JCHR (2022) 12(3), 409-419

Journal of Chemical Health Risks

www.jchr.org

ORIGINAL ARTICLE

Determination of Ultra Trace Amounts of Carmoisine in Food Specimens by Ultrasound-assisted Surfactant-enhanced Emulsification Microextraction Method Coupled with UV-Visible Spectrophotometry

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(Received: 16 January 2021 Accepted: 1 April 2021)

KEYWORDS

Ultrasound-assisted surfactant emulsification–Microextraction;
Carmoisine;
Food dyes;
Spectrophotometry;
Box–Behnken design

ABSTRACT: In this research, an ultrasound-assisted surfactant emulsification microextraction technique was established as a facile, practicable and eco-friendly method for preconcentration of carmoisine (CMS) before its spectrophotometric measurement. Zephiramine and CCl_4 were selected as the emulsifier and organic extractant solvent respectively. Box–Behnken design was employed for the optimization of various influencing factors in the extraction process. Under the optimized conditions, the preconcentration and enrichment factors were 666 and 630 respectively.. The limit of detection (LOD) of the designed analytical that was calculated as three times the signal-to-noise ratio (S/N) was 0.15 ng. mL^{-1}. The limit of quantification (LOQ) was 0.47 ng. mL^{-1} and the working dynamic range was 0.5-80 ng. mL^{-1} with the correlation coefficient of 0.9995. At the end, the applicability of the designed extraction technique for the quantitation of CMS in four real specimes was also inspected and all of the calculated recovery values were between 97.5-104.2% showed the designed technique can be employed for CMS measurement in real specimens.

INTRODUCTION

Synthetic colors are utilized in the cosmetics, food, pharmaceutical and textile industries all over the world. These type of dyes are used in the production of foodstuffs and soft drinks in order to amend the color, appearance and texture, as well as to preserve the natural color during the processing and storage [1]. Due to the fact that synthetic food dyes have azo functional groups and aromatic rings in their chemical structure, they have irreversible adverse effects on the health of human beings. In recent years, the concentration of non-natural colorants in the edible products have strictly been controlled because of the consumer health concerns (especially for children's health) [2]. Carmoisine (CMS), the structure of which is presented in Figure 1, is a highly-consumed anionic azo dye in the

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DOI: 10.22034/jchr.2021.1923785.1265

food industry in the manufacture process of different products such as juices, ice cream, candy and jelly gum. The acceptable daily intake (ADI) dosage of CMS is 4 mg kg^{-1} body weight/day [3]. Despite the fact that the concentration of CMS added to the food products is strictly controlled, its usage exceeds the permitted levels in some cases. Therefore, it is very important to determine CMS in highly consuming products such as beverages.

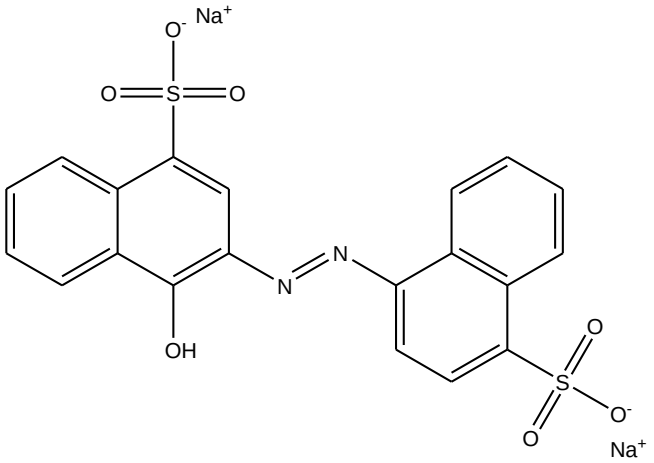

Figure 1. The structure of CMS

To date, different analytical methods, including capillary electrophoresis, stripping voltammetry, high-performance liquid chromatography, differential pulse polarography and UV-Visible spectrophotometry have been reported for the measurement of synthetic colors in food specimens [4-10]. Sample pretreatment step plays a crucial role in the analysis procedure in order to attain accurate and sensitive results. In the recent decade, straightforward and miniaturized of sample pretreatment techniques have emerged new orientations in the analytical chemistry by expanding the usage of green and non-toxic solvents and decreasing the consumption of organic solvents. Microextraction methods are rapid, straightforward, economic, eco-friendly and compatible with most of the analytical instruments [11-13]. Various sample preparation techniques including ionic liquid supramolecular solvent-based microextraction (IL-SUPRAS-ME), liquid–liquid extraction (LLE), solid-phase extraction (SPE), cloud point microextraction (CPE), dispersive liquid-phase microextraction with solidification of floating organic drop (SFO–DLPME), and dispersive solid-phase microextraction (DSPME) have been designed for the determination of food dyes [4, 14-18].

Assadi et al. have established a rapid, simple, and low-cost microextraction method named Dispersive Liquid-Liquid Micro Extraction (DLLME) with a great enrichment factor for the measurement of an immense range of analytes [19]. However, the main disadvantage of DLLME is that the utilized dispersive solvent reduces tangibly the partition coefficient of the analyte to the extraction phase [20]. As an alternative method, Regueiro et al. proposed a novel liquid-liquid microextraction technique with the name of ultrasound-assisted emulsification microextraction (USAEME) [21]. In this method, the microvolume of the water-immiscible organic extractant solvent is emulsified in the specimen solution with the aid of ultrasound power and consequently, there is no need to use a secondary solvent for dispersion. Surfactants are surface active materials that have two different hydrophobic and hydrophilic parts in their molecular structure and have various applications in analytical chemistry [20]. The hydrophobic section of the molecule entails a neutral carbohydrate group that can be in straight, cyclic, aromatic and branched forms. The surfactants play the role of an emulsifying agent to augment the dispersion of organic solvents in the aqueous phase [21]. Under ultrasound radiations the surfactant speeds up the creation of microdroplets of the organic extractant solvent in the aqueous phase and as a consequence, the extraction time decreases considerably. The defined method

is named ultrasound-assisted surfactant-enhanced emulsification microextraction (UASEME) which has the advantages of both DLLME and USAEME techniques [22]. In this work, USAEME as a new, straightforward and highly sensitive microextraction method was used for CMS determination. All experimental parameters affecting the microextraction process were optimized by the response surface methodology (RSM) based on a Box–Behnken design. Then, the applicability of the designed technique was evaluated for the CMS measurement in different real specimens and its figures of merits were compared with the former reports.

MATERIALS AND METHODS

Chemicals and reagents

All of the used chemicals in this research were of analytical reagent grade and utilized without any subsequent purifications. Double-distilled deionized water was used for the preparation of all of the working solutions. CMS, chlorobenzene (C_6H_5Cl), chloroform ($CHCl_3$), carbon tetrachloride (CCl_4), dichloromethane (CH_2Cl_2), sodium hydroxide (NaOH), and sodium chloride (NaCl), acetic acid (CH_3COOH), boric acid (H_3BO_3) and phosphoric acid (H_3PO_4) were purchased from Merck chemical company (Darmstadt, Germany). Tetradecyl dimethylbenzylammonium chloride dihydrate (zephiramine) and hexadecyl trimethylammonium bromide (CTAB) were supplied from Sigma-Aldrich. Universal buffer solutions were prepared by Lurie (1978) [23].

A stock solution of CMS with the concentration of 1000 µg mL^{-1} was prepared by dissolving 0.100 g of CMS powder in 100 mL of water in a volumetric flask. The solutions were stored in a refrigerator at 4 ºC; because, CMS solution was stable at this temperature at least for 1 month. Fresh standard solutions were made each day by dilution of the afore-mentioned stock solution. Food real samples were bought from a local supermarket in Tehran (Tehran, Iran).

Apparatus and software

All absorbance measurements were obtained by a Hewlett-Packard 8453 diode array spectrophotometer controlled with a Hewlett-Packard computer, between 400 and 700 nm digitized every 1 nm. A model 780 digital Metrohm pH meter equipped with a combined glass–calomel electrode was used for the pH adjustments. The centrifuge was performed by a Sigma 3K30). An ultrasonic (VGT-1740QTD, Taiwan) water bath with a temperature control and a digital timer was used to emulsify the extraction solvent. The experimental design was performed with Minitab Version 19.

Multivariate optimization

In the recent decade, using the multivariate approach of 'Experimental design' has become popular in analytical chemistry [24-26]. In these methods, different parameters that can influence the response could be optimized simultaneously by considering the interactions between them. In the UASEME, various factors play a crucial role in the microextraction yield. Hence, Box–Behnken design (BBD) was employed for optimization and scrutinize the interplays between the independent factors (solution pH, surfactant concentration, organic extractant solvent volume and sonication time) on the highest extraction efficiency of CMS from food specimens. BBD is a second-order multivariate method based on a three-level partial factorial designs. Box–Behnken is a spherical, rotatable, or nearly rotatable that consists of a central point and with the mid-points of the edges of the variable space. The number of experiments (N) required for the development of Box–Behnken design is described as $N = 2k(k-1) + C_o$ (where k denotes the number of factors and C_o stands for the number of central points [27, 28]. Thus, 27 trials were implemented for optimizing these 4 variables at 3 levels (low, medium, and high) in the current BBD. All of the experiments were repeated three times at the central point for error estimation.

Analytical procedure

For the UASEME, 4.0 mL of a buffered solution (pH 5.5) and 1.0 mL NaCl 20% were appended to 5.0 mL specimen solution comprising various concentrations of CMS, were

located in a 12 mL screw cap test tube with a conical bottom. 25 µL of carbon tetrachloride as organic extractant and 120µL of 3.0×10^{-2} M solution of zephiramine as the emulsifying agent were appended into the specimen solution. Then, the tube was inserted in the ultrasonic water bath so that the level of both bathwater and specimen was the same. The extraction process was performed under ultrasound waves in 3 min at room temperature. Afterwards, the organic phase was separated from the water by a 3 min centrifugation at 3000 rpm. The upward aqueous phase was emptied with a micropipette and precipitated organic phase was dehumidified by passing nitrogen gas. At the end, the residue was dissolved in 500 µL water. The absorption of the working solutions were measured at the λ_{max} of CMS (515 nm).

Preparation of real samples

Appropriate amounts (1.0 g) of fruit candy, strawberry jelly, smarties and soft beverage specimens were dissolved in deionized water. Then, sample solutions were filtered using membrane filter (0.45 µm) and the filtreted part were diluted to 50 mL in a volumetric flask. An aliquot of the solutions was treated under the proposed UASEME approach and following the spectrophotometric measurement of CMS.

RESULTS AND DISCUSSION

The Uv-Visible spectrum of CMS exhibited that at 515 nm is the maximum absorbance wavelength (λ_{max}) of CMS and the presence of surfactant cannot affect the λ_{max} of CMS. In this regard, all of the absorption measurements were carried out at 515 nm.

The influence of extraction solvent type

Owing to the fact that the physicochemical features of the extraction solvent can have remarkable influences on the emulsification process and consequently the extraction yeild, electing an proper extractant solvent is an impressive point in designing an effective UASEME technique. In this respect, the performance of different halogenated solvents including dichloromethane (CH_2Cl_2), carbon tetrachloride (CCl_4), chloroform ($CHCl_3$), and chlorobenzene (C_6H_5Cl), were investigated as the possible organic extractant solvent and the findings of evaluating their emulsification and extraction efficiency are presented in Figure 2. As it is clear, the highest extraction yield was observed when carbon tetrachloride was utilized as the organic solvent; hence, this substance was chosen as the extractant.

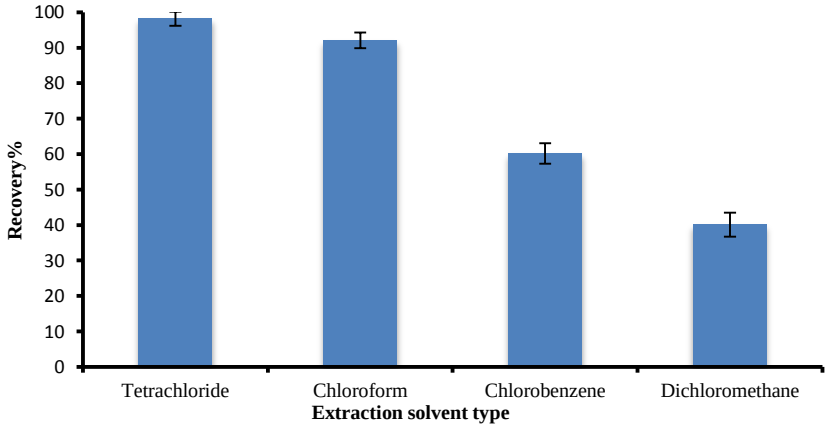

Figure 2. Impact of extractant solvent nature on the extraction yield of CMS.
Extraction conditions: concentration of CMS, 20 ng mL^{-1}; extraction temperature, 25 ºC; extraction time, 3 min; sample pH, 5.5; concentration of Zephiramine, 3.6×10^{-4} M; extraction solvent, 25µL; concentration of NaCl, 2% w/v.

The influence of surfactant nature

The second parameter that has substantial impacts on the extraction efficiency in the UASEME method is the surfactant quiddity. The performances of two cationic surfactants including zephiramine and CTAB as the emulsifier, were evaluated in this research and the obtained results demonstrated that the recovery value was higher in the case of zephiramine, thus this surfactant is better than CTAB. It should be noted that only cationic surfactants were investigated here because CMS is an anionic dye and cationic surfactants have stronger interactions with CMS because of electrostatic forces.

The influence of ionic strength

To scrutinize the impact of ionic strength on the extraction yield, the extraction process was performed on the four solutions with different concentrations of NaCl (0-3% w/v). With incrementing the concentration of sodium chloride from 0-2% the extraction efficiency increased proportionally because of the salting out effect and then remained almost constant. Indeed, sodium chloride decreases the CMS solvability in the water and enhances the transference of CMS molecules to the extractant solvent. Besides, salt addition increases the density difference between the organic and aqueous phases and as a consequence makes the separation of phases easier.

The influence of temperature

Due to the fact that both mass transfer and emulsification processes can be influenced by the temperature, this parameter can have a remarkable effect on the extraction efficiency. In this respect, the temperature influence on the extraction process was evaluated in the span of 25 to 45˚C. The findings exhibited the temperature did not affect the extraction efficiency tangibly. Therefore, further experiments were performed at the ambient temperature (25±2˚C) for the convenience of the work.

Box–Behnken analysis

Some initial tests were implemented for determining the used ranges and levels in the next experiments. The chosen ranges for independent variables were the concentration of the surfactant (A: 0.10–0.60 mmol L^{-1}), the pH (B: 2.0–8.0), the volume of the extraction solvent (C: 10–30 µL), and ultrasound emulsification time (D: 1 –5 min). Box–Behnken experimental design was employed for statistical evaluation and optimization of the important variables. Based on the Box-Behnken matrix, 27 experiments containing three replicates at the central point were implemented randomly to reduce the bias of uncontrolled variables. In order to represent the relevance between input variables and responses, experimental data were fitted with a mathematical equation of the second order polynomial (Eq. 1).

$$Y = - 0.7454 + 0.2328\,A + 0.1937\,B + 0.03734\,C + 0.1518\,D - 0.03053\,A\times A - 0.01236\,B\times B - 0.000482\,C\times C - 0.02290\,D\times D - 0.002267\,B\times C \quad (1)$$

Analysis of variance (ANOVA) was applied for determining the importance of each factor and interaction terms (Table 1). The model p-value of 0.0000 for the quadratic model indicates that it is significant. All the variables had significant effects. A “Lack of Fit p-value” of 0.648 implies that the Lack of Fit is not significant relative to the pure error and explains that the quadratic model is statistically significant for the response. Also the coefficients of R^2 (96.69%) and adjusted R^2 (94.93%) indicate a good relationship between responses and the fitted model. For the statistical analysis of the experimental data, it is necessary to assume that the data come from a normal distribution. The normal residual plot (Figure 3) shows an admissible correlation between the predicted and experimental data.

Table 1. Analysis of variance (ANOVA) for response surface quadratic model.

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Model	9	0.392516	0.043613	55.12	0.000
Linear	4	0.158399	0.039600	50.05	0.000
A	1	0.027456	0.027456	34.70	0.000
B	1	0.066722	0.066722	84.33	0.000
C	1	0.054244	0.054244	68.56	0.000
D	1	0.009976	0.009976	12.61	0.002
Square	4	0.215621	0.053905	68.13	0.000
A×A	1	0.194158	0.194158	245.40	0.000
B ×B	1	0.065949	0.065949	83.35	0.000
C×C	1	0.012391	0.012391	15.66	0.001
D×D	1	0.044750	0.044750	56.56	0.000
2-Way Interaction	1	0.018496	0.018496	23.38	0.000
B×C	1	0.018496	0.018496	23.38	0.000
Error	17	0.013451	0.000791		
Lack-of-Fit	15	0.011705	0.000780	0.89	0.648
Pure Error	2	0.001746	0.000873		
Total	26	0.405967			

R^2 = 96.69; adjusted R^2 = 94.93; predicted R^2 = 90.92.
DF, degree of freedom; SS, sum of squares; MS, mean square.

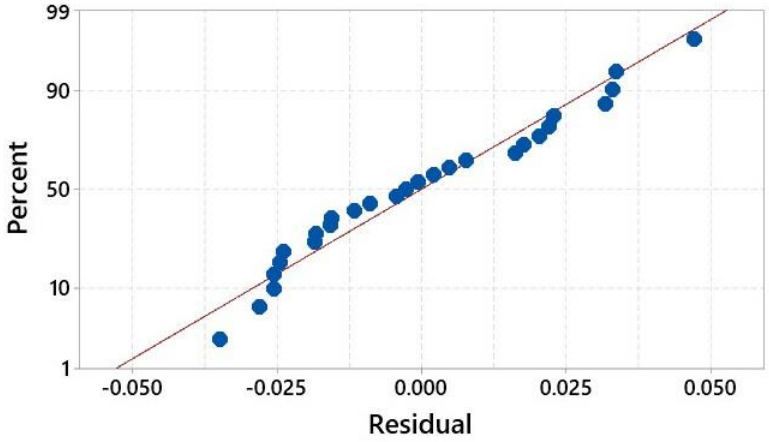

Figure 3. The normal probability plot of residuals.

At the end, analysis of results by RSM was studied for depicting the response as a function of various factors to assess the interplay between the factors and optimum levels was assessed. The concentration of the used surfactant plays a key role in the emulsification microextraction method. Micelle is a molecular aggregation of surfactant molecules and the minimum concentration of the surfactant for the formation of micelle in the solution is called critical micelle concentration (CMC). The obtained results revealed that the extraction efficiency reduced gently when the concentration of zephiramine in the specimen solution increased gradually from its CMC (3.7×10^{-4} M).

This can be due to the competition of the analyte penetration between the extraction solvent and the excess micellar aggregates in the aqueous sample solution. Consequently, the CMS molecules remained in the aqueous

phase instead of being transferred into the extractant solvent. According to the provided data in Figure 4, 3.6×10^{-4} mol L^{-1} was elected as the optimum concentration of zephiramine. As can be seen from the surface plots in Figure 4, the response enhances by increasing of the initial solution pH from 2.0 to 5.5, But, when the solution pH exceeds a value of 5.5, the response declines significantly. The pH of the aqueous phase plays a crucial role in increasing the analyte partition coefficient between the aqueous and surfactant-rich phases which eventuates to the enhancement of the extraction efficiency. Moreover, the obtained responses indicated that the CMS extraction yield reached the highest value at a carbon tetrachloride volume of 25μL. However, the extraction yield decreased gradually by further increasing the volume of extractant solvent. Time in this kind of extraction is defined as the time interval between the addition of extraction solvent and the end of sonication before the centrifugation onset. Time has an important impact on both emulsification and mass transfer processes. The findings proved that the extraction efficiency improved by incrementing the extraction time to 3 min, but it decreased gradually by further increasing the extraction time. The calculated values for the critical point for the extraction of CMS are pH (5.5), the volume of carbon tetrachloride (25 μL), concentration of zephiramine (3.6×10^{-4} M) and time (3 min).

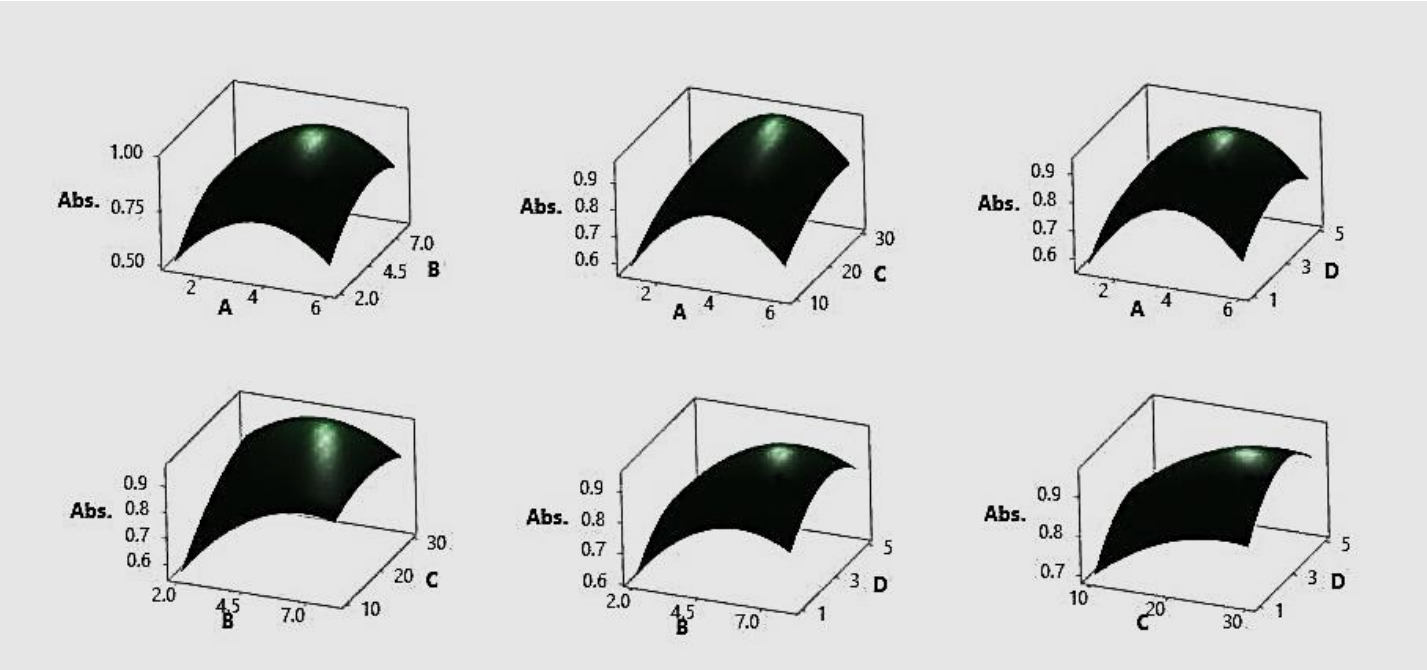

Figure 4. Three-dimensional response surface plots representing the effect of process variable on absorbance: (A) volume of carbon tetrachloride; (B) sample pH; (C) concentration of zephiramine; and (D) time.

Analytical performance

After optimization of all the effective operational factors, the analytical parameters of the designed technique were calculated for the CMS measurement. A calibration curve was depicted for CMS measurement and the results indicated a linear relationship of the absorption with the CMS concentration over a wide range (0.5-80.0 ng mL^{-1}) with the equation of A= 0.0204X + 0.0026 and a correlation coefficient of 0.9995. The limit of detection is defined as $LOD=3S_b/m$, where Sb denotes the standard deviation of 10 blank signals after 10 replications and m is the slope of the obtained calibration curve. For a sample with a volume of 10 mL, it was found to be 0.15 ng mL^{-1}. The preconcentration factor of the method was calculated as the ratio of the highest sample volume to the lowest final volume, yielding a value of 666. The enrichment factor of the method was calculated as the ratio of the calibration

curve slope after extraction to the calibration curve slope before the extraction, yielding a value of 630. The repeatability (intra-day) and reproducibility (inter-day) of the designed technique were evaluated by measuring the absorption of spiked water samples at five different times during a single day and on five subsequent days respectively. Intra-day precision was 3.1% for a 10 ng mL^{-1} CMS solution, while the inter-day precision was 3.5% for the same CMS solution, which indicates that the proposed technique is highly reproducible. The obtained results are presented in Table 2.

Table 2. Analytical figures of merit for UASEME method for CMS determination

Parameter	CMS
Linear range (ng mL^{-1})	0.5–100.0
Calibration equation	A= 0.0204X + 0.0026
Correlation coefficient (R^2)	0.9995
Limit of detection (ng mL^{-1})	0.15
Limit of quantification (ng mL^{-1})	0.47
Preconcentration factor (PF)	666
Enrichment factor (EF)	630
Repeatability (RSD, n = 5)	3.1%
Reproducibility (RSD, n = 5)	3.5%

The selectivity of the proposed method

The selectivity of an analytical technique has an important effect on the accuracy of the obtained results. In this respect, the effects of various anionic and cationic species were investigated on the analytical response of the designed method. For this purpose, a 20 ng mL^{-1} solution of CMS was prepared, different amounts of the interfering species were added to the solution, and then the absorption of the sample was measured in the presence of other interfering species. Then, the tolerance limit, defined as the maximum amount of interfering species that cause an error not higher than ±5% in the measurement of CMS was calculated for the studied interfering species. The obtained results showed that the tolerance limits were 1000 for Ni^{2+}, Cd^{2+}, Ca^{2+}, Mn^{2+}, Na^{+}, K^{+}, NH_4^{+}, Br^{-}, and F^{-}, 500 for Co^{2+}, Pb^{2+}, 200 for oxalate, tartarate, and citrate and 100 for Fe^{3+}. Therefore, the proposed method has an admissible selectivity towards CMS over a wide range of ionic species.

Real sample analysis and comparison with the former reports

To scrutinize the performance of the suggested technique for the measurement of CMS, it was applied for CMS measurement in four spiked food samples, including soft beverages, smarties, strawberry jelly, and fruit candy, and the findings are presented in Table 3. As it is obvious, all the calculated recovery values are between 97.5 and 104.3% which indicates that the proposed technique can be used accurately for the quantitation of CMS in real food samples.

The figures of merits of the developed microextraction technique are compared with those of the previously reported analytical methods in Table 4. As it is clear, the designed UASEME method has the lowest detection limit and %RSD among all of the reported analytical techniques. Moreover, the proposed UASEME method is eco-friendlier because the volume of the consumed organic solvent is lower than those of other extraction techniques and no dispersive solvent is used in this technique. Therefore, the UASEME method proposed in this work is better than the former analytical techniques.

Table 3. Analytical figures of merit of UASEME method for CMS measurement under the optimized conditions.

Samples	Added concentration ($ng\ mL^{-1}$)	Founded concentration ($ng\ mL^{-1}$) ± SD[a]	Recovery (%) (n = 5)
Soft beverage	0.0	20.4 ± 0.5	–
	5.0	25.9 ± 0.8	98.1
	10.0	31.4 ± 0.7	103.3
Smarties	0.0	15.5 ± 0.2	–
	5.0	20.4±0.4	99.5
	10.0	34.6 ± 0.6	97.5
Strawberry jelly	0.0	21.3 ± 0.3	–
	5.0	26.5± 0.9	100.8
	10.0	30.9 ± 0.5	98.8
Fruit candy	0.0	9.3 ± 0.4	–
	5.0	14.9± 0.5	104.2
	10.0	19.8 ± 0.6	102.6

[a]Standard deviation

Table 4. Comparison of analytical figures of merit of the suggested UASEME method with former reports

Sample preparation	Detection	LOD[a] ($ng\ mL^{-1}$)	LR[b] ($ng\ mL^{-1}$)	PF[c]	RSD[d] (%) ($ng\ mL^{-1}$)	Ref.
CPE	Spectrophotometry	17	20-3500	-	4.4	[9]
CPE	Spectrophotometry	7.2	50-5000	-	<5	[11]
DLLME	Spectrophotometry	2	10-2000	-	<6	[29]
UASEME	Spectrophotometry	0.15	0.5-80	666	<3.5	This work

a. Limit of detection, b. Linear dynamic range, c. Preconcentration factor, d. Relative standard deviation, DLLME Dispersive liquid–liquid microextraction, CPE Cloud point extraction,UASEME Ultrasound-assisted surfactant-enhanced emulsification microextraction.

CONCLUSIONS

CMS is a highly consumed dye in the food, cosmetics, textile and pharmaceutical industries, which has adverse effects on the health of human beings; Hence, its measurement is of great importance. In this respect, the UASEME method was coupled with UV-Visible spectrophotometry in this research to provide a simple, efficient, and green methodology for the measurement of CMS in food specimens. Besides, this technique is characterized by its short analysis time and being economic. The impact of several experimental factors, including extraction solvent, solution pH, surfactant and salt concentrations, extraction time, and temperature, were scrutinized and optimized here. The findings revealed that the designed technique provided straightforward procedure and high efficiency for the ultra-trace quantitation of CMS. In addition, the designed method has good repeatability, a very low detection limit, and high preconcentration factor. The method does not also require any special expensive instrumentation, such as HPLC or electrochemical techniques, and is therefore inexpensive and eco-friendly.

ACKNOWLEDGEMENTS

The authors appreciate the research council of Islamic Azad University of Yadegar-e-Imam Khomeini (RAH) Shahre-rey branch for supporting this project.

Conflict of interests

The authors declare that they do not have any conflict of interest.

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