ISGC 2019
May 13rd - 17th

N°500 / PC
TOPIC(s) : Alternative solvents

Tailoring the properties and bioavailability of the anti-tuberculosis drug isoniazid through green approaches

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PURPOSE OF THE ABSTRACT

In recent years, the relevance of green chemistry in biomedicine applications as well as for improvement of pharmaceutical formulations through the increase of drug properties and their bioavailability have been recognized. Alternative and sustainable approaches can contribute to tune the properties of the drugs and prevent polymorphism that could be associated to solid forms of drugs.

Tuberculosis is an infectious disease caused by mycobacterium tuberculosis complex. It is a disease that remains one of the top 10 causes of morbidity and mortality in worldwide and the World Health Organization estimated 10.4 million of new cases of tuberculosis, in 2016, and 1.7 million died from the disease.1-3 The treatment of the active stage of the disease involves the administration of a combination of prolonged regimens of anti-bacterial drugs, for example, isoniazid, ethambutol, pyrazinamide and rifampicin, that are used as first-line anti-tuberculosis drugs.2,3

In this context, it is important to develop and improve strategies that provide shorter drug regimens for preventing drug resistance and toxicity of the antimicrobials. For improving the bioavailability of anti-tuberculosis drugs, such as isoniazid, we firstly studied the possibility to protonate the original drug by suitable combination with biocompatible counter-ions based on alkylsulfonate and sugar-derivates. Some of these combinations can contribute to prepare salts and ionic liquids based on isoniazid. In parallel, we have been developed alternative solvents for therapeutic approaches related to tuberculosis, preparing eutectic mixtures where the active pharmaceutical ingredient (API) is incorporated form therapeutic deep eutectic solvents (THEDESs) 4,5

The chemical and thermal characterization of the THEDES and ionic liquids based on isoniazid have been performed. Nuclear magnetic resonance (1H and 13C NMR), differential scanning calorimetry (DSC), infrared spectroscopy and elemental analysis were used to evaluate the purity and chemical stability of each compound. The cytotoxicity was evaluated in Caco-2 cell line, comparing with the bioactive itself; solubility and permeability studies were also performed in phosphate buffered saline at 37ºC, to simulate physiological conditions. The knowledge of these properties presented by THEDESs and therapeutic ionic liquids are essential for further studies and evaluation of the performance of the drugs in bacteria, in order to improve therapeutic activity of the drugs in tuberculosis treatment.

Acknowledgements:
The research leading to these results has received funding from the European Union Horizon 2020 Program, granted through the project Des.solve (ERC Consolidator). ERC-2016-CoG 725034 and by the Associate Laboratory for Green Chemistry-LAQV which is financed by national funds from FCT/MCTES (UID/QUI/50006/2013).

FIGURES

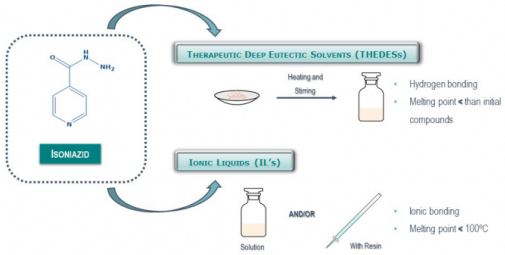

FIGURE 1

Figure 1

Different approaches for preparing THEDES and ionic liquids with isoniazid.

FIGURE 2

KEYWORDS

Therapeutic deep eutectic solvents | ionic liquids | isoniazid

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