

Popular science summary in English

Colorectal cancer is one of the most commonly diagnosed malignant tumors worldwide and remains a leading cause of cancer-related mortality. Despite advances in diagnostics and treatment, the effectiveness of current therapies—especially systemic chemotherapy—remains limited due to the lack of drug selectivity and the occurrence of severe side effects, which significantly reduce patients' quality of life. Many anticancer drugs are toxic to healthy tissues, and an additional challenge is the poor solubility of some active compounds in the aqueous environment of the body. Therefore, there is an urgent need to develop advanced drug delivery systems that enable targeted and controlled release of therapeutics directly at the tumor site while minimizing adverse effects.

The aim of this research project is to develop an innovative, two-level drug delivery system for the treatment of colorectal cancer. The proposed system consists of two complementary components: nanocapsules and hydrogel macrocapsules. The first level comprises nanocapsules fabricated using the layer-by-layer (LbL) method, which involves the alternate deposition of oppositely charged polyelectrolytes (e.g., poly(allylamine) and sodium hyaluronate) on a liquid-core template containing an oil phase. The core consists of a mixture of chloroform, the surfactant AOT, and a hydrophobic anticancer drug such as camptothecin or paclitaxel. This architecture allows for the efficient encapsulation of poorly water-soluble drugs and precise control over the carrier's properties, including drug release kinetics. The second level consists of hydrogel macrocapsules formed by crosslinking natural polysaccharides—sodium alginate or pectin—using calcium ions. The nanocapsules are embedded within the hydrogel matrix, providing additional mechanical and chemical protection. The hydrogel acts as a protective barrier that stabilizes the system in the acidic environment of the stomach and enables pH-responsive release of the drug in the colon, where conditions are more favorable for the action of cytotoxic compounds.

The planned research includes the physicochemical characterization of the nanocapsules (hydrodynamic diameter, polydispersity index, zeta potential, morphology via scanning electron microscopy), assessment of the internal structure of the macrocapsules and the distribution of nanocapsules within the hydrogel matrix (confocal and electron microscopy), *in vitro* drug release studies under conditions simulating the gastrointestinal environment (pH 2–7), thermal analysis of the hydrogel capsules (DSC), quantitative analysis of drug loading and release (UV-VIS, HPLC), and cytotoxicity tests (MTT assay) on colorectal cancer cell lines. These studies will allow for a comparison of the activity of the free drug, drug-loaded nanocapsules, empty nanocapsules, and the complete hydrogel formulation.

The most important expected outcome of the project is the development of a functional, selective, and safe drug delivery system capable of protecting the active substance in the gastrointestinal tract and enabling its controlled release in the colon. The use of natural, biocompatible materials enhances the system's translational potential and compatibility with the requirements of personalized medicine. This interdisciplinary project combines nanotechnology, materials chemistry, and bioengineering, aligning with global trends in the development of intelligent therapeutic systems. The results will provide a solid foundation for future biological studies, including *in vivo* testing, and will support the further advancement of modern, targeted cancer therapies.