SOLID-STATE CIRCULAR DICHROISM (CD) SPECTROSCOPIES AS A TOOL FOR SUPPORTING THE DEVELOPMENT OF MEDICINAL CHEMISTRY

Chirality is of prime importance in a wide range of Life Sciences since most of the basic compounds found in living organisms, from the simplest viruses to the most complex forms, are chiral. It means that they exist only in a single enantiomeric form among two or more viable options. Until recently most synthetic drugs have existed as racemate, *i.e.* equal amounts of *left*- and *right*-handed enantiomers of a chiral molecule. On the other hand, the chiral drugs from natural sources *e.g.* morphine, ephedrine, betulin, are in the form of a pure enantiomer. Nowadays, however, pharmaceutical companies put much effort into substitution of registered racemic mixture drugs with their enantiopure forms. This is because although the enantiomers have identical physical and chemical properties, they have different pharmacological profiles. Indeed, the spatial structure of drugs is one of the key elements determining their pharmaceutical effects, potency at the same receptor as well as rates and pathways of metabolic dispositions. Thus, one of the most important tasks of both modern organic chemistry and pharmaceutical industry is an unambiguous assignment of the spatial structure determining the chirality of the molecules. In the world of drugs, special attention is devoted to polymorphism phenomena. Despite polymorphs having an identical chemical composition, they are differing in bioavailability, solubility, chemical stability, and many other properties. Consequently, the polymorphic behaviour of each single active pharmaceutical ingredient (API) must be carefully investigated and all forms found must be precisely characterised.

Circular dichroism (CD) spectroscopies, both in the electronic and vibrational ranges, are one of the most sensitive tools for monitoring structural changes of chiral substances. Therefore, within this project, we will use and extend the applicability of these chiroptical methods towards their new applications in the field of analysis of chiral solid APIs. We will apply for the first time a **high-resolution vibrational circular dichroism (VCD*i*)** spectroscopy for stereochemical analysis having fundamental importance in drug chemistry and detailed descriptions of pills containing the same API but formulated by different pharmaceutical companies. Finally, we want to develop **diffused reflection circular dichroism (DRCD)** technique which may become a simple and convenient alternative to currently used ECD methodologies for probing chiral solids.

We believe that by using new strategies in solid-state CD spectroscopy, a more accurate characterisation of solid pharmaceuticals will be carried out. This will substantially contribute to a significant progress in the structure analysis of chiral drugs which play a significant role in the field of modern medical chemistry.