MS28 Navigating crystal forms in molecular and pharmaceutical materials

MS28-04
Learning the intermolecular history of an API through the application of Hirshfeld surface analysis tools
V. Psycharis [1]
[1]*Institute of Nanoscience and Nanotechnology NCSR 'Demokritos', - Agia Paraskevi (Greece)*

Abstract
Cocrystals have attracted the intense interest of researchers working on pharmaceuticals because there is a need in many cases to change the physical properties of Active Pharmaceutical Ingredients (APIs) [1]. The packing and arrangement of APIs, in pharmaceutical crystals, where they exist as molecular entities or as molecular adducts, influence the physical and in some cases the chemical properties and thus their overall performance [2]. Further to this research area, another field that has been emerged in parallel is the use of APIs as ligands in transition metal complexes which have been used as therapeutic and diagnostic agents [3]. Following the path of crystallization of different APIs in the structure of a polymorph, an adduct or a complex and studying the specific intermolecular interactions that play the major role in the packing of the corresponding structure, the complete information for the behaviour of the API molecule in the crystalline phase is gathered. In the present study, the intermolecular interactions of two APIs (Levofloxacin and Acetylsalicylic Acid) are examined in all of crystalline forms found in CSD with the analysis tools of Crystal Explorer software, which are based on the Hirshfeld Surface (HS) concept [4,5]. Ball and stick model, dnorm and Shape index Hirshfeld surfaces for the Levofloxacin molecule in its free (top three pictures, [6]) and coordinated forms (bottom three pictures [7]) are shown in Figure-1. Points within ellipses are contact points of the API that they are observed in both compounds. As the HS analysis tools consider all the intermolecular interactions that are involved in the packing of the API molecule in the crystal structure under study, and not only those that are deemed important, the role of each specific active atomic site of the API can be revealed. Thus, through this study, all information concerning the protected, the available donor or the acceptor sites of an API for intermolecular interactions, upon coordination or adduct formation, and the corresponding sites of the API in its polymorphs will be gained. All this information is expected to help in the design of new cocrystals with improved performance of the specific API or to passivate specific sites upon coordination which are involved in side effects during its bioactivity.

References
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Ball and stick models, dnorm & Shape decorated HSs