Molecular docking studies of mixed ligand complexes using flavonoids as precursors

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Abstract - Flavonoids are a group of plant phenolics which provide various health benefits through cell signaling pathways and antioxidant effects. In the present study, a new series of transition mixed ligand complexes of Co(II), Ni(II), Cu(II) and Zn(II) were synthesized by incorporating curcumin and quercetin flavonoid precursors. The structural features of the synthesized complexes had been explored by UV-Vis, NMR and conductivity measurements. These data support an octahedral geometry of the synthesized complexes. *In silico* biological activity score for the ligand was predicted using PASS online software. Based on the *in silico* results molecular docking studies was carried out to find out the interaction between the targets like cancer DNA (1 BNA), 6-COX enzyme and the synthesized compounds using HEX 8.0

Keywords: Flavanoids; curcumin Schiff base; VLS3D; Molecular Docking

1. INTRODUCTION

Curcumin (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) is a yellow component of the Indian spice turmeric, manufactured from the rhizome of the perennial herb *Curcuma longa* [1]. Curcumin has been referred to as "curecumin"[2,3] because it possesses various biological activities like antitumoral, antimicrobial, anti-inflammatory, antioxidant, anticancer, antihepatotoxic, antihyperlipidemic, antiviral and anti-Alzheimer's disease.

Quercetin is an yellow pigment in plant products which can help to alleviate eczema, sinusitis, asthma and hay fever [4,5]. The literature survey over the past few decades on curcumin reveals that its biological activity is enhanced after forming Schiff base with heterocyclic ring containing compounds like 4-aminoantipyrine. Recent progress explores that the individual biological activity of both the flavonoids is enhanced after forming complexes with metal ions [6, 7]. Increasingly over the last decade, computational (*in silico*) methods have been developed and applied to pharmacology hypothesis development and testing of lead compounds. These *in silico* methods incorporate databases, quantitative structure-activity relationships, pharmacophores, homology models and other molecular modeling approaches, machine learning, data mining, network analysis tools and data analysis tools that use a computer. *In silico* methods are primarily used along with the *in vitro* data create the model as well as to test it. Such models have seen frequently use in the discovery and optimization of novel molecules with affinity towards the target, the clarification of absorption, distribution, metabolism, excretion and toxicity properties as well as physicochemical characterization

Based on the literature survey and the above facts, in the present study, a few mixed ligand complexes using the above biologically active flavanoids (curcumin and quercetin) were synthesized. They have been characterized by UV-Vis, NMR and TGA analytical techniques. The biological activity of the curcumin Schiff base has been predicted by PASS online. As per the results obtained from the above software, Molecular docking studies was carried out in HEX 8.0 and Argus lab software.

2. EXPERIMENTAL

2.1 Synthesis of compounds

2.1.1 Synthesis of Curcumin derived Schiff base (L_1)

Curcumin derived Schiff base was prepared by condensing equimolar concentration of curcumin with 4-aminoantipyrine in 30 mL of ethanol. This mixture was refluxed for *ca* 3 h. Then the volume of reaction mixture was reduced and washed with petroleum-ether for 3 times to remove the reactants. Finally it was poured into water. The red orange precipitate was obtained.