ANTI-INFLAMMATORY RESPONSE OF NOVEL OXAZOLINES

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ABSTRACT

The aim of this work is to screen *in vivo* and *in vitro* anti-inflammatory effects of Novel Oxazoline derivatives.The newly synthesized compounds tested for acute toxicity by OECD-423 guidelines. Anti-inflammatory response screened by *in vitro* method using egg albumin. Using plethysmometer *in vivo* screening of synthesized compounds performed.There were no toxic signs in acute toxicity studies. By invitro studies phenyl ring possesing halogen/hydroxyl/methoxyl group at third/fourth position are found to have good antiinflammatory effect using Diclofenac (100µg/ml)as the standard drug. The same pattern of reducing the inflammatory response observed for invivo studies too. The compounds which showned good anti-inflammatory response found to have certain common features like presence of halogen/hydroxyl/methoxyl functional groups in their structure.

Key words : Carageenan, anti inflammatory, denaturation,oxazolines

No: of Figures: 2 **No: of References: 5**

INTRODUCTION :

Oxazoline is one of the important moiety in heterocyclic chemistry and have wide applications in agriculture industry, pharmaceutical, food industry, natural product, medicine, polymers and various other industries. Oxazoline containing many molecules reported to have antibacterial, antifungal, antimicrobial, antioxidant, antipyretic, anti-HIV, anti malarial, anti tumour, antiviral, anti-inflammatory, CNS stimulant activity etc.

In higher organisms ,inflammation is a defense mechanism in order to protect from infection and injury.[1] At the site of tissue damage, inflammatory response include changes in blood flow, an increase in blood vessel permeability, migration of fluid, proteins and leukocytes from circulation to the site of injury .Most of the anti-inflammatory agents work by inhibiting the effects of certain chemicals –enzymes namely COX enzymes which involve in production of pain mediators – prostaglandins. A reduction in prostaglandin production reduces pain and inflammation.[2]

Carrageenan-induced rat paw oedema is a widely used test to determine anti-inflammatory activity and constitutes a simple and routine animal model for evaluation of pain at the site of inflammation without any injury or damage to the inflamed paw. freshly prepared solution of 1–3% carrageenan in saline as an intraplantar injection in doses of 50–150 µl is commonly used. There are several mediators involved in inflammation. Histamine,serotonine and bradykinin are the first detectable mediators in the early phase of carrageenan-induced inflammation; prostaglandins (PGs) are involved in the increased vascular permeability and are detectable in the late phase of inflammation. Local and/or systemic inflammation is associated with enhanced levels of the pro-inflammatory cytokines TNF-a,IL-1, and IL-6.

MATERIALS AND METHODS

Animals

Young *Swiss-Albino* mice aged about 4–5 weeks with average weight of 25–35 gm and adult wistar albino Rats of either sex having average weight of 150-250 gm. were used for the experiment and maintained in the animal house of the Pushpagiri College of pharmacy. They were housed in standard cages under standard environmental conditions of room temperature at 24 ± 1°C and 55-65% relative humidity with 12 hour dark light cycle and provided with standard food for rodents and water *ad libitum*. The experimental protocol was approved by the institutional animal Ethics committee in Pushpagiri College of pharmacy and was performed according to the CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals) Guidelines. chemicals used for this project were of AR grade and LR grade.

Acute toxicity studies

Acute oral toxicity study for the test extract of the plant was carried out using OECD guidelines 425.Healthy, *Swiss-Albino* mice aged about 4–5 weeks with

average weight of 25–35 gm were used for this study. Animals had been fasted prior to dosing with free access of water. The fasted body weight of each animal is determined and the dose is calculated according to the body weight. Limit test at 2000mg/kg. dose 2000mg/kg of plant extract in 1% tween was administerd orally. The animals are observed individually during the first 24hrs and daily thereafter, for a period of 14 days.

Carrageenan Induced Paw edema[6]

Wistar Albino rats weighing 150 -250 g were used for animal studies. Acute inflammation is provided by injection of 0.1ml of 1% carrageenan into the sub plantar surface of rat hind paw. The animals were grouped into Group 1 served as control 1%sodium CMC, Group 2 received standard diclofenac and 0.1ml of carrageenan, Group 4 received test group and 0.1ml of carrageenan. The paw volume was measured at 0^{th} and 4^{th} hours.

Methodology for In vitro anti-inflammatory activity[5]

The reaction mixture consisted of 0.2 ml of egg albumin (from fresh hen's egg), 2.8 ml of phosphate buffered saline (pH 6.4) and 2 ml of varying concentrations of the test series, by which the concentrations (100µg/ml) . Similar volume of double-distilled water served as control. Then the mixtures were incubated at 37°C ± 2°C in a biological oxygen demand incubator for 15 min and then heated at 70°C for 5 min. After cooling, their absorbance was measured at 660 nm by using vehicle as blank. Diclofenac sodium (100µg/ml) used as reference. The percentage inhibition of protein denaturation was calculated by using the following formula:

% inhibitionof protein denaturation = 100 × ([Vt/Vc] −1). Where, Vt = absorbance of test sample, Vc = absorbance of control.

Statistical analysis

All the values are expressed in mean ± SEM. Statistical significance was calculated by one way ANOVA with Dunnett's test

RESULT

None of the tested compounds are superior to Diclofenac sodium which was the standard.

There is no sign of toxicity. All compounds exhibited anti-inflammatory activity among tested 25 oxazoline derivatives LJ1,LJ2,LJ5,LJ9,LJ10,LJ11,LJ15,LJ23 shows significant anti-inflammatory activity.(shown in figure I and 2)

Figure 1 :Evaluation of *In Vivo* Anti-Inflammatory Activity of Oxazolines

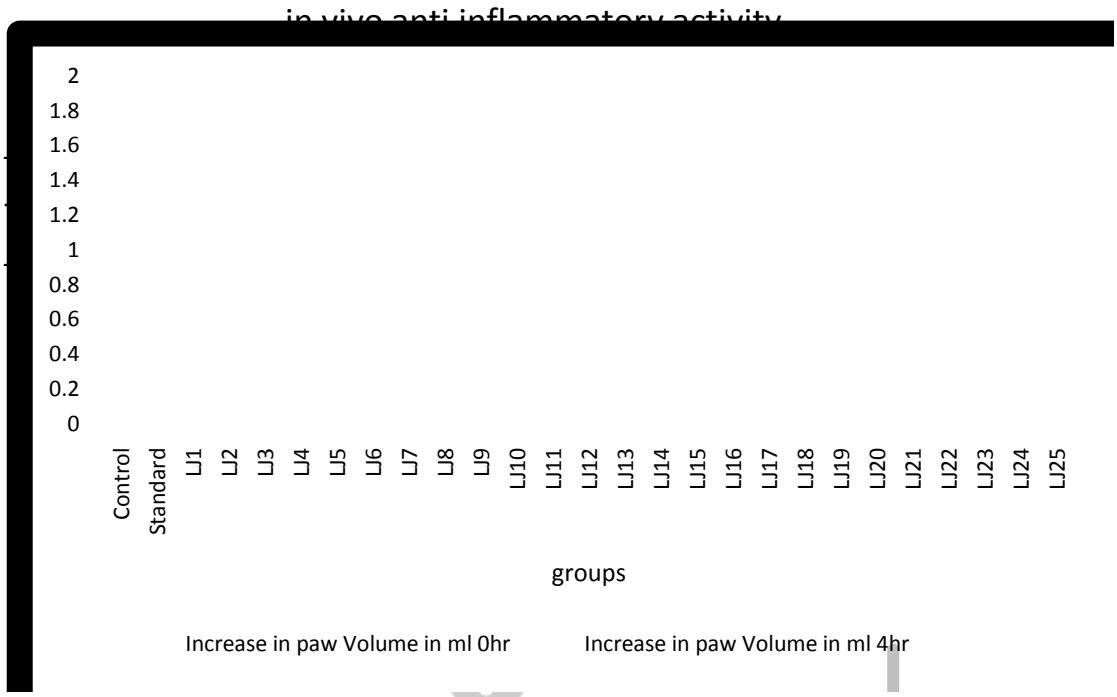
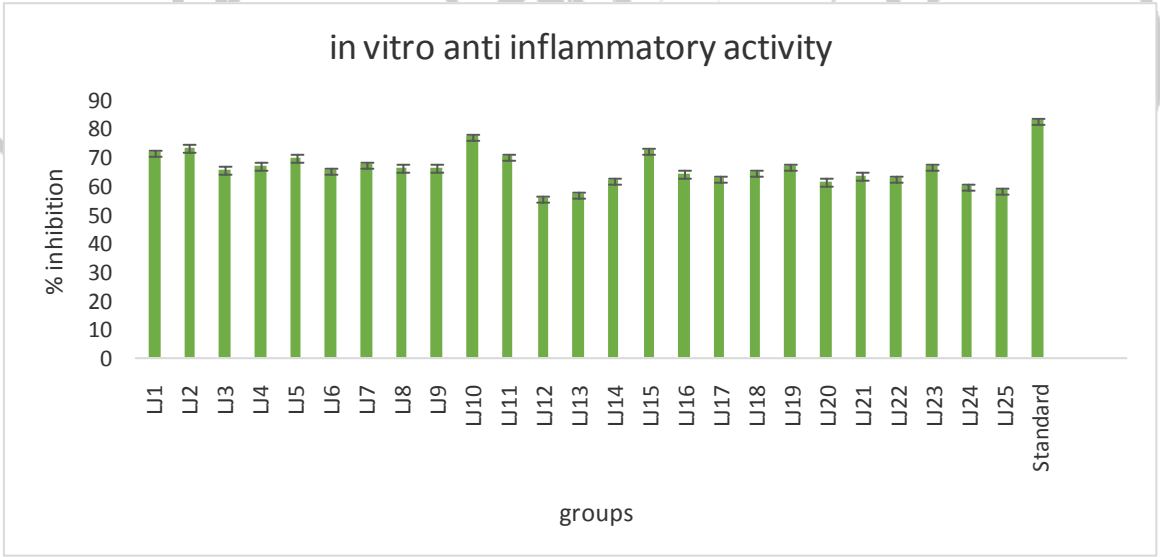


Figure 2 :Evaluation of *In Vitro* Anti-Inflammatory Ativity of Oxazolines



DISCUSSION

Twenty five Oxazoline derivatives are prepared,characterized and among the tested compounds LJ1,LJ2,LJ5,LJ9,LJ10,LJ11,LJ15,LJ23 shows significant anti inflammatory activity. There were no toxic signs in acute toxicity studies. By *in vitro* studies phenyl ring possesing halogen/hydroxyl/methoxyl group at third/fourth position are found to have good antiinflammatory effect using Diclofenac (100µg/ml)as the standard drug. The same pattern of reducing the inflammatory response observed for *invivo* studies too.The compounds which showned good anti-inflammatory

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Authors Biography

Dr.Lincy has completed her Ph.D in Pharmaceutical sciences . She have guided & Supervised many PhD and postgraduate students in Pharmaceutical Sciences. She have ample of publications in many reputed journals and authored different text books. She have presented many papers and attended various conferences held at national and International level. Currently she is working as Professor at Pushpagiri college of Pharmacy,Kerala-India.