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 investigation of molecular interactions of these materials with mucins.

![Image of testing mucoadhesive properties of tablets using texture analyser](image1.png)

**Fig.1.** Testing mucoadhesive properties of tablets using texture analyser
Recent publications on mucoadhesion and mucoadhesive polymers:


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:


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.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 \textit{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.

![Change in environment](image)

\textbf{Fig.4.} Gelation of aqueous dispersion of a polymer caused by changes of environment

\textbf{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.

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

**Fig.5.** Polymeric nanoparticles formed by complexation between poly(acrylic acid) and methylcellulose in aqueous solutions

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.

![Novel organosilica nanoparticles](image)

**Fig.6.** Novel organosilica nanoparticles

**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](image)
Recent publications on multilayered assembly and coatings:


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.
Recent publications on ocular drug delivery and biomaterials


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**

- Nualkaekul S., Lenton D., Cook M.T., Khutoryanskiy V.V., Charalampopoulos D. Chitosan coated alginate beads for the survival of microencapsulated Lactobacillus plantarum in pomegranate juice, *Carbohydrate Polymers*, 90, 1281-1287 (2012)
- Nualkaekul S., Cook M.T., Khutoryanskiy V.V., Charalampopoulos D. Influence of encapsulation and coating materials on the survival of Lactobacillus plantarum and Bifidobacterium longum in fruit juices, *Food Res. Int.*, 53, 304-311 (2013)

**Cationic polymers for gene delivery**

Many human diseases have a genetic origin and replacing defective genes with healthy substitutes offers an excellent approach for treatment. However the possibility of using DNA as a drug is still quite challenging because gene expression occurs only when DNA is transported inside the cell nucleus of the target cells. Cationic polymers can bind negatively charged DNA electrostatically and form compact particles known as *polyplexes*. Within the polyplex particles, DNA is protected from enzymatic degradation...
and can migrate into the cell nucleus. Our research efforts in this direction are concentrated on chemical modification of commercially-available and synthesis of novel cationic polymers and evaluation of their potential as vectors for gene delivery.

![Fig.10. Fluorescence of cells transfected with polyplexes formed by polyethyleneimine and GFP-expressing DNA plasmid.](image)

**Recent publications on cationic polymers for gene delivery:**


**Alternatives to animal experimentation**

Currently approximately 2.7 million animals are used in scientific procedures in the UK each year (Home Office data), under the regulation of The Animals (Scientific Procedures) Act 1986. According to this Act, the development of alternatives which Replace animal use, Reduce the number of animals used, or Refine the procedures involved to minimise suffering (3Rs principle) is an urgent need.

We are interested in development and evaluation of animal alternative approaches to test drug delivery systems. In particular, we are developing novel materials to mimic the properties of mucosal membranes which can be used as substrates for examining mucoadhesive properties of new polymeric dosage forms in place of animal tissues. Additionally, we apply the methodology reported by Adriaens et al (*Pharm. Res.*, 1999, 16, 1240-1244; *Pharm. Res.*, 2001, 18, 937-942) on the use of terrestrial slugs as “lower” organisms in assessment of biocompatibility of chemicals.
Recent publications on applications of 3Rs principles