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Application of computer-aided drug design strategies for optimization of anticancer activity of phenazinamine derivatives

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We have carried out efficient group based quantitative structure–activity relationships (GQSAR) exploring the relationship between the structures of a new promising family of 2-phenazinamine derivatives and their anti-cancer activities. We have developed residential evocative model, in order to aid in further optimization and expansion of newer anticancer agents containing novel pharmacophore. G-QSAR was performed on VLife molecular design suite (MDS) 4.2 version software. The extrapolative authority of the G-QSAR was checked through the cross-validation method and also by separating some compounds as fraction for external test set. The synthesis of five novel 2-phenazinamine derivatives was carried out successfully by chemical modifications suggested by the GQSAR model developed and by making use of its molecular descriptors. The screening of *in vitro* anticancer activity on K562 cell line was done in Tata Memorial Cancer Research Center Mumbai, India. The results display an improvement in anti-cancer activity. Phenazinamine and the analogues have better binding interactions with Oxidoreductase (PDB: 1YYD.) The binding energies of the protein-ligand interactions also confirm that the ligands fit into the active pockets of receptor tightly. The docking scores of PDB cavity (most hydrophobic area) and ligand suggests efficient binding interactions. These studies have been performed by using Autodock 4.2 version software. Thus, the synthesized phenazinamine derivatives can be used as a lead for further preparing promising future anticancer drug candidates.

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Chemical constituents of sandbox tree (*Hura crepitans* Linn) and anti-hepatotoxic activity of the leaves and stem bark extracts

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Background: The use of natural products derived from plants for therapeutic purpose is as ancient as human civilization. Sandbox tree, *Hura crepitans* L. (Euphorbiaceae) is one of such plants and has been reported to have many ethno-medicinal applications especially as antimicrobial, anti-inflammatory and anti-hepatotoxic effects.

Purpose of the study: This recent study was designed to determine the anti-hepatotoxic activity of the ethylacetate soluble fraction of the leaves and stem bark of *H. crepitans* and to isolate secondary metabolites.

Methods: Chromatographic technique was used for isolation and Ultraviolet-Visible (UV), Infra-red (IR) and Nuclear Magnetic Resonance (NMR) spectroscopies were used for structural elucidation. Anti-hepatotoxicity study was carried out using carbon tetrachloride (CCl4) induced rat model and biochemical parameters: alanine aminotransferase (ALT), aspartate aminotransferase (AST), L-γ-glutamyltransferase (GGT), urea and creatinine (CREA) were assayed on the serum. Phytomicrographs of the liver samples were also taken and analyzed.

Results: Our present study showed that biochemical studies of blood samples of CCl4 treated rats with value 105.0±0.001 AU in ALT showed significant increase in the level of serum enzyme activities reflecting liver injury but, 69.0±13.23 AU for leaves and 53.3±2.52 AU for bark ($p<0.05$) indicated protection of hepatic cells. AST, GGT, urea and CREA also reduced significantly. Daphnane diterpenes, daphnetoxin acid and huratoxin were isolated from H. crepitans in this recent study along with apocynin and methylpentadecanoate.

Conclusion: *H. crepitans* significantly reduced the level of biochemical parameters indicating protection against hepatocellular injury. Isolates obtained from this plant could also serve as lead compounds in therapy of diseases involving hepatic injury.

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