Université catholique de Louvain **UCL** SECTEUR DES SCIENCES ET TECHNOLOGIES

Institut de la Matière Condensée et des Nanosciences

Invitation à la soutenance publique de thèse

Pour l'obtention du grade de Docteur en Sciences

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Master en sciences chimiques, à finalité didactique

Insights and Advances in Cocrystal Screening: a focus on Levetiracetam/Etiracetam with achiral coformers

Cocrystals have been especially developed in pharmaceutical sciences for their ability to modulate the physico-chemical properties of a drug product showing non-optimal parameters. Selecting likely coformers to form a cocrystal with a given active pharmaceutical ingredient (API) among the millions of potential candidates is however not trivial, as there are many factors coming into play in varying manners.

In this thesis, we thus investigated ways of improving the selection of coformers to limit the trial-and-error proportion of the procedure. For that matter, we first performed an experimental cocrystal screen on the enantiopure and racemic versions of a selected API, Levetiracetam. By comparing the results of their respective cocrystal screenings, we showed a tendency for them to form cocrystals with identical non-chiral partners. We also discovered a stable conglomerate of cocrystals, which is only the second report of such a case. Notably, this conglomerate is formed with the lactol tautomer of alpha-ketoglutaric acid, which had never been isolated in the solid-state up to now.

In a second phase, we examined the possibility of using Isothermal Titration Calorimetry (ITC) to measure interactions between an API and complexing agents in solution. We showed that interactions in solution between non-charged compounds can be detected by ITC but that they are not sufficient to identify cocrystal formers of a given API.

Similarly, we considered the use of some of the CSD solid-form modules to validate the results of the experimental cocrystal screenings of Levetiracetam and Paracetamol. Doing so, we demonstrated how knowledge-based informatics can help take decisions concerning coformer selection and experimental prioritization, and how one can optimally apply them to a given system.

Jeudi 29 septembre 2016 à 16h30

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