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Abstract

Ionic and Aerogel Levothyroxine Formulations with Improved Bioavailability Properties †

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Thyroid diseases affect a considerable portion of the population, with hypothyroidism being one of the most commonly reported thyroid diseases [1]. Levothyroxine (T4) is clinically used to treat hypothyroidism; however, the narrow therapeutic index of this drug, the need for frequent administration, and the influence of gastrointestinal diseases, foods and other drugs on its absorption represent shortcomings related to the oral administration of T4 [2–8]. There are several approaches to enhancing the drug solubility and bioavailability, such as particle size reduction, nanosuspension, the use of surfactants, salt formation, and solid dispersion, among others [3]. In this work, an attempt to improve T4 solubility is made through the synthesis of T4 salts based on Ionic Liquids (ILs) and on T4's dispersion in biocompatible aerogel matrices. ILs based on pharmaceutical drugs (API-ILs) are a class of salts with promising therapeutic properties [4–6]. Herein, T4 was used as an 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 applications in the biomedical and pharmaceutical fields due to their open pore structure and high surface area capable of active adsorption and releasing desired compounds [7]. The use of polysaccharides for the synthesis of aerogel matrices has additional benefits such as biodegradability and biocompatibility, which make them promising drug encapsulation and delivery systems [7]. In this work, composite aerogels based on locust bean gum and κ-carrageenan were used as T4 carriers, and delivery studies were performed allowing for the determination of the drug solubility. The water and serum solubilities of the prepared T4-ILs were compared with the original T4 drug, as was the thermal analysis, which was carried out through differential scanning calorimetry (DSC) studies. The poorly water-soluble pharmaceutical drug T4 was loaded into the aerogel matrices 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.

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