

Molecular modelling, chemical synthesis and evaluation of antinociceptive effects for some phenazone analogues

S. M. Bensaber¹, Z. S. Abood², A. Aremash¹, A. El-Zitrini², I. A. Mureema¹, A. Gbaj^{1,2} and M. I. Joaeda¹

¹University of Tripoli, Libya

²National medical research center, Libya

A wide range of pain relievers are available today, but they are different in their efficacy, safety and cost. Phenazone has long history of analgesic effect and at the same time it is may be work by different mechanism in comparison with other NSAIDs. The toxicity of phenazone and its derivatives was largely studied by many research groups and some results indicated that the toxicity may diminished by introducing imine functionality (azapropazone). In the current study, we aimed to develop new potent and safe analgesic agents depending on structural modifications of phenazone depending on Schiff's base (imine) formation. 4-Aminophenazone was condensed with several aldehydes to produce the designed imine derivatives utilizing reflux or microwave techniques for the synthesis. The purification of the synthesized compounds was performed as required for each derivative and monitored by the TLC and HPLC techniques. The spectroscopic characterization of all derivatives (sixteen compounds) was performed using infra red, ¹HNMR and ¹³CNMR spectroscopic techniques. The possible interaction of all compounds and the active site of the targeted cyclooxygenase 2 (COX2) enzymes were studied using AutoDock 4.2 program for molecular modelling. The obtained docking results indicated that some of the targeted compounds showed better interaction at the active site in comparison to the phenazone. *In vitro* investigation of the inhibitory activity of the designed compounds against COX₂ enzyme was conducted and showed that a significant activity. Some of the synthesized compounds showed good *in vivo* antinociceptive effects using animal models and some of the compounds also showed more activity than phenazone itself.

salahpharm2@yahoo.com