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CO-CRYSTALLIZATION- TOWARDS ENHANCED BIOLOGICAL ACTIVITIES EXAMPLES OF CRYSTAL ENGINEERING APPROACH

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Leishmaniasis is caused by protozoa parasites of the genus Leishmania, a biologically diverse group of flagellate parasites. Leishmaniasis is endamic in tropical and subtropical regions, particularly Afghanistan, Iran, China, Nepal, Bangladesh, etc. Based on the high prevalence of Leishmaniasis in Pakistan and associated morbidity, our research group has started to work on this disease by using different strategies. Present lecture will cover the results of structural modification of antileishmanial natural product and a commercially available drug by using a crystal engineering approach co-crystallization. Co-crystals are crystalline structures made up of two or more components in a definite stoichiometric ratio linked through non-covalent interactions in same crystal lattice. They differ in their biological and physiochemical properties from their components. They have wide applications in drug designing and in analysis of active pharmaceutical ingredients (APIs). The co-crystals of anti-leishmainal natural product, sesselin (1) and an anti-cancer drug exemestane (2) with thiourea were synthesized by using neat grinding followed by liquid assisted grinding and solution methods. Both the pure sesseline, exemestane and their co-crystalized form with thiourea, (1 and 2, respectively) were evaluated for their anti-leishmanial activity in vitro against L. major promastegoates. The co-crystal (1) exhibited improved leishmanicidal activity (IC50 = 13.2 + 1.2 ug/mL) in comparison to that of sesseline (IC50 = 29.4 + 1.0 ug/mL). However, the co-crystal of exemestane with thiourea (2) found to be in active.

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