Title: Sustainable ionic-liquid-based strategies for the downstream processing of interferon α-2b from *Echerichia coli*

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Abtract: Over the last decades, society has been facing an increment of chronic diseases due to the higher human life expectancy and the lack of efficient treatments for several pathologies. In this regard, biopharmaceuticals have become one of the most effective clinical treatments for a broad range of diseases, including cancer, metabolic and neurodegenerative disorders [1]. Among biopharmaceuticals, the role of interferons, particularly interferon α-2b (IFNα-2b), should be underlined, as they have been marketed for over 30 years with a considerable impact on the global therapeutic proteins market [2]. Usually based on the recombinant DNA technology, the manufacturing process of biopharmaceuticals encompasses two main stages: the upstream and downstream stages. Typically, the upstream phase includes recombinant protein production processes in a suitable host microorganism, such as *Escherichia coli* [3], while the general downstream processing of biopharmaceuticals comprises four stages - recovery, isolation, purification and polishing -, which are responsible for the majority of the production costs of biopharmaceuticals (50–90%) [3]. The downstream processing is a time-consuming and multi-step process, for which the development of cost-effective purification processes is mandatory to decrease their costs and environmental impact. In this context, two ionic-liquid-(IL)-based strategies were investigated in this work for the purification of IFNα-2b recombinantly produced from *E. coli* fermentation broth. ILs have been used as adjuvants in aqueous two-phase systems (ATPS) and applied in supported materials as alternative ligands. The obtained results demonstrate that ILs have a tailoring ability and contribute to the development of more effective and sustainable downstream processes of biopharmaceuticals.

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Acknowledgements: The authors acknowledge the funding by FEDER through COMPETE 2020 – Programa Operacional Competitividade e Internacionalização (POCI), and by national funds (OE), through FCT/MCTES from the project "IL2BioPro" – PTDC/BII-BBF/30840/2017. This work was developed within the scope of the project CICECO – Aveiro Institute of Materials, UIDB/50011/2020 & UIDP/50011/2020, and CEMMPRE project UID/EMS/00285/2020, financed by national funds through FCT/MCTES and when appropriate co-financed by FEDER under the PT2020 Partnership Agreement. Márcia C. Neves acknowledges the research contract CEECIND/00383/2017, and Leonor S. Castro acknowledges FCT for her Ph.D. grant 2020/05090/BD.