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Contribution of artificial intelligence in the studies of isothiazole derivatives to design new and selective inhibitors of HCV polymerase NS5B

Abstract:

A QSAR investigation was carried out on a diverse collection of thirty-eight isothiazole derivatives acting as NS5B inhibitors. The research methodology involved the utilization of various statistical techniques including multiple linear regression/MLR and artificial neural network/ANN. The displaying satisfactory results in terms of internal and external validation parameters (R2MLR=0.811; R2adj (MLR) =0.781; Q2LOO (MLR)= 0.737; FMLR=26.794; R2test(MLR) =0.891) and (R2ANN = 0.991; R2cv (ANN) = 0.939; R2test (ANN) = 0.839). The highly commendable statistical outcomes achieved for this model strongly indicate its reliability in predicting the activity of new inhibitors. Consequently, a series of potent NS5B inhibitors were crafted, and their inhibitory potential was confirmed through molecular docking simulations using Autodock software. Through in silico scrutiny, four innovative compounds, namely N7, N8, N9, and N10, were devised, demonstrating hydrophobic and hydrogen bond interactions, as well as carbon-hydrogen bonds and electrostatic interactions, with the active site 221 binding pockets. Additionally, these newly formulated compounds displayed favorable ADMET characteristics, with molecular dynamics investigations revealing a stable energetic state and dynamic equilibrium, as indicated by such as RMSD and RMSF which are respectively called root mean square deviation and root mean square fluctuation and also hydrogen bonding models. The findings of this research underscore the significance of NS5B inhibition in the treatment of HCV.

Biography

Salah Belaidi is currently professor and research director in the Department of Chemistry; University of Biskra. He is the head of the "Computational and Medicinal Chemistry" group. He received his MSc and PhD in macrolide chemistry. My research interests span the areas of chemical design of biomolecules, virtual screening in drug discovery and drug design, QSAR models and molecular docking, as well as molecular dynamics. He has published more than 100 articles in reputed journals and has been a noted member of the editorial board of several journals.