Title: Rational way of taste masking by inhibition of taste receptors

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Abstract

Taste masking of bitter drugs plays a vital role in patient acceptability and compliance especially in case of liquid formulation for pediatrics. Taste masking can be achieved by physical or chemical methods, which involve avoiding the direct contact of the drug molecules with the bitter taste receptors. The well explored methods for achieving this include use of sweetening and flavouring agents, microencapsulation, ion exchange resins, use of vehicles such as oils, surfactants, poly-alcohols and inclusion complexation of bitter drugs with macromolecules such as cyclodextrins etc.

This project involves various lesser explored techniques for taste masking including the use of milk proteins, synthesis of a prodrug and several molecular modeling approaches.

This research work was performed in three parts

Taste improvement using milk proteins are promising because of their biocompatibility, as well as health benefits. Milk proteins such as β-lactoglobulin (β-LG), α-lactalbumin, lactoferrin, and casein were subjected to molecular modeling based understanding of their interaction with a bitter drug risperidone (RIS). Good binding of RIS with β-LG and sodium caseinate (NaCAS) were observed, which were further studied using Induced Fit Docking (IFD), Molecular Dynamic (MD) simulation, Molecular Mechanics-Generalized Born Surface Area **(**MMGBSA) and fluorimetry which indicated good binding of RIS with NaCAS and β-LG. Experimental taste assessments were performed by palatability study using a suitable standardized rat based assay. NaCAS was found to be effective in taste improvement of RIS while β-LG was ineffective.

Meloxicam pivalate as a novel prodrug was synthesized using conventional synthetic method and extensively characterized. Its taste assessment was performed using single bottle-test model using rats. Palatability of meloxicam pivalate solution improved significantly as compared to meloxicam.

Taste is mediated through several G protein-coupled receptors. As the structure of bitter receptors is not elucidated by X-ray crystal structures or NMR spectroscopy, homology modeling was used to derive three- dimensional (3-D) structures. MD simulation of bitter drugs,

RIS, azithromycin (AZT), clarithromycin (CLR) with β-cyclodextrin (β-CD) and (2-hydroxypropyl)-β-cyclodextrin (HP-β-CD) were performed. Interaction studies showed that RIS-β-CD, RIS-HP-β-CD, AZT-β-CD, AZT-HP-β-CD, CLR-β-CD, and CLR-HP- β-CD in 1:1 ratio led to the formation of stable complexes and these complexes do not interact with taste receptor studied. Hence, the present study could be utilized for further screening of taste masking agents computationally before the actual experiments are carried out.