

The search for new drugs includes basically two strategies. The first one is the synthesis of new chemical entities (NCEs) dedicated to a specific disease, whereas the second one is based on a search for new applications for active pharmaceutical ingredients (APIs), previously used in the pharmacotherapy of other diseases. The advantage of the latter strategy is usually a well-established safety profile of the drug demonstrated in a long-term clinical practice that considerably shortens the time necessary for the successful transfer of the concept to the clinic.

It is estimated that 40% of the drugs used in the pharmacotherapy are poorly soluble in water. Similarly, among NCEs developed as promising drug candidates even 90% are poorly soluble. It results in a high fall-out rate at early stages of the drug development when the dissolution of the compound in organic solvents, shows promising results *in vitro*, but finally fails *in vivo*, because the drug does not dissolve in the aqueous environment of the gastrointestinal tract, which is crucial for absorption. To face this problem, throughout the recent years, the supersaturated drug delivery systems (SDDS) have been proposed. They are able to present APIs to the intestinal milieu at concentrations above their equilibrium solubility, called supersaturation.

From technological point of view, it could be achieved by e.g. the reduction of particle size (micro- or nanonization), or dispersion of the drug in hydrophilic carriers. However, the large diversity of physicochemical properties of APIs, makes the selection of the right technology difficult. In addition, drug interactions with carriers, induced in technological processes, is often difficult to predict. It is therefore necessary to understand the mechanism responsible for the limited solubility of a particular active ingredient. For this purpose, the application of advanced, interdisciplinary analytical tools is needed. This is of particular importance when deciding on the further development of a new compound that has promising pharmacodynamic properties, but limited water solubility.

In the current project, it is assumed that the empirical base of knowledge created using the experience gained during research on improving the solubility of APIs with known properties, will facilitate the development of effective methods of solubility improvement for newly synthesized compounds. For this reason, APIs having potential new therapeutic indications, have been selected as models in this study. Their selection is also dictated by their relevance from a social point of view, such as the treatment of neurodegenerative diseases or the prevention of cancer. As far as the newly synthesized compounds are concerned, a candidate for a new anti-epileptic drug with a unique hybrid structure, intended for oral administration will be analysed. In this case, the improvement of solubility is to guarantee its absorption from the gastrointestinal tract. An attempt to increase the solubility of a new compound intended for topical application, with a view to developing a supersaturated system intended for topical sun protection, will be an additional aspect undertaken in the project. Interestingly, preparations of this kind in some countries are classified as OTC drugs (USA, Canada, Australia). In order to ensure effective photoprotection, the manufacturing process requires the dissolution of the organic UV filter in the components of the formulation in the highest possible concentration (e.g. supersaturated system), but after application its percutaneous absorption is undesirable due to safety reasons.

The supersaturated systems will be prepared using a new technology, i.e. nano spray drying, which enables the development of nanostructured carriers for active ingredients based on both hydrophilic polymers and lipids. Their assessment will include, among others studies on solubility, stability, absorption, and irritation. The analyses will be performed *in vitro* using physicochemical tools, compendial, biochemical tests, and research on cell lines.

Based on the project outcomes, an interdisciplinary knowledge base will be created, which in the future may facilitate *in silico* modelling, and development of new original therapies, despite the adverse physicochemical properties of the active ingredient. This will reduce the time it takes to develop new drugs, which can increase access to the latest treatments for all social groups.