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ORIGINAL ARTICLE

Solvent extraction of dopamine by heptakis (2,3,6-tri-O-acetyl)-β-cyclodextrin

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Abstract The possibility of modified cyclodextrin, heptakis (2,3,6-tri-O-acetyl)-β-cyclodextrin (TA-β-CD) to act as extracting agent for dopamine from aqueous phase into the organic phase has been investigated. Thus, by means of an ion-pairing mechanism, dopamine was extracted by modified cyclodextrin in the presence of counter ions such as picrate and tropaeolin 00. The results showed that the modified cyclodextrin can be used as extractant for dopamine. Some aspects of dopamine extractability concerning the pH and the nature of anion used as counter ion have been studied.

Keywords Extraction · Dopamine · Recognition · Modified cyclodextrins

Introduction

Many research groups focus on the recognition and selective determination of catecholamines, especially dopamine, with optical detection methods [1–3]. Dopamine [2-(3,4-dihydroxyphenyl)ethylamine, DA] is a biogenic amine that plays an important role in the body as neurotransmitter [4, 5]. Moreover, dopamine plays a key role in research on neurodegenerative processes such as Parkinson's disease [6]. The effects of this neurotransmitter are complex and poorly understood. Because the physiological level of dopamine is as low as 0.018–0.020 g mL^{-1}, analytical methods must be very sensitive. In pharmaceutical preparations dopamine concentration is several orders of magnitude higher (ca. 40 g L^{-1}), so less sensitive spectrophotometric methods can be applied. The development of fast, sensitive and selective methods for quantitative determination of dopamine is therefore necessary. The solvent extraction of catecholamines, including DA, was investigated from both points of view, of inclusion complex formation between macrocyclic receptor and DA, and of large-scale separation [1, 7].

In particular, the molecular recognition of dopamine by macrocyclic receptors became one of the most important subjects in macrocyclic chemistry. Among the macrocyclic receptors, cyclodextrins and their derivatives were intensively involved in the studying of characteristic interactions present in host–guest chemistry [8–14].

Due to their unique ability to form inclusion complexes with a large number of biological compounds, including amines, either in solution or in solid state, cyclodextrins and their derivatives were extensively used in the separation of chemical and biochemical compounds by chromatographic or electrophoretic techniques [15]. In order to improve their physicochemical properties and inclusion capacities, different kinds of cyclodextrin derivatives have been synthesized [16] and applied in specific fields of chemistry and pharmacy.

In our previous work [17] we investigated the solvent extraction and transport through liquid membrane of some native aromatic amino acids and their methylester derivatives, by using heptakis (2,3,6-tri-O-acetyl)-β-cyclodextrin (TA-β-CD) as receptor. The experimental results suggested that aromatic amino acid native and methylesters were

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extracted from aqueous phase (pH = 5.5) into organic phase and transported through chloroform liquid membrane by heptakis TA-β-CD by an active transport assisted by pH gradient.

In the present work the ability of heptakis TA-β-CD (Chart 1) to act as extractant agent for the solvent extraction of dopamine from aqueous phase into chloroform phase has been studied. The physicochemical parameters, like pH and the nature of anion used as counterion are discussed.

Experimental

Reagents

All the reagents used were of analytical grade. Dopamine (Chart 1) was purchased from Fluka (3-Hydroxytyramine Hydrocloride purriss H8502-5G) at the purity ≥98.5% and the heptakis TA-β-CD (Chart 1) was obtained from Ciclolab (Budapest, Hungary) and used without further purification. Double distilled water was used throughout all experiments. The organic solvent chloroform was HPLC purity, purchased from Sigma-Aldrich Steinheim, Germany (dielectric constant $\varepsilon_r = 4.81$ [18] and used without further distillation.

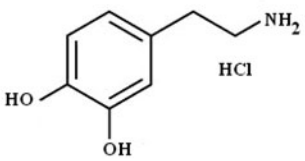
The absorbance was determined by spectrophotometric measurements carried out by means of UV–Vis-NIR Spectrometer:JASCO V-670. The pH was measured by the digital MV-870 pracitronic pH-meter with glass electrode and saturated calomel electrode.

Liquid–liquid extraction

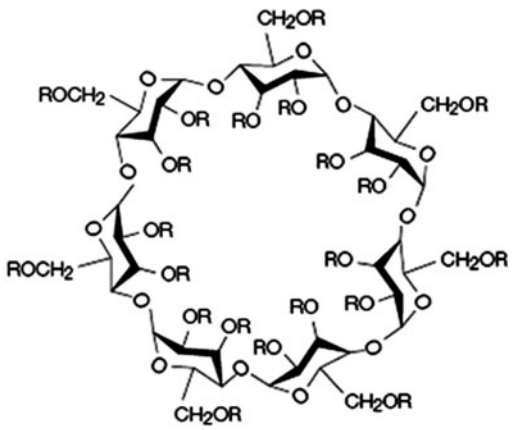
Equal volumes (10 mL) of aqueous solution of DA (3×10^{-4} M) and chloroform solution (10 mL) of heptakis TA-β-CD (10^{-3} M) were mixed and shaken for 25 min at T = 298.15 K. Chloroform and water were saturated with each other, in order to prevent volume change during extraction. The extraction measurements of DA from aqueous phase into chloroform were performed according to Pedersen's procedure [19]. The extraction efficiency was calculated as the ratio $E\,[\%] = (A_0 - A)/(A_0) \times 100$, where A_0 and A are the absorbance of the aqueous phases before and after the extraction with heptakis TA-β-CD, respectively. The absorbance measurements (A_0) were made against a blank solution with the same matrix as sample solutions before the extraction (concentration of picric acid or tropaeolin 00), without containing DA. For A measurements the blank had the same composition as before, plus the addition of heptakis TA-β-CD and this solution was subjected to extraction in chloroform as the samples were.

The absorbance of DA was performed at 280 nm, in accordance with the absorbance maximum present in UV spectra for this compound, 345 nm in the presence of

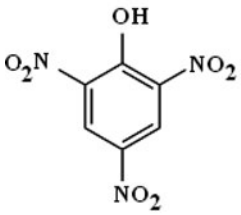
Chart 1 The chemical structure of compounds used throughout the experiments



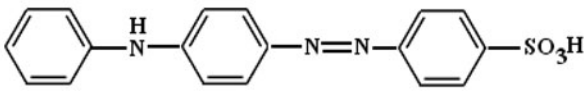
Dopamine



Heptakis (2, 3, 6-tri-O-acetyl)-_-cyclodextrin, R = acetyl.



Picric acid



Tropaeolin 00

picrate anion and 407 nm in the presence of tropaeolin 00. Each experiment was performed five times.

Results and discussion

The extraction abilities of heptakis TA-β-CD 10^{-3} M upon DA substrate, have been investigated from aqueous phases to chloroform as organic phase. The obtained extractability of 3×10^{-4} M concentration of DA was unsatisfactory, respectively, E [%] = 9.5. Taking into account the DA structure, we suspected that pH may have an important influence upon the extractability in this system. In order to obtain DA solutions at different pH values and at constant concentration, two solutions of DA were prepared with the same concentration of DA (3×10^{-4} M): first, in 1×10^{-2} M HCl and second in 1×10^{-2} M NaOH. The experimental results show that the extractability depends strongly upon the pH of the DA aqueous solution, reaching a maximum value of 23.45.

To improve the efficiency of the liquid–liquid extraction process a counter ion was introduced in the system. Therefore, 8×10^{-5} M picric acid was included in each of the two solutions of DA prepared as described above and the yields value of extraction efficiency at all pH values are higher, with a maximum of E [%] = 38.72. This increase in efficiency can be explained by increasing of hydrophobicity of ion pair complex formed between dopamine, modified cyclodextrin and picrate ion. Moreover by using the tropaeolin 00 as the anion forming the ion pair, the yields of dopamine extractability was increased by relatively three fold at Ph = 4.54 (65.21%).

The experimental data of the extractability of dopamine from aqueous phase into chloroform phase by heptakis TA-β-CD in the presence of picrate anion and tropaeolin 00 are given in Fig. 1.

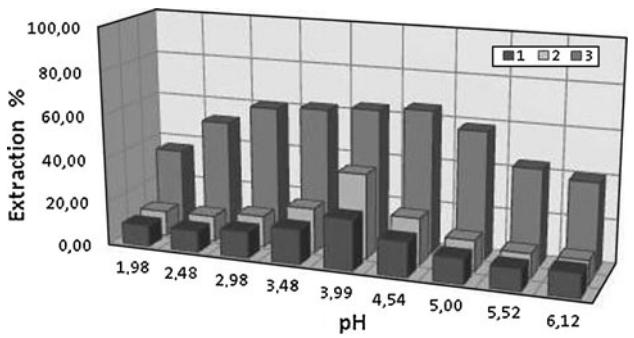


Fig. 1 The influence of the pH upon extractability into chloroform phase of DA by heptakis TA-β-CD at T = 298.15 K. *1* DA (3×10^{-4} M) + heptakis TA-β-CD (1×10^{-3} M); *2* in the presence of picric acid 8×10^{-5} M; *3* in the presence of tropaeolin 00 (6×10^{-4} M)

From the data displayed in Fig. 1 one can conclude that heptakis TA-β-CD exhibits good extractability for dopamine in the presence of tropaeolin 00 as counter ion at pH = 4.54. The effect of the pH would be helpful in our next study regarding the dopamine transport through membrane with heptakis TA-β-CD.

Conclusions

The present study shows that the extractability of dopamine by modified cyclodextrin, heptakis TA-β-CD is strongly controlled by pH of aqueous solution of dopamine, the maximum value being recorded at pH 4.00. By means of an ion-pairing mechanism, dopamine was extracted by modified cyclodextrin in the presence of counter ions such as picrate and tropaeolin 00. The dopamine exhibited good extractability by modified cyclodextrin from aqueous phase into the organic phase. The main goal of our investigations was to determine the optimal conditions for separation of dopamine through solvent extraction.

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