INVESTIGATION OF CINNARIZINE AND β-CYCLODEXTRIN INCLUSION COMPLEX IN D_2O USING NMR SPECTROSCOPY

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Cinnarizine (CIN) is a piperazine derivative with a broad spectrum of biological activity ranging from antihistaminic to calcium channel-blocking. It is mainly used for the treatment of nausea, vertigo, and other vestibular disorders [1]. According to the Biopharmaceutical Classification System (BCS), it is a Class II drug characterized by high permeability and low solubility, which, unfortunately, poses a major challenge in drug formulation. Cyclodextrins (CDs), the cyclic oligosaccharides with a central hydrophobic cavity and a hydrophilic outer surface, represent a potential answer to this challenge by forming inclusion complexes that can improve the solubility and bioavailability of the drug. Of the many CDs available, beta-cyclodextrin (β-CD) and its derivatives are the most commonly used due to the convenient size of their central cavity and low cost. As far as we know, there are only two previous studies on CIN/CD inclusion complexes using NMR spectroscopy: an older one by Tokumura et al, which showed that complexation of CIN/β-CD occurs in 0.1 M DCl [2], and the more recent one by Patel et al, which investigated the complexation of CIN with HP-β-CD in DMSO [3]. Therefore, we set out to obtain a more comprehensive picture of the binding mode between CIN and β-CD by using 1D and 2D NMR techniques in D_2O with added DCl – a medium that reflects the pH-dependent solubility of CIN. [4] Our NMR studies have confirmed the encapsulation of CIN in β-CD and provide new insights into its binding mode, confirming the formulation potential.

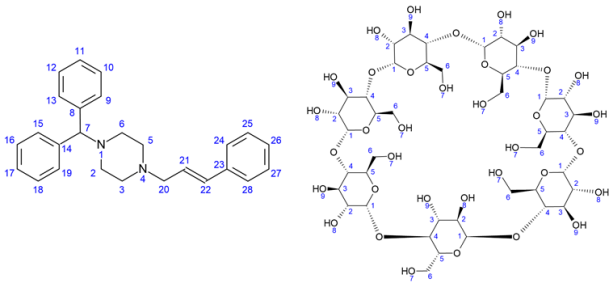

Figure 1. Structure and numbering of cinnarizine and β-cyclodextrin.

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