OPTIMIZATION OF CHIRAL SEPARATION OF DERIVATIVES OF 2,6-DIKETOPIPERAZINES WITH β-CYCLODEXTRIN AND HYDROXY ACIDS AS COMPONENTS OF MOBILE PHASE IN HPLC

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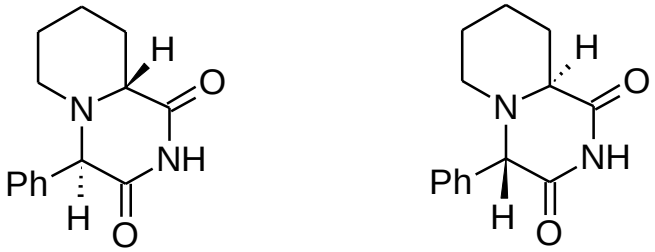
Cyclodextrins (CDs) are a cyclic polymers of alpha-D-glucopyranose. They have been widely used for all types of chiral separations by virtue of its availability, and low cost, exhibits limited aqueus solubility [1]. It has been found that the addition of organic hydroxy carboxylic acids, such as citric and tartaric acid enable forming complexes with β-cyclodextrins and improve their solubility [2].

The model compounds were bicyclic 2,6-diketopiperazines derivates (2,6-DKPs). DKPs are known to possess various pharmaceutical activities, such as antitumor, anticonvulsant and antiviral. Their usefulness for medicinal chemists greatly depends on chirality[3]. Their chemical formula is presented below.



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Scheme 1. Chemical structure of derivatives of bicyclic 2,6 diketopiperazines (2,6-DKPs).

The bicyclic 2,6-diketopiperazines derivates (2,6-DKPs) were resolved by liquid chromatography using β–cyclodextrin as a mobile phase additive and hydroxy acids as enhance of its solubility.

The mechanism for enantiomer separation with β-cyclodextrin in the presence of hydroxy acids was discussed. The effect of β-cyclodextrin, hydroxy acids concentration, pH of mobile phase on retention and enantioseparation were investigated. The system with higher concentration of β-cyclodextrin improves resolution and reduces the retention time for 2,6-DKPs. The best selectivity for the model compounds were obtained for β–cyclodextrin with DL-tartaric acid.

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