931/E2/Poster

Sitosterol palmitate can bind to human glucocorticoid receptor as an agonist: an *in silico* study

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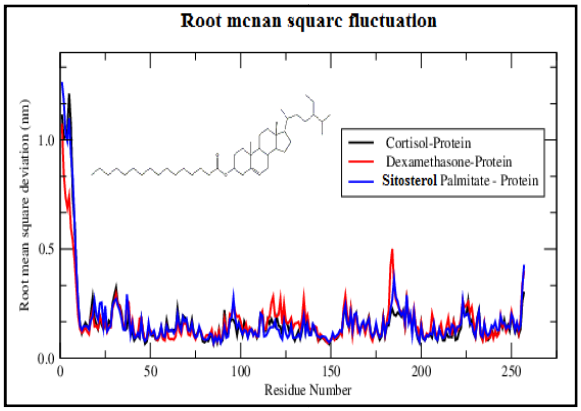
The "Sri Lankan Flora" is an online database of force field parameters and several structural parameters of compounds that can be used in molecular modeling. The database contains nearly 200 compounds isolated and identified from the flora of Sri Lanka and is freely accessible at http://www.science.cmb.ac.lk/tools/slflora web address. Glucocorticoid receptor (GR) belongs to the super family of nuclear receptors and act as a steroid hormone trans-activated transcriptional factor expressed in almost all cells in the body. It is known to regulate growth, stress response, metabolism, homeostasis, immune function, and development. Cortisol is the main physiological ligand for the GR and in the absence of the ligand, GR resides in the cytosol in an inactive form associated with several chaperone proteins. The ligand binding domain of the GR intercedes to receptor activity via glucocorticoids. The molecular docking procedure with DOCK6 software was conducted to predict binding affinity of cortisol to GR protein and the binding affinity recorded. The same docking procedure was used for the seven (07) steroids found from Sri Lankan flora and a *synthetic glucocorticoid, dexamethasone* and respective grid scores were recorded. Out of seven steroids only one, sitosterol palmitate, showed high binding affinity towards the GR. The complexes of cortisol, dexamethasone and sitosterol palmitate with GR were pursued for molecular dynamics (MD) simulation study for 30 ns each to investigate the stability of the complexes in aqueous medium. The stability of the above systems was studied in terms of root mean square deviations (RMSD), radius of gyration (Rg), root mean square fluctuations (RMSF) and total solvent accessible surface area (SASA). The MD analysis, specially the RMSF analysis indicates that cortisol, dexamethasone and sitosterol palmitate complexes behaved in a relatively similar manner in aqueous medium. Therefore, it could be concluded that the binding of sitosterol palmitate to GR as an agonist may produce biological effects similar to that produced by glucocorticoids and could be recommended for *in vitro* testing.



Acknowledgement: Financial assistance by the University of Colombo Research grant (AP/3/2/2014/RG/01)

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