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# Ionic Liquids-Polymer Nanoparticle Systems as Breakthrough Tools to Improve the Leprosy Treatment

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**Abstract :** The Mycobacterium leprae causes a chronic and infectious disease called leprosy, which the most common symptoms are peripheral neuropathy and deformation of several parts of the body. The pharmacological treatment of leprosy is a combined therapy with three different drugs, rifampicin, clofazimine, and dapsone. However, clofazimine and dapsone have poor solubility in water and also low bioavailability. Thus, it is crucial to develop strategies to overcome such drawbacks. The use of ionic liquids (ILs) may be a strategy to overcome the low solubility since they have been used as solubility promoters. ILs are salts, liquid below 100 ºC or even at room temperature, that may be placed in water, oils or hydroalcoholic solutions. Another approach may be the encapsulation of drugs into polymeric nanoparticles, which improves their bioavailability. In this study, two different classes of ILs were used, the imidazole- and the choline-based ionic liquids, as solubility enhancers of the poorly soluble antileprotic drugs. Thus, after the solubility studies, it was developed IL-PLGA nanoparticles hybrid systems to deliver such drugs. First of all, the solubility studies of clofazimine and dapsone were performed in water and in water: IL mixtures, at ILs concentrations where cell viability is maintained, at room temperature for 72 hours. For both drugs, it was observed an improvement on the drug solubility and [Cho][Phe] showed to be the best solubility enhancer, especially for clofazimine, where it was observed a 10-fold improvement. Later, it was produced nanoparticles, with a polymeric matrix of poly(lactic-co-glycolic acid) (PLGA) 75:25, by a modified solvent-evaporation W/O/W double emulsion technique in the presence of [Cho][Phe]. Thus, the inner phase was an aqueous solution of 0.2 % (v/v) of the above IL with each drug to its maximum solubility determined on the previous study. After the production, the nanosystem hybrid was physicochemically characterized. The produced nanoparticles had a diameter of around 580 nm and 640 nm, for clofazimine and dapsone, respectively. Regarding the polydispersity index, it was in agreement of the recommended value of this parameter for drug delivery systems (around 0.3). The association efficiency (AE) of the developed hybrid nanosystems demonstrated promising AE values for both drugs, given their low solubility (64.0 ± 4.0 % for clofazimine and 58.6 ± 10.0 % for dapsone), that prospects the capacity of these delivery systems to enhance the bioavailability and loading of clofazimine and dapsone. Overall, the study achievement may signify an upgrading of the patient's quality of life, since it may mean a change in the therapeutic scheme, not requiring doses of drug so high to obtain a therapeutic effect. The authors would like to thank Fundação para a Ciência e a Tecnologia, Portugal (FCT/MCTES (PIDDAC), UID/DTP/04567/2016-CBIOS/PRUID/BI2/2018).

**Keywords :** ionic liquids, ionic liquids-PLGA nanoparticles hybrid systems, leprosy treatment, solubility
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