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Structure activity relationship (SAR) investigation on the binding properties of ligands similar to combretastatin to colchicine binding site of tubulin protein as anti-cancer drug

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Background and Aims: Combretastatin is a potent tubulin polymerization inhibitor, which binds to colchicine domain in microtubule's molecule. As respects the increasing affinity of the drug to colchicines domain led to greater drug efficacy, studies in destroying cancer cells are always looking to find molecules that have agreater tendency to colchicine domain. The present study was designed to introduce new structures with more affinity to colchicine domain of tubulin protein.
Methods: Data mining of structures with 80% similarity to combretastatin using the PubChem at NCBI database, retrieved 1600 structures. The Protein Data Bank (PDB) File of tubulin 3D structure with colchicine was taken from RCSB PDB and protein 3D structure was optimized with Swiss-PDB Viewer software. Docking of ligands to colchicine site of tubulin performed with leadIT software (version 2.1.0 BioSolveIT, GmbH, Germany) and the interaction energy of different compounds was obtained.
Results: 60 compounds from 1600 similar structures to combretastatin had highest absolute interaction energies compared to combretastatin as a reference ligand.
Conclusions: These findings could be the basis for pharmaceutical chemistry to develop anti-cancer compounds with higher activity and low toxicity compared to combretastatin.

Keywords: Cancer; Combretastatin; Tubulin; Chemoinformatics; Docking