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Title

Máximum 2

Design of a liquid-liquid extraction platform for the resolution of chiral pharmaceuticals

Abstract Body

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Enantiomers have different pharmacological properties, which can hinder the treatment of pathologies using racemic drugs. Racemates represent around 90 % of the commercialized chiral drugs, raising concerns by the FDA (Food and Drug Administration of United States) and EMA (European Medicines Agency). Therefore, the commercialization of the therapeutically active isomer should be preferential. Obtaining the pure enantiomer relies on direct synthesis or resolution of the existing racemates. Resolution is often considered a simpler and cheaper alternative. Enantioselective liquid-liquid extraction (LLE) is a promising separation process that can be operated in a continuous mode. LLE are composed of two tunable immiscible phases that allow the optimization of enantioseparation by the addition of a chiral selector, which is responsible for the chiral recognition. If the two immiscible phases are composed mainly of water, then the system is an aqueous biphasic system (ABS). Since the majority component of ABS is water, they are considered green, economical and reliable systems. A major advantage of LLE is that it can comprise both enantiomeric recognition and solvent extraction on a single technique. Ionic liquids are alternative solvents with great structural diversity, allowing the design of task-specific solvents, including chiral ionic liquids (CILs). The introduction of CILs in LLE may contribute to high performant extraction/separation systems. Another promising class of green chiral selectors is the tartaric acid esters family which in conjugation with boric acid appear as promising adjuvants for the LLE systems. In this work, two different approaches were explored for the purification of propranolol enantiomers using LLE and ABS. In the first one, CILs and tartaric acid esters were used in LLE systems as chiral selectors, and in the second one, CILs and tartaric acid esters were used as chiral selectors in polymer-polymer-based ABS. The best outcome was scaled-up resorting to centrifugal partition chromatography (CPC).

Images and Tables

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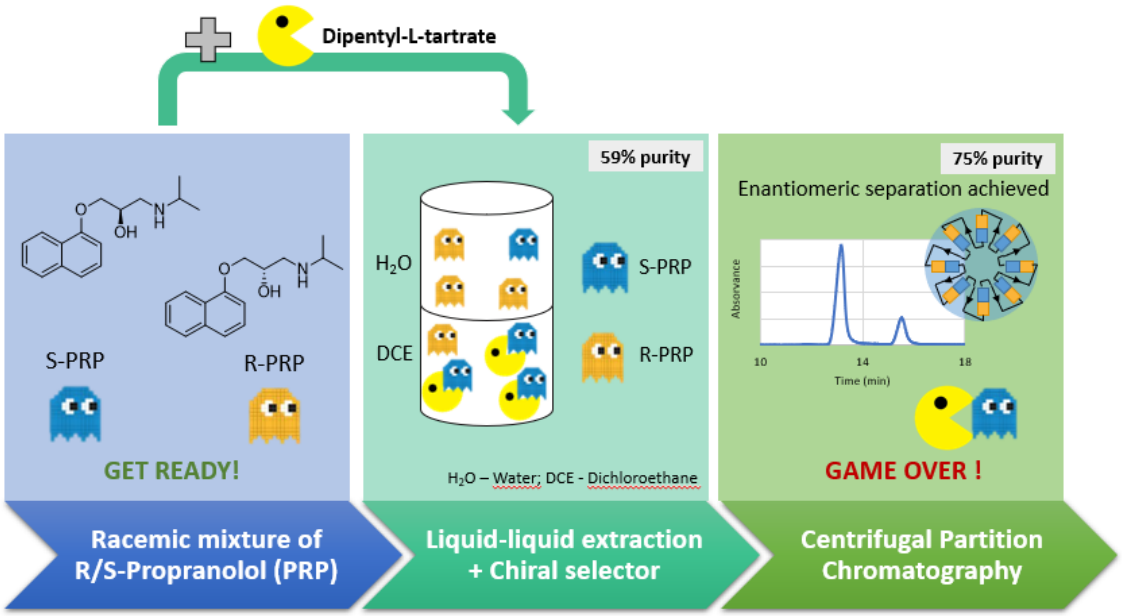

Figure 1. Schematic representation of the developed liquid-liquid extraction platform.

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