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Programmed drug release via rolled-up biopolymer capsules

Project summary

The pharmacokinetics of many drugs, namely their resorption, distribution, metabolism and elimination depend on the hour of administration. As the consequence, these drugs are more effective and/or better tolerated if taken at appropriate time. Synchronization of drugs administration with the circadian cycle is not always possible or convenient. For instance, the anti-cancer drug 5-FU (5 Fluorouracile) should be taken at 4 a.m. to allow for a 50 percent improvement with respect to the non-chronomodulated treatment. Non-uniform distribution of medicaments in oral dosage forms (tablets or capsules) constitutes an advanced approach to programming of optimized diffusion-controlled drug release. However, creation of such systems with desired 3D-distribution of the drugs is a challenging issue. Within the framework of this research project, we propose a simple and cheap method to create biopolymer capsules with arbitrary complex spatial distributions of the drugs in them, and aim to explore the potential of the method for chronotherapies.

In vitro release kinetics of drugs (carbamazepine, ranitidine, heparin, nonsteroidal anti-inflammatory drugs (NSAIDs), 5-fluorouracil, lorazepam, synthetic anti-inflammatory glucocorticoid medications, like methylprednisolone, triamcinolone, and prednisolone) from the capsules immersed in the classical physiological media defined in the 9th European Pharmacopeia (phosphate buffers, etc) will be monitored by fluorimetry, pH-metry, and high performance liquid chromatography. The experimental research will be accompanied by theoretical Fourier-Bessel analysis and by random-walk simulation of the drug release processes from the capsules.

The method's potential for chronotherapy and chronopharmacology will be explored for drugs, known for their chronokinetics effects, on animal models. The *in vitro* and *in vivo* tests will be realized in accordance with the official EU and FDA guidelines. This project will have a significant impact on the materials engineering sector and on the health sector. When realized, the technology for time-programmed drug release can lead to considerable improvements in quality of life and the wellbeing of the patients (less of adverse and/or undesirable, toxic effects) who should take medicaments known for their chronopharmacokinetic properties. The new approach will also allow the patients with rare diseases to profit the advantages of chronomodulated therapies, and will bring new possibilities for personalized medicine.

The research is effectuated under the scientific supervision of V. Luchnikov (IS2M) and T. Vandamme (UNISTRA), in collaboration with R. Pedron, another PhD student, involved in the project, and the colleagues from IS2M and UNISTRA (C. Vaulot, L. Delmotte, T. Petithory, N. Anton, J. Wallyn).