

Therapeutic Efficacy of *Clompanus Pubescens* Leaves Fractions via Downregulation of Neuronal Cholinesterases/ $\text{Na}^+\text{-K}^+$ ATPase/ $\text{IL-1 } \beta$ and Improving the Neurocognitive and Antioxidants Status of Streptozotocin-Induced Diabetic Rats

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Abstract : The increasing global burden of diabetes mellitus has called for the search for a therapeutic alternative that offers better activities and safety than conventional chemotherapy. Herein, we evaluated the neuroprotective and antioxidant properties of different fractions (ethyl acetate, N-butanol and residual aqueous) of *Clompanus pubescens* leaves in streptozotocin (STZ)-induced diabetic rats. Our results revealed a significant elevation in the levels of blood glucose, pro-inflammatory cytokines, lipid peroxidation, neuronal activities of acetylcholinesterase, butyrylcholinesterase, nitric oxide, epinephrine, norepinephrine, and Na^+/K^+ -ATPase in diabetic non treated rats. In addition, decreased levels of enzymatic and non-enzymatic antioxidants were observed. Treatment with different fractions of *C. pubescens* leaves resulted in a significant reversal of the biochemical alteration and improved the neurocognitive deficit in STZ-induced diabetic rats. However, the ethyl-acetate fraction demonstrated higher activities than the other fractions and was characterized for its phytoconstituents, revealing the presence of Gallic acid (713.00 ppm), catechin (0.91 ppm), ferulic acid (0.98 ppm), rutin (59.82 ppm), quercetin (3.22 ppm) and kaempferol (4.07 ppm). Our molecular docking analysis revealed that these compounds exhibited different binding affinities and potentials for targeting BChE/AChE/ $\text{IL-1 } \beta/\text{Na}^+/\text{K}^+$ -ATPase. However, only Kampferol and ferulic exhibited good drug-like, ADMET, and permeability properties suitable for use as a neuronal drug target agent. Hence, the ethyl-acetate fraction of *C. pubescens* leaves could be considered a source of promising bioactive metabolite for the treatment and management of cognitive impairments related to type II diabetes mellitus.

Keywords : diabetes mellitus, neuroprotective, antioxidant, pro-inflammatory cytokines

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