

HPLC-FLUORESCENCE METHOD FOR THE ENANTIOSELECTIVE ANALYSIS OF PROPRANOLOL IN RAT SERUM USING IMMOBILIZED POLYSACCHARIDE-BASED CHIRAL STATIONARY PHASE

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Tstereoselective high-performance liquid chromatographic (HPLC) method was developed and validated to determine S-(-)- and R-(+)-propranolol in rat serum. Enantiomeric resolution was achieved on cellulose tris(3,5-dimethylphenylcarbamate) immobilized onto spherical porous silica chiral stationary phase (CSP) known as Chiralpak IB. A simple analytical method was validated using a mobile phase consisted of n-hexane-ethanol-triethylamine (95:5:0.4%, v/v/v) at a flow rate of 0.6 mL min⁻¹ and fluorescence detection set at excitation/emission wavelengths 290/375 nm. The calibration curves were linear over the range of 10–400 ng mL⁻¹ (R = 0.999) for each enantiomer with a detection limit of 3 ng mL⁻¹. The proposed method was validated in compliance with ICH guidelines in terms of linearity, accuracy, precision, limits of detection and quantitation, and other aspects of analytical validation. Actual quantification could be made for propranolol isomers in serum obtained from rats that had been intraperitoneally (i.p.) administered a single dose of the drug. The proposed method established in this study is simple and sensitive enough to be adopted in the fields of clinical and forensic toxicology. Molecular modeling studies including energy minimization and docking studies were first performed to illustrate the mechanism by which the active enantiomer binds to the β-adrenergic receptor and second to find a suitable interpretation of how both enantiomers are interacting with cellulose tris(3,5-dimethylphenylcarbamate) CSP during the process of resolution. The latter interaction was demonstrated by calculating the binding affinities and interaction distances between propranolol enantiomers and chiral selector. Chirality 00:000–000, 2014.

Key Words: propranolol; enantioselective; Chiralpak IB; HPLC-FD; molecular modeling.

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