activities. Some selected molecules from these series were also evaluated for analgesic and anti-inflammatory potential.

The antibacterial activity was studied against both gram positive (*Bacillus subtilus*) and gram negative (*Escherichia coli*) bacterial strains and also evaluated as antifungal activity against *Aspergilus niger* strain. We have also investigated their toxicity through hemolytic and thrombolytic activities using blood as a substrate. Analgesic and anti-inflammatory activities for selected compounds were performed using *swiss albino mice,* which showed very encouraging results.

Out of seven prepared series, the series (6a-s) in wihich piperidine ring is replaced with oxadiazole moiety shows most significant results. Two of the derivatives (6b & 6h) from this series (6a-s) found more potent antibacterial activity when compared with diclophenac sodium standard. From same series 6l & 6p showed improved hemolytic activity while 6e & 6f exhibited better thrombolytic activity as compared to piperine.

7a-p series have aryl derivatives of oxadiazole-amide functionalities and in this series 7b showed the maximum antimicrobial activity while 7l and 7e of this series exhibited better hemolytic and thrombolytic activities respectively. A minor change in carbon chain for the series 8a-p as compared to 7a-p display overall decrease in activities, however prominent antibacterial and antifungal activities were shown by 8a and 8d.

Schiff base containing derivative, 10l showed prominent hemolytic activity among the other members of this series. Sulphonamide bearing derivatives 11a-e showed moderate thrombolytic and hemolytic activity but 11e exhibited maximum antibacterial & antifungal activities. Oxatraizole containing derivative 12b and 12f found to have better thrombolytic activity as well as good antimicrobial agents.

Selective derivatives were analyzed against analgesic and anti-inflammatory activities. Addition to Schiff Base moiety to piperine (10h) showed maximum analgesic activity (tail + hot plate method) even higher than Diclofenac sodium standard, while simple oxadiazole (5) and alkyl substituted oxadiazole (6o) showed maximum anti-inflammatory activities.

Overall it is concluded that introduction of new functionality to piperine alkaloid made the molecules potent than the parent in most of the cases.

ABSTRACT

Piper nigrum is a medicinal plant and commonly used as household spice, having piperine alkaloid as major and active ingredient. Piperine is an antibacterial compound and its multiple uses have already been established in literature, therefore it is widely used in folk. There are many other potent antibiotics available in the market that contain substituited-1,3,4-oxadiazole heterocyclic ring structures.

The high resistivity of microorganisms towards the prevailing drugs motivated us to synthesize new bioactive molecules by combining the piperine backbone to biological active oxadiazole system. It was assumed that 2,5 – disubstituited-1,3,4- oxadiazole heterocyclic ring may act as potent biological active molecules that boost the pharmacological activities to the new limits. The presented research work comprises the synthesis of some novel multifunctional derivatives followed by structural characterization & biological evaluation.

Piperine alkaloid is extracted in lab using soxhlet apparatus, purified, further derivatized and characterized. Piperine, by basic hydrolysis, is converted to piperic acid, which on esterification changed into ethyl piperate and upon reaction with hydrazine lead to piperine hydrazide molecule, which acts as backbone for further derivatization. Piperine hydrazide in three different routes changed to 1-oxadaizole moiety by reacting with CS_2 in aprotic solvents, 2- Imine functionality bearing molecules by reacting with various aldehydes, 3-sulphonamide functionalities by reacting with various aryl sulphonyl chlorides. Oxadiazoles further converted to oxatriazole by reacting with hydrazine. Overall we have synthesized 83 derivatives of piperine, with oxadiazole, oxatriazole, amide, imine and sulphonamide functionalities. The compounds presented in this work were synthesized according to available protocols in the literature and has been mentioned in seven schemes in detail (at the end of Chapter 1: Introduction).

These synthesized compounds were purified through chromatographic techniques including column chromatography and preparative chromatography. Structures of all these were elucidated through IR, EIMS, ^{1}H and ^{13}C NMR spectroscopic techniques.

As literature showed that various molecules containing these type of functionalities are biologically active and used for the treatment of various diseases. This encouraged us to evaluate piperine derivatives to search for more biological active or potent molecules. We have evaluated antibacterial, antifungal, hemolytic and thrombolytic