Molecular Docking and ADMET Studies on Wattakaka volubilis Root and Evaluation of its Effect on Diabetes Mellitus induced Memory Dysfunction in Rats

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Abstract:
The study was undertaken to evaluate the neuroprotective activity of alcohol extract of Wattakaka volubilis root on diabetes associated memory dysfunction. Studies have indicated that Diabetes mellitus affects the CNS and induces pathological changes in brain characterized by mild-to-moderate cognitive deficits. Single intraperitoneal injection of Streptozotocin (STZ) 60 mg / kg was used to induce Diabetes. Diabetic animals were segregated into groups and administered with glimepiride (0.5 mg/kg), donepezil (5 mg/kg), alcohol extract of W. volubilis root 200 and 400 mg/kg for 30 days. Behavioural studies were performed by open field, jumping box and Morris water maze. After 30 days, brain levels of Malondialdehyde (MDA), reduced Glutathione (GSH), Superoxide dismutase (SOD), Nitric oxide synthase (NOS), Advanced Glycation End Products (AGEs) and Acetylcholinesterase (AChE) were estimated.

The alcohol extract significantly (p<0.001) inhibited progression of hyperglycemia and cognitive impairment with significant (p<0.001) improvement in behavioural parameters compared with the untreated diabetic control ones. Levels of MDA, NOS, AChE and AGEs were significantly (p<0.001) decreased and those of SOD and GSH was significantly (p<0.001) increased in alcohol extract treated groups. Results were comparable with the results of standard groups. Certain of phytoconstituents of W. volubilis were identified which showed good binding interactions with target proteins in brain insulin signalling pathways. This includes mehoxywogonin which showed best docking score against MAPK, GSK3 β, amyloid γ-secretase, tau-protein, AChE and aldose reductase. Aeridin showed best docking score against PDE2, eNOS and NFKB. Marsdenin showed best docking score against AKT. Volubilol with amyloid β-secretase and dregeoside Da1 with NMDA. Qikprop tool was used to predict the pharmacokinetic properties and toxicity of the selected phytoconstituents using Schrodinger drug design suite.

Conclusion: It is concluded that W. volubilis root provides neuroprotection and ameliorates the possible cognitive impairment associated with Diabetes mellitus.