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Liquid-liquid Extraction System Based on Non-ionic Surfactant -salt-H_2O and Mechanism of Drug Extraction

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Abstract: Extraction behavior of chlorpromazine hydrochloride (CPZ) and procaine hydrochloride (PCN) in the system described in the title was studied. Research shows that the extraction efficiency of CPZ can amount to 96% by twice extraction, while that of PCN is 77%. This system produces the distribution coefficients (K_D) of 12.3 and 2.6 respectively for CPZ and PCN. Extraction mechanism is deduced according to ultraviolet and molecular fluorescence spectra variation of the drugs in the system studied.

Keywords: Non-ionic surfactant-salt-H_2O extraction system, polyethylene glycol-1000, chlorpromazine hydrochloride, procaine hydrochloride, mechanism of extraction.

The utilization of solid-liquid extraction system based on polymer-$(NH_4)_2SO_4$-H_2O on separation of metal ions and bio-active substances has been summarized[1]. Cloud point extraction (CPE) benefits the environment and has been used in separation of metal chelates, biomacromolecules and in pretreatment of environmental samples[2-4].

In a 10 mL color comparison tube 20% PEG-1000 and 2.5 g $(NH_4)_2SO_4$ were chosen as phase separation condition at pH 5.5. The average extraction efficiencies were $\overline{E}_{CPZ}$ = 85% and $\overline{E}_{PCN}$ = 55% respectively. If twice continuous extraction was conducted on CPZ, the extraction efficiency $\overline{E}'_{CPZ}$ = 96% and quantitative extraction was reached, while that of PCN was $\overline{E}'_{PCN}$ = 77%. The distribution coefficients K_D of CPZ and PCN at pH 5.5 are shown in **Table 1**.

Table 1 The distribution coefficients (K_D) of CPZ and PCN

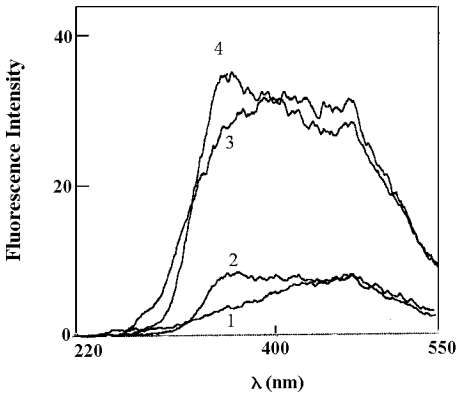
Drug (μg/mL)	4.0	6.0	8.0	10.0	12.0	14.0	16.0	18.0	24.0	30.0	RSD (%)
K_D^{CPZ}	12.2	11.8	12.4	12.6	12.4	*22.0	*44.9				2.5
K_D^{PCN}	2.4	2.2	2.4	2.4	2.6	2.8	2.6	2.6	2.8	2.8	7.9

* Not taken in RSD calculation

The average distribution coefficients are: K_D^{CPZ} = 12.3, K_D^{PCN} = 2.6. This result can be explained by the mechanism of liquid-liquid extraction. In water solution λ_{max} of CPZ is at 254 nm, while that of PCN is at 290 nm. In PEG phase λ_{max} of CPZ is at 256 nm, while that of PCN is at 295 nm, but the absorptions of CPZ and PCN are

stronger than in water solution. This is caused by hydrogen bonds formed between PCN and PEG. The ether oxygen atom in PEG forms a hydrogen bond with the hydrogen atom in $-NH_2$. Seen from the fluorescence spectra of drugs (in **Figure 1**), the fluorescence intensities of the two drugs are higher in PEG phase than in water phase, which proves that both drugs can form hydrogen bond with PEG, thus the molecular rigidities are strengthened and the fluorescence intensities are boosted. It can also be inferred from **Figure 1** that the fluorescence intensity of PCN is greater than that of CPZ, both in PEG phase and water phase.

Figure 1 The fluorescence spectra of drugs



λ_{EX}=210 nm, *C*=10 μg/mL, pH=5.5
1, 2-CPZ, PCN in water phase; 3, 4-CPZ, PCN in 20% PEG phase

Hydrogen bond and hydrophobic interaction exist in the extraction system of drugs, both of which directly affect the distribution coefficients and the extraction efficiencies of drugs. PCN forms stronger hydrogen bond and weaker hydrophobic interaction, thus the hydrogen bond is the major effect and the hydrophilic property of the drug is stronger, therefore it has smaller distribution coefficient and extraction efficiency; CPZ forms weaker hydrogen bond and stronger hydrophobic interaction, thus the major effect is hydrophobic interaction and the lipophilic property of the drug is stronger, therefore it has greater distribution coefficient and extraction efficiency.

Besides the advantages shown in the solid-liquid system, better reproducibility and convenient continuous extraction are achieved. It is possible to apply the liquid-liquid extraction system reported in this paper as the pretreatment process for instrumental analysis, such as HPLC, FIA, and CE, *etc*.

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