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FOOD ANALYSIS

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Determination of Curcumin in Food with Homogenous Liquid-Phase Microextraction Preconcentration and Spectrophotometric Determination

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ABSTRACT

Antioxidants play a role in the transformation of free radicals into more stable chemical structures. Work on phenolic antioxidants has accelerated in recent years. Curcumin is a natural phenolic with antioxidant properties. In this study, a salt-supported homogenous liquid-phase microextraction method was used for preconcentration and spectrophotometric determination of curcumin for the first time. The curcumin was transferred into the organic phase using cyclohexylamine as the extraction solvent at pH values between 2.0 and 7.0 and determined by spectrophotometry. The results showed that the performance of the method for curcumin was unaffected by pH. The pH of the sample solution, the mass of salt, and the volume of the solvent were optimized, and the influence of the matrix types was investigated. The limits of detection and quantification were 1.44 and 4.80 μg L^{-1} for curcumin. The developed method was employed for the analysis of food samples.

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KEYWORDS
Curcumin; cyclohexylamine; salt supported homogeneous liquid phase microextraction; spectrophotometry; phenolics

Introduction

In the last decade, there has been an interest to develop natural preventive agents derived from plants for disease prevention. These active ingredients are expected to play an essential role in synthesizing new and better agents (Nakata et al. 2007). Curcumin is a natural extract derived from turmeric and is known to have various therapeutic effects. It has traditionally been used to treat inflamed joints, parasitic skin diseases, the liver, and urinary diseases. Some studies have demonstrated the pharmacological effects of antineoplastic, antioxidant, and chemo-preventive compounds (Vakilinezhad et al. 2019). Curcumin has good tolerability and safety profiles even at doses between 4000 and 8000 mg/day and of doses up to 12,000 mg/day of 95% concentration of curcumin, bisdemethoxycurcumin, and demethoxycurcumin (Hewlings and Kalman 2017). Since

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its quantity in food, herbal drugs, and spices is important, it is necessary to determine it correctly across a wide range of concentrations.

There are many studies in the literature for the extraction and determination of curcumin in samples. Spectrophotometry (Hazra et al. 2015; Kadam et al. 2013; Sharma, Agrawal, and Gupta 2012; Savale 2017), spectroflourimetry (Gupta, Nahata, and Dixit 2010; Karimi et al. 2020), infrared spectroscopy (Lestari et al. 2017; Tanaka et al. 2008), chromatography (Jayaprakasha, Rao, and Sakariah 2002; Inoue et al. 2008; Jadhav, Mahadik, and Paradkar 2007; Osorio-Tobón et al. 2016) and electroanalytical techniques (Cittan, Altuntaş, and Çelik 2020; Arslan and Çakır 2014; Çakır, Biçer, and Yılmaz Arslan 2015; Burç, Güngör, and Duran2020; Basmaz and Öztürk 2017; Tigari and Manjunatha 2020; Stanic, Voulgaropoulos, and Girousi 2008; Ziyatdinova, Nizamova, and Budnikov 2012) have been used for the determination of curcumin. As spices and herbs are commonly analyzed, an extraction method is needed for the determination of curcumin. Dispersive liquid-liquid microextraction (Hashemi et al. 2013; Asfaram et al. 2016; Ünsal, Tüzen, and Soylak 2019) is a frequently used method for the isolation of curcumin from real samples. Ionic liquid microextraction (Gökdemir, Baylan, and Çehreli 2020; Sahne et al. 2017), deep eutectic solvent microextraction (Aydın, Yılmaz, and Soylak 2018; Altunay, Elik, et al. 2020; Altunay, Elik, et al. 2020), floating drop microextraction (Xie et al. 2020; Afkhami, Pirdadeh-Beiran, and Madrakian 2017), Soxhlet extraction (Revathy et al. 2011), microwave and ultrasound-assisted extraction (Mandal, Mohan, and Hemalatha 2008; Patil, Pathak, and Rathod 2021; Shirsath et al. 2017), surfactant-free microemulsion extraction (Degot et al. 2021), and cloud point extraction (Rahimi, Hashemi, and Nazari 2014) methods have also been used.

Salt supported homogenous liquid phase microextraction is based on the phase separation of a homogeneous mixture of the aqueous (including analytes) and organic phases and the simultaneous extraction of the analytes into one of the separated phases by the salting out effect. The method is useful in terms of reducing the use of hazardous organic solvents, reducing sample preparation time and cost, and ease of use (Manousi et al. 2022). To our best knowledge, this approach has not been used to extract curcumin from solid samples.

A new method has been developed for effective and quantitative extraction, preconcentration, and spectrophotometric determination of trace curcumin with salt-supported homogenous liquid-phase microextraction. Curcumin in food samples was extracted into the organic phase with salt support, and the organic phase was diluted with methanol and analyzed at 500 nm by spectrophotometry. The developed method was employed for the analysis of food samples.

Materials and methods

Apparatus and chemicals

A Hitachi UH 5300 spectrophotometer (Tokyo, Japan) was used to determine curcumin. A Precisa 125 A SCS analytical balance (Dietikon, Switzerland), a Fisons 12665 model vortex (London, UK), a Hettich Rotofix 32 A model centrifuge (Tuttlingen, Germany), a Sartorius PT–10 model pH meter (Goettingen, Germany), and a Millipore Milli-Q-

Direct 18 model water purification system (Darmstadt, Germany) were also used in the experiments.

Curcumin (analytical standard >98%), cyclohexylamine (analytical grade > 99%), NaCl (>99.5%), o-H_3PO_4 (>85.0%), and $NaH_2PO_4{\cdot}H_2O$ (99.0 – 102.0%) were purchased from Merck (Darmstadt, Germany). All solutions were prepared in 18.2 MΩ deionized water.

Methods

Method optimization was performed in 10 mL model solutions containing 3×10^{-6} mol L^{-1} curcumin. The pH 3.0 buffer, 300 µL of cyclohexylamine (as the extraction phase), and 3 g of sodium chloride (NaCl) (as the salting out agent) were added to the sample solution in 50 mL centrifuge tubes. The mixture was vortexed for 3 minutes to provide a homogeneous turbid solution. This solution was centrifuged at 4000 rpm for 10 minutes.

After centrifugation, two phases were obtained as the aqueous phase and the extraction phase. The lower water phase was removed with a syringe. The remaining extraction phase volume was measured with a micropipette, and the final volume was obtained with methyl alcohol to 500 µL. The solution was analyzed by spectrophotometry at 500 nm using a calibration curve. The same process steps were carried out with the blanks.

Preparation of samples

The developed method was applied to tea, turmeric powder, and saffron purchased from an herbalist, Kayseri, Turkey. 2.0 g of tea were weighed into a 150 mL beaker and 100 mL of deionized water was added. The extraction process was carried in an ultrasonic bath for 30 minutes.

For turmeric and saffron powders, 10 mg sample and 25 mL methanol were added into a 50 mL beaker, and the extraction was carried out in an ultrasonic bath for 30 minutes. All extraction procedures were carried out at the room temperature and the liquid was separated from the solid by centrifugation. The extraction of each sample was repeated twice and the obtained liquid fractions were combined. The final volumes of the samples were adjusted two-fold with solvent.

Results and discussion

pH

The isolation of trace curcumin from the aqueous phase to the extraction phase depends on the pH. Model solutions were prepared from pH 2.0 to 7.0 using buffers to determine the optimum value for the extraction of curcumin. The absorbance of the samples following the microextraction was determined by spectrophotometry. All results from pH 2.0 to 7.0 were quantitative. The optimum pH was selected to be 3.0 for subsequent measurements. These results show that the isolation of curcumin was unaffected by pH.

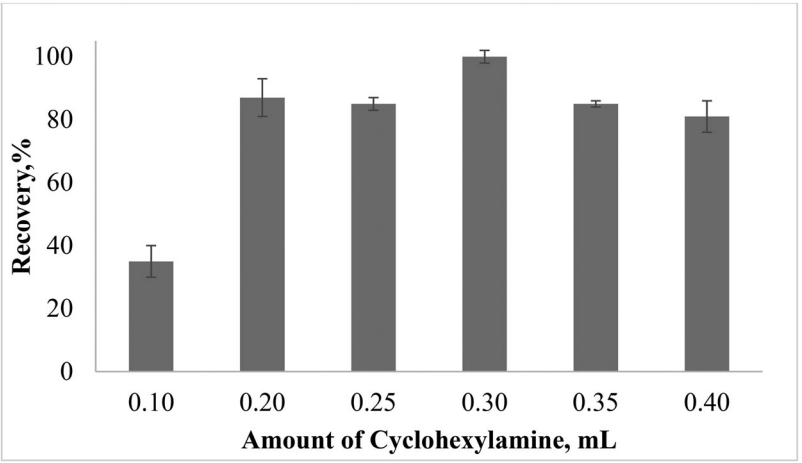


Figure 1. Influence of the volume of organic phase upon the recovery of curcumin. Conditions: concentration of curcumin: 3.0 x 10^{-6} M, pH: 3.0, concentration of NaCl: 3.0 g, centrifugation time: 10 min.

Volume of extraction solvent

In micro-extraction-based separation and enrichment studies, the type and quantities of the components that make up the extraction phase must be optimized. Hence, the influence immiscible and micelle-forming organic solvents such as cyclohexylamine upon the recovery of curcumin was investigated. Solutions containing volumes of cyclohexylamine from 100 µL to 400 µL were prepared to determine the optimum value.

Figure 1 shows that quantitative recovery of curcumin was obtained using 300 µL of cyclohexylamine. Therefore, this volume was employed in subsequent measurements. The reduced extraction efficiency at other volumes may be due to the balance between the volume of the aqueous sample in the medium, the volume of the extraction phase, and the mass of salt.

Mass of NaCl

In the extraction protocol, the sodium chloride salt dissolves in the aqueous phase and forces the organic substances in the aqueous phase to pass into the organic phase. NaCl masses from 2.0 to 4.0 g were added to the model solutions containing curcumin. Figure 2 shows that the recovery values were quantitative for more than 2.0 g of NaCl. The highest recovery was obtained using 3 g of NaCl which was used in subsequent measurements. The enhancement is based on the decreased solubility of the less polar solvent or analyte with increased salt concentration, leading to two-phase separation.

Sample volume

The influence of sample volume upon the recovery of curcumin under optimum conditions was investigated. For this purpose, the developed method was applied to model solutions with volumes between 10 and 30 mL. The results were quantitative using a

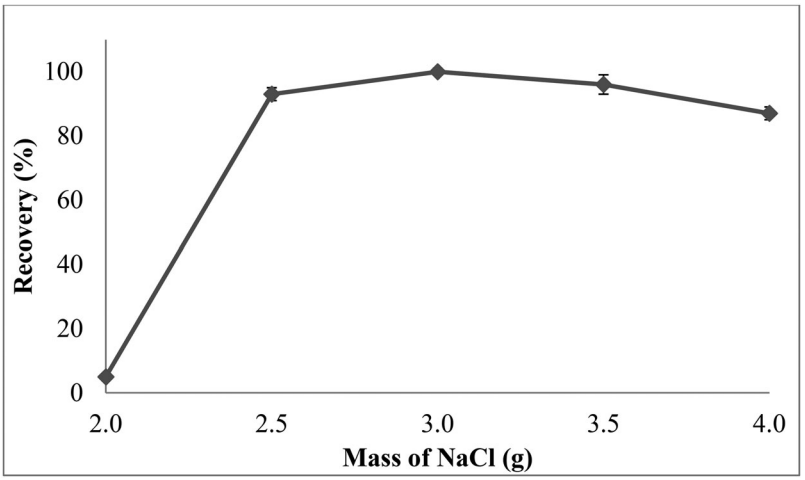


Figure 2. Influence of the NaCl mass upon the recovery of curcumin. Conditions: pH: 3.0, concentration of curcumin: 3.0 x 10^{-6} M, volume of cyclohexyamine: 300 µL, centrifugation time: 10 min.

Table 1. Tolerable concentrations of interferent species ($n = 3$).

Species	Added as	Added concentration (mg L^{-1})	Recovery (%)
K^{+}	KCl	1000	99 ± 1*
Fe^{3+}	$Fe(NO_3)_3.9H_2O$	0.5	93 ± 1
SO_4^{2-}	Na_2SO_4	1000	102 ± 4
CO_3^{2-}	Na_2CO_3	250	94 ± 4
Ca^{2+}	$Ca(NO_3)_2.4H_2O$	250	96 ± 4
Pb^{2+}	$Pb(NO_3)_2$	5.0	95 ± 2
Zn^{2+}	$Zn(NO_3)_2.6H_2O$	5.0	108 ± 4
Co^{2+}	$Co(NO_3)_2.6H_2O$	2.5	97 ± 3
Mn^{2+}	$Mn(NO_3)_2.4H_2O$	1.0	101 ± 4
B^{3+}	$Na_2B_4O_7.10H_2O$	5.0	94 ± 6
Karmin	Karmin	5.0	101 ± 1
Brillant black	Brillant black	9.0	102 ± 5
Cochenille red	Cochenille red	6.0	100 ± 5

*: $\bar{x} \pm s$

10 mL sample volume. There was a 20-fold enrichment factor because the final volume was 0.5 mL.

Matrix species

The influence of anions, cations, and organic species present in real samples was investigated. The tolerable concentrations are summarized in Table 1. The results for all species were quantitative at tolerable concentrations. The results show that the developed method may be employed without influence by the matrix.

Analytical performance of the method

To determine the limit of detection (LOD) and limit of quantification (LOQ), 23 parallel 10 mL blank samples were prepared. The limit of detection was calculated by

Table 2. Results of the real sample analyses as mean ± standard deviation and recovery values.

Sample	Added (μg)	Found (μg)	Recovery, %
	0	1.18 ± 0.15	–
Turmeric powder	7.37	8.57 ± 1.02	100
	14.74	15.01 ± 1.34	94
	0	1.84 ± 0.05	–
Curcumin tea	3.68	5.41 ± 0.64	97
	7.37	9.55 ± 0.49	104
	0	0.67 ± 0.01	–
Saffron	1.84	2.37 ± 0.05	92
	3.68	3.68 ± 0.10	88

Table 3. Comparison of this work with literature methods for the determination of curcumin.

Method	Linear range (μg L^{-1})	Relative standard deviation (%)	Limit of detection (μg L^{-1})	Reference
Dispersive liquid liquid microextraction	0-5	2.2	1.2	Hashemi et al. 2013
Dispersive liquid liquid microextraction	10-2000	2.3	0.233	Asfaram et al. 2016
Dispersive liquid liquid microextraction	0.05 – 100	2.87	28	Safdarian, 2012
Ultrasound-assisted ionic liquid-dispersive liquid liquid microextraction	0-5000	4.1	0.51	Ünsal, Tüzen, and Soylak 2019
Deep eutectic solvent microextraction	5-300	1.7-3.7	1.81	Altunay, Elik, et al. 2020
Salt supported homogenous liquid-phase microextraction	3 – 3000	3.6	1.44	This work

dividing three times the standard deviation of the absorbance values (3 s) by the slope (m) of the calibration curve. The limit of quantification was determined by dividing 10 times the standard deviation of the absorbance values by the slope (m) of the calibration curve. The limit of detection for curcumin was 1.44 μg L^{-1}; the limit of quantification was 4.80 μg L^{-1}.

The calibration relationship was $y = 0.413x + 0.0068$ with a coefficient of determination (R^2) of 0.997 where y is the absorbance and x is the concentration (μg L^{-1}). The linear range was between 3 and 3000 μg L^{-1}. The enrichment factor was 20 and the relative standard deviation was 3.6%.

Analysis of food samples

To characterize the accuracy of the method, curcumin was added to the tea, saffron, and curcumin powdered samples and the recoveries were evaluated. Curcumin was added to triplicate samples and the results are shown in Table 2. The concentrations were determined by spectrophotometry (Ünsal, Tüzen, and Soylak 2019).

Conclusions

The results demonstrate that the salt-supported homogenous liquid-phase microextraction was reliable for the determination of curcumin in food samples. The method was

employed for the first time for the analysis of turmeric, tea, and saffron for curcumin. The comparison of the developed method with the literature is provided in Table 3, demonstrating comparable analytical figures of merit. The determination of curcumin in food was carried out rapidly and inexpensively and this approach is suitable for the routine determination of curcumin.

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