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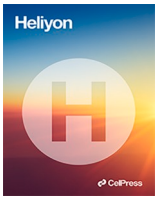

Sensitive determination of daunorubicin in plasma of children with leukemia using pH-switchable deep eutectic solvents and HPLC-UV analysis

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ABSTRACT

An environmental friendly, fast, easy and inexpensive liquid-liquid microextraction (LLME) in combination with pH-switchable deep eutectic solvent (DES) method followed by HPLC was investigated for the separation and determination of daunorubicin (DNR) in human plasma samples. For this purpose, first, 9 DESs were prepared based on previous studies and their switchability in aqueous solution was evaluated by changing the pH. Non-switchable DESs were discarded and switchable DESs were used to extract DNR. The parameters affecting the extraction efficiency were optimized (DES type, volume of DES, concentration of KOH, volume of HCl, salt addition and extraction time). After optimizing the conditions and drawing the calibration curve, figures of merit were calculated. Relative standard deviations (%RSDs) based on 7 replicate with 50 μg L^{-1} of DNR in plasma were 2.7 for intra-day and 4.8 % for inter-day. A wide linear range from 0.15 to 200 μg L^{-1} was obtained. The detection limit of the method based on signal-to-noise 3 and the quantification limit of the method based on signal-to-noise 10 were 0.05 and 0.15, respectively. After spiking plasma samples with different concentrations of DNR, relative recoveries were obtained in the range of 91.0–107.8 %.

1. Introduction

Daunorubicin (DRN) is an aminoglycoside anticancer drug from the anthracycline class that is obtained from Streptomyces peucetius and other species [1]. Daunorubicin is used in the treatment of erythroleukemia, acute lymphoblastic leukemia, acute myelocytic leukemia and acute monocytic leukemia. Its use is also recommended in the treatment of neuroblastoma, non-Hodgkin's lymphoma, Ewing's sarcoma, Wilms' tumor and chronic myelocytic leukemia [2]. Chemotherapy and the use of anticancer drugs such as daunorubicin are widely recognized as the cornerstones of treatment for most malignancies. In this regard, a lot of research is being

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done to determine the effectiveness, side effects, and concentration effects of anticancer drugs on the derma process, as well as the combined effect of anticancer drugs in the chemotherapy process [3]. Controlling the dose of daunorubicin during chemotherapy is very important, and in order to further improve the therapeutic effect of the drug and reduce its side effects, it seems necessary to develop a suitable method for quantitative measurement of DNR [4].

So far a few methods such as capillary zone electrophoresis (CZE) [5], high performance liquid chromatography (HPLC) [6], fluorescence [7] and electrochemical methods [8] have been reported for determination of DNR in biological samples. Chromatographic methods are more sensitive than other methods. In other words, HPLC is the superior technique in drug analysis for the following reasons: no need for derivatization, ability to be coupled with different detection systems and no temperature limitation. However, despite the invention of all kinds of very sensitive instrumental analysis methods, preparation of sample before analysis is mandatory. Because some real sample matrices are complex and not compatible with analytical instruments. As a result, it is necessary to prepare the sample before analysis. Dispersive liquid-liquid microextraction (DLLME) is the best versions of LPME, which was presented in 2006 by Asadi and co-workers [9]. This method, with all its advantages, has disadvantages such as the use of toxic solvents as extractants and the high consumption of disperser solvents. To overcome the problem of toxic extraction solvents in DLLME, the use of organic solvents lighter than water [10], ionic liquids (ILs) [11], supramolecular [12] and deep eutectic solvents (DESs) [13] have been replaced. DESs are a new class of extraction solvents obtained from renewable sources, characterized by a significant melting point reduction compared to their constituents [14]. DESs are easily obtained by mixing one compound as hydrogen bond acceptor (HBA) with another compound as hydrogen bond donor (HBD) [15]. In some cases, these solvents can be made of three or more components. DESs are environmentally friendly because they are synthesized from natural compounds, and their greenness has been proven in scientific articles [16,17]. So far, safe and environmentally friendly DESs have been used as extractants in the DLLME method for the preconcentration of various organic and inorganic species [18−21]. Another disadvantage of DLLME is the use of a large volume of dispersing solvent (about one cc) to disperse the extractant in the aqueous solution. To solve this problem, vortex and ultrasonic methods have been used instead of the disperser solvent to disperse the extractant in the aquatic environment [18,19]. Vortex and ultrasonic are associated with energy consumption and are usually time consuming.

Recently, a method has been developed using DESs, which does not require disperser solvent, vortexing or ultrasonication, and dissolving the extraction solvent in the aqueous phase, as well as separation of organic and aqueous phases, happens with alkalinity and acidification of the environment. This method is called pH-switchability DESs [20,21]. In the presented method, after adding DES, the medium becomes alkaline with a concentrated KOH solution, during which DES is completely dispersed in the aqueous phase and establishes a high contact surface with the analytes. Then acid is added drop by drop to the sample solution to neutralize the alkalinity of the environment. In the meantime, DES extracts analytes by obtaining its molecular form and separates from the aqueous phase.

The aim of this research is to develop an simple, efficient and cheap procedure for selective and accurate extraction of DNR from plasma of children with leukemia. For this purpose, first, 9 DESs were prepared based on previous studies and their switchability in aqueous solution was evaluated by changing the pH. Non-switchable DESs were discarded and switchable DESs were used to extract DNR in plasma samples.

2. Material and methods

2.1. Reagents and materials

Ethylene glycol (EG), (1S)-(+)-camphor-10-sulfonic acid (CSA), *p*-aminophenol, salicylic acid (SA), methyltrioctylammonium-chloride (MTOAC), *n*-butanoic acid (BA), 1-undecanol, *l*-menthol, 1-octanol, thymol and pure standard of daunorubicin hydrochloride (purity higher than 95 %) were purchased from Sigma-Aldrich (St. Louis, MO, USA). Acetone, acetonitrile (for spectroscopy), methanol (HPLC grade), sodium dodecyl sulfate (SDS), decanoic acid, 1-decyl-3-methylimidazolium chloride ([DMIM]Cl), Tetrabutyl ammonium chloride (TBAC), Na_2HPO_4, NaCl, KOH and HCl (37 %) were purchased from Merck (Darmstadt, Germany). A stock solution of DNR at 1000 mg L^{-1} was prepared in 1 % (v/v) formic acid in water:methanol (50:50 % v/v). Working solutions were prepared by daily dilution of the stock solution.

2.2. Instrumentation

An HPLC system (Knauer, Berlin, Germany) equipped with a Polaris $C_{18\text{-A}}$ column 25 cm × 4.6 mm, with particle size of 5 μm, connected with a guard precolumn (Phenomenex, Torrance, CA, USA), a binary pumps (Smartline-1000), a UV detector (Smartline-2500, variable wavelength programmable, Berlin, Germany) and a Chromgate software (version 3.1) was used for the analysis of DNR. A manual sample injector fitted with a 20 μL injection loop (model 7725i, Rheodyne, Cotati, CA, USA) was applied for sample injection. The mixture of 20 mM formic acid solution and methanol (60:40 %v/v) in isocratic elution with a flow rate of 0.8 mL min^{-1} was used as mobile phase. The wavelength of the device for DNR detection was set at 254 nm.

2.3. Sampling and sample preparation

A drug-free blank sample was received from a 12-year-old female who had not been treated with any drugs for more than one year. Real samples were received from two males and two females with acute leukemia who were treated with daunorubicin at Dr. Kermanshahi Hospital in Kermanshah, Iran. The age range of the patients was 6–14 years. The samples were kept at a temperature of −18 °C until analysis.

To preparation of the samples, 100 μL of plasma was placed in a test tube and 300 μL aqueous solution of ZnSO4 (15 % w/v) and 200 μL acetonitrile were added to the test tube. The resulting mixture was vortexed for 10 min. After centrifuging for 5 min at a speed of 4000 rpm, the supernatant was transferred to another test tube and diluted to a volume of 5 mL using pure water to reduce the matrix effect. The obtained phase was then subjected to the presented method.

2.4. Preparation of DESs

In this work, 9 DESs were synthesized based on previous studies. These solvents have been characterized in previous studies and their synthesis in our laboratory was according to the agenda of previous studies. For this purpose, nine DESs including DES-I (MTOAC: *n*-butanol, 1:3) [14], DES-II (*l*-menthol:EG, 1:1) [15], DES-III (*l*-menthol:SA, 4:1) [22], DES-IV (*l*-menthol:CSA, 5:1) [23], DES-V (*l*-menthol:phenol, 1:1) [24], DES-VI ([DMIM]Cl:1-undecanol, 1:2) [25], DES-VII ([DMIM]Cl:*n*-butanoic acid, 1:2) [18], DES-VIII (TBAC:*p*-aminophenol, 1:2) [26] and DES-IX (thymol:decanoic acid, 1:2) [27] were synthesized and investigated. The DESs features, along with their references, are presented in Table 1.

2.5. Extraction procedure

In this method, 5 mL of the diluted and pre-treated plasma was placed in a 10-mL glass tube, and 50.0 μL of selected DES-IV was added. To dissolve the DES in the sample phase, 100 μL of 5 mol L^{-1} KOH solution was added to the tube and it is shaken manually for several seconds. Then, 105 μL of 5 mol L^{-1} HCl is added drop by drop to the test tube. In the meantime, the DES-IV extracts analytes by obtaining its molecular form and separates from the aqueous phase. The DES-IV was collected on the surface of the sample solution without centrifugation. By placing the test tube in the freezer, the extractant phase solidifies in a short period of time. The solidified phase is transferred to a clean container with a spatula to melt at room temperature. It was injected into the HPLC for analysis (Scheme 1).

3. Results and discussion

In this research, LLME based on pH-switchable DES combined with HPLC-UV was employed for the extraction and analysis of DNR in plasma samples. The effect of different parameters including type of DES and its volume, KOH concentration, HCl volume, salt effect and extraction time were investigated and optimized.

3.1. Effect of the type of DES

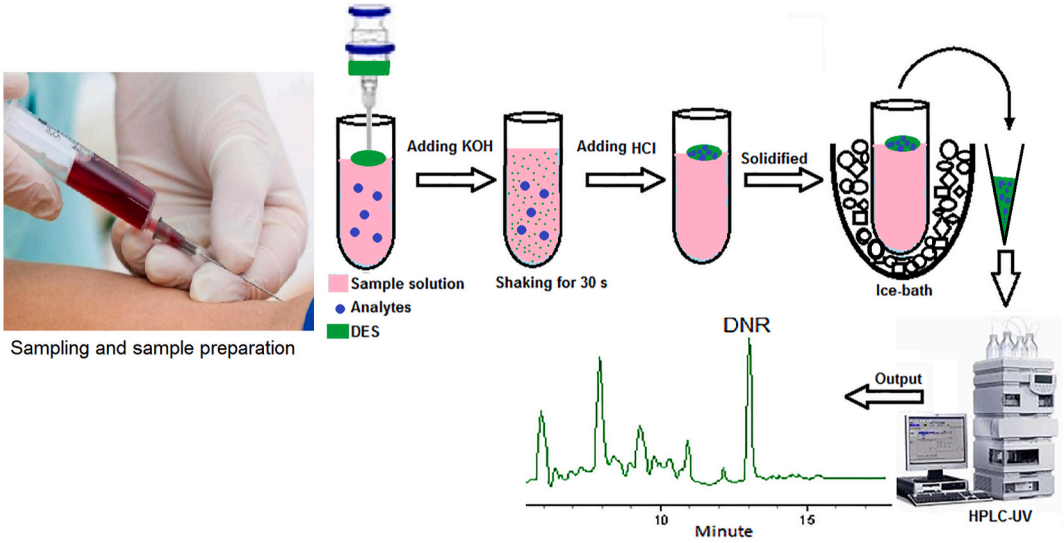
The interaction of DESs with analytes is different due to their different structure. In this research, the pH-switchability of nine sensitized DESs was investigated. As shown in Table 1, four of the DESs including DES-I, DES-VI, DES-VII and DES-VIII did not have the pH-switchability and were discarded. The extraction recovery of other DESs that had the pH-switchability were investigated to extraction and preconcentration of DNR. The results in Fig. 1(A) show that extraction recovery of DNR using DES-IV (*l*-menthol:CSA, 5:1) is better than other solvents and has a lower %RSD. As a result, DES-IV was the best choice.

3.2. Effect of the volume of DES

In liquid-liquid microextraction based DESs, selectig of the DES volume is a significant parameter that must be optimized. The DES volume should be large enough to extract the analytes, but not so large as to reduce the enrichment factor. To optimize the DES volume on the extraction efficiency of DNR, different tests were done using different DES volume ranging from 30 to 80 μL. The results in Fig. 1 (B) show that by increasing the volume of DES from 30 to 50 μL, the extraction efficiency of the DNR increases. With a further increase in the DES volume, the extraction efficiency remains constant or decreases slightly due to the dilution effect. Volumes less than 30 μL often do not have stable extraction recovery and have significant fluctuations due to the difficult collection of the floated phase. Therefore, 50 μL of DES-IV was chosen as the optimum volume.

Table 1
The properties and characteristics of the nine DESs investigated for the extraction of daunorubicin.

Reference	Component-1	Component-2	Molar ratio	Abbreviation	pH-Switchability
[14]	MTOAC	*n*-butanol	1:3	DES-I	Non-switchable
[15]	*l*-menthol	EG	1:1	DES-II	Switchable
[22]	*l*-menthol	SA	4:1	DES-III	Switchable
[23]	*l*-menthol	CSA	5:1	DES-IV	Switchable
[24]	*l*-menthol	Phenol	1:1	DES-V	Switchable
[25]	[DMIM]Cl	1-Undecanol	1:2	DES-VI	Non-switchable
[18]	[DMIM]Cl	*n*-Butanoic acid	1:2	DES-VII	Non-switchable
[26]	TBAC	*p*-aminophenol	1:2	DES-VIII	Non-switchable
[27]	Thymol	Decanoic acid	1:2	DES-IX	Switchable



Scheme 1. Schematic diagram of the proposed procedure.

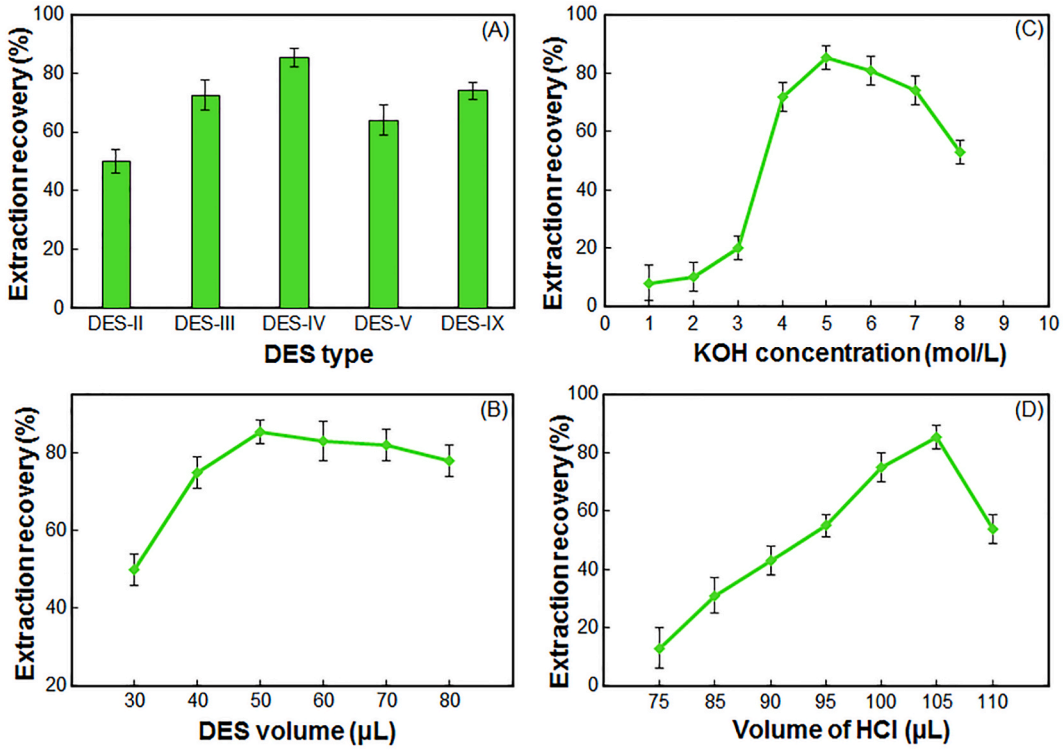


Fig. 1. The effect of the DES type (A), volume of DES (B), effect of the KOH concentration (C) and volume of HCl (D) on the extraction recovery of daunorubicin in plasma samples obtained from LLME based on pH-switchable DES/HPLC–UV.

3.3. Selection of KOH concentration

In the conventional LLME based on DES, vortex, ultrasonic, or disperser solvent are used to disperse the DES in the sample solution, each of which has its own disadvantages. In this study, the DES is dissolved in the aqueous solution only by making the medium alkaline using KOH solution and creates a homogenous system. Considering a constant volume of KOH solution (about 100 μL), its concentration should be optimized to be able to dissolve the DES in the aqueous solution. For this purpose, various experiments were done by using 100 μL of KOH with different concentrations in the range of 1–10 mol L^{-1}. As seen in Fig. 1(C), at concentrations less

than 4 mol L^{-1}, 100 μL of KOH solution cannot completely dissolve the DES in the sample solution and a homogeneous system is not created. By increasing the KOH concentration from 4 to 5 mol L^{-1}, the extraction recovery of DNR increases. By increasing the concentration from 5 to 8 mol L^{-1}, the extraction efficiency decreases. At concentrations higher than 8 mol L^{-1}, phase separation does not occur using the optimized volume of HCl. Therefore, the concentration of KOH was set at 5 mol L^{-1}.

3.4. Effect of HCl volume

As described in section 2.5, by gradually adding HCl solution and neutralizing the KOH solution, separation of phases and anaytes extraction occurs at the same time. Since 5 mol L^{-1} concentration was selected to optimize the concentration of KOH, the solution of HCl with the same concentration of 5 mol L^{-1} was used to neutralize the environment. As a result, the volume of HCl solution should be optimized to obtain the highest extraction recovery of DNR. So, various experiments were performed using different volumes of HCl solution including 55, 65, 75, 85, 90, 100, 105 and 110 μL. The results in Fig. 1(D) show that phase separation does not occur in volumes less than 75 μL. By increasing the volume of HCl from 75 to 105 μL, the phase separation improves, and the extraction recovery of analytes reaches the maximum in the volume of 105 μL. In volumes greater than 105 μL of HCl, the desired analyte loses its orginal form and its solubility in sample solution increases, which leads to a decrease in extraction recovery. As a result, 105 μL of the HCl was selected.

3.5. Salt addition

In the presented study, adding salt increases the extraction efficiency by reducing the solubility of analytes, and on the other hand, by reducing the solubility of the extractant, it increases the volume of the extractant phase and reduces the enrichment factor. These two opposing effects approximately cancel each other out and the effect of salt becomes weak. Nevertheless, various experiments were performed in the absence of salt and in the presence of different concentrations of salt. The results showed that the increase of salt has no effect on the extraction efficiency of DNR.

3.6. Investigation of extraction time

In LLME based on pH-switchability DES, the time from adding alkali to the moment when adding acid starts is called extraction time. Extraction times from 0 to 5 min were used for DNR extraction. The results showed that only 30 s is enough time for extraction, and no change in extraction efficiency is obtained after 30 s. In less than 30 s, DES does not spread completely in the sample phase. Therefore, 30 s was chosen as the best extraction time.

3.7. Quantitative analysis

The analytical performance of the presented procedure was evaluated by investigation of the linearity, LOD, LOQ, accuracy, precision, extraction recovery and enrichment factor. The linear range of DNR were obtained in the blank plasma spiked with various concentrations of DNR in the range of 0.05–500 μg L^{-1} and the samples were analyzed in triplicate. Linear range was 0.15–200 μg L^{-1} with coefficient of determinations (r^2) of 0.9988. The accuracy and precision was investigated by analysis of plasma sample spiked at concentrations of 10, 50 and 100 μg L^{-1}. The plasma samples were analyzed in 7 replicates on the same day (intra-day studies), and the same samples were analyzed on 7 consecutive days (inter-day studies). After extraction and HPLC analysis of DNR, the amount recovered from plasma was calculated. Intra–day and inter–day RSDs were 2.7 and 4.8 %, respectively. The inter-day and intra-day accuracy ranged from 91.0 to 107.8 and 90.3−108.0 %, respectively. The LODs (S/N = 3) and LOQs (S/N = 10) were 0.05 μg L^{-1} and 0.15 μg L^{-1}, respectively. The EF was defined as the ratio between the concentration of analyte in the floated phase (C_{flo}) and initial analyte concentration (C_0) within the sample (Equation (1)).

$$EF = \frac{C_{flo}}{C_0} \tag{1}$$

Table 2
Analytical characteristics of LLME based pH-switchable DES followed by HPLC−UV for determination of daunorubicin.

Parameter	Analytical feature
Linear range (μg L^{-1})	0.15–200
RSD% (Intra-day, $n = 7$)	2.7
RSD% (Inter-day, $n = 7$)	4.8
Accuracy% ((Intra-day, $n = 7$)	91.0–107.8
Accuracy% (Inter-day, n = 7)	90.3–108.0
r^2	0.9988
Limit of detection (μg L^{-1}) (S/N = 3, $n = 7$)	0.05
Limit of quantification (μg L^{-1}) (S/N = 10, $n = 7$)	0.15
Extraction recovery (%)	85.3
Enrichment factor	106.6

The %ER was obtained from the following formula: was defined as the ratio between the amount of the analyte in the floating phase (n_{flo}) and the initial amount of the analyte (n_0) within the sample (Equation (2)).

$$ER\% = \frac{n_{flo}}{n_0} \times 100 = \frac{C_{flo}.V_{flo}}{C_0.V_{sample}} \times 100 \quad (2)$$

n_{flo} = amount of the analyte in the floating phase; n_0 = initial amount of the analyte within the sample; V_{flo} = volume of the floating phase and V_{sample} = volume of the sample solution.

The EF and the ER% of DNR (at a concentration of 50 μg L^{-1}) were 106.6 and 85.3 %, respectively. The results of the competence figures are collected in Table 2.

By spiking the samples at different concentration levels with DNR, the matrix effect was investigated. The relative recoveries in the range of 91.0–107.8 % showed that the sample matrix has a negligible effect on analyte extraction with the presented method.

3.8. Analysis real samples

To demonstrate the applicability of the developed LLME based on pH-switchable DES, it was applied to the extraction of DNR from blank and real plasma samples. A blank plasma sample from a healthy volunteer and 4 real plasma samples from 4 patients who were treated with daunorubicin were subjected to the presented extraction method and each experiment was repeated three times. The results showed that daunorubicin was not found in the blank sample, but it was detected in all 4 real samples in the concentration range of 58.7–188.3 μg L^{-1}. The results are presented in Table 3. To investigate the effect of the sample matrix, all samples were spiked at three different concentration levels (10, 50 and 100 μg L^{-1}) as presented in Table 3. The results showed that the relative recoveries of DNR in plasma samples were in the range of 91.0–107.8 %, with RSD<7. Fig. 2 shows the chromatograms of direct injection of DNR standard at concentration level of 10 mg L^{-1} (A), plasma sample taken from 9 year-old male (B) and the corresponding spiked ones at concentration of 50 μg L^{-1} for DNR (C). The obtained relative recoveries showed that the effect of the matrix on the efficiency of the proposed method for the extraction of drugs in plasma samples is negligible.

3.9. Comparison with other methods

Some analytical figures of the LLME based on pH-switchable DES procedure in combination with HPLC−UV for the extraction and determination of DNR in biological samples were compared with other reported methods in Table 4 [1–3,5,28]. The proposed procedure has low LOD (0.05 μg L^{-1}), wide liner range (0.15−200 μg L^{-1}), and comparable RSD (<3 %) with respect to the compared analytical procedures. In addition, the extraction time (<2 min) of the method was shorter than the other methods and also the enrichment factor (106.6) was higher. Obtained results were acceptable for an analytical approach which to be an efficient, sensitive, and robust technique for the analysis of drugs in biological samples.

4. Conclusion

In this research, a LLME based on pH-switchable DES followed by HPLC−UV was optimized for the extraction and determination of

Table 3
Determination of daunorubicin in plasma samples and relative recovery of spiked daunorubicin in these samples.[a]

Plasma samples	Added (mg L^{-1})	Found, mean ± SD[b] (n = 3) (mg L^{-1})	Relative recovery (%)
Blank (taken from 12-year-old healthy female volunteer)	0	–	–
	10	10.3 ± 0.8	103
	50	47.6 ± 3.4	95.2
	100	102.5 ± 7.2	102.5
Taken from a patient under daunorubicin treatment (9-year-old male)	0	58.7 ± 2.9	–
	10	67.8 ± 4.2	91
	50	108.4 ± 8.5	99.4
	100	165.2 ± 10.7	106.5
Taken from a patient under daunorubicin treatment (13-year-old male)	0	134.6 ± 9.8	–
	10	145.3 ± 11.4	107
	50	181.5 ± 10.6	93.8
	100	241.0 ± 18.4	106.4
Taken from a patient under daunorubicin treatment (6-year-old female)	0	96.3 ± 5.2	–
	10	105.8 ± 7.3	95
	50	150.2 ± 9.2	107.8
	100	203.1 ± 15.4	106.8
Taken from a patient under daunorubicin treatment (14-year-old female)	0	188.3 ± 11.2	–
	10	197.6 ± 12.5	93
	50	235.2 ± 14.8	93.8
	100	295.3 ± 17.3	107

[a] These data are based on the diluted volumes of plasma samples and dilution effect was considered for calculation of them.
[b] Standard deviation.

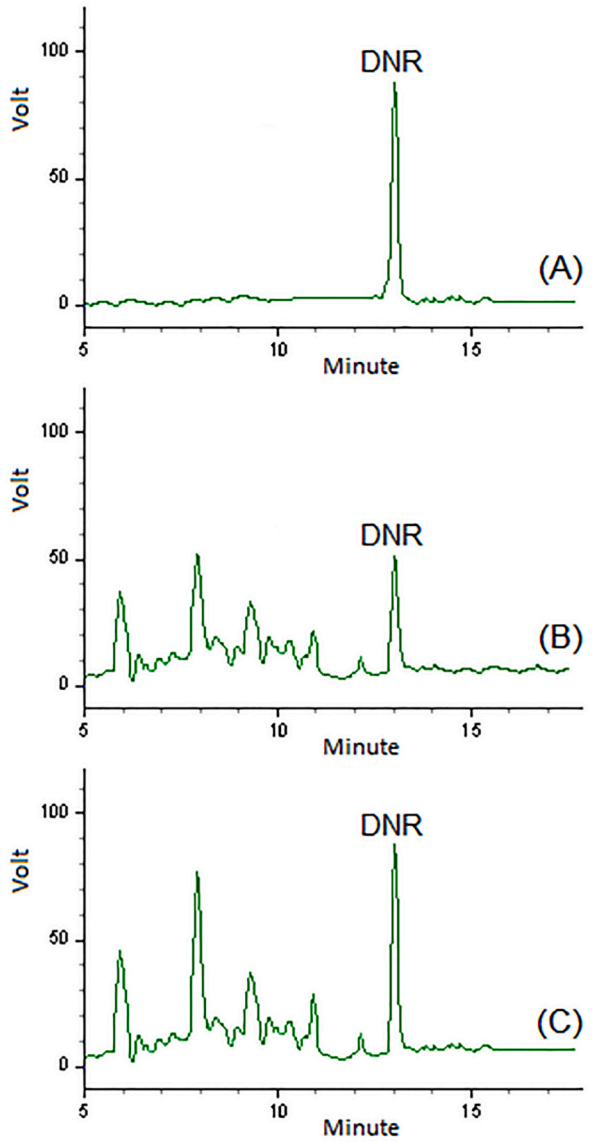


Fig. 2. The chromatograms of direct injection of DNR standard at concentration level of 100 mg L^{-1} (A), plasma sample taken from 9 year-old male (B) and the corresponding spiked ones at concentration of 50 μg L^{-1} for DNR (C).

Table 4
Comparison of the proposed method with other techniques for determination of daunorubicin in biological samples.

Method	Sample	Linear range (μg L^{-1})	LOD (μg L^{-1})	RSD%	Reference
LC–ESI–MS/MS	Cancer cells	0.211–132	0.068	2.8–5.9	[1]
Fluorescence and UV–vis	Serum and urine	400–6000	27–375	1.5–4.4	[2]
LC–MS/MS	Rat plasma	0.25–100	–	3.5–9.7	[3]
LLE−CE	Plasma	2–40000	0.7	2.7–12.5	[5]
CZE−AD	Urine	500–100000	400	0.98–1.22	[28]
LLME−DES−HPLC−UV	Plasma	0.15–200	0.05	2.7	This work

DNR in human plasma samples. To the best of our knowledge, this is the first time the pH-switchable DES composed of l-menthol:EG with molar ratio of 1:1 was used in the extraction of DNR in plasma samples. The important advantages of the method is that disperser organic solvents are not used, and time-consuming and energy-consuming steps such as vortexing and ultrasonication have been eliminated. Short extraction time and a simple extraction procedure are other advantages of the method. Homogenization of extractant and aqueous solution mixture as well as phase separation is done only by changing the pH. The method has good LOD, LR, sensitivity,

accuracy, and precision. The method was then proved as a suitable method for the extraction of DNR from plasma samples and can therefore be potentially applied to different drugs in biological samples.

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Ethics statement

This study was approved by the Research and Ethics Committee of Kermanshah University of Medical Sciences (IR.KUMS.REC.1400.823).

Data availability statement

Data will be made available on request.

Additional information

No additional information is available for this paper.

CRediT authorship contribution statement

Reza Akramipour: Supervision, Investigation. **Homa Babaei:** Methodology, Formal analysis. **Fidel Castro-Cayllahua:** Writing - review & editing, Supervision. **Mohammad Reza Golpayegani:** Writing - original draft, Investigation. **Nazir Fattahi:** Visualization, Resources, Data curation. **Farshad Fattahi:** Project administration, Data curation.

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.

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References

[1] P. Krumpochova, A. Kocurova, P. Dolezel, P. Mlejnek, Assay for determination of daunorubicin in cancer cells with multidrug resistance phenotype, J. Chromatogr. B 879 (2011) 1875–1880.
[2] J. Tian, S. Liu, Z. Liu, J. Yang, J. Zhu, M. Qiao, X. Hu, Fluorescence quenching and spectrophotometric methods for the determination of daunorubicin with meso-tera (4-sulphophenyl) porphyrin as probe, Spectrochim. Acta, Part A 120 (2014) 7–13.
[3] Y. Yang, Development and validation of a high-performance liquid chromatography–tandem mass spectrometric method for quantification of daunorubicin in rat plasma, Talanta 71 (2007) 596–604.
[4] N. Zare, H. Karimi-Maleh, M. Saei Moghaddam, Design and fabrication of new anticancer sensor for monitoring of daunorubicin using 1-methyl-3-octylimidazolinium chloride and tin oxide/nitrogen-doped graphene quantum dot nanocomposite electrochemical sensor, Environ. Res. 215 (2022), 114114.
[5] G. Hempel, P. Schulze-Westhoff, S. Flege, J. Boos, Quantification of daunorubicin and daunorubicinol in plasma by capillary electrophoresis, J. Chromatogr. B 758 (2001) 221–228.
[6] S. Li, S. Zeng, B. Wei, Q. Wu, C. Liu, P. Song, Determination of free and encapsulated cytarabine and daunorubicin in rat plasma after intravenous administration of liposomal formulation using ultra-high performance liquid chromatography tandem mass spectrometry, J. Chromatogr. B 1200 (2022), 123275.
[7] M.T. Htun, Photophysical study on daunorubicin by fluorescence spectroscopy, J. Lumin. 129 (2009) 344–348.
[8] M. Alizadeh, P.A. Azar, S.A. Mozaffari, H. Karimi-Maleh, A.M. Tamaddon, Evaluation of Pt,Pd-doped, NiO-decorated, single-wall carbon nanotube-ionic liquid carbon paste chemically modified electrode: an ultrasensitive anticancer drug sensor for the determination of daunorubicin in the presence of tamoxifen, Front. Chem. 8 (2020) 677.
[9] M. Rezaee, Y. Assadi, M.R.M. Hosseini, E. Aghaee, F. Ahmadi, S. Berijani, Determination of organic compounds in water using dispersive liquid–liquid microextraction, J. Chromatogr. A 1116 (2006) 1–9.
[10] M.A. Farajzadeh, M.B. Aghdam, M.R. Afshar Mogaddam, A.A. Alizadeh Nabil, Simultaneous derivatization and lighter-than-water air-assisted liquid–liquid microextraction using a homemade device for the extraction and preconcentration of some parabens in different samples, J. Separ. Sci. 41 (2018) 3105–3112.
[11] H. Sehrawat, N. Kumar, R. Tomar, L. Kumar, V. Tomar, J. Madan, S.K. Dass, R. Chandra, Synthesis and characterization of novel 1,3-benzodioxole tagged noscapine based ionic liquids with in silico and in vitro cytotoxicity analysis on HeLa cells, J. Mol. Liq. 302 (2020), 112525.
[12] N. Altunay, A. Elik, M. Tuzen, M.F. Lanjwani, M.R. Afshar Mogaddam, Determination and extraction of acrylamide in processed food samples using alkanol-based supramolecular solvent-assisted dispersive liquid-liquid microextraction coupled with spectrophotometer: optimization using factorial design, J. Food Compos. Anal. 11 (2023), 105023.
[13] N.D. Oktaviyanti, Kartini, A. Munim, Application and optimization of ultrasound-assisted deep eutectic solvent for the extraction of new skin-lightning cosmetic materials from Ixora javanica flower, Heliyon 5 (2019), e02950.

[14] M.R. Golpayegani, R. Akramipour, S. Gheini, M.V. Amini, F. Fattahi, A. Mohebbi, N. Fattahi, Sensitive determination of vincristine in plasma of children with leukaemia using vortex-assisted dispersive liquid–liquid microextraction based on hydrophobic deep eutectic solvent, RSC Adv. 12 (2022) 3611–3617.
[15] T. Ahmadi Jouybari, H. Ahmadi Jouybari, M. Shamsipur, N. Babajani, A. Kiani, Z. Nematifar, K. Sharafi, M. Moradi, N. Fattahi, Trace determination of triazine herbicides in fruit and vegetables using novel hydrophobic deep eutectic solvent-based dispersive liquid-liquid microextraction followed by high-performance liquid chromatography-ultraviolet, J. Separ. Sci. 45 (2022) 4448–4459.
[16] K. Zhang, R. Guo, Y. Wang, J. Wang, Q. Nie, B. Li, G. Zhu, Temperature-controlled air-assisted liquid–liquid microextraction based on the solidification of floating deep eutectic solvents for the determination of triclosan and alkylphenols in water samples via HPLC, Microchem. J. 182 (2022), 107864.
[17] K. Zhang, R. Guo, Y. Wang, Q. Nie, G. Zhu, One-step derivatization and temperature-controlled vortex-assisted liquid-liquid microextraction based on the solidification of floating deep eutectic solvents coupled to UV–Vis spectrophotometry for the rapid determination of total iron in water and food samples, Food Chem. 384 (2022), 132414.
[18] M. Pirsaheb, H. Hosseini, H. Mohamadi Sorkali, N. Fattahi, N. Noori, Preconcentration and determination of amoxicillin and ceftriaxone in hospital sewage using vortex-assisted liquidphase microextraction based on the solidification of the deep eutectic solvent followed by HPLC–UV, Int. J. Environ. Anal. Chem. 99 (2019) 112–123.
[19] T. Ahmadi-Jouibari, Z. Shaahmadi, M. Moradi, N. Fattahi, Extraction and determination of strobilurin fungicides residues in apple samples using ultrasound-assisted dispersive liquid-liquid microextraction based on a novel hydrophobic deep eutectic solvent followed by HPLC-UV, Food Addit. Contam. 39 (2022) 105–115.
[20] N. Fattahi, B. Hashemi, F. Shiri, M. Shamsipur, N. Babajani, Extraction of parabens from personal care products using a pH-responsive hydrophobic deep eutectic solvent: experimental design and COSMO-RS evaluations, New J. Chem. 46 (2022) 15851–15859.
[21] B. Yu, R. Shi, C. Liu, Z. Liu, P. Shen, J. Hu, F. Shi, pH-responsive gelatin polymer-coated silica-based mesoporous composites for the sustained-release of indomethacin, Heliyon 9 (2023), e13705.
[22] A. Abri, N. Babajani, A. Moshtaghi Zonouz, H. Shekaari, Spectral and thermophysical properties of some novel deep eutectic solvent based on l-menthol and their mixtures with ethanol, J. Mol. Liq. 285 (2019) 477–487.
[23] T. Ahmadi Jouybari, H. Ahmadi Jouybari, F. Hosseini, M. Nesari, N. Fattahi, Evaluation of blood lead levels in opium addicts and healthy control group using novel deep eutectic solvent based dispersive liquid–liquid microextraction followed by GFAAS, Environ. Sci. Pollut. Res. 30 (2023) 24553–24561.
[24] D. Raj, Thin-layer chromatography with eutectic mobile phases—preliminary results, J. Chromatogr. A 1621 (2020), 461044.
[25] M. Pirsaheb, N. Fattahi, Development of a liquid-phase microextraction based on the freezing of a deep eutectic solvent followed by HPLC-UV for sensitive determination of common pesticides in environmental water samples, RSC Adv. 8 (2018) 11412–11418.
[26] A. Jouyban, M.A. Farajzadeh, F. Khodadadeian, M. Khoubnasabjafari, M.R. Afshar Mogaddam, Development of a deep eutectic solvent-based ultrasound-assistedhomogenous liquid-liquid microextraction method for simultaneousextraction of daclatasvir and sofosbuvir from urine samples, J. Pharm. Biomed. Anal. 204 (2021), 114254.
[27] E. Lim, B. Kim, M. Seok Oh, J.B. You, Microfluidic formation of surface nanodroplets using green deep eutectic solvents for liquid–liquid nanoextraction and controlled precipitation, J. Colloid Interface Sci. 643 (2023) 82–91.
[28] Q. Hu, L. Zhang, T. Zhou, Y. Fang, Determination of daunorubicin in human urine by capillary zone electrophoresis with amperometric detection, Anal. Chim. Acta 416 (2000) 15–19.