

SUMMARY OF DOCTORAL DISSERTATION

Designing co-delivery drug systems based on graft copolymer carriers prepared from
biofunctionalized monomeric ionic liquids

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The innovative ionic graft polymers were designed as a carriers for antibacterial drug delivery. The presented systems are derived from choline-based monomeric ionic liquids (MILs) containing pharmaceutical anions.

The preparation of biofunctionalized MIL involved the introduction of pharmaceutical anions by exchange of anion in the [2-(methacryloyloxy)ethyl]trimethylammonium chloride (TMAMA). Drug anions selected for this study are: fusidate (FUS), cloxacillin (CLX), ampicillin (AMP), *p*-aminosalicylate (PAS), piperacillin (PIP), tazobactam (TAZ), ibuprofen (IBU), diclofenac (DIC), naproxen (NAP), nalidixic (NAL), valproate (VPA), cholic (CHA), and aspartic (APT). Successfully biofunctionalized MILs (TMAMA/FUS, TMAMA/CLX, TMAMA/AMP, TMAMA/PAS, TMAMA/PIP, TMAMA/TAZ, TMAMA/DIC, TMAMA/IBU, and TMAMA/VPA) were subsequently copolymerized with methyl methacrylate via controlled atom transfer radical polymerization (ATRP) by *grafting from* multifunctional macroinitiator. This generated the well-defined graft copolymers with polymerized ionic liquids (PILs) in side chains defined as ionic graft polymer-drug conjugates. However, the polymerizations of TMAMA modified with FUS, CLX, AMP, PAS and PIP were successful. The grafting degree of side chains was defined by macroinitiator, and the length of side chains was adjusted during polymerization to develop polymer conjugates with precisely tailored structural parameters and drug contents.

Besides single drug delivery systems, the carriers for combination therapies were designed in analogous manner. This involved copolymerization of two biomodified MILs with different pharmaceutical anions. The obtained dual-drug conjugates contained FUS-CLX and AMP-CLX drug anion pairs. During self-assembly of amphiphilic PAS-conjugates into micellar structures, isoniazid (ISO) was encapsulated to produce another type of co-delivery systems. Furthermore, ion exchange was conducted on PIP-conjugates to introduce tazobactam (TAZ) ions. Consequently another type of dual-drug conjugates carrying PIP-TAZ anions were generated.

The drug release behavior evaluated *in vitro* typically demonstrated initial burst release phase, followed by a sustained release lasting up to 72 hours. The kinetic of drug release was influenced by the chemical nature of the drugs and the structure of polymer matrix. Overall, the designed choline-based polymer systems indicated high drug-loading capacities and effective encapsulation, underscoring their potential as advanced carriers for antibacterial therapy, including drug co-delivery in combined therapy.