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Design, synthesis, and *in silico* ADME and anticancer evaluation of 4-amino-5-phenyl-1,2,4-triazole-3-thiol Schiff bases

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ABSTRACT A series of five new 4-amino-5-phenyl-1,2,4-triazole-3-thiol Schiff base derivatives (**4a-4e**) was rationally designed, and successfully synthesized by the condensation reaction between 4-amino-phenyl-4*H*-1,2,4-triazol-3-thiol and aromatic aldehydes, *in silico* absorption, distribution, metabolism, and excretion (ADME) studies were conducted using the Swiss ADME platform to assess drug-likeness and pharmacokinetic behavior. The predicted results indicated favorable physicochemical properties, good oral bioavailability, high gastrointestinal absorption, and compliance with Lipinski, Veber, and Egan rules, with no predicted blood–brain barrier permeability. The anticancer activity of the synthesized compounds was evaluated *in vitro* using MTT viability assay against the HepG2 human hepatocellular carcinoma cell line, with WRL-86 normal hepatic cells used for comparison. Compound **4a** exhibited a concentration-dependent cytotoxic effect against HepG2 cells, while showing comparatively lower toxicity toward WRL-68 cells, suggesting a possible degree of selectivity toward cancer cells. However, the observed anticancer activity was modest and was more pronounced only at higher concentrations. Overall, the combined synthetic, structure, *in silico* ADME, and preliminary biological evaluation indicated that these 1,2,4-triazole-based Schiff base derivatives represent promising scaffolds for further structure optimization and extended biological investigations.