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Investigation of the applicability of fatty acid-based deep eutectic solvent based air assisted liquid liquid microextraction for the rapid determination and extraction of butylparaben in cosmetic products

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ABSTRACT

In this research paper, fatty acid-based deep eutectic solvents (FA-DESs) were prepared and investigated for the extraction of butylparaben (BP) from cosmetic products by air assisted liquid liquid microextraction (AA-DLLME). The amounts of BP were determined by UV/Vis spectrophotometry. By combining single factor optimization and Box-Behnken design based multivariate approach, key extraction parameters affecting the FA-DES AA-LLME procedure were systematically optimized. Under the optimized conditions, wide working range ($5\text{--}800\ \mu\text{g L}^{-1}$) was obtained with a good $r^2:0.9972$ and high enrichment factor (205). For three replications run of $10\ \mu\text{g L}^{-1}$ (low), $300\ \mu\text{g L}^{-1}$ (medium) and $600\ \mu\text{g L}^{-1}$ (high) of BP, the percent extraction recovery and relative standard deviation were in the range of $92 \pm 4\%$ - $98 \pm 2\%$ and $1.8\text{--}2.6\%$, respectively. The limit of detection and the limit of quantification were $1.5\ \mu\text{g L}^{-1}$ and $5\ \mu\text{g L}^{-1}$, respectively. The study of the matrix effect showed that the proposed method has high selectivity for measuring BP in the selected samples. Therefore, it has great potential in sample pre-treatment and quantification of trace BP in cosmetic products.

1. Introduction

Parabens are esters of p-Hydroxy benzoic acid. It is possible that cosmetic products contain one or more parabens as methylparaben, ethylparaben, propylparaben, butylparaben (BP) or benzylparaben. They are highly preferred due to their effectiveness against microbiological contamination and their low cost (Nowak et al., 2021). Parabens, which are considered a good preservative, are both poisonous and toxic (Fransway et al., 2019). They cause irritation and allergic reactions such as eczema on the skin. Parabens are also known as substances that mimic the estrogenic hormone in the body (Oishi, 2002). For this reason, they are taken in large amounts or accumulate in the body over time; causes hormone disruption and irritation. Estrogenic activity is associated with certain forms of breast cancer, which has been found to contain BP (Shanmugam et al., 2010). Based on these results, personal care products including deodorants, antiperspirants, hand-face creams and sprays we apply directly to our bodies increase our risk of developing breast cancer (Lincho et al., 2021). Therefore, it is very important to develop new analytical techniques for the determination of BP from these products.

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UV-vis spectrophotometer is widely used for the determination of organic species due to its simplicity, cheapness, rapid measurement and availability in almost every research laboratory (Doğan et al., 2020). The biggest problem in this determination technique is that the analyte concentration to be determined is too low and the determination cannot be made correctly due to interferences originating from the matrix solution (Mello et al., 2013). Therefore, to obtain reliable results, an effective and simple separation and preconcentration method is needed prior to analysis step. Many sample preparation methods including fabric phase sorptive extraction (FPSE) (Gülle et al., 2019), vortex-assisted liquid-liquid microextraction (VA-LLME) (Ge et al., 2020), syringe-assisted liquid-liquid microextraction (SA-LLME) (Rajabi et al., 2017), magnetic solid phase extraction (MSPE) (Yusoff et al., 2017), matrix solid-phase dispersion coupled with supramolecular solvent-based microextraction (MSPD-SUPRAS) (Yıldız and Çabuk, 2018) and syringe-to-syringe dispersive magnetic nanofluid microextraction procedure (SS-DMNF-ME) (Dil et al., 2021) were commonly used for the separation and preconcentration of trace concentrations of BP in cosmetic products.

Solvents are the most important area of Green Chemistry research. They represent a significant challenge for Green Chemistry because their amount is often wasted in syntheses and processes. In addition, conventional solvent is toxic, flammable and corrosive. In order to eliminate all these deficiencies, chemists have turned to producing safer solutions. In recent years, the trend towards environmentally friendly processes has increased the interest in green solvents (Pacheco-Fernández and Pino, 2019). A system consisting of a mixture of two or more Lewis acids and bases and having a much lower melting point than the initial components is defined as a deep eutectic solvent (DES) (Shishov et al., 2017). In other words, the DES are prepared by mixing at least two chemicals, a hydrogen bond acceptor (HBA) and a hydrogen bond donor (HBD), whose freezing point is much lower than that of each component (Santana-Mayor et al., 2021). Amide, amine, fatty acids, sugars, alcohol and metal salts can be used as HBDs. The fact that they are non-flammable and non-volatile, recyclable, low vapor pressure and high boiling point has led to an increased interest in DES (Florindo et al., 2018). Although DESs and ionic liquids have similar physical properties, they show different chemical properties (Vanda et al., 2018). As an alternative to ionic liquids, DESs overcome their main disadvantages such as high cost and toxicity, while maintaining their negligible vapor pressure, easy adjustability, and excellent dissolution properties. In addition, the DESs have lower melting point than room temperature, immiscibility with water, and easy dispersion into water. (Vanda et al., 2018; Florindo et al., 2018).

The main purpose of this study is to investigate the applicability of DESs to chemometric optimization and extraction of BP. Fatty acid-based DES was suggested as a new extraction solvent for the air assisted liquid liquid microextraction of BP from cosmetic products. Based on the results of the preliminary experiments performed, four main variables including FA-DES volume, pH, extraction cycles and NaCl amount were optimized by Box-Behnken design. The accuracy and precision of the proposed method was experienced with reproducibility and repeatability studies. To our knowledge, there are no reports of FA-DES application for analysis of BP in cosmetic products. Moreover, the results shown that the FA-DESs reported in the literature can be applied in different chemical species.

2. Materials and methods

2.1. Standards and reagents

All reagents were of analytical reagent grade. Butylparaben (purity >99%), were purchased from Sigma-Aldrich (Spruce, USA) and its stock solution was prepared by dissolving the appropriate amount in methanol and stored in a refrigerator at 4 °C. Working solutions and calibration solutions were prepared by daily sequential dilution of this stock solution. Methanol (purity ≥98) was bought from Merck (Germany). Phosphate buffer solution (0.2 mol L⁻¹ pH = 6.6) was prepared by mix 18.75 mL of 0.2 mol L⁻¹ dibasic sodium phosphate with 31.25 mL monobasic sodium phosphate in 50 mL the water. Different concentrations of NaCl solutions were prepared from its stock solid (purity ≥99%, Merck). Reagents including n-octanoic acid (C8, purity ≥98, Merck), nonanoic acid (C9, purity ≥96, Sigma), decanoic acid (C10, purity ≥98, Sigma), undecanoic acid (C11, purity ≥99%, Merck) and dodecanoic acid (C12, purity ≥96, Merck) were used in the preparation of low viscous fatty acid-based deep eutectic solvents.

2.2. Instrumentation and software

An UV-Visible Spectrophotometer (Shimadzu UV-1800 PC model, Tokyo, Japan) was used in determination step. Ultrasonic bath (A SK5210LHC Kudos, Shanghai, China) and digital pH-meter (Mettler Toledo FE28, Zurich, Switzerland) were used in the extraction and sample pre-treatment steps. Ultra-pure water was obtained from Milli-Q water purification system (Millipore, USA). Design-Expert® software version 12.0.1 (Stat-Ease Inc., Minneapolis), was used for ANOVA analysis and multivariate optimization.

2.3. Cosmetic products

Cosmetic products including shampoo, shower gel, hair cream, moisturizing cream, suntan cream, hand cream, anti-acne cream, face care gel, liquid soap, face moisturizing gel, gel soap, tooth paste, eye area care cream, argan extract hair mask, face clay mask, hemp oil foot mask, facial cleansing gel, firming body lotion, antibacterial liquid soap, hair care mask, solid soap and clay hand mask were obtained from EZEL cosmetic company in Sivas, Turkey. Sample pre-treatment of these products was carried out according to the method previously reported in the literature (Huang et al., 2013). First, solid (1 g) and liquid samples (5 mL) were spiked to 50 mL-centrifuge tubes. Then, 10 mL of ethanol was poured into the tubes. Then, the tubes were placed in an ultrasonic bath, and were sonicated at 52 kHz for 10 min at room temperature. Then, the resulting mixture was filtered using a 0.22 µm millipore membrane filter. Finally, the FA-DES AA-LLME procedure was applied to 5 mL of the supernatant obtained.

2.4. Preparation of fatty acid-based DESs

In this study, seven fatty acid-based DESs such as C8:C12, C9:C12, C10:C12, C11:C12, C8:C10:C12, C8:C11:C12 and C9:C10:C12 were prepared and investigated for the extraction of BP. These fatty acid-based DESs were prepared according to the previously

reported method (El-Deen and Shimizu, 2020). The fatty acid-based DESs were prepared by mixing HBD and HBA at various molar ratios in beakers at 60 °C until homogeneous clear solutions were formed. Here, the shorter alkyl chain fatty acids act as HBA, while the longest fatty acids act as HBD (Florindo et al., 2018). From phase change materials to green solvents: Hydrophobic low viscous fatty acid-based deep eutectic solvents. *ACS Sustainable Chemistry & Engineering*, 6(3), 3888-3895.). The use of acids smaller than C8 (hydrophilic acids) was not used in this study due to the chemical instability of DES (leaching of acids into water) when in contact with water. As a result, FA-DESs were prepared as shown in Table 1.

2.5. Optimization strategy

Optimization studies were carried out randomly to minimize the effects of uncontrolled variables. Since it is not possible to complete all studies in a single working day, the studies were divided into two blocks and carried out in two consecutive days to avoid possible variations. Based on the results of the preliminary experiments performed, four main variables including FA-DES-1 volume (A), pH (B), extraction cycles (C) and NaCl amount (D) were chosen for optimization. For each variables, high and low points were selected using Box-Behnken design (BBD) (see Supplementary Material Table S1). The BBD was used to optimize values for each variable based on extraction recovery (ER%). The BBD consisted of 29 trials at three levels (-1, 0, +1) for the four variables (see Supplementary Material Table S1). Optimization studies were expressed according to following quadratic equation-1.

$$y = b_0 + \sum_{i=1}^k b_i x_i + \sum_{i=1}^k b_{ii} x_i^2 + \sum_{1 \leq i < j \leq k} b_{ij} x_i x_j + \varepsilon \quad (1)$$

Where y was response, x_i was variables, k was factor number, b_0 was constant, b_i was linear coefficient, b_{ij} was interaction coefficient, b_{ii} was quadratic coefficient, and ε was residue. Moreover, the terms $X_i X_j$ and X_i^2 represent the interaction and quadratic terms, respectively.

2.6. FA-DES AA-LLME procedure

The experimental steps of the FA-DES AA-LLME procedure were summarized below. Firstly, 875 μL of FA-DES-1 (molar ratio at 1:2) was added to a falcon centrifuge tube containing the 5 mL of sample solution (spiked with BP at 100 $\mu\text{g L}^{-1}$). After the pH of the solution was adjusted to pH 6.6 using phosphate buffer solution, 4.0 (w/w) % of NaCl solution was added to the obtained mixture. Next, the 10 mL syringe was inserted into the mixture and seven extraction cycles of suction and injection were performed into the tube for dispersion. After seven extraction cycles, a cloudy solution was obtained. Following this, the falcon tube was kept in an ice-water bath for 2 min to solidify the floating FA-DES-1. The aqueous phase at the bottom of the falcon tube was removed using a syringe. Finally, the solidified DES phase melted at room temperature. The final volume of the resulting measurement phase was diluted 250 μL with methanol and transferred to micro-quartz cuvette for spectrophotometric analysis (265 nm). All studies were carried out in triplicate with sample blank. The spectrum obtained depending on the BP concentration was given in Supplementary Fig. 1.

2.7. Calculation of enrichment factor and extraction recovery

Extraction recovery (ER%) and enrichment factor (EF) was used to indicate the best value of the optimized microextraction parameters. The ER% and EF were calculated according to the following equation-2 and 3:

$$\text{ER}\% = \times 100 [C_{\text{measured}} - C_{\text{real}}] / C_{\text{spiked}} \quad (2)$$

$$\text{EF} = m_m / m_i \quad (3)$$

Where C_{measured} was the detected concentration of BP in sample solution after adding a certain amount of the standard BP solution, C_{real} was the concentration of BP in sample solution without addition of standard BP solution, C_{spiked} was the concentration of standard BP solution spiked into the sample solution, m_m and m_i were the slope of the calibration graphs obtained before and after extraction, respectively.

Table 1

Summary of the components, molar ratios and melting temperatures of the prepared fatty acid-based DES.

Abbreviation	HBA	HBD	Molar ratio	Freezing point (°C)
FA DES-1	C9	C12	2:1	7.8
FA DES-2	C8	C12	2:1	19.5
FA DES-3	C10	C12	2:1	21.9
FA DES-4	C11	C12	2:1	23.4
FA DES-5	C8: C10	C12	1:1:1	13.5
FA DES-6	C8: C11	C12	1:1:1	13.4
FA DES-7	C9: C10	C12	1:1:1	13.4

C8: n-octanoic acid.

C9: nonanoic acid.

C10: decanoic acid.

C11: undecanoic acid.

C12: dodecanoic acid.

3. Results and discussion

3.1. Selection of experimental design parameters

3.1.1. Selection of suitable FA-DES

The most important parameter to be optimized in extraction studies is the selection of the extraction solvent. The extraction solvent should ensure efficient, rapid and selective extraction of the investigated analyte from the sample solution. In addition, due to the toxic properties of organic solvents, extraction solvents were preferred to be environmentally friendly. In recent years, deep eutectic solvents have been used as extraction solvents due to their environmentally friendly, inexpensive and easy preparation. For these reasons, seven the FA-DESs were prepared and tested for the extraction of BP in this study. The composition and molar ratios of the FA-DES were given in Table 1. These prepared FA-DESs were investigated for the extraction of BP. The FA-DES were used in equal volumes (500 μ L). The obtained results were in Fig. 1a. According to the results, the ER% of BP for the studied FA-DES were FA-DES-1 (92.9%) > FA-DES-4 (84.1%) > FA-DES-5 (77.3%) > FA-DES-3 (65.8%) > FA-DES-2 (60.4%) > FA-DES-6 (60.1%) > FA-DES-7 (58.5%). The best analytical results in FA-DES-1 are probably due to stronger interactions between n-octanoic acid and dodecanoic acid during FA-DES formation. Accordingly, the BP interacts with the hydrophilic part of DES-1 and is easily extracted. Based on the results obtained, the FA-DES-1 was chosen as the suitable extraction solvent for the extraction of BP.

3.1.2. Effect of molar ratio of selected DES components

Because the FA-DES provides with H-bond, the effectiveness of this bond depends on the molar ratio of the components in the aqueous solution. Therefore, appropriate molar ratios of the main components of FA-DES should be investigated to ensure efficient and easy phase separation of the investigated analyte. So, different molar ratios of C9:C12 bromide forming FA-DES-1 were mixed and investigated for the extraction of BP. The obtained results (see Fig. 1b) showed that the ER% of BP increased rapidly as the molar ratio increased from 3:1 to 1:2, and then remained constant. The probable reason for this may be that the hydrogen bonding occurs more easily and effectively by increasing the electron exchange depending on the increasing concentration of C12 in the composition. Therefore, the appropriate molar ratio of FA-DES-1 was chosen as 1:2 for further extraction steps.

3.2. Optimization of the significant variables using Box-Behnken design

3.2.1. Statistical analysis and model fitting

The levels of coded extraction variables and the respective response values of the BBD were given in Supplementary Material Table S2. Using Design-Expert® software, these variables and values were processed through full quadratic regression model to calculate and plot the 3D response surface and analysis of variance (ANOVA) of the BBD. The ANOVA (see Table 2) was applied to evaluate the model and to obtain response surfaces for optimization of extraction variables. If p-value (smallest level of significant) in ANOVA results is lower than 0.05, then indicates that the established model is statistically significant. When the results in Table 2 are examined, it indicates that the p-values of all interactions (linear, binary and quadratic) are less than 0.05, thus all variables are significant for the established model. Additionally, the “lack of fit” explains the model’s failure to represent extraction results at the point not included in the ANOVA analysis. The p-value of the “lack of fit” (0.8724) shown that the established model used to fit response variables was significant and adequate to represent the relationship between the ER% and the independent variables.

The goodness of fit for the established model is explained by the coefficients of determination (R^2 , adjusted- R^2 , predicted - R^2). The R^2 (0.9997) helps explain the amount of variance around the mean results explained by the established model. The adjusted- R^2 (0.9994) for the number of terms in the established model is used. Here, as the number of variables that do not contribute to the model increases, the value of the adjusted- R^2 decreases. In addition, the predicted - R^2 value (0.9989) is used only for the variables that contribute to the established model. High R^2 values (see Table 3) indicated that the established model could be reliably used to explain and optimize the effects of extraction variables on the ER% of BP. Based on the results, the relationship between the response and extraction variables can be expressed by the following equation-4:

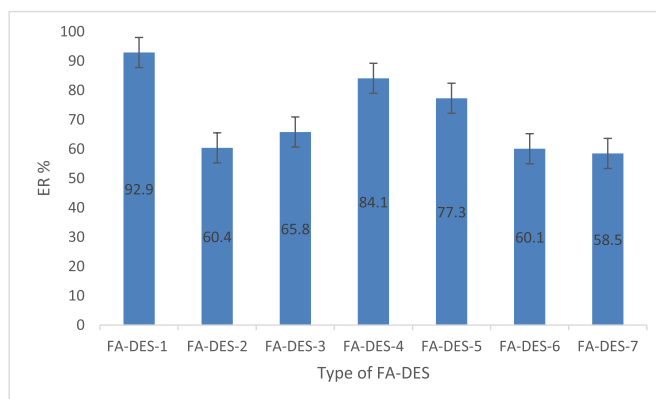


Fig. 1a. Effect of type of FA-DES on the ER% of BP.

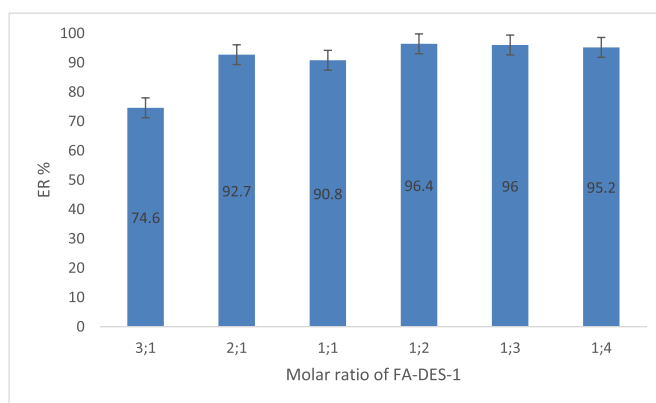


Fig. 1b. Effect of molar ratio of FA-DES-1 on the ER% of BP.

Table 2
Analysis of variance (ANOVA) for the BBD.

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	5136.4	14	366.9	3474.1	< 0.0001	significant
A	333.9	1	333.9	3161.9	< 0.0001	
B	35.4	1	35.4	334.9	< 0.0001	
C	401.0	1	401.0	3797.4	< 0.0001	
D	189.4	1	189.4	1793.2	< 0.0001	
AB	235.6	1	235.6	2231.12	< 0.0001	
AC	182.3	1	182.3	1725.8	< 0.0001	
AD	9.6	1	9.6	91.0	< 0.0001	
BC	285.6	1	285.6	2704.5	< 0.0001	
BD	21.6	1	21.6	204.8	< 0.0001	
CD	86.8	1	86.8	821.7	< 0.0001	
A ²	834.7	1	834.7	7903.9	< 0.0001	
B ²	1393.3	1	1393.3	13193.9	< 0.0001	
C ²	1226.8	1	1226.8	11616.9	< 0.0001	
D ²	1726.6	1	1726.6	16349.4	< 0.0001	
Residual	1.5	14	0.1056			
Lack of Fit	0.7665	10	0.0766	0.4306	0.8724	not significant
Pure Error	0.7120	4	0.1780			
Cor Total	5137.83	28				

Table 3
Fit statistical parameters of the established model.

Std. Dev.	0.3250	R ²	0.9997
Mean	71.36	Adjusted R ²	0.9994
C.V. %	0.4554	Predicted R ²	0.9989

$$ER(\%) = 94.56 + 5.27A - 1.72B + 5.78C + 3.97D - 7.67AB - 6.75AC + 1.55AD - 8.45BC - 2.33BD + 4.66CD - 11.34A^2 - 14.66B^2 - 13.75C^2 - 16.32D^2 \quad (4)$$

Results in Fig. 2a show that most of the data points are distributed near the regression line. This indicated a good correlation between the predicted ER% and actual ER% and a good fit for the quadratic model. In addition to these results, residual graphs are randomly distributed (see Fig. 2b). This means that the variance of the experimental results is constant for all values of the ER% of BP.

3.2.2. Interaction between extraction variables

3D response surfaces graphs were plotted to obtain more details of the extraction variables associated with the ER% of BP. These graphs help explain the relationship between the ER% of the two variables simultaneously, while keeping the other variables constant at their central level. 3D response surface plots (see Fig. 3a–c) represent the relationship between ER% of BP and four extraction variables (FA-DES-1 volume, pH, extraction cycles and NaCl amount). Fig. 3a describes the effect of LW fatty acid-based DES-1 volume and extraction cycles on the ER % of BP under constant extraction conditions. The ER % of BP was increased with increasing extraction cycles from 1 to 7 and FA-DES-1 volume from 200 μ L to 900 μ L. In addition, with a further increase FA-DES-1 volume from 900 μ L to 1100 μ L, the ER % of BP was partially decreased. These results indicate that approximately 7 extraction cycles are sufficient for the FA-

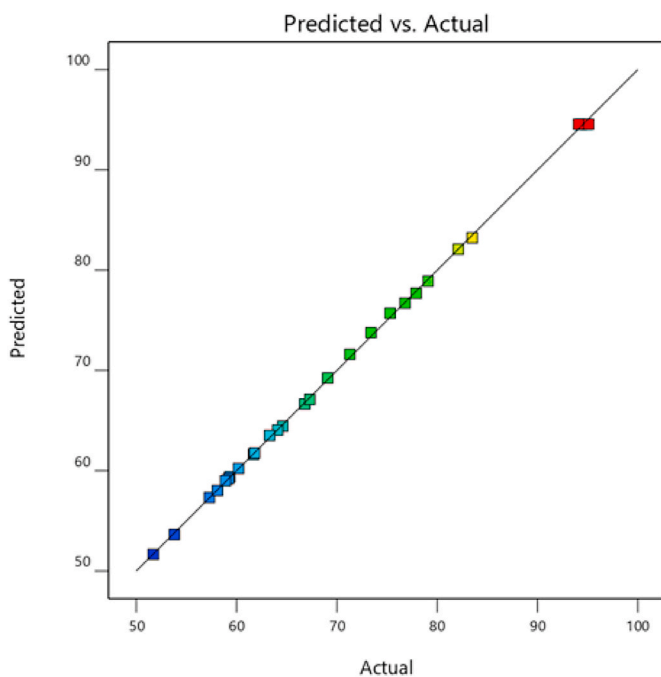


Fig. 2a. The predicted response vs. the observed response.

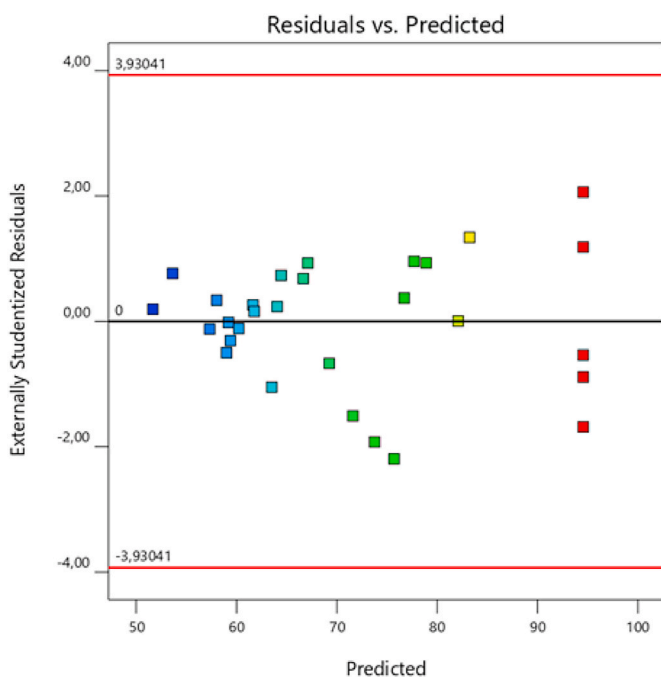
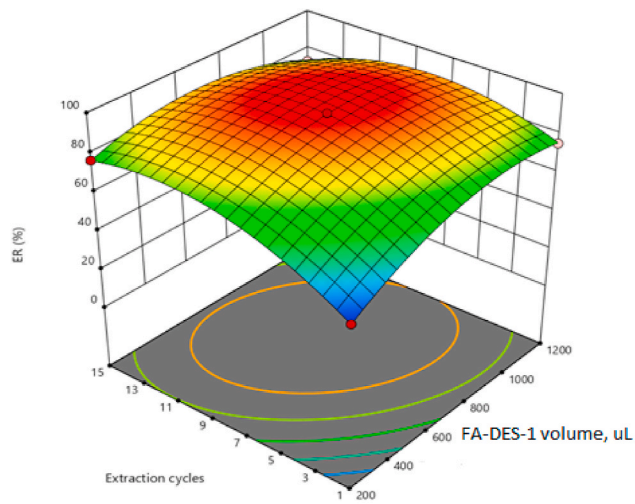
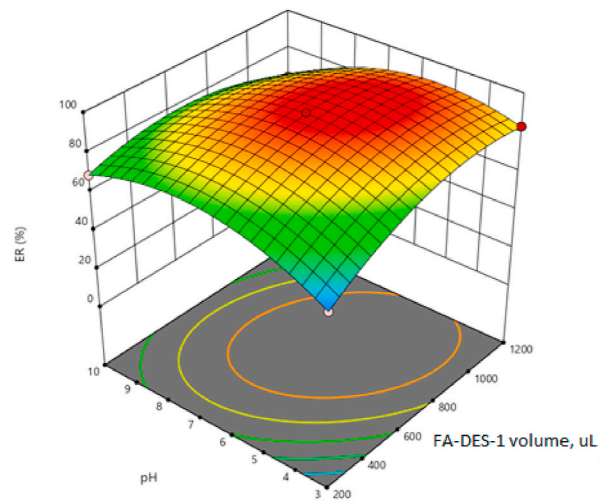


Fig. 2b. A plot of the internally studentized residuals vs. the predicted response.

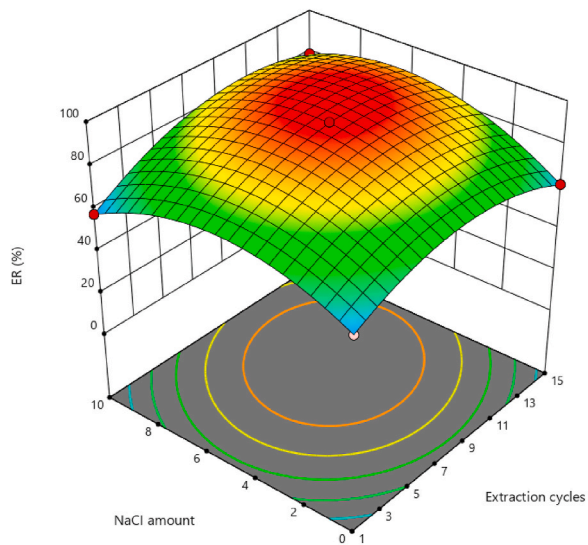
DES-1 to form microspheres that will provide phase separation. The effect of the interaction between pH and FA-DES-1 volume on the ER % of BP is presented in Fig. 3b. Here, it can be said that the ER % of BP is increased when the pH is increased from 3 to 7 and the increase FA-DES-1 volume is below 900 μL , and there is a drastic decrease in the ER % of BP if the pH is above 8 and the LW fatty acid-based DES-1 volume is above 1000 μL . In particular, the H bond formation, which is the main factor of DES formation, has decreased due to the increased OH^- ions in the environment due to the increase in pH value, and accordingly the ER % of BP has decreased. The effect of the interaction between extraction cycles and NaCl amount on the ER % of BP is presented in Fig. 1c. In microextraction



(a)



(b)



(c)

Fig. 3. (a) 3D response surface for the FA-DES-1and extraction cycles on the ER% of BP, (b) 3D response surface for the FA-DES-1and pH on the ER% of BP, (c) 3D response surface for the extraction cycles and NaCl amount on the ER% of BP.

studies using DES (as extraction solvent), the increase in the ionic strength of the sample solution both accelerates the microsphere formation of DES and facilitates the phase separation. When looking at Fig. 3c, it is seen that quantitative recoveries were obtained in approximately 7 extraction cycles and 4%(w/w) NaCl solution. Moreover, there was no significant change in recovery at higher NaCl amounts and higher extraction cycles.

3.2.3. Variables optimization

According to the result of Box-Behnken design, the optimized extraction variables of FA-DES AA-LLME procedure were as follows: FA-DES-1 volume 875 μL , pH 6.5, extraction cycles 7 and NaCl amount 4 (w/w)%. Under the optimal extraction conditions, a predicted maximum ER% of BP was 92.7%. To test the suitability of the model, triplicate validation studies were performed under these selected optimal extraction conditions. The average ER% of BP was $93.5 \pm 2.1\%$. The obtained analytical data indicated that the model and its quadratic equation were reliable.

3.3. Method validation and application for analysis of personal care products

3.3.1. Quantitative features of the proposed method

To investigate the performance quality of the FA-DES AA-LLME procedure under optimal extraction conditions, quantitative features of the method were determined. For this, analytical parameters like working range, regression equation, determination coefficient (r^2), limit of detection (LOD), limit of quantification (LOQ), enrichment factor (EF), extraction recovery (ER) and relative standard deviation (RSD) were examined, and calculated in the personal care products. Analytical results were presented in Table 4. To investigate the working range and linearity of the method, sample solutions including fifteen different concentrations of BP were prepared, and after the FA-DES AA-LLME procedure, the calibration curve was plotted. For the BP, wide working range (5–800 $\mu\text{g L}^{-1}$) was obtained with a good r^2 :0.9972 and high EF (205). For three replications run of 10 $\mu\text{g L}^{-1}$ (low), 300 $\mu\text{g L}^{-1}$ (medium) and 600 $\mu\text{g L}^{-1}$ (high) of BP, the ER% and RSD were in the range of $92 \pm 4\%$ - $98 \pm 2\%$ and 1.8–2.6%, respectively. LOD (1.5 $\mu\text{g L}^{-1}$) and LOQ (5 $\mu\text{g L}^{-1}$) were calculated using the according to the following equations-5 and 6:

$$\text{LOD} = 3s_{\text{blank}} / m \quad (5)$$

$$\text{LOQ} = 10s_{\text{blank}} / m \quad (6)$$

Where s_{blank} was the standard deviation of the sample blank, m was the slope of the calibration graphic, respectively.

3.3.2. Selectivity study

Different chemicals species with BP in the personal care products can potentially extracted together in the extraction solvent. Accordingly, it reduces the extraction efficiency of the FA-DES AA-LLME procedure for BP. A series of experiments were designed using standard solutions of 50 $\mu\text{g L}^{-1}$ BP in which appropriate amounts of different chemical species was added. The FA-DES AA-LLME procedure was applied to these solutions under the optimized conditions that were already established for extraction of BP. Then, the tolerable limit was determined for each chemical species. The tolerance limit of the chemical species does not cause deviation of more than $\pm 5\%$ in absorbance of BP. Moreover, analytical results including RSD and recovery for the chemical species were given in Table 5. As shown in Table 5, the studied chemical species do not interfere with the extraction and determination of the BP by the proposed method. As a result, the FA-DES AA-LLME procedure has good selectivity for measuring BP in the personal care products.

3.3.3. Repeatability and reproducibility studies for accuracy and precision

The precision and accuracy of the FA-DES AA-LLME procedure were evaluated based on the RSDs and recoveries, respectively. In this context, the repeatability/reproducibility RSDs and recoveries were tested by spiking personal care products at three fortification concentration (10, 300 and 600 $\mu\text{g L}^{-1}$) of BP with six parallel studies. As a result, the RSDs ranged from 1.8% to 2.5% for repeatability studies, and varied between 2.1% and 2.9% for reproducibility studies. In addition, the recovery ranged from 94.5% to 98.1% for repeatability studies, and varied between 92.3% and 96.9% for reproducibility studies. The obtained analytical data showed that the FA-DES AA-LLME procedure exhibits good accuracy and precision.

3.3.4. Analysis of personal care products

The applicability of the FA-DES AA-LLME procedure was evaluated by the determination and extraction of trace amounts of BP in a total of 22 personal care products such as shampoo, shower gel, hair cream, moisturizing cream, suntan cream, hand cream, anti-acne cream, face care gel, liquid soap, face moisturizing gel, gel soap, tooth paste, eye area care cream, argan extract hair mask, face clay mask, hemp oil foot mask, facial cleansing gel, firming body lotion, antibacterial liquid soap, hair care mask, solid soap and clay hand mask. Table 6 shows analytical value of standard solution (at concentration of 100 and 600 $\mu\text{g L}^{-1}$ of BP), spiked the personal care products (at concentration of 100 and 600 $\mu\text{g L}^{-1}$ of BP), and the BP without spiked. The spiked and without spiked BP were analyzed after the FA-DES AA-LLME procedure was applied to these solution, while the standard solution was injected directly. Butyl paraben could not be found in any of the analyzed personal care products. Relative recoveries of BP were calculated by multiplying by 100 the ratio between the concentration found in each sample and the concentration found in deionized water spiked at the same level. In brief, these results demonstrated that the FA-DES AA-LLME procedure could be effectively used to analyze trace levels of BP in the personal care products with the good recoveries ($90 \pm 2\%$ - $106 \pm 3\%$) and acceptable relative standard deviations ($3.3\% \leq$). Moreover, these

Table 4
Quantitative features of the FA-DES AA-LLME procedure.

Analytical parameters	After FA-DES AA-LLME procedure	Before FA-DES AA-LLME procedure
Regression equation $A=(a \pm SD_a)c + (b \pm SD_b)$	$A=(0.8628 \pm 0.0197)C-(0.0962 \pm 0.0088)$	$A=(0.0042 \pm 0.0028)C+(0.0095 \pm 0.0039)$
r^2	0.9972	0.9985
Working range. $\mu\text{g L}^{-1}$	5-800	220-4500
LOD. $\mu\text{g L}^{-1}$	1.5	66.7
LOQ. $\mu\text{g L}^{-1}$	5.0	220
RSD	1.8-2.6	-
ER	92 ± 4 - 98 ± 2	-
EF	205	-

A. absorbance of BP; c. BP concentration in real samples (ng mL^{-1}); a. slope; b. intercept; SD_a and SD_b . standard deviations of slope and intercept. respectively.

LOD: Linear dynamic range.

r^2 : Determination coefficient.

LOD: Limit of detection.

LOQ: Limit of quantification.

RSD: Relative standard deviation for 10 $\mu\text{g L}^{-1}$ (low), 300 $\mu\text{g L}^{-1}$ (medium) and 600 $\mu\text{g L}^{-1}$ (high) of BP.

ER: Extraction recovery for 10 $\mu\text{g L}^{-1}$ (low), 300 $\mu\text{g L}^{-1}$ (medium) and 600 $\mu\text{g L}^{-1}$ (high) of BP.

EF: Enrichment factor.

Table 5
Selectivity results for BP of the FA-DES AA-LLME procedure (N = 3).

Matrix ions	Tolerable limit ^a	RSD (%)	Recovery (%)
K^+	2000	1.8	99 ± 4
Na^{2+}	2000	1.8	98 ± 3
Mg^{2+}	2000	1.9	98 ± 1
Cl^-	2000	1.6	98 ± 2
HPO_4^{2-}	2000	1.5	99 ± 2
CO_3^{2-}	1500	1.9	97 ± 3
Cu^{2+}	1500	1.5	98 ± 4
K^+	1500	1.6	97 ± 3
PO_4^{3-}	1500	1.8	99 ± 2
F^-	100	2.2	98 ± 3
Ca^{2+}	1000	1.9	97 ± 4
Sn^{2+}	1000	1.6	98 ± 3
Mn^{2+}	1000	1.6	97 ± 3
SO_4^{2-}	750	2.1	98 ± 4
Co^{2+}	750	2.0	98 ± 3
Pb^{2+}	500	1.9	96 ± 4
Cr^{3+}	500	2.1	97 ± 3
Cd^{2+}	500	2.3	97 ± 2
Fe^{3+}	500	2.3	96 ± 3
Tricosane	250	2.0	95 ± 3
Zn^{2+}	250	1.9	95 ± 2
Isopropylparaben	150	2.2	96 ± 3
Benzyl paraben	150	2.3	96 ± 4
Ethylparaben	75	2.5	94 ± 3
Methylparaben	75	2.7	94 ± 5

^a [Matrix ions concentration. $\mu\text{g L}^{-1}$ /BP concentration. $\mu\text{g L}^{-1}$].

results indicate that the FA-DES AA-LLME procedure did not show the matrix effect.

3.4. Comparison with other analytical methods

The key analytical parameters of the FA-DES AA-LLME procedure (working range, LOD, EF, ER, RSD and extraction time) were compared with some techniques. The analytical data were summarized in Table 7. The working range of the FA-DES AA-LLME procedure was found to have a wider range than the analytical techniques reported. The EF was better than the analytical techniques reported and the extraction time of our method was shorter than all analytical techniques reported. The obtained LOD and ER were satisfactory and comparable to the analytical techniques reported. The precision of the method was satisfactory and the RSD values were comparable to those of the analytical techniques reported. In addition, the FA-DES AA-LLME procedure is more repeatable than the other methods which is due to the reduced number of sample preparation steps.

4. Conclusions

Although new methods aiming to simplify and speed up sample preparation need to be developed, this may not always be possible due to the complex nature of cosmetic matrices. Future trends in this area are towards the development of new extraction procedures

Table 6
Application results of BP in cosmetic products using FA-DES AA-LLME procedure.

Cosmetic products	Intra-day (N = 3)				Inter-day (N = 3 × 3)		
	Spiked ($\mu\text{g L}^{-1}$)	Found ($\mu\text{g L}^{-1}$)	Recovery \pm SD ^a (%)	RSD (%)	Found ($\mu\text{g L}^{-1}$)	Recovery \pm SD ^a (%)	RSD (%)
Shampoo	100	96	96 \pm 2	2.2	95	95 \pm 3	2.9
	600	588	98 \pm 3	2.6	582	97 \pm 2	3.2
Shower gel	100	94	94 \pm 3	2.3	92	92 \pm 4	2.7
	600	576	96 \pm 2	2.5	570	95 \pm 4	3.0
Hair cream	100	93	93 \pm 4	1.9	91	91 \pm 5	2.2
	600	570	95 \pm 3	2.2	564	94 \pm 3	2.5
Moisturizing cream	100	91	91 \pm 2	2.0	90	90 \pm 5	2.4
	600	564	94 \pm 4	2.3	576	93 \pm 3	2.7
Suntan cream	100	96	96 \pm 3	2.2	93	93 \pm 2	2.6
	600	588	98 \pm 2	2.8	582	97 \pm 2	3.0
Hand cream	100	103	103 \pm 1	2.4	96	96 \pm 3	2.8
	600	606	101 \pm 2	2.9	588	98 \pm 3	3.1
Anti-acne cream	100	95	95 \pm 4	2.3	106	106 \pm 2	2.9
	600	582	97 \pm 4	2.7	612	102 \pm 3	3.3
Face care gel	100	103	103 \pm 3	2.3	95	95 \pm 4	2.6
	600	612	102 \pm 3	2.5	576	96 \pm 4	2.9
Liquid soap	100	94	94 \pm 2	1.9	92	92 \pm 3	2.0
	600	582	97 \pm 3	2.2	570	95 \pm 3	2.5
Face moisturizing gel	100	96	96 \pm 2	2.0	104	104 \pm 2	2.3
	600	588	98 \pm 3	2.4	612	102 \pm 2	2.8
Gel soap	100	97	97 \pm 3	2.1	103	103 \pm 3	2.4
	600	594	99 \pm 1	2.5	624	104 \pm 2	2.7
Tooth paste	100	102	102 \pm 1	2.3	96	96 \pm 3	2.8
	600	606	101 \pm 2	2.8	588	98 \pm 4	3.1
Eye area care cream	100	95	95 \pm 4	1.8	94	94 \pm 4	2.2
	600	588	98 \pm 2	2.1	582	97 \pm 2	2.5
Argan extract hair mask	100	97	97 \pm 3	2.4	95	95 \pm 3	2.8
	600	594	99 \pm 3	2.9	588	98 \pm 2	3.1
Face clay mask	100	94	94 \pm 4	2.5	92	92 \pm 4	3.0
	600	582	97 \pm 2	2.8	564	94 \pm 3	3.3
Hemp oil foot mask	100	96	96 \pm 2	2.4	94	94 \pm 4	2.7
	600	582	97 \pm 3	2.6	570	95 \pm 5	2.9
Facial cleansing gel	100	93	93 \pm 3	1.9	92	92 \pm 5	2.1
	600	588	98 \pm 2	2.2	576	96 \pm 3	2.6
Firming body lotion	100	98	98 \pm 4	2.0	95	95 \pm 3	2.4
	600	594	99 \pm 3	2.4	582	97 \pm 2	2.8
Antibacterial liquid soap	100	96	96 \pm 2	1.8	104	104 \pm 4	2.2
	600	588	98 \pm 1	2.1	612	102 \pm 3	2.5
Hair care mask	100	94	94 \pm 3	2.3	91	91 \pm 4	2.8
	600	588	98 \pm 2	2.7	570	95 \pm 3	3.1
Solid soap	100	95	95 \pm 3	2.1	93	93 \pm 3	2.9
	600	582	97 \pm 3	2.4	576	96 \pm 3	3.2
Clay hand mask	100	96	96 \pm 4	2.2	94	94 \pm 3	2.6
	600	588	98 \pm 2	2.6	582	97 \pm 3	2.9

^a Standard deviation (N = 3. 95% confidence interval).

that allow the extraction of cosmetic samples, thereby avoiding interfering species without loss of sensitivity. Based on these facts, A simple and green fatty acid-based deep eutectic solvent based air assisted liquid liquid microextraction coupled with UV/Vis spectrophotometry for the rapid determination and extraction of BP in cosmetic products was described in the study. New types of fatty acid-based deep eutectic solvents were prepared and tested for the first time as extraction solvents for extraction of BP. By combining single factor optimization and the BBD based multivariate approach, important extraction parameters affecting the FA-DES AA-LLME procedure were systematically optimized. Under the optimized extraction condition, a very low LOD was good $1.4 \mu\text{g L}^{-1}$, a wide working range of $8\text{--}950 \text{ ng mL}^{-1}$, and a short extraction time equal to 2 min was obtained. In addition, the FA-DES AA-LLME procedure has the following advantages: high extraction efficiency, high EF, low LODs and no requirement for organic solvents and expensive reagents. The FA-DES AA-LLME procedure has good accuracy in analysis of BP in cosmetic products. The study of the matrix effect showed that the proposed method has high selectivity for measuring BP in the selected samples. Therefore, it has great potential in sample pre-treatment and quantification of trace BP in cosmetic products.

Author contributions section

Ayşenur Öztürk Altunay: Validation, Investigation, Adil Elik: Supervision, Writing -original draft, Writing - review & editing.

Table 7
Comparison of the FA-DES AA-LLME procedure with other methods.

Analytical method	Working range ($\mu\text{g L}^{-1}$)	LOD ($\mu\text{g L}^{-1}$)	EF	ER (%)	RSD (%)	Extraction time (min)	References
SS-DMNF-ME HPLC-UV	5-100	0.8	85.9	89-99	≤ 5.2	5	Dil et al. (2021)
DLLME GC-MS	1-100	0.46	240	73.6-106.3	≤ 10.8	5	Han et al. (2010)
FPSE-HPLC/UV	5-500	0.58	–	91.6-98.8	≤ 2.6	40	Kaur et al. (2020)
SPE-UHPLC-DAD	5-20000	1.0	–	92-101	≤ 6.0	24.7	Ali et al. (2020)
DES-VALLME HPLC-UV	–	5.2	–	90-97	≤ 1.27	10	Dalmaz, & Özak, (2022)
DF- μ LPME HPLC-UV	–	2.6	8.8	84-100	≤ 5.74	5	Ramos-Payan et al. (2017)
FA-DES AA-LLME- UV/Vis spectrophotometry	5-800	1.5	205	92-98	≤ 2.6	2	This study

LDR: Linear dynamic range; LOD: Limit of detection; LOQ: Limit of quantification; RSD: Relative standard deviation; ER: Extraction recovery; EF: Enrichment factor.
 FA-DES AA-LLME: Fatty acid-based deep eutectic solvent based air assisted liquid liquid microextraction.
 DLLME GC-MS: Dispersive liquid–liquid microextraction combined with gas chromatography-mass spectrometry.
 SS-DMNF-ME HPLC-UV: Syringe-to-syringe magnetic fluid phase microextraction high-performance liquid chromatography-UV detector.
 FPSE-HPLC/UV: Fabric-phase sorptive extraction and high-performance liquid chromatography with UV detection.
 SPE-UHPLC-DAD: Solid-Phase Extraction and Ultra-High Performance Liquid Chromatography/Diode Array Detector.
 DES-VALLME: Deep eutectic solvent-based vortex-assisted liquid–liquid microextraction.
 VA-DLLE: vortex-assisted dispersive liquid–liquid extraction.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

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Appendix A. Supplementary data

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