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REGULAR ARTICLE

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Fast liquid chromatography for racemic atenolol acetate separation––The analytical protocol

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Abstract

Kinetic resolution of (*R*,*S*)-atenolol is a faster strategy to produce (*S*)-atenolol. Since this racemate is a less soluble compound, resolution of its ester offers high concentrations in the process. A good analytical method is required to observe the enantiomer concentrations. This paper described application of ultra-fast liquid chromatography on the atenolol ester separation using different resolution media and analytical procedures. Chiralcel OD column resolved the ester. The chromatograms indicated different characteristics of the process. The enantiomers could be recognized by the column in less than 1 (one) hour. Symmetrical peaks were obtained, but several procedures produced peaks with wide bases and slanted baselines. Efficient enantioresolution was obtained at high mobile phase flow rate, decreased concentration of amine-type modifier, but increased alcohol content in the mobile phase. High UV detection wavelength was required. At 1.0 mL/min, the (90/10/0.5) composition resulted $\alpha = 1.46$ and $R_S = 0.9998$ that were good separation.

KEYWORDS

atenolol, Chiralcel OD, enantiomers separation, kinetic resolution, ultra-fast liquid chromatography

1 | INTRODUCTION

Switching (*R*,*S*)-atenolol to (*S*)-atenolol would develop lesser side effects as the single enantiomer avoids the side effects generated by the racemate,[1] and (*R*)-atenolol has not lacked of the side effects.[2,3] Many pathways were studied to form the (*S*)-atenolol either synthesis or resolution routes.

Assymetric syntheses of the (*S*)-atenolol were conducted using chiral or achiral raw materials, which required the chiral catalysts or addendums such as (*R*,*R*)-Co-(salen) complexes, (*R*)- or (*S*)-epichlorohydrin being present during the syntheses.[4-10] Enzymatic resolutions of the racemic compound by immobilized lipases were developed via enantioselective esterification or and hydrolysis.[11-15] Kinetic resolutions of the (*R*,*S*)-atenolol to give the (*S*)-atenolol could be done microbially using *Rhizopus arrhizus* or *Geothricum candidum*; however, the (*R*,*S*)-atenolol acetate was used as well to give the single enantiomeric atenolol.[11] Since the racemic atenolol acetate could develop the single enantiomeric compound, it is important

