

TITLE: Aqueous biphasic systems as chiral purification platform

AUTHORS: Ferreira, A.M.; Carreira, A.R.F.; Sintra, T.E.; Coutinho, J.A.P.

INSTITUTION: CICECO – Aveiro Institute of Materials, Chemistry Department, University of Aveiro, Portugal

ABSTRACT:

The differences in the pharmacological activities of enantiomers may result in serious problems in the treatment of diseases using racemates. Even when a drug is commercialized as a racemate, both FDA (Food and Drug Administration of United States) and EMA (European Medicines Agency) possess restricted guidelines, being mandatory to perform a complete pharmacological and toxicological characterization of both enantiomers and racemate. Indeed, the commercialization of the therapeutically active isomer should be prioritized. Considering the increased difficulty in the production of pure enantiomers by direct synthesis, the synthesis of racemates followed by their chiral resolution is a simpler, more flexible and cheaper alternative. Aqueous biphasic systems (ABS) appear as interesting candidates to turn enantioseparations since several processing steps can be combined into a single operation, allowing continuous operation and showing to be a low-cost process [2]. Furthermore, ABS are composed of two immiscible aqueous-rich phases, valuable when dealing with biologically active compounds [2]. Ionic liquids are alternative solvents with an enormous degree of structural diversity, allowing the design of task-specific solvents and, by their introduction in ABS, of highly performant extraction/separation approaches. The chiral ionic liquids (CILs) could be seen as a potential alternative to tailor the selectivity aiming at increasing the enantiomers purification. In this work two different approaches were investigated for the purification of propranolol enantiomers using ABS. More specifically, in the first one, CILs were used as phase component of the ABS and as a selector chiral, and in the second one, CILs were used as selector chiral in polymer-polymer-based ABS. Moreover, to improve the purification yield, several operational parameters, such as pH, temperature and tie-line length (TLL) were optimized through a factorial design of experiments.

BIBLIOGRAPHY

[1] B. Schuur, B.J.V. Verkuil, A.J. Minnaard, J.G. de-Vries, H J. Heeres, B.L. Feringa, *Org. Biomol. Chem.*, 2011,9, 36-51.

[2] M.G. Freire, A.F. Cláudio, J.M. Araujo, J.A. Coutinho, I.M. Marrucho, J.N. Canongia Lopes, L.P. Rebelo, *Chem. Soc. Rev.* 2012, 41, 4966-95.

Keywords: Chiral ionic liquids, aqueous biphasic systems, enantiomer separation, propranolol

Development Agency: This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, FCT Ref. UID/CTM/50011/2019, financed by national funds through the FCT/MCTES. This work was also financially supported by the project POCI-01-0145-FEDER-030750 (PTDC/EQU-EPQ/30750/2017)- funded by FEDER, through COMPETE2020 - Programa Operacional Competitividade e Internacionalização (POCI), and by national funds (OE), through FCT/MCTES.