Chiral determination of various adrenergic drugs by thin-layer chromatography using molecularly imprinted chiral stationary phases prepared with α-agonists

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Thin-layer chromatography (TLC) based on molecularly imprinted polymers (MIPs) of α-agonists as chiral stationary phases was applied to the determination of enantiomers of various adrenergic drugs including α- and β-agonists and β-antagonists (β-blockers). In this study, three MIPs imprinted with (+)-ephedrine, (+)-pseudoephedrine and (+)-norephedrine plus a non-imprinted polymer (non-MIP) were prepared, processed and coated on a glass support as thin layers. Then enantiomeric determination of adrenergic drugs was carried out by development of their racemates on the TLC plates, using established conditions. From the results, the racemates of the compounds used as print molecules were well separated into two isomers on the MIP-plates, except on the plate based on MIP of (+)-norephedrine. Most adrenergic drugs structurally related to print molecules were completely resolved into two spots with the MIP plates. In general, the retention of (+)-isomers (or 1S-isomers) was greater than that of (−)-isomers (or 1R-isomers), indicating the stereoselectivity of the MIPs with the former isomers. Moreover, the role between the chemical structures of the analytes with chiral recognition of the MIPs has been investigated. The proposed method enables rapid determination of enantiomers and screening of large numbers for optical purity of adrenergic drugs.

Introduction

The chiral determination for verifying enantiomeric purity/composition of pharmaceutical drugs is a growing concern to analytical chemists and the pharmaceutical regulatory agencies. The reason for this is that optical isomers of pharmaceutical drugs can have differences in pharmacological activities, side effects and even toxic effects. In this context, it is necessary to find reliable, sensitive and rapid methods for analysis and characterization of enantiomers of optically active compounds.

Most enantiomeric determinations are performed using spectroscopic and chromatographic methods. Spectroscopic methods are extremely valuable in the stereochemical analysis of drugs, however, they present difficulties during the analysis of a pure enantiomeric drug.1 Chromatographic methods such as HPLC, GC and TLC provide satisfactory determination of enantiomeric composition or purity.2 Chromatographic procedures have been developed with both direct methods using chiral stationary phases (CSPs) or chiral mobile phase additives (CMAs), and indirect methods using a chiral derivatizing reagent.3–6 Both GC and HPLC methods are sensitive but time consuming, costly and restricted to a certain class of compounds,3,5,6 whereas TLC possesses several advantages over other methods such as simplicity, rapidity, low cost and simultaneous detectability.

Molecular imprinting is a technique for the preparation of tailor-made chiral selectors, which is rapidly growing in the field of chiral separation. During the last decade, MIPs have been prepared for numerous classes of either achiral or chiral compounds, e.g., amino acid,7–9 sugars,10 and a number of pharmaceutical drugs,11–16 mostly for HPLC application. There are several advantages of the employment of MIP in chiral discrimination. Firstly, the enantiomeric order of elution is foreseen by predetermining of the enantiomer selected as the print molecule. A MIP permits molecular recognition for several types of compounds varying according to chiral template, whilst other chiral selectors have enantioselectivity only with certain types of compounds. MIP can be reused after removing the print molecule from such a polymer. Finally, the need to screen a range of CSPs to find one that affects a given separation can be dismissed when a MIP is used and subsequently the cost of analysis is reduced. From the advantages stated above of TLC separation and imprinting technique, the application of MIP in TLC will be a useful tool for enantiomeric determination of chiral drugs. The first report on the employment of MIP as a TLC stationary phase was made by Kriz et al.,17 involving the separation of enantiomers of amino acid derivatives. Our group further applied this approach for enantiomeric separations of a number of pharmaceutical drugs.18–20 Adrenergic drugs are agents that exert pharmacological and therapeutic effects on the autonomic nervous system producing either stimulation (adrenergic agonist) or decrease (adrenergic antagonist) in sympathetic activity. They contain at least one asymmetric carbon which provides the molecule in more than two stereoisomeric forms. As the pharmacological and/or pharmacokinetic action of each form of these drugs are different,21–24 the separation of enantiomers of these drugs is therefore important. The most simple and rapid method used for the determination of optical purity of adrenergic drugs is thin-layer chromatography; one which can be performed by an indirect method with the use of a chiral derivatizing reagent25–28 or complex–ligand exchange plate29 or a chiral ion pair reagent as mobile phase additive.30,31 Recently, we reported the direct enantioseparation of four adrenergic agonists including nor-
ephedrine, pseudoephedrine, ephedrine and epinephrine by TLC based on MIPs of both (−)-norephedrine and (−)-pseudoephedrine as CSPs. The result shows the potential of this method for chiral resolution of such compounds.

The objective of this work was to separate and determine enantiomers of a number of adrenergic drugs by applying the previous work. The adrenergic drugs studied included four α-agonists, two β-agonists and four β-blockers, widely used in clinical therapeutics. (Their chemical structures are given in Tables 2 and 3.) In order to extend the previous work, we imprinted the polymers with (+)-pseudoephedrine, (+)-norephedrine and (+)-ephedrine by the use of a thermal polymerization method. Note that the latter compound has not yet been subjected to this approach. The preparation procedure of the TLC plate of MIPs was entirely adopted from our previous work. The suitable chromatographic conditions for chiral determination by TLC of each compound were examined.

Experimental

Reagents

Ethylene glycol dimethacrylate (EDMA) and methacrylic acid (MAA) were obtained from Aldrich (Milwaukee, WI, USA). 2,2′-Azobis (butyronitrile) (AIBN) was purchased from Janssen Chimica (Geel, Belgium). (+)-Ephedrine and racemic ephedrine were obtained from Sigma (St. Louis, MO, USA). (+)-Pseudoephedrine, (−)-pseudoephedrine, (−)-ephedrine HC1, (−)-norephedrine and (+)-norephedrine HC1 were obtained from Aldrich. Racemic norephedrine, epinephrine, isoproterenol, propanolol HCl, oxprenolol HCl and pindolol were obtained from Aldrich. Nadolol was a generous gift from Schwartz (Monheim, Germany). The free bases were prepared by neutralization of the aqueous solution of the salts with 1 M NaOH. All other reagents (ACS certified reagent grade) were used without further purification.

The preparation of polymeric materials

The preparation procedure of the polymers (Table 1) was similar to that outlined by Vlatakis et al. Methacrylic acid and ethylene glycol dimethacrylate were used as functional monomer and cross-linking monomer, respectively. A print molecule (3 mmol) was dissolved in dichloromethane (40 ml) and then MAA (12 mmol), EDMA (0.31 mol) and initiator (AIBN) (0.1 mmol) were added. The mixture was degassed under vacuum in an ultrasonic bath for 5 min and then purged with nitrogen for 5 min. The polymerization was carried out by heating of the mixture at 40 °C for 16 h. The bulk polymer was ground to a fine powder in an agate pestle and mortar and sieved through a 100 μm mesh. The sifted particles were collected and the remaining particles were reground. Then, the polymer was stirred in a solvent mixture of acetic acid and methanol (1 + 9 v/v) for 24 h, and filtered. The precipitate was washed with methanol. Finally, the polymer was dried under vacuum. Non-MIP included as the control was prepared in the absence of the print molecule.

Particle size data of each polymer were acquired using an Aerosizer (Amherst, MA, USA). A Jeol 5700 scanning electron microscope (JSM 5800 LV; Palo Alto, CA, USA) was used to determine particle morphology.

Thin-layer chromatography

TLC plates were prepared according to the method described in previous work. Each polymer (1 g) and CaSO4 (1 g) were carefully mixed with distilled water (3 ml) by means of a pestle and mortar. The slurry was poured on standard glass microscope slides (76 × 26 mm), which were spread as a thin layer with a layer thickness of 0.25 mm. The plates were dried for 24 h at room temperature. The polymeric materials of the same batch were exploited to maintain consistency of their physical properties. The analytes were four α-agonists; pseudoephedrine, norephedrine, ephedrine and epinephrine, two β-agonists; salbutamol, isoproterenol and four β-antagonists; propranolol, oxprenolol, pindolol and nadolol. An analyte was dissolved in methanol (2–3 mg ml⁻¹) and 1 μl of solution was applied manually to TLC plates by use of a Hamilton syringe (Altech, Deerfield, IL, USA). The plate was then dried in air and developed with eluent in which a satisfactory retention and/or resolution can be obtained (see Table 2 for eluents of α- and β-agonists and Table 3 for eluents of β-blockers). The solvent fronts were a left to migrate approximately 60 mm and development time was typically 5 min. To detect a spot, after being sprayed with detection reagent (listed in Tables 2 and 3 for each analyte), the plate was heated gently with the hot air of a blower until the spot intensely appeared. The racemates of ephedrine, pseudoephedrine, norephedrine, epinephrine and propanol were analyzed for each enantiomer by spotting of a pure enantiomer of these compounds alongside. RSl of separated enantiomers (or racemate) were measured and presented in the Tables as hRf values (Rf × 100). For unseparated racemate, hRf of each enantiomer was displayed in equal value as that of one spot. Chiral separation factor (α) was calculated according to previous work. Duplicate determinations for each separation were performed.

Results and discussion

Molecularly imprinted polymer-based chiral stationary phases for TLC

Although imprinted polymer can be obtained either by photopolymerization methods or thermal polymerization methods, in this study the preparation of polymers was based on a thermal polymerization method. The polymerization was carried out at 40 °C, which is lower than that (60 °C) described by Vlatakis et al. with the purpose of reducing the degradation of the print
molecules during polymerization. The use of methacrylic acid as functional monomer with dichloromethane as solvent in the polymerization process gave the polymeric materials the capability of coating as a stationary thin layer on a glass support. Besides α-agonists, we tried to use a β-agonist, (−)-isoproterenol, as a print molecule. In preparation of this polymer, THF was employed as a solvent in the polymerization process due to low solubility of (−)-isoproterenol in a non-polar solvent. It was found that the stationary layer obtained with this polymer was easily rubbed off. This observation was also found in earlier work made by the authors for preparation of the polymers with the same method of polymerization but different types of print molecules and functional monomer. However, this result was not found when THF was used as a solvent in preparation of the polymer by photo-initiation at low temperature (4 °C), as observed by our group. From this finding in both the present and previous work, we can conclude that the type of solvent employed in the polymerization process has a significant influence on the characteristics of the MIP-stationary layer.

Physical properties of the polymeric materials

SEM of all the polymers was carried out. Fig. 1 shows SEM images obtained from non-MIP (A) and MIP of (+)-ephedrine (B). It can be seen from Fig. 1, non-MIP was composed of irregularly shaped particles having a smooth surface and MIP imprinted with (+)-ephedrine was mostly agglomerates of random irregular particles, which was similar to other MIPs (their electron micrographs are not shown). These results show the difference between the morphologies of non-MIP and MIPs, which were prepared in the absence and presence of print molecule, respectively, under given conditions.

Physical properties of TLC–adsorbent often reflect on the adhesion of adsorbent on a support or the characteristic of the TLC layer obtained or the chromatographic efficacy, i.e., the retention of analyte on a stationary phase. The physical data of polymer particles used is shown in Table 1. The size distributions of the polymer particles were 30–40 μm. Typically, the polymers had a surface area approximately 0.20 m² g⁻¹ and a bulk density of 0.45 g ml⁻¹. The polymers having

<table>
<thead>
<tr>
<th>Compound</th>
<th>Eluent</th>
<th>Detection reagent</th>
<th>Color of spot</th>
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<tbody>
<tr>
<td>α-Agonist—</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ephedrine</td>
<td>10% Acetic acid in acetonitrile</td>
<td>Ninhydrin reagent</td>
<td>Purple–blue</td>
</tr>
<tr>
<td>Pseudoephedrine</td>
<td>5% Acetic acid in acetonitrile</td>
<td>Acidified potassium permanganate reagent</td>
<td>Brown</td>
</tr>
<tr>
<td>Norephedrine</td>
<td>10% Acetic acid in acetonitrile</td>
<td>Ninhydrin reagent</td>
<td>Purple–blue</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>10% Acetic acid in acetonitrile</td>
<td>Ninhydrin reagent</td>
<td>Purple–blue</td>
</tr>
<tr>
<td>β-Agonist—</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoproterenol</td>
<td>5% Acetic acid in acetonitrile</td>
<td>Acidified potassium permanganate reagent</td>
<td>White (on brown background)</td>
</tr>
<tr>
<td>Salbutamol</td>
<td>10% Acetic acid in acetonitrile</td>
<td>Acidified potassium permanganate reagent</td>
<td>White (on brown background)</td>
</tr>
</tbody>
</table>
such physical properties produced desirable layers, except the MIP imprinted with (+)-isoproterenol, which gave a brittle layer. It should be noted that the polymer imprinted with (−)-isoproterenol had swelling ability and low bulk density, which caused layer-coating problems.

**TLC chromatographic conditions**

We examined several solvent systems to use as a chromatographic eluent and found that acetonitrile was appropriate for elution-development of α- and β-agonists, while a non-polar solvent such as dichloromethane was preferred for that of β-blockers which are less polar than α- and β-agonists. In addition, we found that modification of both solvents with acetic acid in the range of 5–10% resulted in the analytes being less retained and enabled better separation of the enantiomers as well as improving the spot shape.

Although the analytes were UV absorbing, most of this activity was lost on the MIP-plate surface due to the strong absorbance of MIP in UV light. Moreover, the residual print molecule in the polymer (determined quantitatively by an IR method described elsewhere18–20) may interfere in the spot visualization, hence its amount would have to be kept low so as not to cause such interference. In this study, the spot detection of analytes was based on the use of detection reagents. Nonetheless, the MIPs also responded themselves by giving color reactions with the detection reagents. Thus, a sensitive and selective detection reagent was required. In the search for detection reagents of adrenergic drugs, three reagents were found. The ninhydrin reagent was suitable for detection of ephedrine, norephedrine and epinephrine with the greatest sensitivities. The acidified potassium permanganate reagent enabled the detection of pseudoephedrine, isoproterenol and salbutamol. The anisaldehyde reagent enabled the visualization of all β-blockers. The potassium permanganate reagent gave a brown background with white spots for salbutamol and isoproterenol, or in a reverse manner in the case of pseudoephedrine. The reaction spots by the anisaldehyde reagent were unstable with the chromatographic zone fading quickly after 5 min. Of all the detection reagents used the ninhydrin reagent gave the most stable spots.

**Separation of adrenergic drugs on MIP prepared against (+)-ephedrine**

Table 4 gives the retention and resolution data of ten adrenergic drugs for CSP based on MIP of (+)-ephedrine. This CSP could enantiomerically resolve seven out of ten racemates of adrenergic drugs and the rest were not separated into individual isomers. Seven racemates that separated into isomers were ephedrine, pseudoephedrine, norephedrine, sabutamol, pindolol, propranolol and oxprenolol. In these resolutions, the $hR_F$ values of (+)-isomers were lower than those of (−)-isomers, indicating greater affinity of the former isomers. Also, the racemates of β-

<table>
<thead>
<tr>
<th>Compound</th>
<th>Eluent</th>
<th>Detection reagent</th>
<th>Color of spot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nadolol</td>
<td>7% Acetic acid in dichloromethane</td>
<td>Anisaldehyde reagent</td>
<td>Pink</td>
</tr>
<tr>
<td>Pindolol</td>
<td>7% Acetic acid in dichloromethane</td>
<td>Anisaldehyde reagent</td>
<td>Purple–blue</td>
</tr>
<tr>
<td>Propranolol</td>
<td>5% Acetic acid in dichloromethane</td>
<td>Anisaldehyde reagent</td>
<td>Blue</td>
</tr>
<tr>
<td>Oxprenolol</td>
<td>5% Acetic acid in dichloromethane</td>
<td>Anisaldehyde reagent</td>
<td>Purple–blue</td>
</tr>
</tbody>
</table>

Table 3 Eluent and detection conditions used for β-blockers
blocks except nadolol were completely separated into two spots. When the resolution of racemic propranolol occurred, the $hR_s$ value of the (+)-R-enantiomer was however higher than that of the (−)-S-enantiomer (as the two spots obtained from racemic propranolol were identified). Generally, for the enantiomerically separated case, this CSP produced the $\alpha$ values $> 1.3$ with tailing of the spot up to 10–12 mm.

No enantiomeric resolution was observed for racemic epinephrine, isoproterenol and nadolol on this CSP. It should be noticed that the first two racemates possess the catechol substituent in their structures and the latter racemate has two hydroxyl groups on the ring extended from the benzene ring (see Tables 2 and 3). The catechol group increases hydrophilicity of the molecule, resulting in the change in retention of an analyte. It is reasonable for the retention results that were obtained for catechol derivatives because the CSP contains the polar carboxyl groups; racemic epinephrine and isoproterenol moderately or less retained with the polar eluent, while with a non-polar solvent, racemic nadolol was significantly retained. However, racemic salbutamol was completely resolved into two spots with this CSP, although its structure is closely related to those of the catechol derivatives.

Separation of adrenergic drugs on MIP prepared against (+)-pseudoephedrine

Table 5 shows the $hR_s$ data and the $\alpha$ values of ten adrenergic drugs for CSP based on MIP of (+)-pseudoephedrine. Chromatographic behaviors of adrenergic drugs on this CSP were similar to those on CSP based on MIP of (+)-ephedrine. On this CSP, the retention values of the enantiomers of adrenergic drugs, omitting those of isoproterenol and propranolol, were highest compared with those obtained on other CSPs. As expected, this CSP was able to resolve the print molecule into two spots, providing a higher $hR_s$ value of the (−)-isomer than that of the (+)-isomer. The racemates of all $\alpha$-agonists were completely resolved into two spots but the tailing spots occurred in the case of epinephrine. However, the highest $\alpha$ value was achieved for racemic epinephrine, which was hardly separated on other CSPs.

This CSP did not afford the enantiomeric resolution for racemic salbutamol, whilst the CSP based on MIP of (+)-ephedrine exhibited moderate enantiomeric resolving capability for this compound. Like CSP based on MIP of ephedrine, this CSP enabled resolution of the enantiomers of $\beta$-blockers but not in the case of nadolol, and again, the (−)-isomer of propranolol was more retarded than the (+)-isomer. Generally, with this CSP, the $\alpha$ values of the separated spots were more than 1.2, this value being close to that obtained with CSP based on MIP of (+)-ephedrine.

Separation of adrenergic drugs on MIP prepared against (+)-norephedrine

Table 6 displays the retention and resolution data of ten adrenergic drugs for CSP based on MIP of (+)-norephedrine. From the results, this CSP showed chiral resolving ability with
γ-agonists and β-blockers other than α-agonists. Rather surprisingly, and contrary to our anticipation, this CSP could not separate the enantiomers of compounds corresponding to the print molecule but enabled the separation of the enantiomers of related compounds such as pseudoephedrine. In the previous work,19 the CSP based on MIP of (−)-norephedrine, prepared by use of the photo-polymerization method, resolved the enantiomer of print molecules rather than other α-agonists. This suggests that MIPs prepared with different methods may produce the difference in enantiomeric resolving capability of MIP.

Not only was this CSP able to resolve racemic isoproterenol into two spots, but it also provided the best enantiomeric resolution; that was achieved for the separation of racemic salbutamol (α value = 2.3). Again, β-blockers except racemic nadolol were completely separated into two spots with the same elution order of propranolol enantiomers as that obtained on other CSPs. With this CSP, when the resolution occurred, the α values of 1.3–2.3 were produced.

The examination of TLC behavior of ten adrenergic drugs on the control plate based on non-MIP was also performed. It was found that none of the adrenergic drugs were resolved into two spots on this type of plate (data not shown). This result confirmed the enantiomeric discrimination contributed by the MIPs.

In this work, the MIPs demonstrate good TLC chromatographic characteristics and efficient enantiomeric resolution with various adrenergic drugs under given conditions. In addition, the resolution results of some adrenergic drugs such as ephedrine, pseudoephedrine and propranolol are similar to those in the previous work on HPLC,14 regarding the determination of mimicked adrenoceptor binding evaluated from recognition properties of MIPs prepared against (+)-ephedrine and (+)-pseudoephedrine.

The results have shown that the chiral determination for optical purity of three classes of adrenergic drugs is feasible with the employment of TLC based on MIPs of three α-agonists. In addition, it would be very interesting to determine the enantiomeric compositions of these drugs; however, there will have to be a further search for a detection reagent providing a highly stable reaction spot. The TLC chromatograms of the high degree of stereoselectivity obtainable with this method are presented in Fig. 2. The plates A, B, C, D and E illustrate the separation of the enantiomers of norephedrine, pseudoephedrine, salbutamol, propranolol and oxprenolol, respectively, on CSPs described in the figure caption.

### Table 6 Retention and resolution data of adrenergic drugs on MIP prepared against (+)-norephedrine

<table>
<thead>
<tr>
<th>Compound</th>
<th>hRf value</th>
<th>Isomer 1</th>
<th>Isomer 2</th>
<th>α</th>
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<tr>
<td>α-Agonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ephedrine</td>
<td>22</td>
<td>22</td>
<td>1.00 (+)</td>
<td></td>
</tr>
<tr>
<td>Pseudoephedrine</td>
<td>40</td>
<td>60</td>
<td>1.50 (+)</td>
<td></td>
</tr>
<tr>
<td>Norephedrine</td>
<td>18</td>
<td>18</td>
<td>1.00 (+)</td>
<td></td>
</tr>
<tr>
<td>Epinephrine</td>
<td>31</td>
<td>31</td>
<td>1.00 (+)</td>
<td></td>
</tr>
<tr>
<td>β-Agonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoprenalol</td>
<td>37</td>
<td>57</td>
<td>1.54 (+)</td>
<td></td>
</tr>
<tr>
<td>Salbutamol</td>
<td>18</td>
<td>42</td>
<td>2.33</td>
<td></td>
</tr>
<tr>
<td>β-Blocker</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Nadolol</td>
<td>11</td>
<td>11</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Pindolol</td>
<td>31</td>
<td>40</td>
<td>1.29</td>
<td></td>
</tr>
<tr>
<td>Propranolol</td>
<td>57</td>
<td>71</td>
<td>1.25 (−)</td>
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</tr>
<tr>
<td>Oxprenolol</td>
<td>42</td>
<td>60</td>
<td>1.43</td>
<td></td>
</tr>
</tbody>
</table>

The hRf values at room temperature are averages of two determinations, the standard deviation being less than 0.5. α = hRf(isomer 2)/hRf(isomer 1). The sign of the optical rotation of the retained isomer is shown in parentheses.

In this study, the enantiomeric determination was performed with a wider range of structures of adrenergic drugs than in the previous study,19 giving additional information concerning chiral recognition of the MIPs imprinted with the α-agonists. All of the compounds studied have three functionalities in common: the aromatic ring, β-hydroxy group and α-amine, but the aryl and amine substituents vary. In addition, there is a –O–CH2-group situated between the aromatic ring and the hydroxyl carbon in β-blockers (see the chemical structures in Tables 2 and 3). The results show that besides the print molecule, the MIPs can enantiomerically resolve closely related compounds with different chiral separation factors, indicating the role of other substituents of the molecule to chiral recognition of the MIPs. To investigate this, the α values obtained for the MIPs were compared and elucidated.

The α value > 1 was obtained for several compounds having either a symmetric or asymmetric carbon atom at the α-position and the amine substituents differ from those of the print molecules, particularly in the case of β-blockers, indicating that the α-carbon and amine side chain are less important for the chiral recognition of the MIPs. The enantiomeric resolution of β-blockers with all the MIPs implies that the –O–CH2-linkage, or on the other hand the extension of distance between the aromatic ring and the amine group did not affect the enantiomeric resolution of the MIPs. The conclusions described above are in agreement with those on a MIP-column.14

As exemplified by β-blockers, the substituents on the aromatic region, particularly the lipophilic group, did not influence the chiral recognition of the MIPs. However, the catechol group renders negative resolution on MIPs, for example in the case of racemic epinephrine and isoproterenol. This behavior might be a result of the steric hindrance of two hydroxyl groups in catechol on the interaction of the aryl group...
with the enantiomeric binding site. Furthermore, the highly hydrophilic characteristics of compounds owing to the polar hydroxyl groups is virtually considered as a concomitant effect. With regard to the hydrophilic effect, the polar molecule may be quickly eluted with the polar solvent and consequently decrease the binding in favor of the antipode with receptor. On the other hand, the steric effect is expressed with nadolol eluted with a non-polar solvent due to the presence of the polar hydroxyl groups on the aryl moiety. The observed effect is also decreased by a change in functional group hydrophilicity to a less polar group, such as the case of salbutamol; methyl alcohol substituting for the m-hydroxyl group of cathecol. In spite of that, there are some exceptions to this behavior of catechol derivatives, for example, racemic epinephrine was resolved on CSP based on MIP of (+)-pseudoephedrine. The reason for this is unclear, but may have been due to the more favorable hydrophilic characteristics of compounds owing to the polar hydroxyl groups is virtually considered as a concomitant effect. Furthermore, the highly hydrophilic characteristics of compounds owing to the polar hydroxyl groups is virtually considered as a concomitant effect.

Conclusions

The employment of MIPs as stationary phases in TLC is a substantially useful method of determining optical isomers for enantiomeric purity. Although the previous chiral determinations of adrenergic drugs, using indirect methods in TLC have been reported in the literature, the chiral determinations obtained with the proposed method are rapid and effective with many classes of adrenergic drugs. With this method, the screening for optical purity of a large number of adrenergic drugs will be possible. The observed correlation between structurally related compounds could also be useful in predicting whether it is possible to determine the enantiomers of optically active compounds on MIP.

References


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