# Multiple molecular targets mediated antioxidant activity, molecular docking, ADMET, QSAR and bioactivity studies of halo substituted urea derivatives of α-Methyl-L-DOPA

## ABSTRACT

A series of novel α-methyl-L-DOPA urea derivatives viz., 3-(3,4-dihydroxyphenyl)-2-methyl-2-(3-halo/trifluoromethyl substituted phenyl ureido)propanoic acids (**6a-e**) have been synthesized from the reaction of α-methyl-L-DOPA **(3)** with various aryl isocyanates **(4a-e)** by using triethylamine (**5**, TEA) as a base catalyst in THF at reflux conditions. The synthesized compounds are structurally characterized by spectral (IR, 1H & 13C NMR and MASS) and elemental analysis studies and screened for their in-vitro antioxidant activity against DPPH, NO and H2O2 free radical scavenging assays and identified compounds **6c** & **6d** as potential antioxidants. The acquired in vitro results were correlated with the results of molecular docking, ADMET, QSAR and bioactivity studies performed for them and predicted that the recorded in silico binding affinities are in good correlation with the in vitro antioxidant activity results. The molecular docking analysis has comprehended the strong hydrogen bonding interactions of **6a-e** with 1CB4, 1N8Q, 3MNG, 1OG5, 1DNU, 3NRZ, 2CDU, 1HD2 and 2HCK proteins of their respective SOD, LO, PRXS5, CP450, MP, XO, NO, PRY5 and HCK enzymes. This has sustained the effective binding of **6a-e** and resulted in functional inhibition of selective aminoacid residues to be pronounced as multiple molecular targets mediated antioxidant potent compounds. In addition, the evaluated toxicology risks of **6a-e** are identified with in the potential limits of drug candidates. The conformational analysis of **6c & 6d** prominently infers that urea moiety uniting α-methyl-L-DOPA with halo substituted aryl units into a distinctive orientation to comply good structure-activity to inhibit the proliferation of reactive oxygen species in vivo.