

Amphiphilic polymers with self-assembly abilities reach nanoparticle sizes, which are attractive to play the role of carriers in controlled and "intelligent" drug delivery systems. Most drugs are insoluble in aqueous solutions, and the use of a polymeric carrier improves the drug's solubility and its efficient transport through the cell membrane allowing for effective uptake and biodistribution in the body. Macromolecules in such systems protect against the accumulation of too high a concentration of a drug in the blood that can cause serious side effects. The carrier designing consists in obtaining a polymer with a specific structure that allows the drug to be released at a controlled rate.

One of the methods of chemotherapy is combination therapy with two or more drugs used as "conventional drug cocktails", which are commonly used in anti-cancer therapy. On the other hand, with respect to polymeric carriers, the strategy of combining drugs in one polymer matrix is the latest trend in drug delivery studies, which requires the achievement of basic knowledge about the co-releasing and interaction of bioactive compounds.

The project proposes the preparation of double-bioactive systems based on ionic graft polymers, which contain pharmaceutical anions with antibacterial activities. The ionic liquid is chosen as a monomer, i.e. 2-[(methacryloyloxy)ethyl]trimethylammonium chloride (ester derivative of choline), which will be polymerized according to a controlled radical mechanism by grafting technique using a multifunctional macroinitiator. Exchange of chloride anion on pharmaceutical one (acetylsalicylate, piperacillin, fusidate, clavulanate, cloxacillin, *p*-aminosalicylate) is a convenient way of introducing a biological activity that will be doubled by drug encapsulation through a polymer with a pharmaceutical anions (piperacillin/tazobactam, fusidate/rifampicin, fusidate/clindamycine, clavulanate/amoxicillin, *p*-aminosalicylate/isoniazid) or copolymerization of two monomers differing in pharmaceutical anion (fusidate/cloxacillin). The choice of pharmaceuticals (antibiotics, anti-tuberculosis drugs) is targeted for bacterial diseases of modern civilization, i.e. pneumonia or tuberculosis (caused by *Streptococcus pneumonia*, *Mycobacterium tuberculosis*), whereas their ineffective treatment can lead to chronic state, and then to the development of cancer.

Interdisciplinary studies involve the design, synthesis and biochemical characterization of polymer carriers, i.e. systems that combine two types of pharmaceutical anions and a pharmaceutical anion in combination with an encapsulated drug. It is expected that the proposed graft copolymers should store a greater amount of bioactive substance compared to linear polymers without exceeding the toxicity threshold as the therapeutic process begins only after their gradual release by diffusion. It is assumed that the encapsulated drug will be released at a higher rate because of their physical interaction with the matrix, which should be weaker than the ionic bonds maintaining the bioanions in the polymer structure. The release of the bioanions based on the exchange generated by the salts in the medium imitating physiological fluid should be slower because of the ionized form, but their absorption will be more effective in acidic than alkaline environments. The rate of co-release may also be depended on polymer structure (degree of grafting, content of ionic units corresponding to the distribution of charges) and interactions between bioactive molecules.

New systems obtained within the project after defining basic correlations structure vs. release and the biological studies on the selected bacterial strains and cell lines (assays of mutagenicity, cytotoxicity, genotoxicity, proinflammatory cytokine activities, oxidative stress) can be used as universal models for further development of potential dual-active systems for combination therapy.