Study of caffeine and coumarin extraction kinetics in an aqueous two-phase system based on polyethylene glycol 1500

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Abstract. Caffeine and coumarin are organic compounds of plant origin, which have biological activity and have found wide application in medicine, pharmaceutical, perfumery and food industries. Recovery of caffeine and coumarin from aqueous solutions using liquid-liquid extraction is the most effective method. In the present work the kinetic dependences of caffeine and coumarin in the aqueous two-phase system (ATPS) of PEG 1500 - Na₂SO₄ - H₂O were experimentally obtained. It was established that equilibrium in the system is achieved after 17 minutes for caffeine and after 12 minutes for coumarin. The effect of ultrasound on the extraction rate of caffeine and coumarin in an aqueous two-phase system was also studied.

Keywords: extraction, aqueous two-phase system, caffeine, coumarin, ultrasound

1. Introduction
The recovery of bioactive compounds from aqueous solutions is an urgent issue that requires special attention. To extract organic substances from aqueous solutions, filtration [1], sorption [2], extraction [3-5], chromatography [6], etc. [7-9] are mainly used. Today, numerous works are aimed at the development of environmentally friendly, effective methods for the extraction of organic compounds that are not inferior to classical extraction systems based on toxic and harmful organic solvents [10-12]. The aqueous two-phase system is of great interest as an alternative extraction system, which is eco-friendly, easy to utilize, efficient and cost-effective [13-17]. Yazdabadi A et al. established the regularities of caffeine extraction in the system based on tetrabutylphosphonium bromide and sorbitol [18]. de Araujo Sampaio D et al. conducted the study on the caffeine extraction in a system based on polyethylene glycol 400 and sodium sulfate at different temperatures, which showed that caffeine is mainly distributed in the polymer phase [19]. All these research results show the prospects of ATPS application for the extraction of organic compounds. However, little information is presented in the literature on the kinetics of extraction of substances in ATPS, which is necessary for the calculation of mass transfer characteristics and the design of extraction equipment [20,21].

Recently, mass transfer processes, including liquid-liquid extraction, are undergoing greater modernization, and combining with the method of ultrasonic intensification [22-26]. However, attempts to intensify, using ultrasound, the processes of metal ion extraction are accompanied by a
decrease in the quantitative characteristics of extraction. Gradov et al. carried out an experimental study of the interphase distribution dependence of Fe (III) ion using an aqueous two-phase system on the time of phase contact with the ultrasonic exposure use and in its absence [27]. It was found that the use of ultrasound irradiation has the effect of slowing down the extraction of this metal ion into the PEG phase. Hu Y et al. studied the effect of ultrasound on the lactic acid extraction from the fermentation solution. Lactic acid was extracted into extractant after 10-15 minutes with ultrasound exposure, which is several times faster than without ultrasound [28].

Caffeine and coumarin, widely used in the pharmaceutical, food and perfume industries, were chosen as model objects. In this work, the caffeine and coumarin extraction kinetics in an aqueous two-phase system based on polyethylene glycol 1500 and sodium sulfate with constant interphase area was studied for the first time. The time to achieve equilibrium in the distribution of the studied substances between the polymer and salt phases was determined. The kinetic dependencies of caffeine and coumarin distribution in ATPS under the influence of ultrasound were obtained for the first time.

2. Experimental details

2.1. Reagents
Polyethylene glycol with a molecular weight of 1500 was purchased from Fluka (Shanghai, China). Na$_2$SO$_4$ was used as phase-forming salt and was purchased from Chimmed (Moscow, Russia). Caffeine and coumarin were used from Sigma-Aldrich (St. Louis, MO, USA) (99% purity). All solutions were prepared using distilled water purified in a UPVA-5 unit for the production of analytical grade water (Livam, Belgorod, Russia). The structural formulas of the research objects are shown in Figure 1.

![Figure 1. The structural formulas of caffeine and coumarin.](image)

2.2. Experiment method
To carry out the extraction experiment, a glass cylinder with an interphase area value of 5.31 cm$^2$ was used when mixing equal volumes (15 ml) of polymer and salt phases. The recoverable substance of a given concentration was prepared by dissolution in the salt phase. Both phases were mixed using a top-driven stirrer with a stirring speed of 100 rpm. We used an ultrasonic generator with a frequency of 35 kHz and a maximum power of 110 W. Figure 2 shows the installation for an extraction experiment.
The concentration of recoverable compounds was detected in the polymer phase by spectrophotometry in the ultraviolet region of the spectrum ($\lambda = 270$ nm) using a fiber optic probe with an optical path length of 10 mm. Measurement of optical density was carried out on the Cary-60 spectrophotometer (Agilent Tech., USA). Determination of the optical density of caffeine and coumarin in experiments without ultrasound was carried out online in a cylinder every 10 seconds. With ultrasound, measurement of optical density carried out every minute at the initial site of dependence before the establishment of constant values of optical density, then the measurement frequency was reduced to 5 minutes. The spectrophotometer was controlled and the results were processed using the Cary WinUV software. All presented experimental data were the result of a series of experiments and processed by the methods of mathematical statistics.

3. Results and Discussion

3.1. Caffeine and coumarin extraction kinetics in PEG 1500 - Na$_2$SO$_4$ - H$_2$O system with and without the use of ultrasound

The dependence of interphase distribution of caffeine (initial concentration of 0.00225 mol/L) and coumarin (initial concentration of 0.002 mol/L) in an aqueous two-phase system (PEG 1500 (15 wt%) – Na$_2$SO$_4$ (9 wt %) – water) on time was experimentally investigated. Figures 3 and 4 illustrate the data obtained without ultrasound. The equilibrium in the system is achieved in 17 and 12 minutes for caffeine and coumarin, respectively, which is probably due to the low interphase tension of the ATPS. Comparing the results with the experiments obtained by Kaplanow I et al. where the mass transfer of lysozyme and bromelain was studied in the PEG system 4000/sodium citrate, the equilibrium of caffeine and coumarin in the system proposed here is achieved faster than the one of proteins [29]. The rapid transition of caffeine and coumarin can be justified by the use of polyethylene glycol with a
lower molecular weight. The results obtained can be used to calculate the mass transfer coefficient and extraction rate for the design of liquid-liquid processes [30,31].

Figures 5 and 6 show the kinetic dependencies for caffeine and coumarin with ultrasound exposure. Comparing the results obtained, it can be seen that the time to reach equilibrium between caffeine and coumarin remains unchanged. It can be noted that in the case of caffeine and coumarin extraction in ATPS it is not necessary to use additional effects, because the equilibrium in the system is reached quickly enough, unlike the results in other works [32].

![Figure 3](image1.png)  
**Figure 3.** Concentration profile of caffeine in the polymer phase over the time of extraction in the PEG 1500 - Na₂SO₄ - H₂O system without ultrasound.

![Figure 4](image2.png)  
**Figure 4.** Concentration profile of coumarin in the polymer phase over the time of extraction in the PEG 1500 - Na₂SO₄ - H₂O system without ultrasound.

![Figure 5](image3.png)  
**Figure 5.** Concentration profile of caffeine in the polymer phase over the time of extraction in the PEG 1500 - Na₂SO₄ - H₂O system with ultrasound.

![Figure 6](image4.png)  
**Figure 6.** Concentration profile of coumarin in the polymer phase over the time of extraction in the PEG 1500 - Na₂SO₄ - H₂O system with ultrasound.
Conclusions
In this work, the kinetics of extraction of caffeine and coumarin in an aqueous two-phase system based on polyethylene glycol 1500 and sodium sulfate was studied. It was established the time after which equilibrium is reached in the system for caffeine and coumarin, equal to 17 and 12 minutes, respectively. The effect of ultrasound on the extraction of the studied compounds in aqueous two-phase system was evaluated.

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