1) Final publishable Summary Report

With “CEREPep” (Crystal Engineering of Rare Earth containing Peptides) we have developed a new approach for the discovery of new crystalline materials in which peptides connected to each other by lanthanide complexes were to be synthesised and characterised.

The final scope of the project was to obtain rare earth containing metallopeptides with luminescent and magnetic properties which then would be targeted as model compounds for applications in medical and biochemical research (e.g. biological imaging, contrast agents, etc). A wide interdisciplinary campus was covered to produce and sufficiently analyse new materials for medicinal or biological chemistry.

Even though we were not able to meet this target and the formation of rare earth containing peptide could not be proven by analytical methods yet, the project brought new important and valuable structural insights into a whole class of anti-cancer drugs (taxanes) as well as the role of hydrogen bonding in stabilizing the 5'-deoxyadenosyl radical from coenzyme B12. Both outcomes were published in leading scientific journals.

One of the most significant results was that the crystal structures of anhydrous and hydrated paclitaxel and docetaxel, widely-used well-established antineoplastic agents for the treatment of a large variety of cancers, were obtained for the first time.

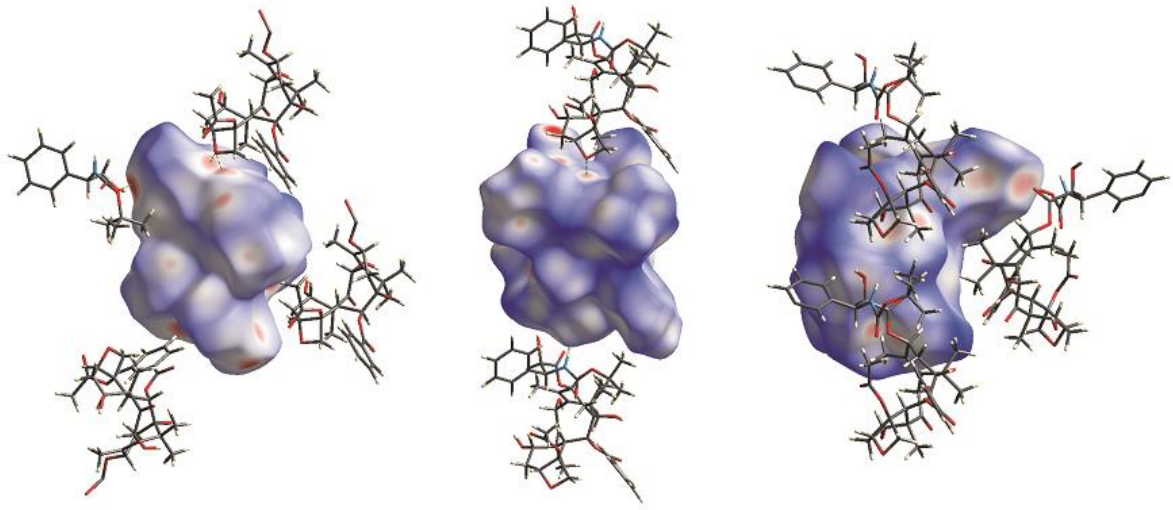

Figure 1. Hirshfeld surface of docetaxel trihydrate at 20°C (left), docetaxel trihydrate at 70°C (centre) and anhydrous docetaxel at 110°C.

Due to their poor solubility taxanes have to be administered intravenously in a formulation of surfactants and ethanol; both of which are biologically and pharmacologically active, giving rise to substantial clinical problems. The investigations of paclitaxel clearly showed the large influence of solvent inclusion on the crystal structure of taxanes; they provided valuable explanations for the difference in solubility between different solvates. Thus, crystal forms of taxanes with much better solubility (e.g. another solvate) might be available through cocrystallisation or the formation of solvates.

In this project we have shown that theobromine can be considered a “text book” case study of the interplay between molecular shape, hydrogen bonding, and materials property. New crystal structures showed surprising hydrogen patterns and will help to gather new insights and conclusions for one of the most important scope of crystal engineering: The understanding of the intermolecular interactions in the context of crystal packing and the utilization of such understanding in the construction of crystalline materials.

Conclusion

“CEREPep” has led to the successful opening of a new gateway for a series of rare earth materials with biologically activity exhibiting new and potential important structural features. Our new approach towards the “design” of rare earth containing peptides showed some very encouraging results and opened the door to a completely new area.

Due to its interdisciplinary quality this project brought together a number of fruitful collaborations and future projects joined by scientists and industrial companies with advanced scientific experience and newcomers in different fields of research situated in four countries of the European Union (United Kingdom, Germany, Malta, Italy). A very competitive network was created, with rich potential to establish a strong position for further research activity after this project, funded and represented by European scientists and the 7th European Framework Program.

Contact details:

Dr. Ulrich Baisch

Department of Chemistry
University of Malta
Msida MSD 2080, Malta

Homepage: https://www.um.edu.mt/profile/ulrichbaisch