Repurposing conventional antimycobacterial drugs using ionic liquids

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Introduction

Nontuberculous mycobacteria, namely the species belonging to the Mycobacterium avium complex, are highly infectious opportunistic pathogens, which incidence is increasing worldwide. Treating these infections is challenging, due to long duration, high toxicity, and low effectiveness of available drugs. It is therefore urgent to find new therapeutic strategies, including the repurposing of old drugs. Ionic liquids (ILs) are organic salts made by the combination of two molecules with opposite polarities, which are gaining attention in drug development. Combining the right ions, it is possible to create ILs that could avoid polymorphism and solubility issues presented by solid conventional drugs, improving their absorption and desired dissolution rate. Besides increasing the bioavailability, the main goals when formulating a new IL is keeping or improving the bioactivity and cytotoxicity properties of the parental drug(s). The aim of our work is to evaluate the ability of ILs based on conventional antimycobacterial drugs, like clofazimine, aminosalicylic acid, and fluoroquinolones, to inhibit the viability and growth of M. avium in axenic culture and inside macrophages.

Results

Direct activity against mycobacteria

Toxicity against host cell

Activity against intracellular mycobacteria

The ILs maintain the same activity presented by the parental compounds

The ILs are not more toxic than the parental compounds

The ILs are more active than the parental compounds

Conclusions

Our results show that the ILs are like their parental compounds, both in terms of direct antimycobacterial activity and toxicity to the host cells. Moreover, against intracellular bacteria, the ILs are more active than their parental compounds when administered individually and equivalent to the combined administration of the parental compounds. Confirmation on better solubility and thermal stability profiles of the ILs will corroborate the potential of these new formulations as alternatives to conventional antimycobacterial drugs.

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