Contribution ID: **11** Type: **not specified**

Single Crystal X-Ray Crystallography lights up pharmaceutical compounds: main investigations and structural insights

Wednesday, 11 May 2022 11:10 (20 minutes)

X-ray Crystallography plays a crucial role in the structural investigation of drugs and provides a fundamental support for drug design and quality control in the drug development process [e.g., monitoring and quality check of Active Pharmaceutical Ingredient (API) and finished products]. Depending on the size of crystals (i.e., fraction of mm or a few μm), the kind of source (i.e., X-ray laboratory source or synchrotron radiation), or the wanted structural information, the crystallographic study can be carried out by single crystal or microcrystalline powder diffraction data. X-ray powder diffraction data (XRPD) provide a bulk information and allow to perform qualitative and quantitative phase analysis, detection of impurity phase(s), study of phase transitions, estimation of the crystallinity degree and percentage of the amorphous component, investigation of polymorphism, drug quality control and crystal structure solution [1,2]. In case of laboratory X-ray sources, if crystals of suitable size (i.e., fractions of mm) are available, their structural characterization can be carried out by single crystal X-ray diffraction data (SCXRD), via structure determination process, to be preferred to the structure solution by XRPD, because, thanks to the best quality of SCXRD, a more detailed structure model can be obtained and more complex structures can be successfully characterized. Contrarily to the case of XRPD, SCXRD allow to locate H atoms via difference Fourier synthesis, and, consequently, to accurately detect the main interatomic interactions. The correct position of H atoms enables also to establish whether a material exists as a salt or cocrystal phase [3]. A correct and accurate crystal structure determination is fundamental to confirm the expected crystal structure or reveal a new one, e.g., a new polymorph, that can have different physical properties (e.g., in terms of solubility, bioavailability,...) [3,4]; determination of the absolute configuration, that can be a critical step for the pharmaceutical industry: opposite enantiomers of a drug can have different biological properties [5]. Nowadays, the structure solution process by SCXRD is usually a routinary task and, at the same time, is greatly useful for understanding the structure-property relationship of drugs and providing key elucidating answers both to pharmaceutical sciences and industries. The increasing access to non-conventional powerful X-ray sources (i.e., synchrotron radiation) allows to reduce the size of the single crystals that can be successfully investigated and to enhance the complexity of the crystal structures that can be solved by SCXRD. Examples of application of single crystal diffraction to investigate pharmaceutical compounds will be shown, together with some cases of structure solution based on single-crystal synchrotron X-ray microdiffraction data, that allowed to characterize microcrystals for which, due to their small size, the use of synchrotron radiation revealed itself an obliged choice, i.e., the only way for succeeding in solving the crystal structure [6,7].

[1] Powder Diffraction Theory and Practice, Eds. R.E. Dinnebier and S.J.L. Billinge, (2008). RSCPublishing, Cambridge, UK.
[2] A. Altomare, C. Cuocci, G.D. Gatta, A. Moliterni and R. Rizzi (2017). 'Methods of Crystallography: powder X-ray diffraction', EMU Notes in Mineralogy, Vol. 19, Chapter 2, 79-138.
[3] Special Issue on Pharmaceuticals, drug discovery and natural products (2013). Acta Cryst C. 69, Ed. C. S. Frampton.
[4] Virtual Issue on Polymorphism (2011). Acta Cryst C., Ed. A. Linden, https://journals.iucr.org/special_issues/2011/polymorphism/
[5] Virtual Issue on Absolute structure (2012). Acta Cryst C., Ed. H. D. Flack https://journals.iucr.org/special_issues/2012/absolutestructure
[6] Giacobbe, C., Di Giuseppe, D., Zoboli, A., Lassinantti Gualtieri, M., Bonasoni, P., Moliterni, A., Corriero, N., Altomare, A., Wright, J., Gualtieri, A.F. (2021). IUCrJ 8, 76-86. DOI:10.1107/S2052252520015079
[7] Titi, A., Touzani, R., Moliterni, A., Giacobbe, C., Baldassarre, F., Taleb, M., Al-Zaqri, N., Warad, I. 'Ultrasonic clusterization process to prepare [(NNCO)6Co4Cl2] as novel double-open-Co4O6 cubane cluster: SXRD-interactions, , physicochemical, thermal, and Bio-mimicking of catecholase activity', (2022). ACS Omega, Submitted.

Presenter: Dr MOLITERNI, Anna (CNR - Istituto di Cristallografia)

Session Classification: Sessione