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IONIC LIQUIDS OF CIPROFLOXACIN

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ABSTRACT

Ciprofloxacin (1-cyclopropyl-6-fluoro-4-oxo-7-piperazin-1-yl-quinoline-3-carboxylic acid) is a quinolone antibiotic which is commonly prescribed for treatment of urinary tract infection due to its broad spectrum against bacteria. However, Ciprofloxacin (CIP) is categorized as a group IV compound of Biopharmaceutics Classification System (BCS) with a poor solubility and permeability, which therefore reduces the bioavailability of this drug. There are limited number of commercial pharmaceuticals of CIP at present. Among them, the most common one is formulated as hydrochloride salt in tablets. This salt demonstrated a higher solubility than the pure CIP, however, it was seen to incompletely dissolve in intestinal fluid, therefore partially limit the bioavailability of this antibiotic.

Ionic liquids (ILs) have been becoming an emerging research area over the last decades. ILs are defined at low melting salts with the melting point < 100 ^{o}C. The great advantage of ILs is their simple preparation with tunable physicochemical properties including solubility, permeability, stability, etc. Besides, the diversity of counterions which are utilized to generate ILs also offers a greater opportunity for ILs to be applied in pharmaceutics.

The molecular structure of CIP contains both carboxylic group and secondary amino group. However, salt formation of CIP mainly focuses on the amino group whereas there is little literature on carboxylic group – based salt forms of CIP. Therefore, the aim of this research is trying to prepare the ILs of CIP, considering its acidic and basic aspects by using various bases and acids.

A number of cationic and anionic counterions for CIP were screened in this work. Three methods of production were tested: dry grinding, metathesis and cooling crystallization. The resulting compounds were assessed by differential scanning calorimetry (DSC), powder X-ray diffraction (PXRD) and Fourier transform infrared spectroscopy (FTIR). No new ionic phase was identified when CIP was co-processed with cationic counterions. In relation to monocarboxylic acids, only propionic acid resulted in a new phase, which may be classified as an IL, however this new phase was thermally unstable. A number of salts was obtained when CIP was reacted with dicarboxylic acids and these new salts were seen to have different solid state properties when subjected to dehydration.

Overall, while this project showed that CIP easily form salts with dicarboxylic acids but a limited potential to form ILs with cationic counterions and monocarboxylic acids.

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List of Abbreviations and Symbols

CIP	Ciprofloxacin
2θ	2 theta (diffraction angle)
C3	Propionic acid
C4	Butyric acid
C5	Valeric acid
C6	Hexanoic acid
C7	Heptanoic acid
C8	Caprylic acid
C10	Capric acid
DDAB	Didecyldimethylammonium bromide
Bz.HCl	Benzalkonium hydrochloride
DSC	Differential Scanning Calorimetry
PXRD	Powder X-ray Diffraction
FTIR	Fourier Transform Infrared Spectroscopy
ILs	Ionic liquids
API	Active pharmaceutical ingredient
DCM	Dichloromethane
TGA	Thermal gravimetric analysis

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