Poster

Exploring co-crystallisation as a technique for taste-masking of nevirapine

K. Edkins[1], Y. Shen[2], M. Aucamp[3], H.E. Abdelhakim[4]

[1]Institute for Pharmacy and Biomedical Sciences,University of Strathclyde, Glasgow, UK, [2]School of Health Sciences, University of Manchester, Manchester, UK, [3]School of Pharmacy, University of the Western Cape, Capetown, South Africa, [4]Global Business School for Health, University College London, London, UK

Katharina.edkins@strath.ac.uk

The bitter taste of pharmaceuticals majorly impacts patient adherence. Co-crystallisation has been proposed as a novel way for taste masking using sweetener-based co-formers, while other co-formers also have a positive effect. We hypothesise that the sweetness of the co-formers is not the key factor but rather the supramolecular interactions between the drug and co-former. These interactions can influence the dissolution characteristics of the co-crystal leading to a delayed dissolution and hence a reduced taste. Furthermore, interaction between the drug and the co-former in solution may lead to an altered shape of the aggregate that inhibits a strong binding with the taste receptor pocket. In our hypothesis, the stronger the interaction, the better the taste masking effect. Here, we explore the supramolecular aggregation between the bitter-tasting drug nevirapine and five co-formers in the crystal and in solution. The co-crystals formed with benzoic acid, glutamic acid and maleic acid show a 1:1 stoichiometry, while saccharin and salicylic acid as co-formers lead to a 2:1 drug/co-former stoichiometry. The aliphatic acids show the anticipated cyclic acid-amide hydrogen bond synthon, while saccharin, benzoic acid and salicylic acid interact with homodimers of nevirapine through hydrogen bonds to the opposite ring nitrogen [1,2]. All co-crystals show a faster dissolution rate than the pure nevirapine material indicating that the reduced drug solubility of the co-crystals is not the mechanism of taste-masking.

Using ^{1}H NMR spectroscopy, the co-formers benzoic acid, salicylic acid and maleic acid show strong interaction with nevirapine, while glutaric acid and saccharin have weak and no interaction, respectively. The taste of the resulting co-crystal, as assessed by the electrical taste sensing system e-tongue, reveals that the bitterness of nevirapine has been covered with the co-crystal benzoic acid, maleic acid and glutaric acid but not saccharin or salicylic acid. From the taste results we deduct that both solution aggregation and the taste of the pure co-former play an important role in taste masking. It is likely that a large variety of co-formers can be used to cover bitter drugs and we show that the investigation of molecular aggregation in solution can help screen the co-formers before any in vitro or in vivo taste test [3].

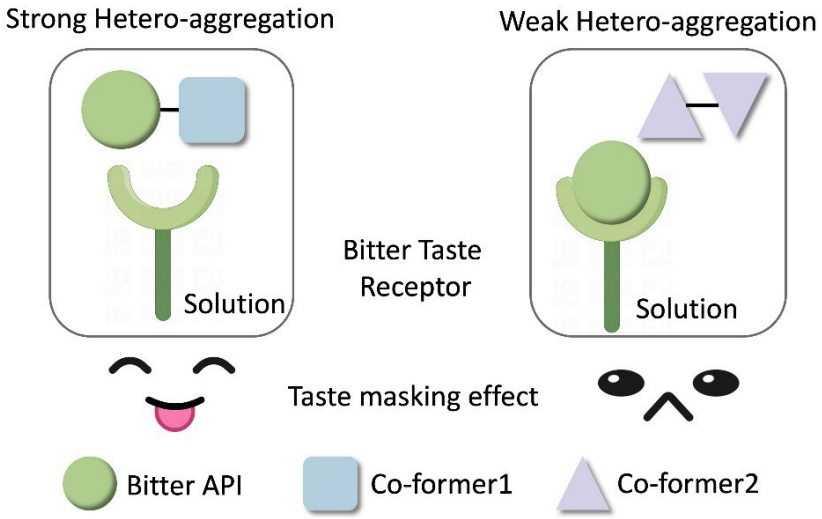

Figure 1. Impact of supramolecular interaction in solution on the use of co-crystallisation for pharmaceutical taste-masking.

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