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Preparative separation of nadolol racemates by fixed-bed liquid chromatography using C18 columns

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Nadolol is a non-selective beta-adrenergic antagonist pharmaceutical drug. This class of pharmaceutical drugs is prescribed mainly, to treat arrhythmias, angina pectoris, hypertension, migraine disorders and for tremor. Nadolol drug is still marketed as a mixture of equal amounts of four stereoisomers. Some authors refer that this fact could be related to some severe risks, such as depression, insomnia, cardiovascular failure among others [1].

An extensive set of experimental results for the separation of nadolol racemates using different achiral C18 columns, such as, XBridge, XBridge Shield RP18, XSelect CSH will be presented: Screening of mobile phase composition, solubility of nadolol racemates using different pure solvents and solvent mixtures, pulses under analytical and preparative conditions, equilibrium adsorption isotherms and breakthrough measurements. Additionally, experimental results will include the preparative separation by fixed-bed chromatography using an Azura Prep LC unit equipped with two 250 mL/min pump heads and a XBridge Prep OBD C18 10 μ m (250x30 mm) column with a 10 μ m particle size diameter [2].

Experimental results presented in this work will stress the advantage of using an intermediate step based on achiral reversed-phase liquid chromatography to perform the separation of the two racemates of nadolol. After this preparative pseudo-binary separation, two binary separations of the two racemates must be performed using a chiral stationary phase, such as Chiralpak IA to achieve the complete separation of all the four stereoisomers of nadolol. These two final preparative separations can be carried out using both fixed-bed or simulated moving bed technologies.

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