INFLUENCE OF HYDROXYBOSENTAN ON DETERMINATION OF BOSENTAN IN HUMAN PLASMA

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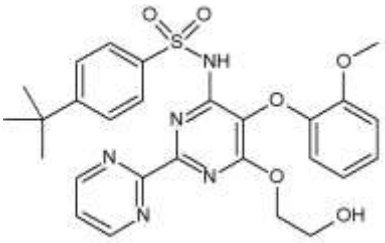
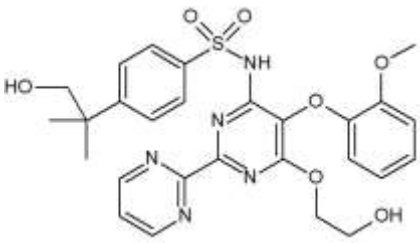


Bosentan



Hydroxybosentan

Bosentan is a drug used in the treatment of pulmonary arterial hypertension. Evaluation of bosentan pharmacokinetics is an important step of the drug development. The aim of our study was to evaluate bioanalytical method reliability by assessing the influence of metabolite on the determination of bosentan in human plasma.

In human body, bosentan is converted to three metabolites. Hydroxybosentan is an only pharmacologically active metabolite and its maximum concentration in plasma reaches 5-8% of the bosentan's maximum concentration [1]. Hydroxybosentan's elimination half-life was reported to be very similar to that of bosentan (5-6 h) [1,2] or slightly greater (6-14 h) [3]. It was observed that times to reach the maximum concentrations are similar for both compounds [1-3].

Combination of high-performance liquid chromatography with UV-Vis detection and liquid-liquid extraction enabled to was determine bosentan in human plasma in the range of 50-4000 $ng \cdot mL^{-1}$. During the method validation, metabolite back-conversion was studied using human plasma samples spkied with hydroxybosentan to obtain concentration of 500 $ng \cdot mL^{-1}$. Additionally, the influence of metabolite on extraction of bosentan and the internal standard was assessed.

We found that there was no influence of metabolite on determination of bosentan in developed bioanalytical method. The method was validated according to European Medicines Agency (*EMA*) [4, 5] and Food and Drug Administration (*FDA*) [6] guidelines, in compliance with the principles of Good Laboratory Practice (*GLP*). All of the validation parameters met acceptance criteria what confirmed method's reliability.

Reference:

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The form of presentation proposed by the Author:
Poster

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