Abstract:

The study designed, synthesized, and characterized novel cuminaldehyde-TZD and veratraldehyde-TZD hybrids to evaluate their *in vitro* α-glucosidase inhibitory potential. Among the synthesized derivatives, compound **6i** (cuminaldehyde-TZD, IC_{50} = 31.29 ± 0.94 μM) and compound **6f** (veratraldehyde-TZD, IC_{50} = 18.16 ± 0.41 μM) demonstrated the most potent inhibition *in vitro*. Enzyme kinetics showed **6i** acts as a mixed-competitive inhibitor, while **6f** acts as a competitive inhibitor. Fluorescence quenching revealed strong static binding, and circular dichroism indicated the compounds induce significant conformational changes in the enzyme's secondary structure. Molecular docking supported the strong binding, highlighting favourable interactions, particularly hydrogen bonding with active site residues (PDB ID: 5NN8). *In silico* ADMET profiling suggested satisfactory oral drug-likeness and low toxicity, confirmed by low cytotoxicity in HEK-293 cells. These findings indicate that cuminaldehyde-TZD and veratraldehyde-TZD hybrids are promising anti-diabetic agents, warranting further *in vivo* studies to validate their hypoglycemic efficacy and safety in diabetic animal models.