In Vitro Antimicrobial Studies of Mesoporous Silica Nanoparticles Comprising Ciprofloxacin Organic Salts

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Infectious diseases are the second major cause of death globally with antibiotic treatments often failing due to drug resistance or insufficient antibiotic activity at the infection site.[1] Mesoporous silica nanoparticles (MSNs) combined with active pharmaceutical ingredients in the form of ionic liquids or organic salts (API-OSILs) offer a promising approach to treating bacterial infections enhancing solubility, bioavailability and reducing polymorphism.[2,3]

Herein, we report a synthetic method to obtain three different sets of nanomaterials, based on the immobilization of fluoroquinolones as counter-ions of cholinium, 3-picolinium and methylimidazolium materials by synthesis of ionic liquids functionalized with a propyltriethoxysilane moiety, which is then grafted on the surface of the MSN. These materials underwent ionic exchange to immobilize antibiotic ciprofloxacin with cholinium, picolinium and imidazolium cations and API-OSILs based on the combination of ciprofloxacin with the cations were also prepared and characterized for comparison. A system consisting of those API-OSILs adsorbed onto the MSNs was also prepared and tested.

Antimicrobial studies against various sensitive and resistant strains including gram-negative *K. pneumoniae* and gram-positive *Enterococcus spp.*, and against sensitive strains of *S. Aureus* and *E. Coli* show that all antibiotic-functionalized materials outperformed free ciprofloxacin in case of resistant species with some reducing the minimum inhibitory concentration (MIC) by 10-fold against resistant *K. pneumoniae* comparing to free ciprofloxacin. The models based on adsorbed API-OSILs demonstrated less activity but were still able to outperform the unmodified ciprofloxacin. Surrogate toxicity studies in human cell lines demonstrated no toxicity of the materials.[4]

All materials were characterized by NMR spectroscopy, FT-IR, elemental analysis, X-ray powder diffraction and N_2 adsorption at 77 K. This method can be extended to engulf a broader range of antimicrobials and ionic liquid combinations, offering a very attractive alternative to the production of novel pharmaceutical ingredients immobilized on nanoparticles and leading to more active formulations, smaller doses and fewer side effects.[5]

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