

Inhibition of *Echis ocellatus* Venom Metalloprotease by Flavonoid-Rich Ethyl Acetate Sub-fraction of *Moringa oleifera* Leaves (Lam.): in vitro and in silico Approaches

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Abstract : Envenoming by *Echis ocellatus* is potentially life-threatening due to severe hemorrhage, renal failure, and capillary leakage. These effects are attributed to snake venom metalloproteinases (SVMPs). Due to drawbacks in the use of antivenom, natural inhibitors from plants are of interest in studies of new antivenom treatment. Antagonizing effects of bioactive compounds of *Moringa oleifera*, a known antisnake plant, are yet to be tested against SVMPs of *E. ocellatus* (SVMP-EO). Ethanol crude extract of *M. oleifera* was partitioned using n-hexane and ethyl acetate. Each partition was fractionated using column chromatography and tested against SVMP-EO purified through ion-exchange chromatography with EchiTab-PLUS polyvalent anti-venom as control. Phytoconstituents of ethyl acetate fraction were screened against the catalytic site of crystal of BaP1-SVMP, while drug-likeness and ADMET toxicity of compound were equally determined. The molecular weight of isolated SVMP-EO was 43.28 kDa, with a specific activity of 245 U/ml, a percentage yield of 62.83 %, and a purification fold of 0.920. The V_{max} and K_m values are 2 mg/ml and 38.095 $\mu\text{mol/ml/min}$, respectively, while the optimal pH and temperature are 6.0 and 40°C, respectively. Polyvalent anti-venom, crude extract, and ethyl acetate fraction of *M. oleifera* exhibited a complete inhibitory effect against SVMP-EO activity. The inhibitions of the P-1 and P-II metalloprotease's enzymes by the ethyl acetate fraction are largely due to methanol, 6, 8, 9-trimethyl-4-(2-phenylethyl)-3-oxabicyclo[3.3.1]non-6-en-1-yl- and paroxypropione, respectively. Both compounds are potential drug candidates with little or no concern of toxicity, as revealed from the in-silico predictions. The inhibitory effects suggest that this compound might be a therapeutic candidate for further exploration for treatment of *Ocellatus*' envenoming.

Keywords : *Echis ocellatus*, *Moringa oleifera*, anti-venom, metalloproteases, snakebite, molecular docking

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