EXECUTIVE SUMMARY OF UGC MINOR RESEARCH PROJECT

GRANT DETAILS

F. No.: 47-976/14 (WRO)

Title: Synthesis, Biological evaluation and virtual screening of novel Pyrazoline derivatives as selective COX-2 inhibitors and anti-inflammatory agents

Name of Principal Investigator: Mr. Chaudhari S. Y.

Duration: 2015-17

College: P. E. S. Modern College of Pharmacy, NIgdi

Effective date of starting the project: 20 Feb 2015

Amount Sanctioned Rs. 2,15,000

SUMMARY OF THE RESEARCH PROJECT

Heterocyclic compounds are important for treatment of various diseases likes anti-inflammatory, antimicrobial anticancer, antitubercular, antidepressant, antimalarial, and hypoglycemic. Compounds possessing different heterocyclic system exhibit a diverse range of biological activities and in great demand in the present day therapy. Medicinal chemistry can interest to prepare novel heterocyclic compounds with potential biological activities

This project is an endeavor this direction, in the synthesis and characterization of novel Pyrazoline derivatives of compounds based on IR, ^{1}H NMR and anti-inflammatory activity.

Pyrazolines are important class of five membered heterocyclic compounds and produce good pharmacological activities. Further, it can be concluded that these molecule can be the best candidate as a lead compound for further development of drug.

In literature survey we have highlightened that pyrazole and 2- Pyrazoline derivatives as potential analgesic and anti-inflammatory agents. Therefore further research and optimization of these compounds may result in highly effective compounds with minimal side effects.

Potent ligands were finding on basis of molecular docking. Docking studies revealed that on the in series-II & IV the change in the functional group R does not bring any major change to the binding affinity. Although the change in the substituents bring about a slight variation in the binding energy, it was not significant.

The binding energy of the Pyrazoline series-I & III were found to be higher with the presence of a Phenyl nitrate group attached to the nucleus at the 1 & 3 positions respectively. This could probably be due to the enhanced electron withdrawing group on aromatic ring system. On other hand if P-SO_2NH_2 and NH_2 functional group added to ring A decreases the binding affinity than

the standard selected. While O-NO_2, P-NO_2 & P-Cl phenyl at fifth position of Pyrazoline shows maximum binding with cyclooxygenase enzyme, this is because of electron withdrawing group. It means that electron withdrawing groups at any ring from A, B, C shows maximum binding with receptor pocket. The docking scores revealed that the designed molecules have good hydrogen bonding interactions with the important amino acids in the selected binding pocket which was studied by using ligplot plus v.1.4.5.

Drug design is also done by using Ramachandran plot, ligplot, Pass Inet application and pre ADMET application.

Selected compounds 1C, 1F, 3D, 3E & 3G having good cox-2 inhibition, lesser cox-1 binding, better NO-donor & analgesic activity with minimum side effects.
Different analogues of 1, 3, 5-triaryl substituted Pyrazolines were synthesized by attaching different substitution at 1^{st}, 3^{rd} and 5^{th} position of Pyrazoline.

The spectral characteristics and physical properties of the synthesized compounds were identified with the help of Melting point, Infra-red and ^{1}H NMR spectroscopy.

The compounds synthesized were evaluated by anti-inflammatory, analgesic and ulcerogenic screening protocol consisting methods like carrageenan induced rat paw edema method, acetic acid induced writhing method and cioli *et al* method of ulcerogenicity.

Active compound (3E) did not induce ulcer in tested animals, so we concluded that these compounds are free from side effects of the commonly used typical analgesic anti-inflammatory agents.

Thus, we conclude that the synthesized compounds have a potential for further development as novel anti-inflammatory and analgesic agent.

Chaudhari S. Y.

Principal Investigator