

Purification of antileukemic drugs through silica-based supported ionic liquids

Mafalda R. Almeida¹, Maria Miguel Albuquerque¹, Carolina Job Carvalho¹, Rui M. F. Bento¹, João C. F. Nunes¹, Márcia C. Neves¹, Valéria C. Santos-Ebinuma², Mara G. Freire¹, Ana P.M. Tavares¹

¹CICECO-Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, 3810-193 Aveiro

²Department of Engineering Bioprocess and Biotechnology, School of Pharmaceutical Sciences, UNESP-University Estadual Paulista, Araraquara, Brazil

L-asparaginase (LA) is an enzyme used as a biopharmaceutical for the treatment of acute lymphoblastic leukemia. LA can be produced via fermentation and its purification usually comprises several steps including precipitation, liquid-liquid extraction and chromatography techniques. Among these, ion exchange chromatography, which is often preceded by precipitation with salts as a first pre-chromatographic step, is the most used. However, these common strategies for protein purification result in low yields and purity, requiring long processing times, while leading to a consequent increase of the process costs. Therefore, the demand for new cost-effective production/purification processes play now a priority role.

This work aims the development of cost-effective technologies to purify LA from the complex fermentation medium from *Bacillus Subtilis*. Silica-based supported ionic liquids (SILs) are investigated as cost-effective purification materials for the target enzyme. The concentration of the extract from the fermentation, material/ extract from fermentation ratio and contact time effects in the purity and yield of LA were optimized. With this strategy, process costs, energy consumed, and waste generated, may be significantly decreased, which may lead to this biopharmaceutical price decrease and wider application.

Acknowledgements:

This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, UIDB/50011/2020 & UIDP/50011/2020, financed by national funds through

the Portuguese Foundation for Science and Technology/MCTES. This work was financially supported by POCI-01-0145-FEDER-031268- funded by FEDER, through COMPETE2020 - Programa Operacional Competitividade e Internacionalização (POCI), and by national funds (OE), through FCT/MCTES. João C. F. Nunes acknowledges SPQ and FCT for the PhD fellowship (SFRH/BD/150671/2020. M. C. Neves acknowledges the research contract CEECIND/00383/2017. A. P. M. Tavares acknowledges the FCT Investigator Programme and Exploratory Project (IF/01634/2015).