Extended Abstract Journal of Clinical & Experimental Toxicology 2021
Vol.5 No.2

HPLC-Fluorescence Method for the Enantioselective Analysis of Propranolol in Rat Serum Using Immobilized Polysaccharide-Based Chiral Stationary Phase - Aymen Al-Suwailem - King Saud University

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Introduction

A stereoselective 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

Introduction:

A stereoselective elite fluid chromatographic (HPLC) strategy was created and approved to decide S-(-)- and R-(+)- propranolol in rodent serum. Enantiomeric goals was accomplished on cellulose tris(3, 5-dimethylphenylcarbamate) immobilized onto round permeable silica chiral fixed stage (CSP) known as chiralpak IB. A basic logical strategy was approved utilizing a portable stage comprised of n-hexane-ethanol-triethylamine (95:5:0.4%, v/v/v) at a stream pace of 0.6 mL min-1 and fluorescence recognition set at excitation/discharge frequencies 290/375 nm. The alignment bends were straight over the scope of 10–400 ng mL-1 (R=0.999) for every enantiomer with a discovery breaking point of 3 ng mL-1. The proposed strategy was approved in consistence with ICH rules as far as linearity, exactness, accuracy, cutoff points of discovery and quantitation, and different parts of scientific approval. Genuine evaluation could be made for propranolol isomers in serum acquired from rodents that had been intraperitoneally (i.p.) managed a solitary portion of the medication. The proposed technique built up in this examination is basic and delicate enough to be embraced in the fields of clinical and criminological toxicology. Atomic demonstrating contemplates including vitality minimization and docking considers were first performed to outline the system by which the dynamic enantiomer ties to the β-adrenergic receptor and second to locate a reasonable understanding of how the two enantiomers are connecting with cellulose tris(3,5-dimethylphenylcarbamate) CSP during the procedure of goals. The last cooperation was exhibited by figuring the coupling affinities and collaboration removes between propranolol enantiomers and chiral selector.

Propranolol is a non cardioselective β-blocker. It is accounted for to have layer balancing out properties, yet it doesn't possess inherent sympathomimetic movement. Propranolol hydrochloride is utilized to control hypertension, pheochromocytoma, myocardial dead tissue, cardiovascular arrhythmias, angina pectoris, and hypertrophic cardiomyopathy. It is likewise used to control manifestations of thoughtful overactivity in the

administration of hyperthyroidism, tension issue, and tremor. Different signs spread the prophylaxis of headache and of upper gastrointestinal seeping in patients with entryway hypertension. This investigation gives an itemized, far reaching profile of propranolol, including recipes, essential examination, and the presence of the medication. Also, the amalgamation of the medication is depicted. The section covers the physicochemical properties, including X-beam powder diffraction, pK, solvency, liquefying point, and methodology of examination (spectroscopic, electrochemical, and chromatographic). Top to bottom pharmacology is additionally introduced (pharmacological activities, restorative dosing, uses, Interactions, and antagonistic impacts and safeguards). In excess of 60 references are given as a proof of the previously mentioned investigations.

A tale perfluoroalkyl-BINOL-based chiral diketone is seen as the principal profoundly enantioselective fluorescent sensor in the fluorous stage. One enantiomer of a chiral amino liquor or diamine at a fixation more prominent than 1 mM can cause an up to 1200–2000-overlap fluorescent improvement of the sensor (0.08 mM), while the other enantiomer gives just a 10–50-overlay upgrade. The fluorous-stage based sensor is found to upgrade the reactivity of the recently announced fluorous insoluble sensor with amino alcohols and grow its chiral acknowledgment capacity. Dynamic light dissipating examinations show the arrangement of totals of altogether different molecule sizes when two enantiomers of a substrate cooperate with the sensor in Perfluorohexane (FC-12). This significant distinction empowers simple separation of the enantiomers with UV-lights or even the unaided eye. NMR, IR, and mass spectroscopic investigations demonstrate that the fluorescent improvement and enantioselectivity ought to start from the fluorous dissolvable advanced nucleophilic expansion of the amino alcohols to the carbonyl gatherings of the sensor.