Hunig's base catalyzed synthesis of new 1-(2,3-dihydro-1H-inden-1-yl)-3-aryl urea/ thiourea derivatives as potent antioxidants and 2HCK enzyme growth inhibitors

ABSTRACT

A series of 1-(2,3-dihydro-1*H*-indan-1-yl)-3-aryl urea/thiourea derivatives (**4a-j**) have been synthesized from the reaction of 2,3-dihydro-1*H*-inden-1-amine **(2)** with various aryl isocyanates/isothiocyanates **(3a-j)** by using *N,N*-DIPEA base (Hunig's base) catalyst in THF at reflux conditions. All of them are structurally confirmed by spectral (IR, ^{1}H & ^{13}C NMR and MASS) and elemental analysis and screened for their *in-vitro* antioxidant activity against DPPH and NO free radicals and found that compounds **4b, 4i, 4h** & **4g** are potential antioxidants. The obtained *in vitro* results were compared with the molecular docking, ADMET, QSAR and bioactivity study results performed for them and identified that the recorded *in silico* binding affinities were observed in good correlation with the *in vitro* antioxidant results. The Molecular docking analysis had unveiled the strong hydrogen bonding interactions of synthesized ligands with ARG 160 residue of protein tyrosine kinase (2HCK) enzyme and plays an effective role in its inhibition. Toxicology studies have assessed the potential risks of **4a-j** and inferred that all of them were in the limits of potential drugs. The conformational analysis of **4a-j** inferred that the urea/thiourea spacer linking 2,3-dihydro-1*H*-inden-1-amino and substituted aryl units has facilitated all these molecules to effectively bind with ARG 160 amino acid residue present on the *α*-helix of the protein tyrosine kinase (2HCK) enzyme specifically on chain A of hemopoetic cell kinase. Collectively this study has established a relationship between the antioxidant potentiality and ligands binding with ARG 160 amino acid residue of chain A of 2HCK enzyme to inhibit its growth as well as proliferation of reactive oxygen species *in vivo*.