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Ionic and Aerogel Levothyroxine Formulations with Improved Bioavailability Properties †

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Abstract: Thyroid diseases affect a considerable portion of the population being hypothyroidism one of the most commonly reported[1]. Levothyroxine (T4) is used clinically to treat hypothyroidism, however, the narrow therapeutic index of this drug, the need for a frequent administration and the influence of gastrointestinal diseases, foods and other drugs on its absorption are the shortcomings related with oral administration of T4.[2] There are several approaches to enhance the drug solubility and bioavailability such as particle size reduction, nanosuspension, use of surfactants, salt formation, solid dispersion, among others[3]. In this work, an attempt to improve T4 solubility through the synthesis of T4 salts based on Organic Salts and Ionic Liquids (OSILs) and on its dispersion into biocompatible aerogels matrixes, is made. OSILs based on pharmaceutical drugs (API-OSILs) is a class of salts with promissory therapeutic properties.[4] Herein, T4 was used as anion in combination with choline and 1-ethanol-3-methylimidazolium [C2OHMIM] cations. All compounds were characterized by 1H- and 13C-NMR, FTIR and elemental analysis in order to confirm their structures and purity levels. Aerogels are a special class of nanoporous materials with growing application in the biomedical and pharmaceutical fields due to their open pore structure and high surface area capable of active adsorption and releasing desired compounds.[5] The use of polysaccharides for the synthesis of aerogel matrices has additional benefits such as biodegradability and biocompatibility, which make them, promising as encapsulation and delivery systems of drug.[5] In this work, composite aerogels based on locust bean gum and κ-carrageenan were used as T4 carriers and delivery studies performed allowing for the determination of the drug solubility. The water and serum solubility of the prepared T4-OSILs as well as the thermal analysis through differential scanning calorimetry (DSC) studies, have been carried out and also compared with original T4 drug. The poor water-soluble pharmaceutical drug T4 was loaded into the aerogel matrixes and the composites were characterized by attenuated total reflectance-Fourier transform infrared spectroscopy (ATR-FTIR) and by DSC; the results were compared with the original T4 drug. Release experiments were performed at physiologic pH using a phosphate buffer solution at pH 7.2.

Keywords: levothyroxine (T4); API-OSILs; aerogels; solubility studies; thermal studies

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