Drug design based on the complementarity between molecules to improve their physicochemical properties

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The antiretroviral drug Nevirapine (NVP) (11-Cyclo-propyl-5,11-dihydro-4-methyl-6H-dipyrido[3,2-b:2´,3´-e][1,4]diazepin-6-one) is a non-nucleoside reverse transcriptase inhibitor, used in the treatment of HIV-1 infection. It is a class II drug according to the Biopharmaceutics Classification System (BSC)[1], exhibiting low solubility and high permeability.

Co-crystallisation has shown promise in the tuning of a range of physical properties including dissolution rate, compressibility and physical stability. Therefore, we propose to increase the NVP dissolution and its bioavailability by obtaining crystalline modification based on co-crystals formation.

The potential co-formers can be restricted to a bunch of compounds, to the hundreds compounds considered as safe for human consumption (included in the GRAS list) or to the millions of known organic compounds. The number of co-crystallisations that can be attempted experimentally is limited; therefore, it is crucial to improve the probability of success using knowledge-based method for reducing efficiently the initial co-former sample. We are using *in-silico* methods developed from the Cambridge Crystallographic Data Centre (CCDC) for saving time and cost to predict and design co-crystals.[2]

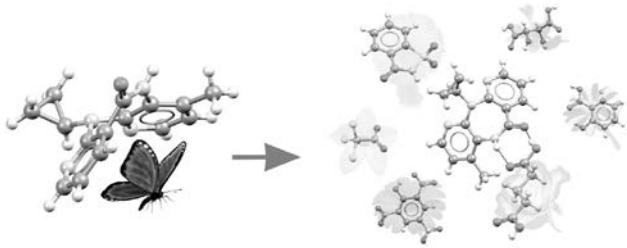

Figure 1: How NVP selects molecules to co-crystallize?

[1] - M. Lindenberg, S. Kopp, J.B. Dressman. *European Journ. of Pharm. And Biopharmaceutics* **2004**, *58*, 2, 265-278.

[2] - P.A. Wood, N. Feeder, M. Furlow, P.T.A. Galek, C.R. Groom, E. Pidcock. *CrystEngComm* **2014**, 16, 5839-5848.