Adsorption Properties of Cyclic Compounds on Cellulose Acetate

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ABSTRACT: The interaction between solutes and semipermeable membranes is an important factor for the membrane-separation process. As an extension to previous works, we studied the adsorption properties of cyclic compounds on cellulose acetate, a material commonly used for semipermeable membranes, in aqueous solution systems by high-performance liquid chromatography (HPLC). Cycloalcohols, cycloethers, amino acids, heterocyclic aromatic compounds, and nucleosides were used in this study. The logarithm of the capacity factor (log k') for these compounds was linearly correlated with the logarithm of 1-octanol/water partition coefficients (log $K_{o/w}$) as well as noncyclic compounds. Cyclic compounds were relatively retained more than were noncyclic compounds in spite of their hydrophilic properties, which indicates the structural effects of the solute molecule on the adsorption. Although noncyclic compounds were retained mainly by hydrophobic interaction, the retention of cyclic compounds was suggested to be controlled by their inclusion within the micropore in cellulose acetate. The adsorption of heterocyclic aromatic compounds was not influenced only by ionic dissociation but also by tautomerism. © 1999 John Wiley & Sons, Inc. J Appl Polym Sci 71: 1657–1663, 1999

Key words: cellulose acetate; membrane; adsorption; cyclic compounds; HPLC

INTRODUCTION

Cellulose acetate is one of the most common materials for semipermeable membranes: reverse osmosis, ultrafiltration, or dialysis membranes. In membrane-separation processes, interaction between the solutes and membrane materials is an important factor to control solute and/or solution permeability. Salts are rejected effectively by a cellulose acetate reverse osmosis membrane, because ionic solutes are excluded from the membrane surface by electrostatic repulsion. On the other hand, adsorption of a solute on the membrane surface may cause reduction of the solution permeability and membrane fouling. Solute permeability may also be influenced by this type of interaction.

In our previous works,[1–3] we showed that liquid chromatography using a column packed with cellulose acetate as a stationary phase can be used to estimate the interaction between cellulose acetate and solutes, because liquid chromatography enables the estimation of even small differences in the adsorption properties by measuring retention times. Cellulose acetate is also known as a stationary phase for chiral separation in liquid chromatography,[4–8] but in that case, organic solvents were included in the mobile phase.

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The retention properties of aliphatic compounds, the logarithm of the capacity factor or the specific retention volume, were correlated linearly with the 1-octanol/water partition coefficient (log $K_{o/w}$), when water was used as the mobile phase. As a result, it has been shown that the adsorption of organic compounds on cellulose acetate was controlled mainly by a hydrophobic interaction. In addition, the following effects have also been found to play an important role in the process: (i) inclusion effects for phenyl compounds, (ii) size-exclusion effects for bulky compounds and polymeric compounds, and (iii) the effects caused by functional groups, the carbonyl groups promoting the retention and the hydroxy group having the opposite effect.

On the other hand, salts were excluded from the cellulose acetate stationary phase due to electrostatic repulsion, and the order of the exclusion for salts was similar to that of the rejection degree.[9]

Based on the interpretation of the adsorption-controlling factors, the orientation of organic solutes on the surface of the membrane could be estimated, and we have discussed the effects of the molecular shape of the organic solute on the permeability.[10]

It is well known that the rejections of phenolic compounds by cellulose acetate membranes are very low or even negative, that is, enrichment in a permeated solution, due to adsorption on the membrane polymer.[11,12] In a high-performance liquid chromatography (HPLC) study, phenyl compounds were found to be retained very strongly, as they were not eluted from a cellulose acetate column when water was used as the mobile phase.[9] Therefore, the retention properties for phenyl compounds and polynuclear aromatic hydrocarbons (PAHs) were examined with methanol as the mobile phase in the column.[13] The results suggest that strong retention for aromatic compounds is due to the inclusion of the aromatic ring in the micropore of cellulose acetate. Nonplanar PAHs were retained less than were planar PAHs. The whole PAH molecule does not interact with cellulose acetate—at most, just two aromatic rings of a fused ring compound do. In other words, cellulose acetate can entrap only one or two aromatic rings of a PAH.[13–15] Alkolta et al.[16] described the retention mechanism based on the calculation of the interaction energy between aromatic compounds and cellulose acetate. They indicated that the micropore formed by four pyranose rings of cellulose acetate is appropriate to include a phenyl group but is too narrow to include a *tert*-butyl group.

As an extension to previous works, we examined the adsorption properties of hydrophilic ring compounds on cellulose acetate using HPLC. Cycloalcohols, cycloethers, and amino acids including a phenyl group, heterocyclic aromatic compounds, and nucleosides were used in this study and the effects of the ring structure are discussed, since saccharides and lactones were reported previously.[2,9] The effects of dissociation were also examined for the electrolytes of the above-indicated compounds. Considering that cellulose acetate is also used as a membrane material for medical and pharmaceutical purposes such as in hemodialysis membranes and microcapsules for drug-delivering systems, the interaction between cellulose acetate and amino acids, nucleic bases, and nucleosides may also yield important information in this field.

EXPERIMENTAL

An HPLC column was prepared by packing cellulose diacetate (acetyl content 39.8%; Kodak 4644, New York) into a stainless-steel column (4.6 mm i.d. $\times$ 250 mm long), where the cellulose acetate was sieved and a fraction of 25–37 μm was used. The HPLC apparatus consisted of an 880-PU pump (JASCO, Japan), a sample injector (Rheodyne 7125, USA), and an 870-UV detector (JASCO) or an 830-RI detector (JASCO). The column temperature was kept at 30 $\pm$ 1°C with a water jacket. Deionized water was commonly used as the mobile phase. When the effects of pH on the retention were examined, 0.2*M* phosphate buffer (pH 2.0, 6.0, 11.6) was used. The flow rate was kept at 0.5, 1.0, or 1.5 mL min^{-1}.

All chemicals were used as purchased without further purification. Deuterium oxide (99.75%, Merck, Germany) was used as the unretained solute. The concentration of aqueous solutions was 0.1% or less and 20 μL of each solution was injected into the column. The solutes used in this study are listed in Tables I and II, where noncyclic compounds were used as the references. The values of the logarithm of the 1-octanol/water partition coefficient (log $K_{o/w}$) and the 1-butanol/water partition coefficient (log $K_{b/w}$) for solutes are also shown in Tables I and II. Here, the values for compounds whose experimental data were not available were calculated by Hansh's method.[17]

Table I List of Alcohols and Ethers

No.	Solute	log $K_{o/w}$ [a]
1	Methanol	−0.77
2	Ethanol	−0.31
3	1-Propanol	0.25
4	1-Butanol	0.88
5	1-Pentanol	1.56
6	1-Hexanol	2.03
7	1-Heptanol	2.57
8	Cyclopentanol	0.66[b]
9	Cyclohexanol	1.23
10	Cyclooctanol	2.37[b]
11	4-Methylcyclohexanol	1.76
12	3,5-Dimethylcyclohexanol	2.29
13	*exo*-Norborneol	1.08[b]
14	*endo*-Norborneol	1.08[b]
15	1-Adamantanol	2.14
16	1,4-Cyclohexanediol	0.08
17	Diethyl ether	0.89
18	Methyl *n*-propyl ether	1.04[b]
19	Ethyl *n*-propyl ether	1.40[b]
20	*n*-Butyl methyl ether	1.58
21	Di-*n*-propyl ether	2.03
22	Tetrahydrofuran	0.46
23	Tetrahydropyran	1.12[b]
24	1,4-Dioxane	−0.27

[a] 1-Octanol/water partition coefficient, obtained from ref. 17.
[b] Calculated value.

The retention property of a solute was characterized by the capacity factor (k') as shown by following equation:

$$k' = \frac{t_R - t_0}{t_0}$$

where t_R and t_0 are the retention times of the solute and the unretained compound (deuterium oxide), respectively.

RESULTS AND DISCUSSION

Cyclo Compounds

For aliphatic noncyclic compounds, it was found that the logarithm of the capacity factor (log k') was linearly correlated with the logarithm of the 1-octanol/water partition coefficient (log $K_{o/w}$).[1] The slopes of the regression lines for noncyclic compounds were similar (0.585–0.688) and independent of the functional groups. The effects of the functional groups were represented by the intercept values. Although the regression analysis was performed between the logarithm of a specific retention volume (log V_g*) and log $K_{o/w}$, the values of the slopes were similar to those between log k' and log $K_{o/w}$. The same regression analysis is used for cyclic compounds to compare them with noncyclic compounds. The plots of log k' versus log $K_{o/w}$ for cycloalcohols and for cycloethers are shown in Figures 1 and 2, respectively. Cycloalcohols were retained slightly more than were *n*-alcohols and the more hydrophilic (lower log $K_{o/w}$) the cycloalcohols are, the more significant the capacity factor is, although 1,4-cyclohexanediol was the exception. The regression lines obtained are referenced by the following equations:

Table II List of Organic Electrolytes

No.	Solute	log $K_{o/w}$ [a]	No.	Solute	log $K_{o/w}$ [a]	log $K_{b/w}$ [b]
30	DL-Alanine	−2.94	34	Purine	−1.23[c]	−0.39[c]
31	DL-Phenylalanine	−1.35	35	Xanthine	−1.16[c]	−0.34
32	DL-Tryptophan	−1.04	36	Adenine	−0.09	0.33
33	L-Tyrosine	−2.26	37	Cytosine	−1.73	−0.68
			38	Hypoxanthine	−1.11	−0.27
45	Phenol	—	39	Uracil	−1.07	−0.40
46	Aniline	—	40	Thymine	−0.65	0.05
			41	Pyridine	0.65	0.84
			42	Adenosine	−1.23	−0.18
			43	Cytidine	—	−0.97
			44	Uridine	—	−0.86

[a] 1-Octanol/water partition coefficient, obtained from ref. 17.
[b] 1-Butanol/water partition coefficient, obtained from ref. 17.
[c] Calculated value.

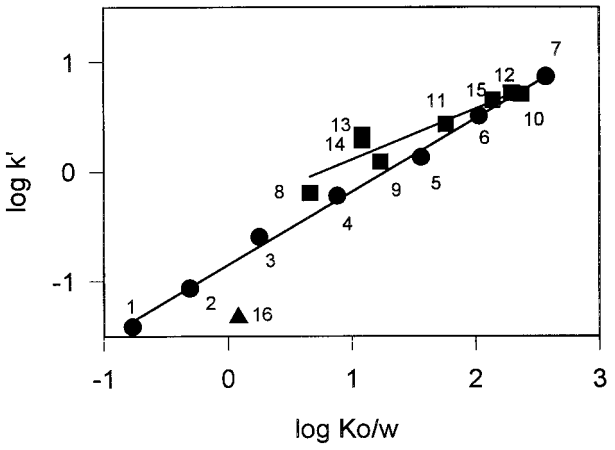


Figure 1 Relationship between log $K_{o/w}$ and log k' (cycloalcohols).

n-alcohols

$$\log k' = 0.668 \log K_{o/w} - 0.849 \qquad (r^2 = 0.9963)$$

cycloalcohols

$$\log k' = 0.463 \log K_{o/w} - 0.352 \qquad (r^2 = 0.9963)$$

noncyclic ethers

$$\log k' = 0.578 \log K_{o/w} - 0.710 \qquad (r^2 = 0.9536)$$

cycloethers

$$\log k' = 0.373 \log K_{o/w} - 0.496 \qquad (r^2 = 0.9860)$$

In the case of ethers, although both noncyclic and cyclic ethers can be correlated with a line, we performed the correlation separately and we show that the regression lines for each group are slightly different. The slope for cycloethers were smaller by 0.2 units than that for noncyclic ethers and this difference was equal to that between n-alcohols and cycloalcohols.

As represented as in our previous work,[1] the values of log k' for lactones appeared above the line for noncyclic esters. The common properties of the retention for cyclic compounds can be summarized as follows: The slopes of the regression lines were smaller than were those for noncyclic compounds and cyclic compounds were retained more easily in spite of their hydrophilic properties. Therefore, it can be pointed out that the retention of cyclic compounds is controlled by effects different from these for noncyclic compounds. Considering that phenyl compounds and PAHs were retained by the inclusion effects by the micropore of cellulose acetate,[13,16] the results suggest that small-size cyclic compounds are also included within the micropore. However, the value for 1,4-cyclohexanediol was plotted lower than the line for n-alcohols and this may be due to the two —OH groups substituted in the parallel position as shown in our previous work[9]: The results for ethylene glycol and glycerol indicated that the —OH group has a negative influence on the retention.

Phenyl and Heterocyclic Aromatic Compounds

Amino acids including a phenyl group, purinic and pyrimidinic bases, and nucleosides were used as hydrophilic aromatic compounds. These compounds were found to be retained in spite of being electrolytes when water was used as the mobile phase, although inorganic salts were eluted at shorter times than was D_2O under the same conditions.[9] The exclusion for salts from cellulose acetate, that is, negative adsorption, is caused by electric repulsion and similar results were obtained for carboxylic acids such as acetic acid. Alanine and glutathione (the latter is not presented in Table II) were also excluded from cellulose acetate either.

Since amino acids containing a phenyl group, purinic and pyrimidinic bases, and nucleosides were retained significantly, regression analysis

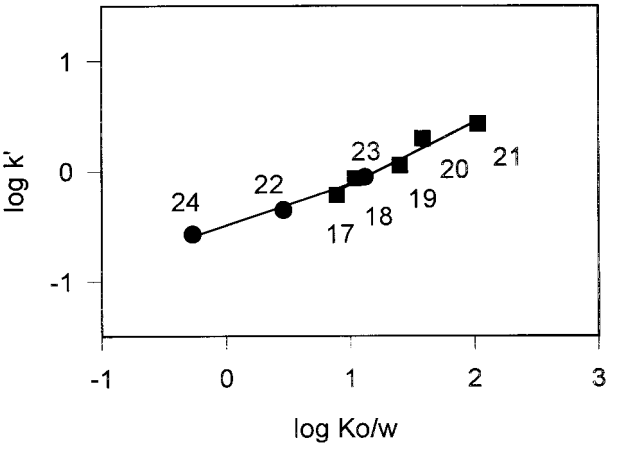


Figure 2 Relationship between log $K_{o/w}$ and log k' (cycloethers).

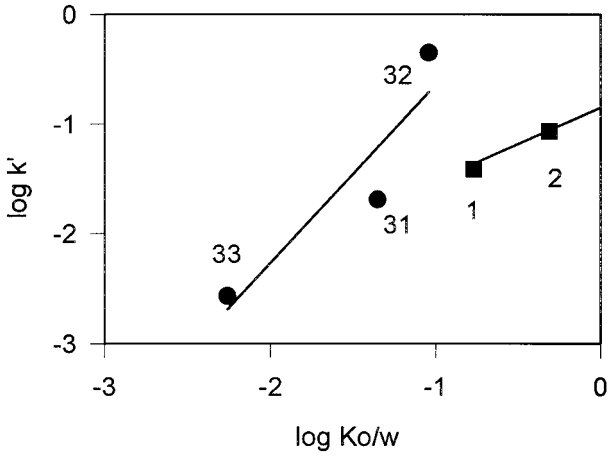


Figure 3 Relationship between log $K_{o/w}$ and log k' (amino acids).

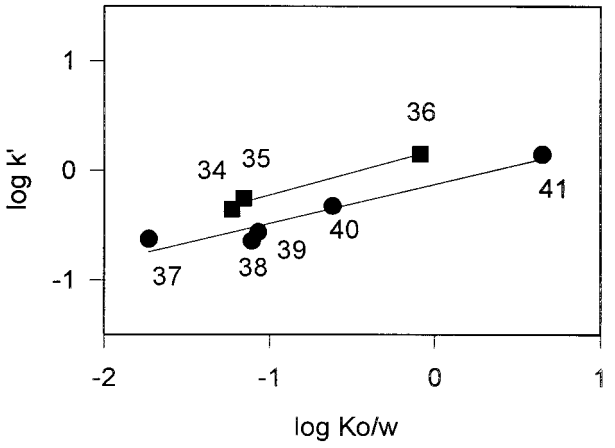


Figure 4 Relationship between log $K_{o/w}$ and log k' (bases).

between log k' and log $K_{o/w}$ was performed. The plots of log k' versus log $K_{o/w}$ for animo acids containing a phenyl group are shown in Figure 3. Here, the regression line for *n*-alcohols is shown together. Although these amino acids showed only a small retention, phenylalanine and tyrosine were plotted near the line for *n*-alcohols and tryptophan show relatively strong retention. As can be appreciated by comparing the results for alanine and amino acids containing a phenyl group, the latter show significant retention and this can be explained by the inclusion effects of the phenyl ring in the cellulose acetate. These inclusion effects overcame the electric repulsive effects.

Purinic and pyrimidinic bases were approximated by different regression lines as shown in Figure 4, where hypoxanthine was an exception. Additionally, pyridine was correlated as a pyrimidinic base group. The plot for these bases was located above the line for the *n*-alcohols and the slopes of the regression lines for these bases were near the slopes for cycloalcohols and cycloethers and are described by the following equations:

purinic bases

$$\log k' = 0.412 \log K_{o/w} + 0.186 \qquad (r^2 = 0.9826)$$

pyrimidinic bases

$$\log k' = 0.359 \log K_{o/w} - 0.125 \qquad (r^2 = 0.9237)$$

The retention for these bases may also be caused by the inclusion of heterocyclic aromatic rings within the cellulose acetate. The difference between purinic bases and pyrimidinic bases will be discussed later.

For nucleosides, the experimental values of log $K_{o/w}$ were not available. On the other hand, since the values calculated by Hansh's method are not accurate enough for these compounds, 1-butanol/water partition coefficients (log $K_{b/w}$) were used instead for the regression analysis. In general, partition coefficients obtained with other organic solvents are linearly correlated with log $K_{o/w}$,[18] and for hydrophilic compounds, log $K_{b/w}$ is a better index, because values of log $K_{o/w}$ are very low. The relationship between log k' and log $K_{b/w}$ for nucleosides and bases are shown in Figure 5.

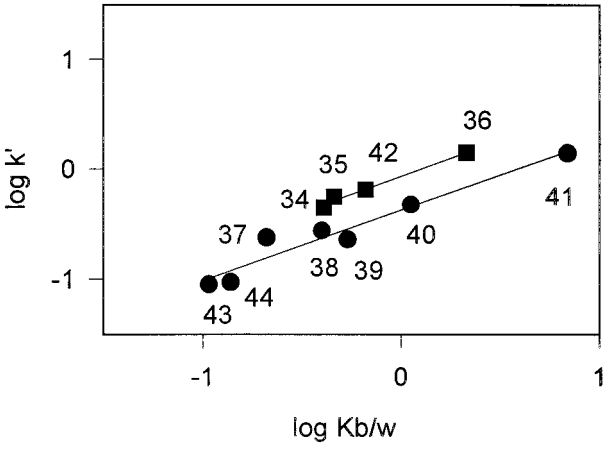


Figure 5 Relationship between log $K_{b/w}$ and log k' (bases and nucleosides).

The correlation for purinic bases and adenosine containing a purine base was approximated with a straight line and pyrimidinic bases and nucleosides containing a pyrimidine base were approximated with another line as shown by the following equations:

purinic bases

$$\log k' = 0.657 \log K_{b/w} - 0.068 \qquad (r^2 = 0.9844)$$

pyrimidinic bases

$$\log k' = 0.641 \log K_{b/w} - 0.376 \qquad (r^2 = 0.9389)$$

The fact that the slopes obtained for both groups are similar and the intercept for the purinic bases is larger than that for the pyrimidinic bases shows a similarity with the results obtained using $\log K_{o/w}$ and indicate that $\log K_{b/w}$ is also a useful index to examine the retention properties for hydrophilic organic compounds. From the fact that a regression line contains values for both nucleosides and bases, it is suggested that a ribose in nucleosides has not induced specific effects. Considering that saccharides showed a slight negative retention,[9] we can assume that only part of the base in the nucleoside was included within the cellulose acetate.

pH Effects

The aromatic compounds mentioned above were retained in spite of being electrolytes and this is in sharp contrast with the retention properties of aliphatic electrolytes. Considering their electrolytic character, however, the retention must be influenced by dissociation. Therefore, phosphate buffers were used as the mobile phase to understand these effects. In these cases, however, it may be pointed out that the ionic strength of the mobile phase may affect even the retention properties of nonionic species, because the solvation properties for cellulose acetate and solutes are affected by the ionic strength.

The effects of pH for electrolytes are summarized in Figure 6. Phenol, aniline, and pyridine were retained in large proportions when the conditions were such that the dominant species was the nonionic molecule (i.e., low pH for the acid, high pH for the bases), while the ionic species (i.e., high pH for the acid, low pH for the bases)

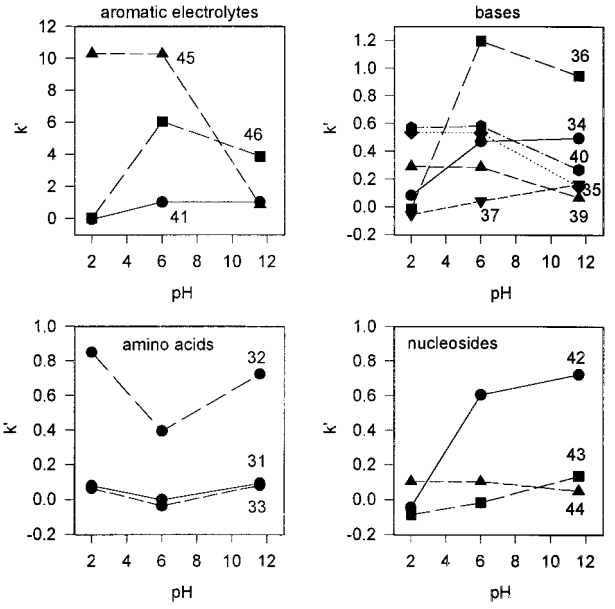


Figure 6 Effect of pH on the retention.

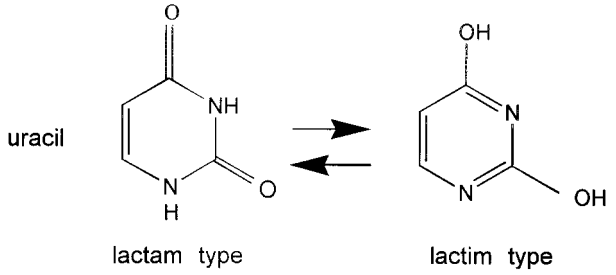
was retained only in small proportions or was completely excluded. Although the capacity factors at pH 11.6 for aniline and adenine were lower than those at pH 6.0, this can be attributed to the hydrolysis of cellulose acetate itself undergone in the alkaline mobile phase. Cellulose acetate is hydrolyzed easily under alkaline conditions and the retentions of organic compounds decrease with the decrease in acetyl content of cellulose acetate.[3]

Comparing the retentions for molecular species, pyridine was retained less than were phenol and aniline. A similar tendency was observed by a batch-type adsorption experiment using a cellulose acetate membrane as the adsorbent.[12] The retention of nonelectrolytic phenyl compounds is considered to be caused by some specific affinity of the phenyl ring with cellulose acetate: The planar structure of the phenyl ring may be a major factor inducing the inclusion effect. The results for pyridine and nucleic bases indicate that the inclusion of heterocyclic aromatic compounds may be affected negatively by heteroatoms such as nitrogen.

The retentions for amino acids were the lowest at almost any isoelectric point. Tryptophan showed larger retention than that of other amino acids. The reasons for these results, however, are not clear at present.

Nucleosides and bases were classified into two groups: One is retained more under acidic conditions and the other is retained more under alka-

line conditions. The former consists of xanthine, hypoxanthine, uracil, thymine, and uridine, and these compounds have a tautomer, one in the lactam form and the other in the lactim form, as shown in the example below:



In general, the lactam form is dominant in the range from acidic to neutral conditions. Since the —OH group affects the retention negatively and the carbonyl group does positively as shown in our previous work,[3] the lactam form may be retained more, and, thus, acidic conditions may be proper for its retention.

The second group consists of purine, adenine, adenosine, cytosine, and cytidine. Since the bases in this group except for cytidine and cytosine have no tautomer, ionic species are dominant under acidic conditions. Accordingly, nonionic species were retained more under alkaline conditions. Although cytidine and cytosine have tautomers, they are substituted by an amino group. The dissociation of this amino group under acidic conditions may affect the retention more strongly.

CONCLUSIONS

The adsorption properties of cyclic compounds on cellulose acetate were examined with HPLC and the results were compared with those for noncyclic compounds. Cyclic compounds were found to be adsorbed more than were noncyclic compounds even if the former are hydrophilic, and this was suggested to be caused by the inclusion effects by the micropore in cellulose acetate. Among electrolytes, those containing a phenyl group or a heterocyclic aromatic ring such as a purinic or pyrimidinic base were retained by cellulose acetate. The retention for those electrolytes was not only influenced by dissociation but also by tautomerism. The results obtained in this work indicate that cellulose acetate has a unique structure suitable for the adsorption of cyclic compounds. This may as well apply for membrane-separation characteristics of organic compounds. Especially, the adsorption properties of amino acids, nucleic bases, and nucleosides may also give useful information in the medical and pharmaceutical fields.

Moreover, the relationship between the retention in liquid chromatography and log $K_{o/w}$ or log $K_{b/w}$ was found to be a useful means to explain the adsorption mechanism for a wide variety of solutes. This may lead to the examination of adsorption of solutes on other membrane materials.

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