moreover, the methanol solvent yield was 41.3 mg g^{-1}, 1.31 times lower than that of the ChCl–Pro solvent. Several studies have reported the extraction efficiency of curcumin/curcuminoids from turmeric using various solvents and techniques, including Soxhlet extraction,[42] supercritical CO_2 extraction,[43] supercritical fluid extraction,[44] microwave-assisted extraction,[33] ultrasound-assisted extraction,[34] enzyme-assisted extraction,[26] and green solvent-based extraction.[45] For example, in a study by Mara *et al.*, the curcuminoid yield (8.43%) was obtained using Soxhlet extraction with isopropyl alcohol and ethanol.[42] In another study, the extraction capacity of curcuminoids from *C. longa* was compared between batch extraction and three-phase partitioning with yields of 52.77 mg g^{-1} and 58.38 mg g^{-1}, respectively.[46] Besides, Sujata *et al.*[34] described the ultrasound-assisted DES-based extraction of curcuminoids from *C. longa* with a maximum yield of 77.13 mg g^{-1}.

3.5. Recovery of curcumin from DESs extract

The recovery of target compounds from DESs is a major challenge because of the non-volatilization property of these solvents. Several methods can be used to recover target compounds from DES extracts, such as supercritical CO_2, recrystallization, column chromatography, liquid–liquid extraction, and adsorption. Nevertheless, these methods require complicated techniques, so are difficult to apply on an industrial scale.[34] Here, DESs are water-soluble, while curcumin is very slightly soluble in water. Therefore, the recovery of curcumin from the DES extract was performed using distilled water. In our study, different volume ratios of the DES extract and distilled water (1 : 10, 1 : 20, 1 : 40, 1 : 80, 1 : 100, v/v) were investigated to evaluate the recovery efficiency through the percentage of curcumin present in the precipitate compared with the original extract (Fig. 6). The result indicated that the recovery yields increased from 77.5% to 99.7% with the ratio of extract : water increasing from 1 : 10 to 1 : 40. Thereafter, the recovery of curcumin decreased with an amount of water equals to 100 times the extract volume. The best recovery (99.7%) was

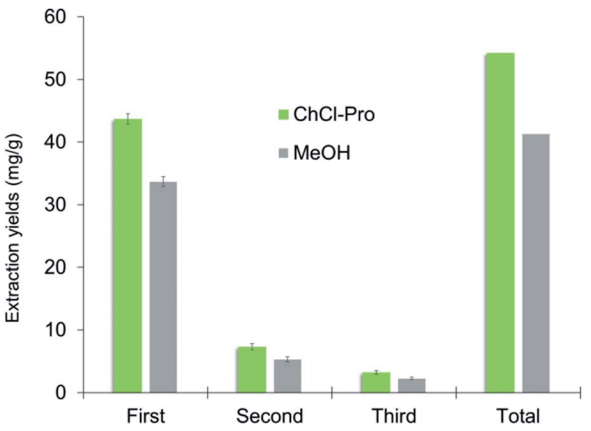

Fig. 5 Extraction yields of curcumin from TR by ChCl–Pro and methanol solvents.

obtained when the water volume was 40-fold that of the extraction volume, whereas in the previous studies by Khadija *et al.*[33] and Sujata *et al.*,[34] the curcuminoids recovery from DESs were 37.5% to 41.97%. Therefore, the use of ChCl–Pro DESs to extract curcumin from the turmeric residue showed a high extraction capacity; moreover, the recovery of most curcumin from the DES extract has great significance for application in industrial practice. The recovered curcumin-containing precipitate was dried and stored in a dry place for further bioactivity tests. The curcumin content in the recovered precipitate was 20.8 ± 0.3%.

3.6. Evaluation of the bioactivities of the recovered curcumin from ChCl–Pro extract

3.6.1. Antioxidant activity. The antioxidant activity of recovered curcumin from the ChCl–Pro extract and methanol extract is illustrated in Table 3. Several studies have indicated that the antioxidant capacity was affected by the number of hydroxyl groups.[47] In this study, the structure of curcumin contained two groups of *o*-methoxyphenols and an enol form of β-diketone. This structure allows the ability to thoroughly trap free radicals in a chain-breaking antioxidant mechanism.[48] In the current study, the IC_{50} value of the recovered curcumin from the ChCl–Pro extract was 25.58 ± 0.51 μg mL^{-1}, while the curcumin extracted by methanol and the positive control had IC_{50} values of 30.02 ± 0.49 and 12.19 ± 0.16 μg mL^{-1}, respectively. The recovered curcumin from the DESs of the ChCl–Pro extract exhibited a higher antioxidant activity than that of the corresponding methanol extract. The content of the substance groups in general and curcumin in particular in the extracts affects the antioxidant capacity.[49] Tanvir *et al.* indicated that the ethanolic and aqueous extracts of *C. longa* from Bangladesh exhibited antioxidant activity with IC_{50} values from 1.08 to 16.55 μg mL^{-1}.[49] Another report by Choi[50] showed the DPPH free radical scavenging activity of five fractions from *C. longa* of H_2O, *n*-hexane, BuOH, MeOH crude extract, $CHCl_3$, and EtOAc with IC_{50} values of 759.28, 280.42, 81.09, 58.17, 16.70, and 9.86 μg mL^{-1}, respectively. Braga *et al.*[42] compared the yield extraction, chemical composition, and antioxidant activity of extracts from *C. longa* using various extraction techniques, including Soxhlet, hydrodistillation, supercritical extraction using CO_2, low-pressure solvent extraction, and cosolvents, in which, the low-pressure and Soxhlet extracts exhibited the strongest antioxidant activity.

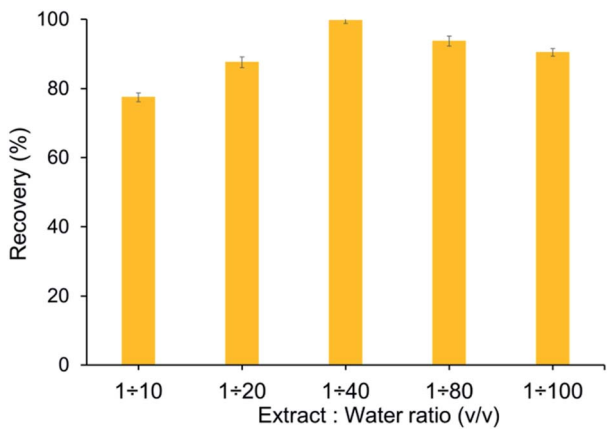

Fig. 6 The recovery of curcumin from the DESs of ChCl–Pro extract.

Table 3 Antioxidant activity of recovered curcumin from the ChCl–Pro extract and methanol extract

Concentration (μg mL^{-1})	Percentage inhibition		
	ChCl–Pro[a]	MeOH[b]	Quercetin
10	33.31	20.09	40.75
20	46.10	38.37	81.03
30	54.04	50.11	100
40	65.17	65.56	100
50	73.23	75.55	100
IC_{50}	25.58 ± 0.51	30.02 ± 0.49	12.19 ± 0.16

[a] Curcumin recovered from ChCl–Pro extract. [b] MeOH extract.

3.6.2. AChE inhibitory activity. In the current study, the AChE inhibitory activity of the recovered curcumin from the ChCl–Pro extract and methanol extract is presented in Table 4. The results showed that the AChE inhibition activity of the recovered curcumin from the ChCl–Pro extract was higher than that of the methanol extract, with IC_{50} values of 19.12 ± 0.83 *vs.* 24.74 ± 0.31 μg mL^{-1}.

In the synaptic cleft, AChE catalyzes the metabolism of acetylcholine to choline and acetate. The inhibition of AChE improves the cognitive function in patients with Alzheimer's disease. Numerous studies have reported the inhibitory effect of curcuminoids in general and curcumin in particular on AChE.[51] According to Wolkmer *et al.*,[52] curcumin inhibited AChE and improved the immunological response in Wistar rats at a dose of 60 mg kg^{-1} body weight. Akinyemi *et al.* also reported that curcumin enhanced memory in albino rats through the inhibition of AChE.[53] In the study by Ahmed and Gilani, curcuminoids inhibited AChE and intensified the memory in rats at a dose of 10 mg kg^{-1}.[54] Zeynep *et al.* compared the AChE inhibitory effects of three curcuminoids (bisdemethoxycurcumin, dimethoxy-curcumin, curcumin) isolated from *C. longa* with IC_{50} values of 2.14 ± 0.78, 19.7 ± 0.2, and 51.8 ± 0.6 μM, respectively.[55] In short, the curcumin extract from TR using DESs of ChCl–Pro showed an inhibition ability against AChE.

Table 4 AChE inhibitory activity of recovered curcumin from ChCl–Pro extract and methanol extract

Concentration (μg mL^{-1})	Percentage inhibition		
	ChCl–Pro[a]	MeOH[b]	Galantamine
12.5	46.22	44.10	100
25	52.11	49.94	100
50	58.44	55.58	100
100	63.55	63.40	100
200	68.44	70.34	100
IC_{50}	19.12 ± 0.83	24.74 ± 0.31	0.33 ± 0.01

[a] Curcumin recovered from ChCl–Pro extract. [b] MeOH extract.

In summary, in the present study, we developed a simple method, using an inexpensive and environmentally friendly chemicals and simple equipment to extract curcumin from waste materials. In addition, we demonstrated the antioxidant activity and AChE inhibition of the obtained curcumin. A series of experiments needs to be implemented in future studies at an industrial scale to confirm the encouraging results of this work.

4. Conclusions

In this experiment, green solvents were used to extract curcumin from TR. The optimized extraction conditions were a ChCl–Pro ratio of 1 : 2, water content in DESs of 20%, solid–liquid ratio of 1 : 40, extraction time of 60 min, extraction temperature of 50 °C, and TR particle size of 0.18 mm. The highest yield of curcumin from TR using ChCl–Pro was 54.2 mg g^{-1}. The extraction efficiency of this method was found to be superior to the traditional method with methanol used as the extraction solvent. Furthermore, distilled water was used in the recovery of curcumin from the DES extract with recovery yields of 99.7%. Finally, the recovered curcumin from the DES extract showed significant antioxidant and AChE inhibitory activities with IC_{50} values of 25.58 ± 0.51 and 19.12 ± 0.83 μg mL^{-1}, respectively, which were better than methanol extract.

Food loss causes substantial economic losses and serious impacts on the environment. Plant-derived wastes still contain a large number of remnant bioactive compounds, which can be used in food and pharmaceutical industries. The design of green extraction techniques can be an effective and sustainable solution to the problems caused by food waste. The use of waste materials to extract biologically active ingredients with green solvents not only can bring economic efficiency but also solves the problem of environmental pollution. This is a potential future perspective.

Author contributions

Conceptualization, Hoai Thi Nguyen; methodology, Nhan Trong Le, Nguyen Thuy Hoang, Hoai Thi Nguyen, Hien Minh Nguyen; validation, Hien Bich Thi Le; investigation, Nhan Trong Le, Nguyen Thuy Hoang, Van Tuong Thi Van, Trieu Phat Dac Nguyen, Ngoc Huyen Thi Chau, Nguyen Thao Nguyen Le; writing—original draft preparation, Nhan Trong Le, Nguyen Thuy Hoang, Hoai Thi Nguyen, Hien Minh Nguyen; writing—review and editing, Nhan Trong Le, Huong Thi Phung, Hien Minh Nguyen; funding acquisition, Hoai Thi Nguyen. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

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