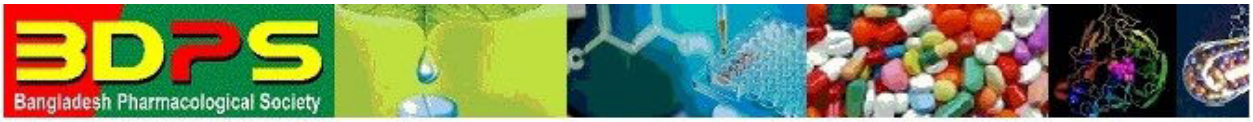
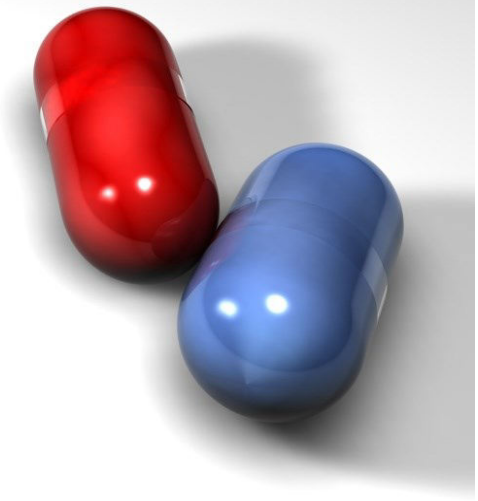


Bangladesh Journal of Pharmacology

Volume 11; Number 3; Year 2016



Cite this article as: Karim N, Ullah R, Khan I, Raza M, Rauf A, Hizbullah SM, Khan I. Anti-inflammatory activity and molecular docking studies of quinolyl-thienylchalcone. Bangladesh J Pharmacol. 2016; 11: 703-704.

A Journal of the Bangladesh Pharmacological Society (BDPS)
Journal homepage: www.banglajol.info
Abstracted/indexed in Academic Search Complete, Agroforestry Abstracts, Asia Journals Online, Bangladesh Journals Online, Biological Abstracts, BIOSIS Previews, CAB Abstracts, Current Abstracts, EMBASE/Excerpta Medica, Google Scholar, HINARI (WHO), International Pharmaceutical Abstracts, Open J-gate, Science Citation Index Expanded, SCOPUS and Social Sciences Citation Index
ISSN: 1991-0088; DOI: 10.3329/bjp.v11i3.28428

Bangladesh J Pharmacol 2016; 11: 703-704

Letter to the Editor

Anti-inflammatory activity and molecular docking studies of quinolyl-thienyl chalcone

Sir,

Chalcones, also known as benzylideneacetophenone, are group of compounds that belong to the flavonoids family and act as a precursur for flavonoid and isoflavonoids occurring in edible plants. Chalcones possesses a broad spectrum of pharmacological activities. They have been shown to possess anti-bacterial, anti-protozoal, anti-malarial (Hayat et al., 2011) and anti-inflammatory activities (Gómez-Rivera et al., 2013). The compound selected for current investigations was synthesized as reported earlier (Rizvi et al., 2012). Previously vascular endothelial growth factor receptor-2 (VEGFR-2) kinase inhibitory activity of the same compound was investigated (Rizvi et al., 2012).

In vivo model was utilized to assess the anti-inflammatory potential of test sample via testing its ability to inhibit the carrageenan-induced hind paw edema, as reported earlier (Winter et al., 1962).

Furthermore, the docking study of COX-2 enzymes were carried out through iGEMDOCK v2.1 and AutoDock Vina (with PyRex tool) software (Trott and Olson, 2010). The docking method of both the software was calibrated through already co-crystallized ligand. The 3-D structures of the chalcone was prepared by Chemdraw (Begam and Kumar, 2012) and Avogadro software (Hanwell et al., 2012). All the default parameters were utilized for the docking studies against COX-2 enzyme.

Intraperitoneal injection of carrageenan in rats showed a time-dependent increase in paw edema. The maximum increase was observed at the 5th hour of carrageenan administration in the control group. Quinolyl-thienyl chalcone at the doses of 80 and 100 mg/kg caused significant inhibition ($p<0.01$; ANOVA followed by Dunnett's post hoc test) in paw edema i.e. 42.8 and 53.8% respectively after 3rd hour and 46 and 59.3% after 5th hour of carrageenan administration whereas 40 mg/kg of quinolyl-thienyl chalcone reduced paw edema significantly ($p<0.05$; ANOVA followed by Dunnett's post hoc test) only after 5 hours of carrageenan administration (26.3% inhibition). The standard anti-inflammatory drug diclofenac sodium (100 mg/kg) was found to be more efficacious and carrageenan induced paw edema was reduced significantly ($p<0.001$; ANOVA followed by Dunnett's post hoc test) after 3rd and 5th hour of carrageenan administration (71.4 and 72% inhibition). The main purpose of the docking studies was to validate the *in vivo* studies and identify the inhibiting potential of quinolyl-thienyl chalcone and diclofenac against COX-2 enzyme from rats.

The docking score of the quinolyl-thienyl chalcone and standard diclofenac are shown in Table I. The predicted docking poses and superimposition of the compound quinolyl-thienyl chalcone along with standard correlate docking results with *in vivo* study. The docking score of quinolyl-thienyl chalcone in both receptors are best than the standard. The interaction analysis of docked quinolyl-thienyl chalcone in the binding pocket of COX-2 (Figure 1) indicated that quinolyl-thienyl chalcone carbonyl group forms one hydrogen bond interaction with the Tyr356 with a distance of 2.90Å while eight

Table I

Docking energies of quinolyl-thienyl chalcone against COX-2 enzyme from rats

Compounds	AutoDock Vina (kcal/mol)	i-GEM DOCK (kcal/mol)			
	Binding affinity	Total energy	van der Waals interaction	Hydrogen bond	Electrostatic interaction
Quinolyl-thienyl chalcone	-9.2	-86	-80	-6	0
Diclofenac sodium	-6.8	-84	-75	-9	0

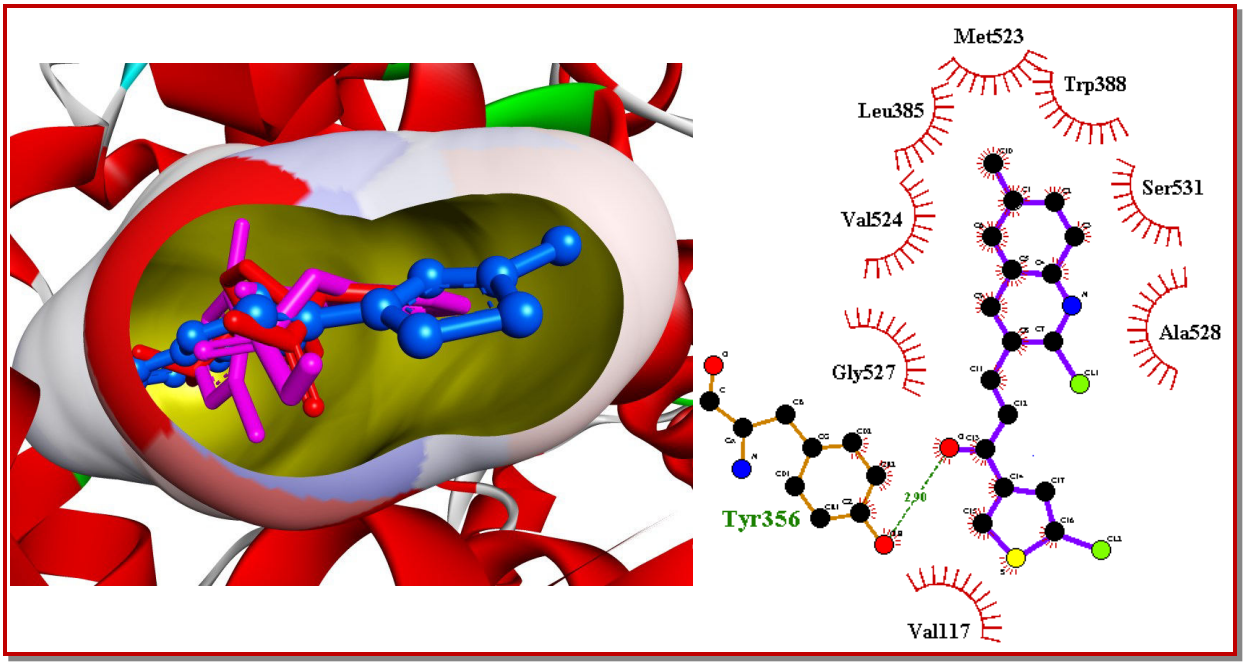


Figure 1: COX-2 enzyme predicted docked poses with quinolyl-thienyl chalcone (ball and sticks blue color), their superimposition on the standard diclofenac (pink color sticks) and Co-crytallized ligand (sticks red color) (Left); Quinolyl-thienyl chalcone docking in the active site of COX-2 enzyme with 2-D schematic presentation (Right)

hydrophobic contacts have been observed from the surrounding residues including them Val117, Leu385, Trp388, Met523, Val524, Gly527, Ala528 and Ser531 with the binding site of COX-2 enzyme.

Thus, quinolyl-thienyl chalcone has the potential for discovery of a compound with potent anti-inflammatory effects and its scaffold could be used for further structural modifications. To the best of our knowledge this is the first study reporting the anti-inflammatory activity of quinolyl-thienyl chalcone.

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