Research activities

Mucoadhesive materials and drug delivery systems

Mucoadhesion is defined as interfacial force interactions between synthetic or natural polymeric materials serving as a dosage form and a mucus layer that covers a mucosal tissue. In the last two decades mucoadhesive polymers have received considerable attention as platforms for controlled delivery due to their ability to prolong the residence time of dosage forms as well as to enhance drug bioavailability. Our current research efforts are focused on evaluation of mucoadhesive properties of various materials and development of systems for transmucosal drug delivery.

Fig.1. Testing mucoadhesive properties of tablets using texture analyser
Recent publications on mucoadhesion and transmucosal drug delivery:

- Brannigan R.P., Khutoryanskiy V.V.* Synthesis and evaluation of mucoadhesive acryloyl-quaternized PDMAEMA nanogels for ocular drug delivery, Colloids and Surfaces B: Biointerfaces, 155, 538-543 (2017)
Polymeric hydrogels

Hydrogels are three-dimensionally cross-linked networks of hydrophilic polymers. The unique ability of hydrogels to swell in water and living tissue-like consistency make them significant candidates for developing various biomaterials and dosage forms. The applications of hydrogels in biomedical and pharmaceutical sciences include soft contact lenses, drug delivery systems, and wound dressings. Our research is focused on design of novel hydrogels, characterisation of their structure and properties and application in drug delivery and tissue engineering.

Recent publications on hydrogels:

- Caló E., de Barros J.M.S., Ballamy L., Khutoryanskiy V.V.* Poly (vinyl alcohol)-Gantrez® AN cryogels for wound care applications, RSC Advances, 6, 105487 -105494 (2016)
- Caló E., de Barros J.M.S., Fernández-Gutiérrez M., San Román J., Ballamy L., Khutoryanskiy V.V.* Antimicrobial hydrogels based on autoclaved poly(vinyl alcohol) and poly(methyl vinyl ether-alt-maleic anhydride) mixtures for wound care applications, RSC Advances, 6, 55211-55219 (2016)

Stimuli-responsive polymers and in situ gelling systems

Stimuli-responsive polymers are materials that undergo phase transitions in response to small changes in their environment. The environmental stimulation can be achieved by changes in temperature, solution pH, ion concentration, electric field, solvent composition and light.

*Fig.2. Different hydrogel samples based on copolymers of 2-hydroxyethylmethacrylate – 2-hydroxyethylacrylate*
Fig. 3. Phase-separation in an aqueous solution of a temperature-responsive polymer

Polymers, which aqueous solutions exhibit sol-gel transitions, triggered by insignificant changes in environment, can be used for development of in situ gelling drug delivery systems. These systems exist as free-flowing liquid formulations and undergo phase transition (gelation) upon administration into the human body. Our current research is focused on the development of polymers, which gelation can be triggered by changes in temperature and solution pH.

Fig. 4. Gelation of aqueous dispersion of a polymer caused by changes of environment

Recent publications on stimuli-responsive polymers:

Nanomaterials for drug delivery

Polymeric micelles and nanoparticles have been extensively used for formulation of poorly-soluble drugs and biopharmaceutical products. We are interested in the development and characterisation of novel polymer colloids by self-assembling of amphiphilic and complex-forming polymers.

![Fig.5. Polymeric nanoparticles formed by complexation between poly(acrylic acid) and methylcellulose in aqueous solutions](image)

We are also interested in the synthesis of novel well-defined nanoparticles for their application in encapsulation technologies and drug delivery. We are looking into the surface-functionalised nanoparticles (thiolated and PEGylated nanoparticles) and how surface functionality affects their interaction with biological tissues and diffusion through various physiological barriers.

![Fig.6. Novel organosilica nanoparticles](image)

Recent publications on nanomaterials:

Multilayered self-assembly and coatings

Layer-by-layer (LBL) sequential adsorption of polymers on solid surfaces is a simple and versatile technique for producing ultrathin polymeric films and coatings. The LBL approach involves an alternating immersion of solid substrates (planar or spherical surfaces) in solutions of interacting polymers resulting in formation of insoluble multilayered polycomplex film, which thickness may be precisely controlled by a number of deposition cycles. The LBL methodology was demonstrated to be useful for encapsulation of drugs, biomacromolecules and living cells, development of solid state electrolytes, ultrathin hydrogel membranes, and coating of surfaces. We are focusing our current research on developing novel multilayered materials by utilising LBL assembly driven by interpolymer hydrogen bonding.

**Fig.7.** Multilayered self-assembly on the surface of glass-slides

Recent publications on multilayered assembly and coatings:

- Khutoryanskaia O.V., Williams A.C., Khutoryanskiy V.V. pH-mediated interactions between poly(acrylic acid) and methylcellulose in the formation of ultrathin multilayered hydrogels and spherical nanoparticles, Macromolecules, 40, 7707-7713 (2007).
Ocular drug delivery and biomaterials

Ocular diseases affect the quality of life of millions of people worldwide. Currently there are about 314 million of visually impaired people with 45 million of them being completely blind. A further growth in the incidence of ophthalmic conditions is expected with the aging population. The leading causes of chronic blindness include cataract, glaucoma, age-related macular degeneration, corneal opacities, diabetic retinopathy, trachoma, and eye conditions in children. The eye is becoming increasingly important target for drug delivery with an urgent need in further advances in ocular therapy. Our research efforts are focused on novel drug delivery systems for ocular drug delivery, development of strategies to enhance drug permeability through the cornea and design of novel ocular biomaterials.

Fig.8. Bovine eye (a), bovine cornea (b) and diffusion Franz cell experiments with bovine cornea to assess drug permeability (c)

Recent publications on ocular drug delivery and biomaterials

- Kandzija N., Khutoryanskiy V.V.* Delivery of riboflavin-5'-monophosphate into the cornea: can liposomes provide any enhancement effects? J. Pharm. Sci., 106, 3041–3049 (2017)
- Brannigan R.P., Khutoryanskiy V.V.* Synthesis and evaluation of mucoadhesive acryloyl-quaternized PDMAEMA nanogels for ocular drug delivery, Colloids and Surfaces B: Biointerfaces, 155, 538-543 (2017)
Encapsulation of living cells into polymer matrices

Incorporation of living cells into the polymeric matrices is of significant interest of researchers because of the number of potential applications. Encapsulation of probiotic bacteria can improve their storage stability and survival during the passage through the gastrointestinal tract. Polymers can also serve as scaffolds for promoting stem cell storage, growth and differentiation towards the formation of tissues that could be used in regenerative medicine. In collaboration with food researchers and cell biologists we are developing novel approaches for microencapsulation of probiotic bacteria and materials used as substrates for stem cells transportation, storage and delivery.

Fig.9. Alginate microcapsule coated with fluorescently-labelled chitosan

Recent publications on encapsulation of living cells

- Cook M.T., Tzortsis G., Charalampopoulos D.*, Khutoryanskiy V.V.* Microencapsulation of a synbiotic into PLGA/alginate multiparticulate gels, Int. J. Pharm., 466 (1), 400-408 (2014)
- Cook M., Tzortzis G., Charalampopoulos D., Khutoryanskiy V.V. Production and Evaluation of Dry Alginate - Chitosan Microcapsules as an Enteric Delivery Vehicle for Probiotic Bacteria, Biomacromolecules, 12, 2834–2840 (2011)