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Chemometric-Based Optimization of Ionic Liquid-Based Dispersive Liquid-Liquid Microextraction for Separation and Preconcentration of Erythrosine from Real Matrices

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Research Article

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ABSTRACT

In this research paper, a simple and economic ionic liquid-based liquid-liquid microextraction (IL-DLLME) procedure was developed to ensure efficient and rapid separation and preconcentration of erythrosine from cosmetic and food samples. Important parameters such as IL volume, temperature, acetone volume, ultrasonic time and pH that may affect the IL-DLLME procedure have been optimized by central composite design (CCD) based on response surface methodology (RSM). The optimum values of IL volume, temperature, acetone volume, ultrasonic time and pH were determined as 440 µL, 35 °C, 120 µL, 9 min and 4.2, respectively. Using these optimum conditions, some analytical data obtained for erythrosine were listed below. Working range, limit of detection and enrichment factor were 2-400 ng mL^{-1}, 0.65 ng mL^{-1} and 79, respectively. The relative standard deviation (RSD%) was 2.4% for 50 ng mL^{-1} of erythrosine. The recovery obtained in the analysis of real samples was in the range of 93.2-108.5%. The analytical data obtained showed that the IL-DLLME procedure was successfully applied to the selected samples.

Keywords: Chemometric optimization, Erythrosine, Ionic liquid, Microextraction, Real matrices.

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Introduction

Food dyes, which constitute an important group among food additives, are used in industry for various purposes such as protecting, increasing or modifying the desired and typical existing color, standardizing the appearance by controlling color change and deterioration, adding decorative features, and creating new products [1,2]. Erythrosine is included in the class of xanthine dyes, containing ortho-iodinated phenonxy groups, in foods (sweets, non-fat confectionery, bakery products, puddings, flavored biscuits and wafer creams, frozen canned crayfish and shrimp, flavored milks, chewing gums, instant jelly mixes, beverage powders, ice products and cookies), pharmaceuticals (tablets and toothpastes) and cosmetics, it is a paint with photoluminous properties, temporarily approved by Food and Drug Administration (FDA) [3-5]. World Health Organization (WHO) and the FDA has recommended an acceptable daily dose of 100 ppm for this dye [6]. It is known that taking more than this dose creates toxic effects for human health [7]. Therefore, it is important to develop accessible, fast and inexpensive methods for monitoring erythrosine in food and cosmetic samples.

Capillary electrophoresis with laser-induced fluorescence detection [8], UV/VIS spectrophotometry [9], cyclic voltammetry [10], ultra-fast liquid chromatography-tandem quadrupole mass spectrometry [11] and high performance liquid chromatography with photo-diode array detector [12] have been used for the determination of erythrosine in different samples. Due to low detection limit of instruments and matrix effect of real samples, separation and preconcentration procedures such as shaking-based ionic liquid dispersive liquid phase microextraction [13], ultrasonic assisted supramolecular solvent-based dispersion solidification liquid–liquid microexraction [14], ultrasonic-assisted cloud point microextraction [15,16] and magnetic solid phase extraction [17] are necessary for the accurate and sensitive determination of food dyes.

Liquid-liquid extraction methods using organic solvents have disadvantages such as time consuming, consuming large amounts of toxic solvents and solvent evaporation steps [18]. For these reasons, the use of ionic liquids with features such as environmentally friendly, inexpensive, effective phase separation and low steam pressure is becoming widespread in microextraction studies [19,20]. One of the most popular microextraction methods is the dispersive liquid liquid microextraction (DLLME) procedure. DLLME consists of two steps; (1) extraction into the aqueous sample containing the analyte and injection of a suitable mixture of dispersive solvents. In this step, the extraction solvent is well dispersed in the aqueous sample as droplets and the analyte is enriched in it. The large surface area between the extraction solvent and the aqueous sample is achieved, the equilibrium state is quickly reached, and the extraction is time-independent. This is the most important advantage of the method. (2) after centrifugation of the cloudy solution,

the analyte in the precipitated phase is determined by an analytical instrument.

It is necessary to optimize important parameters in microextraction studies. In addition to the disadvantages of traditional univariate optimization approaches such as time consuming and excessive chemical consumption, possible interactions between variables are not taken into account. therefore, an accurate, precise and effective optimization step may not be provided [21]. Therefore, chemometric-based statistical optimization approaches have been frequently used in the optimization step in recent years. These approaches provide significant advantages such as less chemical consumption and fewer experiments required [22].

This study was aimed at developing and validating a fast, selective and sensitive liquid-based liquid-liquid microextraction (IL-DLLME) procedure to separate and preconcentrate erythrosine from foods and cosmetics samples for the determination by UV-VIS spectrophotometer. The IL-DLLME procedure have been optimized by central composite design (CCD) based on response surface methodology (RSM). These results show that the optimized IL-DLLME procedure has the potential to be used as one of the alternatives to conventional analytical methods for determination and extraction of erythrosine from real samples.

Materials and Methods

Reagents

Unless stated otherwise, all chemicals studied were of analytical purity. A stock erythrosine was purchased from Sigma–Aldrich (St. Louis, MO, USA). Working and calibration solutions were daily prepared by diluting this stock solution with water. Dispersive solvents including methanol, ethanol, acetonitrile, tetrahydrofuran and acetone were purchased from Merck (Darmstadt, Germany). 1–octyl–3–methylimidazolium hexafluorophosphate ([OMIM][PF_6]) (as extraction solvent) was bought from Sigma–Aldrich. For pH adjustments in optimization studies, buffer solutions such as acetate, borate, citrate and phthalate were used. To minimize all possible contamination, a diluted HNO3 solution was used to wash the glassware and finally rinsed with distilled water.

Apparatus

The quantification measures were performed using an UV–VIS Spectrophotometer (Shimadzu UV-1800 PC model, Kyoto, Japan) equipped with 10 mm quartz cuvette. Ultrasonic bath (Kudos, Shanghai, China), centrifuge (Hettich Universal-320 model, Germany) and digital pH-meter (JP Selecta model, Barcelona, Spain) were used to prepare the selected samples, provide phase separation and adjust the pH of the sample solutions, respectively.

Sampling

In this study, two different sample groups including foods and cosmetics were investigated. All samples were collected from supermarkets in Sivas, Turkey. Cherry juice, pomegranate juice, strawberry juice, pastry cream, jole, and turnip juice were selected as food samples. In addition, lipstick, hair dye, shower gel, and hand cream were chosen as cosmetic samples. Appropriate 0.5 g amounts of the samples were dissolved in the water, filtered, and completed to volume in 50-mL centrifugal tests including 10 mL ethanol. The mixture was stirred in the shaker for about 2 h, as in the case of sausage, to transfer the erythrosine into the ethanol phase. For complete dissolution, the samples were warmed for 5 min and filtered before use. 10 mL of sample solution were then treated using the optimized IL-DLLME procedure for the determination and extraction of erythrosine [5, 23].

Optimization Strategy

A central composite design (CCD) based on response surface methodology (RSM) was created for the optimization of important parameters that may affect the IL-DLLME procedure planned to be developed. After preliminary trials, five parameters (IL volume, temperature, dispersive solvent volume, ultrasonic time and pH) affecting the extraction of erythrosine were determined. A five-variable and three-level CCD was created to optimize these selected parameters effectively and quickly. Design-Expert® trial version 12.0.1. (Stat-Ease Inc., Minneapolis) was used as CCD software. In the CCD design, IL volume, dispersive solvent volume (acetone), temperature, ultrasonic time and pH were symbolized as X1, X2, X3, X4 and X5, respectively. In addition, the levels, units and codes of the optimized parameters are given in Table 1.

Table 1. Codes, units, and levels of variables in chemometric-based CCD design

Parameters	Symbol	Unit	Levels		
IL volume	X1	µL	50	250	450
Temperature	X2	°C	25	40	55
Acetone volume	X3	µL	100	500	600
Ultrasonic time	X4	min	1	6	11
pH	X5		3	6	9

Optimized IL-DLLME Procedure

In this study, 10 mL of sample solution containing the erythrosine at a concentration of 50 ng mL-1 was poured into a centrifugal test tube and the solution pH was adjusted at 4.2 using an acetate buffer solution. Afterwards, 440 µL of [OMIM][PF6] as extraction solvent was quickly injected into the sample solution. 120 µL of acetone was then added as the dispersing solvent. Following this, the tube was placed in an ultrasonic bath and sonicated for 9 min at 35 °C. The mixture was centrifuged for 5 min at 4000 rpm and then the aqueous phase was thrown away. The final volume of the remaining phase was made up to 500 µL with acetone. Finally, measurements were made using a UV-VIS spectrophotometer at 526 nm. All studies were carried out with the sample blank to exclude possible changes in absorbance from the reagents.

Results and Dicussion

Optimization of Parameters in IL-DLLME Step

After preliminary studies, a chemometric-based CCD design was created for five parameters (X1, X2, X3, and X4) affecting the separation and preconcentration of erythrosine. The design results, which include the experimental value and prediction values found as a result of the application of this design, are presented in Table 2. From the results, it is seen that there is no significant difference between the experimental data and the prediction data of the model. The statistical evaluation of these results is explained in detail below.

Statistical analysis

ANOVA analysis of the experimental data in Table 2 was performed with the CCD statistical program [24,25]. Here, the significance or no significance levels of the microextraction parameters and their interactions are determined. First of all, the p-value must be less than 0.05 for the model to be significance. This explanation is valid for all linear, binary and quadratic interactions.

Table 2. Experimental and estimated values obtained as a result of application of CCD design

Run	X1	X2	X3	X4	X5	Experimental Recovery(%)	Prediction Recovery(%)
1	250	55	350	6	6	65.1	65.56
2	250	40	350	6	6	70.4	70.53
3	250	40	350	6	6	69.7	70.53
4	450	25	600	1	9	52.1	52.15
5	450	25	100	11	9	91.2	91.16
6	50	55	100	11	9	82.7	82.63
7	450	40	350	6	6	70.1	70.47
8	50	25	600	1	3	96.7	96.80
9	250	40	350	6	3	71.2	71.37
10	50	25	100	1	9	76.2	76.28
11	250	40	350	1	6	71.1	70.96
12	450	55	600	1	3	56.7	56.65
13	50	25	600	11	9	85.3	85.34
14	250	40	100	6	6	77.2	77.41
15	450	55	100	11	3	96.8	96.66
16	450	25	100	1	3	87.1	87.11
17	250	40	350	11	6	71.2	71.59
18	50	55	600	11	3	41.9	41.85
19	250	40	600	6	6	63.8	63.83
20	250	40	350	6	6	71.5	70.53
21	50	55	600	1	9	84.2	84.22
22	50	55	100	1	3	70.4	70.39
23	250	40	350	6	6	71.5	70.53
24	50	40	350	6	6	75.2	75.08
25	250	40	350	6	9	71.9	71.98
26	450	25	600	11	3	67.2	67.17
27	450	55	600	11	9	56.9	56.80
28	450	55	100	1	9	69.2	69.14
29	50	25	100	11	3	76.2	76.21
30	250	25	350	6	6	75.0	74.79

Statistical data are presented in Table 3. When the results in Table 3 are evaluated, it is seen that the p-value of the model is much smaller than 0.05. Therefore, it is concluded that the established model has meaning. When the same evaluation is made for other interactions, it is seen that only the p-value of X_4, X_5, X_2^2, X_3^2 and X_4^2 interactions is greater than 0.05. F-values should be considered while evaluating the contribution to the established design. The numerical magnitude of the F-value indicates that the model contribution is large. In the light of this explanation, the parameters that contribute the most to linear, binary and quadratic interactions are X_3 (F-value: 2251.26) X_1X_3 (F-value: 812.25) and X_1^2 (F-value:12.39), respectively. R values (R_2, Adjusted R^2 and Predicted R^2) are examined for validation of statistical data. Here, it is desirable that the R^2-value be numerically close to 1 and to each other. In addition, for statistical reliability of the results, the difference between Adjusted R^2 and Predicted R^2 values should be less than 0.2. When the data in Table 3 is analysed, it is seen that the values of R^2, Adjusted R^2 and Predicted R^2 are 0.9992, 0.9975 and

0.9860, respectively. It can be said that this is in accordance with the above explanations. High agreement of R^2 values indicates high agreement between experimental values and predicted values of the model. The quadratic model presented the following equation for the recovery of erythrosine.

$$Recovery\ (\%) = +70.53-2.31X_1-4.62X_2-6.79X_3+0.3167X_4+0.3056X_5+2.33X_1X_2-7.12X_1X_3+5.53X_1X_4-5.10X_1X_5-3.2X_2X_3-0.6250X_2X_4+3.10X_2X_5-5.15X_3X_4+1.70X_3X_5+3.95X_4X_5+2.25X_1^2-0.3536X_2^2+0.0964X_3^2+0.7464X_4^2+1.15X_5^2$$

Table 3. ANOVA analysis result from CCD for erythrosine

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	4244.70	20	212.23	575.93	< 0.0001	significant
X_1-IL volume	95.68	1	95.68	259.64	< 0.0001	
X_2-Temperature	383.64	1	383.64	1041.08	< 0.0001	
X_3-Acetone volume	829.60	1	829.60	2251.26	< 0.0001	
X_4-Ultrasonic time	1.80	1	1.80	4.90	0.0542	
X_5-pH	1.68	1	1.68	4.56	0.0615	
X_1X_2	86.49	1	86.49	234.70	< 0.0001	
X_1X_3	812.25	1	812.25	2204.17	< 0.0001	
X_1X_4	488.41	1	488.41	1325.38	< 0.0001	
X_1X_5	416.16	1	416.16	1129.32	< 0.0001	
X_2X_3	156.25	1	156.25	424.01	< 0.0001	
X_2X_4	6.25	1	6.25	16.96	0.0026	
X_2X_5	153.76	1	153.76	417.25	< 0.0001	
X_3X_4	424.36	1	424.36	1151.57	< 0.0001	
X_3X_5	46.24	1	46.24	125.48	< 0.0001	
X_4X_5	249.64	1	249.64	677.44	< 0.0001	
X_1^2	12.39	1	12.39	33.64	0.0003	
X_2^2	0.3070	1	0.3070	0.8332	0.3851	
X_3^2	0.0228	1	0.0228	0.0620	0.8090	
X_4^2	1.37	1	1.37	3.71	0.0861	
X_5^2	3.23	1	3.23	8.76	0.0160	
Residual	3.32	9	0.3685			
Lack of Fit	0.9690	6	0.1615	0.2064	0.9518	not significant
Pure Error	2.35	3	0.7825			
Cor Total	4248.01	29				
R^2	0.9992		Adjusted R^2	0.9975	Predicted R^2	0.9860

Effect of factors

The 3D-surface graphics of the binary interactions of the optimized parameters were drawn by the CCD. In this study. the graphs drawn for the 3 most important interactions (pH-IL volume, temperature-IL volume and acetone-ultrasonic time) were interpreted. Figure 1a shows the effect of the interaction between pH and IL volume on recovery % of erythrosine. Here, it is seen that quantitative recoveries% for erythrosine are obtained in the range of ionic liquid volume 325-425 µL when the pH value is in the acidic region. In the basic region, the recovery was reduced. The possible reason for this decrease may be that the binding sites of the ionic liquid are affected.

The effect of the interaction between ionic liquid and temperature on recovery % of erythrosine is presented in Figure 1b.

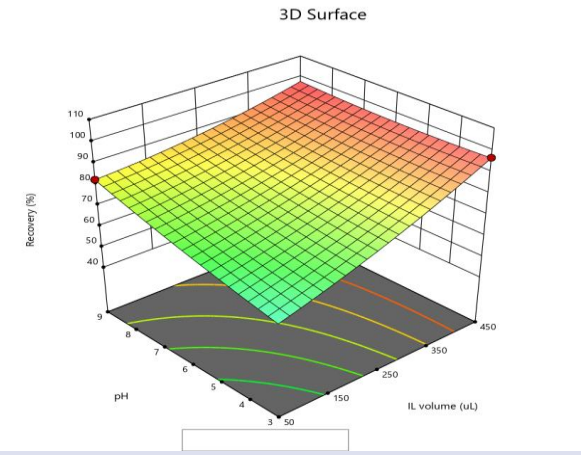

Figure 1a. Effect of pH and IL volume interaction on recovery % of erythrosine

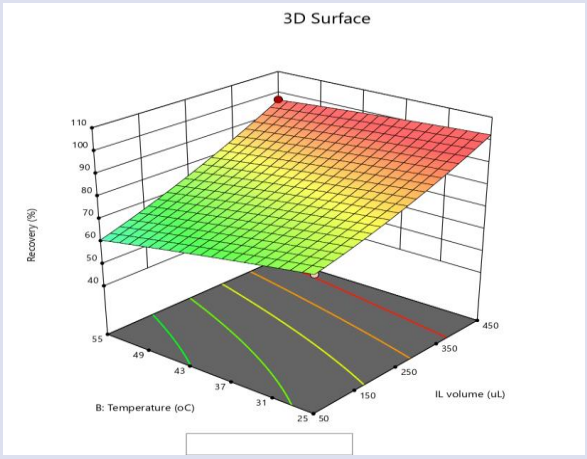

Figure 1b. Effect of temperature and IL volume interaction on recovery % of erythrosine

Here, it can be said that there is a significant decrease in recovery for all ionic liquid volumes above 45 °C. This may be due to a decrease in the separation efficiency of the ionic liquid due to the increase in temperature. For this reason, it is planned to keep the temperature in the works below 45 °C.

The effect of dispersive solvent (acetone) and ultrasonic time on recovery% of erythrosine is presented in Figure 1c. From the related figure, it can be said that the increase in acetone volume does not cause a significant change in recovery, especially above 350 µL. In addition, the best recovery values were obtained in approximately 9 min of ultrasonic time. This shows that the short ultrasonic time is sufficient for the acetone to be effectively dispersed into the sample solution.

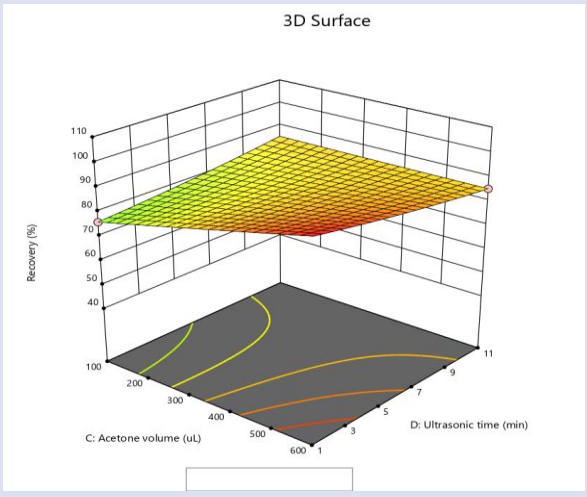

Figure 1c. Effect of acetone and ultrasonic time interaction on recovery % of erythrosine

Optimum conditions

The last step of the chemometric modelling is to determine the optimum conditions of the optimized X1, X2, X3, X4 and X5 parameters. Optimum data for the variables with the highest recovery% for erythrosine were tested. The optimum values for the parameters X1, X2, X3, X4 and X5 were 440 µL, 35 °C, 120 µL, 9 min and 4.2, respectively, for the estimated recovery of over 90% by the CCD. As a result of the repeated experimental studies carried out, it was seen that the average recovery value was compatible with the predicted value of the model. Therefore, these values were chosen as optimum for the optimized parameters.

Foreign ions effect

Since optimization studies are carried out on model solutions, the effect of foreign ions should be investigated before the analysis of real samples. For this reason, different anions, cations and food dyes were added to the model solutions and then the extraction and determination of erythrosine was performed by applying the optimized method. The recovery% value was calculated for erythrosine in the presence of each foreign ion. As can be seen in the results in Table 4, quantitative recoveries (92.4-103.7%) were obtained in the presence of foreign ions studied, indicating that the optimized IL-DLLME procedure is selective for erythrosine.

Table 4. The effect of some foreign ions on the recovery of erythrosine under optimum conditions

Foreign ions	*Tolerable limit	Recovery (%)
Na(I)	20000	97.4
Mg(II)	20000	97.2
Ca(II)	20000	96.8
C_2O_4(II)	10000	98.6
SO_4(II)	10000	97.1
Fe(II)	10000	98.2
Pb(II)	5000	102.4
Cd(II)	5000	97.8
Sn(II)	5000	101.5
Patent Blue V	1000	96.3
Curcumin	1000	103.7
Azorubine	500	96.2
Tartrazine	500	95.8
Allura Red	250	93.5
Carmine	100	92.4

*[Foreign ions amount]/ [erythrosine amount]

Analytical performance

Under optimal conditions, the analytical performance of the optimized IL-DLLME procedure in terms of working range, limit of detection (LOD), limit of quantification (LOQ), correlation coefficient (R^2), accuracy (as recovery%), precision (as relative standard deviation, RSD%), and enrichment factor were investigated. To investigate the working range of the method, the selected samples were spiked with the erythrosine standard at different concentrations (0.5, 1, 2, 10, 50, 100, 200, 400, 800 and 1000 ng mL^{-1}) and the resulting sample was pretreated with the optimized IL-DLLME procedure before UV-VIS spectrophotometric analysis. As a result, the working range was obtained in the range of 2-400 ng mL^{-1} with 0.9975 of R^2. The LOD and LOQ were calculated from the ratio of 3 and 10 times the standard deviation of the

reagent blank to the resulting calibration plot, respectively. The LOD and LOQ was 0.65 ng mL^{-1} and 2.0 ng mL^{-1}, respectively. The EF value was calculated from the formula below.

EF= Slope-1/ Slope-2 (1)

Where Slope-1 and Slope-2 were the slope of the calibration graphs obtained before and after applying the optimized IL-DLLME procedure, respectively. The EF was calculated as 79. The accuracy of the optimized IL-DLLME procedure was tested with relative recovery of added selected samples at 20 and 50 ng mL^{-1} concentrations. The recovery% were ranged from 93.2% to 108.5% (n=3), indicating good reliability and applicability of the optimized IL-DLLME procedure. The precision of the optimized IL-DLLME procedure was tested with RSD%. Intraday precision was tested for three replicate blank analysis of concentrations of 20 and 50 ng mL^{-1} of erythrosine on the same day, while inter–day precision was tested by analysis of the same concentrations on three consecutive days. In the results of working, the RSD% for intraday precision was in the range of 1.9-3.4%, while the RSD% for interday precision was in the range of 2.2-4.7%. The RSDs% indicate good precision and reproducibility of the optimized IL-DLLME procedure. All results were shown in Table 5.

Table 5. Analytical data of the optimized IL-DLLME procedure using optimum conditions

Analytical parameters	Optimum data
Calibration equation after IL-DLLME	y = 3.555c + 0.0008
Calibration equation before IL-DLLME	y = 0.045c − 0.005
Working range (ng mL^{-1})	2-400
R^2	0.9975
LOD (ng mL^{-1})	0.65
LOQ (ng mL^{-1})	2.0
Intraday precision	1.9-3.4
Inter–day precision	2.2-4.7
Accuracy (as recovery%),	93.2-108.5
EF	79

Real Samples Analysis

The feasibility of the optimized IL-DLLME procedure was tested by applying it to foods (pomegranate juice, strawberry juice, pastry cream, jole, and turnip juice) and cosmetic (lipstick, hair dye, shower gel, and hand cream) samples were investigated. In order to investigate the matrix effect of the optimized IL-DLLME procedure, two standard concentrations (20 and 50 ng mL^{-1}) of the erythrosine were spiked to the selected samples. All measurements were repeated three times. Analysis results of selected samples are given in Table 6. These quantitative recoveries obtained show that the optimized IL-DLLME procedure has low matrix effect. Therefore, the optimized IL-DLLME procedure can be reliably applied to the extraction and determination of erythrosine from the analyzed samples. Finally, the amounts of erythrosine in the samples were given in detail in Table 6 along with their RSD%.

Table 6. The results of applying the optimized IL-DLLME procedure to selected samples

Sample	Spiked (ng mL^{-1})	Found (ng mL^{-1})	Recovery (%)
Pomegranate	-	11.2±0.7	-
	20	30.7±1.1	97.4
	50	60.6±2.3	98.9
Juice	-	24.9±0.9	-
	20	43.9±1.5	95.3
	50	73.3±2.7	96.8
Strawberry juice	-	Nd*	-
	20	20.8±1.4	104.0
	50	50.9±1.9	101.8
Pastry cream	-	Nd	-
	20	18.9±0.8	94.6
	50	48.5±2.2	97.0
Jole	-	37.6±2.0	-
	20	56.2±2.7	93.1
	50	85.6±2.9	96.0
Turnip juice	-	Nd	-
	20	20.5±1.3	102.5
	50	50.8±2.0	101.6
Lipstick	-	121.6±5.7	-
	20	141.1±7.2	97.3
	50	170.8±8.3	98.3
Hair dye	-	159.2±6.4	-
	20	180.9±9.5	108.5
	50	211.3±11.8	104.2
Shower gel	-	7.4±0.5	-
	20	26.4±1.1	94.9
	50	55.8±2.3	96.8
Hand cream	-	Nd	-
	20	20.9±0.9	104.5
	50	51.3±1.8	102.6

*could not be determined

Comparison of the Optimized Procedure with the other Reported Methods

Some analytical properties suck as working range, LOD, RSD, EF and recovery% of the optimized IL-DLLME procedure were compared with other extraction procedures and detection techniques reported in the literature. Comparison data were made with publications in references (see Table 7). When the relevant publications were examined, it can be said that the optimized IL-DLLME procedure has a higher EF and wider working range than similar determination techniques. it also appears that the proposed management exhibits high precision and low RSD over expensive techniques. From these results it is clear that the optimized IL-DLLME procedure exhibits significant advantages over the compared methods.

Table 7. Comparison of the proposed method with similar analytical methods

Analytical methods	Working range (ng mL^{-1})	LOD (ng mL^{-1})	RSD (%)	EF	Recovery (%)	Refs.
HIH-LLME-UV-VIS	30-1400	6	≤2.9	37.5	95-101	[5]
UA-SUPRA-MSLLME-UV-VIS	1-100	0.6	≤1.4	142	91-103	[14]
DES-UA-LLME- UV-VIS	0.05–0.25	3.75	≤4.6	40	90-100	[26]
CPE-UV-VIS	30-3000	22	≤3.27	15	-	[27]
VA-DES-DLLME-HPLC	0.5–500	0.1	≤5.6	95	96.8-99	[28]
HP-TLC	20-200 ng/zone	9.8 ng/zone	≤2.7	35	98-101	[29]
IL-DLLME-UV-VIS	2-400	0.65	≤4.7	79	93.2-108.5	Proposed method

HIH-LLME: Heat-induced homogeneous liquid-liquid microextraction, UA-SUPRA-MSLLME: ultrasonic assisted supramolecular solvent based dispersion solidification liquid–liquid microexraction, UA-LLME: Deep eutectic solvent ultrasound assisted liquid-liquid microextraction, CPE: Cloud point extraction, VA-DES-DLLME: Vortex assisted deep eutectic solvent dispersive liquid-liquid microextraction, HP-TLC: high performance thin-layer chromatography

Conclusions

Herein, a simple and economic dispersive liquid-liquid microextraction (DLLME) based on ionic liquid (IL) procedure for the extraction, separation and preconcentration of erythrosine from foods and cosmetics has been optimized using a central composite design (CCD) based on response surface methodology (RSM). In this study, the [OMIM][PF6] (as extraction solvent) and acetone (as dispersive solvent) were used for the extraction of erythrosine for the first time. The optimized IL-DLLME procedure has some advantages including simple, fast, green and economic. As a result of the analysis of the selected samples, it was seen that the optimized method has low matrix effect, high accuracy, wide working range and good sensitivity. These results show that the optimized IL-DLLME procedure has the potential to be used as one of the alternatives to conventional analytical methods for determination and extraction of erythrosine from real samples.

Conflicts of interest

No conflict of interest or common interest has been declared by the authors.

References

[1] Gomes K. M. S., Oliveira M. V. G. A. D., Carvalho F. R. D. S., Menezes C. C., Peron A. P., Citotoxicity of food dyes sunset yellow (E-110), bordeaux red (E-123), and tatrazine yellow (E-102) on Allium cepa L. root meristematic cells, *Food Science and Technology,* 33(1) (2013) 218-223.

[2] Yamjala K., Nainar M. S., Ramisetti N. R., Methods for the analysis of azo dyes employed in food industry–a review, *Food Chemistry,* 192 (2016) 813-824.

[3] Lakdawalla, A. A., Netrawali, M.S., Mutagenicity, comutagenicity, and antimutagenicity of erythrosine (FD and C red 3), a food dye, in the Ames/Salmonella assay, *Mutation Research/Genetic Toxicology,* 204(2) (1988) 131-139.

[4] Ryvolová M., Táborský P., Vrábel P., Krásenský P., Preisler J., Sensitive determination of erythrosine and other red food colorants using capillary electrophoresis with laser-induced fluorescence detection, *Journal of chromatography A*, 1141(2) (2007) 206-211.

[5] Ozkantar N., Yilmaz E., Soylak M., Tuzen M., Separation, enrichment and spectrophotometric determination of erythrosine (E127) in drug, cosmetic and food samples by heat-induced homogeneous liquid–liquid microextraction method, *International Journal of Environmental Analytical Chemistry,* 99(12) (2019) 1135-1147.

[6] Rubio L., Sanllorente S., Sarabia L.A., Ortiz M.C., Determination of cochineal and erythrosine in cherries in syrup in the presence of quenching effect by means of excitation-emission fluorescence data and three-way PARAFAC decomposition, *Talanta,* 196 (2019) 153-162.

[7] World Health Organization. Evaluation of certain food additives: Eighty-sixth report of the joint FAO/WHO expert committee on food additives, World Health Organization, 965 (2019).

[8] Rubio L., Sanllorente S., Sarabia L. A., Ortiz M.C., Determination of cochineal and erythrosine in cherries in syrup in the presence of quenching effect by means of excitation-emission fluorescence data and three-way PARAFAC decomposition, *Talanta*, 196 (2019) 153-162.

[9] Hassan M., Uzcan F., Alshana U., Soylak, M., Switchable-hydrophilicity solvent liquid–liquid microextraction prior to magnetic nanoparticle-based dispersive solid-phase microextraction for spectrophotometric determination of erythrosine in food and other samples, *Food Chemistry,* 348 (2021) 129053.

[10] Nayak D. S., Shetti, N. P., A novel sensor for a food dye erythrosine at glucose modified electrode, *Sensors and Actuators B: Chemical,* 230 (2016) 140-148.

[11] Chen X.H., Zhao Y.G., Shen H.Y., Zhou L.X., Pan S.D., Jin M.C., Fast determination of seven synthetic pigments from wine and soft drinks using magnetic dispersive solid-phase extraction followed by liquid chromatography–tandem mass spectrometry, *Journal of Chromatography A.,* 1346 (2014) 123-128.

[12] Ma K., Yang Y.N., Jiang X.X., Zhao M., Cai Y.Q., Simultaneous determination of 20 food additives by high performance liquid chromatography with photo-diode array detector, *Chinese Chemical Letters,* 23(4) (2012) 492-495.

[13] Wu H., Guo J.B., Du L.M., Tian H., Hao C. X., Wang Z.F., Wang J.Y., A rapid shaking-based ionic liquid dispersive liquid phase microextraction for the simultaneous determination of six synthetic food colourants in soft drinks, sugar-and gelatin-based confectionery by high-performance liquid chromatography, *Food Chemistry,* 141(1) (2013) 182-186.

[14] Shokrollahi A., Pili H.B., Doust K.H., Microspectrophotometric determination of erythrosine in beverage and water samples after ultrasonic assisted supramolecular-based dispersion solidification liquid–liquid microextraction, *Journal of Analytical Chemistry,* 72(6) (2017) 617-623.

[15] Meral S., Elik A., Ultrasonic-assisted cloud point microextraction and spectrophotometric determination of Ponceau 4R in various beverage samples using Non-ionic surfactant PONPE 7.5, *Food Additives & Contaminants: Part A,* 38(4) (2021) 573-585.

[16] Elik A., Interference-free determination of carmine in food samples using ultrasonic assisted cloud point extraction coupled with spectrophotometry, *Cumhuriyet Sci. J.,* 40(2) (2019) 305-316.

[17] Emiroğlu E., Yuvali D., Sarp G., Yilmaz E., Narin İ., Magnetic solid phase extraction of erythrosine (E127) in pharmaceutical samples with Fe3O4/C-nanodots hybrid material prior to spectrophotometric analysis, *Microchemical Journal,* 170 (2021) 106766.

[18] Canales R.I., Brennecke J.F., Comparison of ionic liquids to conventional organic solvents for extraction of aromatics from aliphatics, *Journal of Chemical & Engineering Data*, 61(5) (2016) 1685-1699.

[19] Yu H., Merib J., Anderson J. L. (2016). Faster dispersive liquid-liquid microextraction methods using magnetic ionic liquids as solvents, *Journal of Chromatography A.,* 1463 (2016) 11-19.

[20] Nawała J., Dawidziuk B., Dziedzic D., Gordon D., Popiel S., Applications of ionic liquids in analytical chemistry with a particular emphasis on their use in solid-phase microextraction, *TrAC Trends in Analytical Chemistry,* 105 (2018) 18-36.

[21] Elik A., Demirbaş A., Altunay N., Experimental design of ligandless sonication-assisted liquid-phases microextraction based on hydrophobic deep eutectic solvents for accurate determination of Pb (II) and Cd (II) from waters and food samples at trace levels, *Food Chemistry*, 371 (2021) 131138.

[22] Altunay N., Elik A., Unal Y., Kaya S., Optimization of an ultrasound-assisted alcohol-based deep eutectic solvent dispersive liquid-phase microextraction for separation and preconcentration of quercetin in wine and food samples with response surface methodology, *Journal of Separation Science,* 44(9) (2021) 1998-2005.

[23] Nambiar A.P., Sanyal M., Shrivastav P.S., Performance evaluation and thermodynamic studies for the simultaneous cloud point extraction of erythrosine and tartrazine using mixed micelles in food samples, *Food Analytical Methods,* 10(10) (2017) 3471-3480.

[24] Stalikas C., Fiamegos Y., Sakkas V., Albanis T., Developments on chemometric approaches to optimize and evaluate microextraction, *Journal of Chromatography A.*, 1216(2) (2009) 175-189.

[25] Mousavi L., Tamiji Z., Khoshayand M.R., Applications and opportunities of experimental design for the dispersive liquid–liquid microextraction method–A review, *Talanta*, 190 (2018) 335-356.

[26] Yuvali D., Seyhaneyildizi M., Soylak M., Narin İ., Yilmaz E., An environment-friendly and rapid liquid-liquid microextraction based on new synthesized hydrophobic deep eutectic solvent for separation and preconcentration of erythrosine (E127) in biological and pharmaceutical samples, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy,* 244 (2021) 118842.

[27] Shokrollahi A., Zarghampour, F., Determination of erythrosine in food samples by CPE-scanometry as a new method and comparison with spectrophotometric results, *Analytical and Bioanalytical Chemistry Research*, *3*(2) (2016) 159-168.

[28] Faraji M., Determination of some red dyes in food samples using a hydrophobic deep eutectic solvent-based vortex assisted dispersive liquid-liquid microextraction coupled with high performance liquid chromatography, *Journal of Chromatography A*, 1591 (2019) 15-23.

[29] Nambiar A.P., Sanyal M., Shrivastav, P.S., Simultaneous densitometric determination of eight food colors and four sweeteners in candies, jellies, beverages and pharmaceuticals by normal-phase high performance thin-layer chromatography using a single elution protocol, *Journal of Chromatography A*, 1572 (2018) 152-161.