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# Tubulin polymerization inhibition, molecular structure and ligand-enzyme interactions of [1,3]thiazolo[3,2-a]benzimidazol-3(2H)-one derivatives

It is known that the synthesis of tubulin and microtubules is part of the processes of cell division which makes it a potential target in the development of new chemotherapeutic agents for cancer as well as parasitic infections treatment [1]. Several binding sites are known on the surface of tubulin, but the best studied for the purpose of designing polymerization inhibitors are the colchicine and taxine sites [2]. The potential of the benzimidazole structure in anticancer therapy is well known. There are a number of representatives of this class of compounds that are actively used as anti-cancer agents, such as bendamustine, nocodazole and denibulin [3]. On the other hand, benzimidazole carbamates such as albendazole, mebendazole, carbendazim and other derivatives, show a high therapeutic index, broad spectrum activity against nematodes, cestodes and trematodes. However, anthelmintic resistance limits their action frequently and motivates the discovery of new compounds with anthelmintic activity. Benzimidazole compounds bind to the colchicine binding site of β-tubulin in the parasitic cells, thus effecting its polymerization, disrupting the microtubule functions and leading to the of parasites death. Herein we present an in vitro evaluation on ability of 2-substituted-[1,3]thiazolo[3,2-a]benzimidazol-3(2H)-ones to interfere with tubulin polymerization, DFT characterization of the molecular structure of the compounds and molecular docking study on tubulin-ligands interactions. It was found that Z conformation of the exocyclic double bond is the more stable, and for compounds with a heterocyclic fragment, where rotation about the C-C bond to the aryl fragment leads to distinguishable conformers, s-cis is more favorable. The interaction of the 2-substituted-[1,3]thiazolo[3,2-a]benzimidazol-3(2H)-ones with tubulin was explored by molecular docking at the colchicine binding site and provided useful insights on the structure-activity relationship.

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