ENANTIOMERIC PURITY TESTING OF S-KETOPROFEN IN PHARMACEUTICAL FORMULATIONS BY CE USING A DUAL CYCLODEXTRIN SYSTEM

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A capillary electrophoretic (CE) method was developed for the determination of ketoprofen enantiomers in the presence of sulfanilic acid used as an internal standard.
The CE separation was carried out using uncoated fused silica capillaries and a buffer made of 100 mM phosphoric acid adjusted to pH 2.5 with triethanolamine and containing an anionic cyclodextrin (CD), sulfobutylether-ß-cyclodextrin (SB-ß-CD), in combination with a neutral CD, trimethyl-ß-cyclodextrin (TM-ß-CD). UV detection was performed at 214 nm.
On basis of preliminary studies, the concentrations of both CDs were found to be the most significant factors influencing the enantiomeric resolution of ketoprofen in this CE system.
In order to optimize the concentrations of the two CDs a multivariate approach based on a central composite design at centered face was applied. The selected responses were the three migration times (upslope half-height, apex and downslope half-height) of the peaks corresponding to S-ketoprofen, R-ketoprofen and sulfanilic acid. The main effects, the quadratic terms and the first-order interactions of the factors were evaluated. Several performance criteria, such as the asymmetry factor, resolution and peak efficiency, were then estimated.
Derringer's desirability function was used as a multicriteria decision making tool for all these criteria. From the global desirability optimal concentrations of TM-β-CD (24 - 30 mM) and SBE-β-CD (3.5 - 5.5 mM) could be deduced, leading to very robust experimental conditions.
The suitability of the CE method for its intended use and the reliability of the results within well defined limits were demonstrated by means of a validation procedure. For that purpose, a new approach based on the accuracy profiles (estimation of total error with two-sided confidence limits at 95 %) was used for the selection of the most suitable regression model, the determination of the limits of quantitation (LOQ) and the selection of the concentration range [1].
The proposed CE method was then applied to determine R-ketoprofen in S-ketoprofen raw material and in commercial tablets containing S-ketoprofen.

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