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Direct Separation of Enantiomers by Reversed-phase High Performance Liquid Chromatography on Cellulose Tris(3,5-dimethylphenylcarbamate)

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Various types of enantiomeric drugs were optically separated by reversed-phase high performance liquid chromatography using cellulose tris(3,5-dimethylphenylcarbamate) as a chiral stationary phase.

Tris(phenylcarbamate) derivatives of polysaccharide are used as a chiral stationary phase for the optical resolution of racemic compounds. Especially, silica-based cellulose tris(3,5-dimethylphenylcarbamate)(CDMPC) is useful for the separation of enantiomers of β-adrenergic blockers, anticholinergics and various carboxylic acids.[1,2,3] Direct optical resolution of these compounds has been attained usually by normal-phase HPLC conditions. In this letter, we wish to report an efficient optical resolution for the various drugs by reversed-phase HPLC on CDMPC column using aqueous buffer-acetonitrile eluting systems.

Figure 1 shows the chromatogram of the resolution of sodium 4-[α-hydroxy-5-(1-imidazoyl)-2-methylbenzyl]-3,5-dimethyl-benzoate dihydrate (Y-20811),[4] on CDMPC column, 250 × 4.6(id)mm, (CHIRALCEL OD, DAICEL Chemical Industries, Ltd.,) using a mixture of 0.05 M sodium perchlorate (pH 3.0)-acetonitrile (73:27) as an eluent.

The HPLC resolution is greatly influenced by pH and buffer of the eluting system. The results shown in Tables 1 and 2 indicate that Y-20811 was more effectively resolved in a lower pH region (the optimum pH = 3.5) and by using perchlorate buffer-acetonitrile as an eluent, respectively.

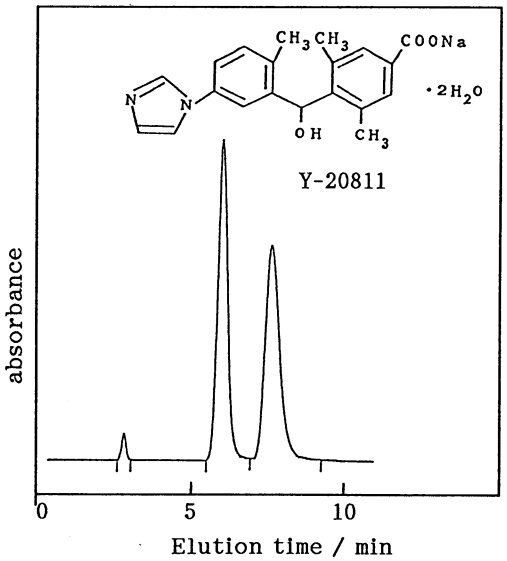

Fig.1. Chromatogram of Y-20811 flow rate, 1cm³min⁻¹; temp 25 ℃.

Table 1. The pH effect on the optical resolution of Y-20811 using perchlorate buffer-acetonitrile(4:1)

pH	K'_1	α	Rs
5.6	3.10	1.38	1.50
4.0	4.82	1.57	2.62
3.5	4.64	1.57	2.68
2.9	4.33	1.63	2.62
2.5	4.98	1.61	2.01

Table 2. The buffer effect on the optical resolution of Y-20811 at pH 4.0

Buffer system	K'_1	α	Rs
NaH_2PO_4-H_3PO_4	2.88	1.33	1.75
CH_3COONH_4-H_3PO_4	2.60	1.37	1.92
CH_3COONa-CH_3COOH	2.86	1.37	1.85
$NaClO_4$-$HClO_4$	4.82	1.57	2.62

In a similar manner, the following enantiomeric drugs were resolved on the CDMPC column (Fig.2).

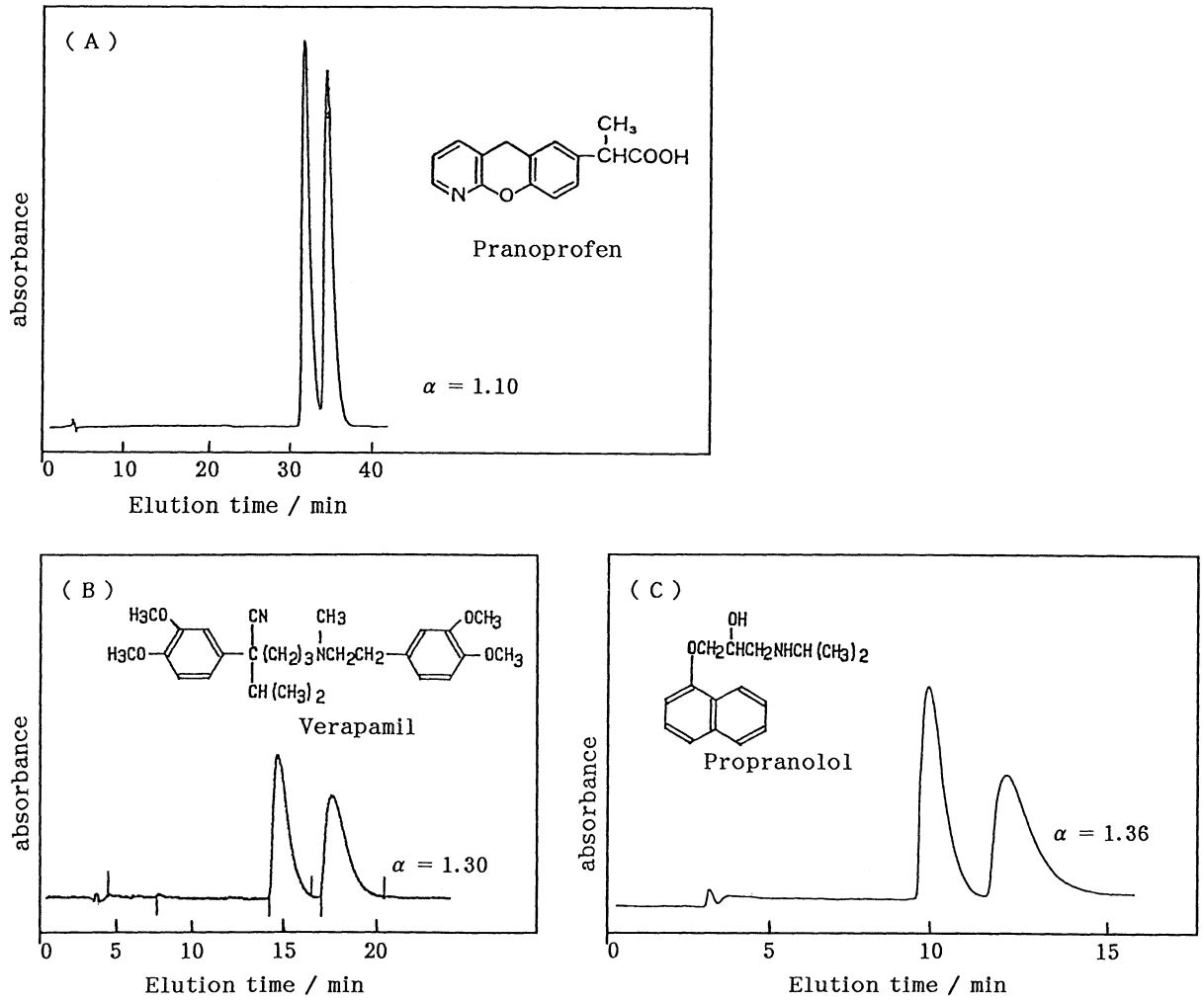

Fig.2. Chromatogram of pranoprofen, verapamil and propranolol.
flow rate, $1cm^3min^{-1}$; temp 25 ℃.
Eluent: (A) H_2O-CH_3CN-CH_3COOH (75:25:0.05)
(B) 0.05M $NaClO_4$(pH 3.0)-CH_3CN (2:1)
(C) 0.05M $NaClO_4$(pH 2.1)-CH_3CN (7:3)

The CDMPC column was quite stable during the present work. Thus, we recommend that this column can be used not only under the normal-phase conditions but also under the reversed-phase conditions.

References

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