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Effect of p-sulfonatocalix [4] resorcinarene on the solubility and bioavailability of an anti-tuberculosis drug isoniazid (INH)

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Tuberculosis (TB) is a serious infectious disease and ranks as the second leading cause of death from an infectious disease worldwide with an estimated 8.6 million incident cases and 1.3 million deaths due to the disease in 2012. Isoniazid (INH) is the major first-line drug used for the treatment of TB, although emergence of its resistance on wide scale has been a matter of great concern for future treatment schedules of TB. Novel approved chemotherapy treatment to tuberculosis is not observed because it is a neglected disease. Pharmaceutical alternatives to isoniazid chemotherapy itself are needed, and in this sense, several ideas have been pursued. In the present research paper, the formation of isoniazid-p-sulfonatocalix [4] resorcinarene (p-SC [4] R) inclusion complex with the aim to enhance the physicochemical and biopharmaceutical properties of the guest molecules were isoniazid by inclusion complexation. The 1:1 stoichiometry ratio for the complex has been suggested based on Job's plot and AL diagram from phase solubility studies. The inclusion complex formation of Isoniazid-p-SC [4] R were characterized by dissimilar analytical techniques including UV-VIS spectroscopy, DSC, TGA and ESI-Mass spectroscopy. An optimized isoniazid-p-SC [4] R complex exhibited improved *in vitro* dissolution profile and decreased *in vivo* acute oral toxicity compared to pure drug isoniazid. The aim of the present research work was to determine the effect of water soluble p-SC [4] R on the dissolution performance of isoniazid. We have designated p-SC [4] R as a drug solubilizing agent owing to the ease of synthesis in upper rim as well as lower rim, availability of 8 phenolic units and a straightforward accessibility. Additionally, they possess open and rigid structure and also number of possible conformations and binding positions with a hydrophilic outer surface and a polar cavity at their center that provides a hydrophobic matrix. Since isoniazid is a flat shape molecule, it can be easily entrapped in the hydrophobic p-SC [4] R cavity to form host-guest complex. The stoichiometries of the inclusion complex and the apparent formation constant have been estimated. We have performed the phase solubility and dissolution studies.

Biography

Nikunj N Valand is pursuing PhD in Department of Chemistry, Gujarat University, Ahmedabad, Gujarat. He is a DST-INSPIRE Senior Research Fellow and his research area is supramolecular chemistry, nanomaterials and organic chemistry. He has expertise in synthesis and biological evaluation of organic as well as pharmaceutical drugs.

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