International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 14, No. 5, May 2025 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_14.5.2025.11

ORIGINAL RESEARCH

Evaluation of anti inflammatory effect of atorvastatin in adult male albino rats

Dr. Vijayarani.R[1], Dr. R.S. Theivanayagi[2], Dr. S.Umadevi[3]

[1,2]Assistant Professor, Department of Pharmacology, Govt Sivagangai Medical College, Sivagangai, India
[3]Associate Professor, Department of Pharmacology, Govt Pudukkottai Medical College, Pudukkottai, India

Corresponding author
Dr. R.S. Theivanayagi
Assistant Professor, Department of Pharmacology, Govt Sivagangai Medical College, Sivagangai, India
Email: theivanayagirs@gmail.com

Received: 25 March, 2025 Accepted: 21 April, 2025 Published: 01 May, 2025

ABSTRACT

Aim and objective: To evaluate the anti-inflammatory effect of Atorvastatin in experimentally induced paw edema in adult male albino rats. **Materials and methods:** Eighteen inbred adult male albino rats weighing about 150-200 gms were selected from Central Animal House, Madurai medical college, Madurai. They were divided into three groups, each group containing six rats. The group I was considered as control group, received normal feed and water.Group II was considered as standard received Tab. Indomethacin 10mg/kg per orally. Group III was considered as test group, received Tab. Atorvastatin 6mg/kg per orally. Paw edema was produced by sub plantar injection of carrageenan. The drugs were administered one hour prior to carrageenan injection. The paw edema was measured by using plethysmography immediately before, after 1 hour, 2 hours and 3 hours of injecting carrageenan. The difference between the left and right paw edema volume was determined and the percentage reduction was calculated and compared to control animals after administrating standard and test drugs. The results were tabulated and analysed by suitable statistical method. **Results:** 6mg/kg Atorvastatin group and 10mg/kg Indomethacin group showed significant anti-inflammatory activity in compared to the control group. **Conclusion:** Atorvastatin has anti-inflammatory activity which is comparable to indomethacin.However studies in chronic models of inflammation are needed to confirm safety.

Key words: Atorvastatin, Indomethacin, Anti inflammatory and carrageenan

INTRODUCTION

Inflammation is the immune system's response to harmful stimuli, such as pathogens, damaged cells, toxic compounds, or irradiation, and acts by removing injurious stimuli and initiating the healing process. Inflammation is therefore a defense mechanism that is vital to health. Usually, during acute inflammatory responses, cellular and molecular events and interactions efficiently minimize impending injury or infection. This process contributes to restoration of tissue homeostasis and resolution of the acute inflammation. Uncontrolled acute inflammation may become chronic, contributing to a variety of chronic inflammatory diseases. At the tissue level, inflammation is characterized by redness, swelling, warmth, pain, and loss of tissue function, which result from local immune, vascular and inflammatory cell responses to infection or injury During the inflammatory process there will be vascular permeability changes, leukocyte recruitment and accumulation, and inflammatory mediator release . Various pathogenic factors, such as infection, tissue injury, or cardiac infarction, can induce inflammation by causing tissue damage. The etiologies of inflammation can be infectious or non-infectious The inflammatory response is the coordinate activation of signaling pathways that regulate inflammatory mediator levels in resident tissue cells and inflammatory cells recruited from the blood[1]. Mediators and Biomarkers of Inflammation include: Reactive oxygen species (ROS) and reactive nitrogen oxide species (RNOS), Cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha, and chemokines, Acute-phase proteins, such as C-reactive protein or CRP, Prostaglandins, Cyclooxygenase (COX)-related metabolites, Inflammation-related growth factors and transcription factors, such as NF-kappa B and major immune cell types[2]

INDOMETHACIN

Indomethacin is the commonly used NSAID. It is an indole derivative and a potent non selective COX inhibitor and also inhibit phospholipase A and C. It acts by reducing neutrophil migration and decreasing T cell and B cell proliferation[3].

DOI: 10.69605/ijlbpr_14.5.2025.11

STATINS

Statins are inhibitors of 3-hydroxyl-3-methylglutaryl coenzyme A (HMG-CoA) reductase, a key enzyme in the synthesis of cholesterol. Currently, statins are widely used to control cholesterol levels and have achieved very good effects in lowering the incidence of cardiovascular events among patients. Atorvastatin is a statin that has become a routine treatment for patients with hypercholesterolemia and atherosclerosis. In addition to its lipid-lowering property, atorvastatin can also produce anti-inflammatory effects[4]. Statins decrease the secretion of pro-inflammatory cytokines IL-6 (interleukin-6) and IL-8 (interleukin-8) from macrophages and inhibit the release of the chemokine CCL2/MCP-1 (macrophage chemotactic protein-1) from these cells[5].Statins have beneficial effects in decreasing serum levels of TNF-α[6]. They have been reported to suppress acute and chronic inflammation by inhibiting edema formation, leukocyte-endothelial adhesion, production of inflammatory cytokines and transcription factors[7]

In this present study the potential anti-inflammatory effects of Atorvastatin in acute local inflammation was compared with Indomethacin, a well known anti inflammatory drug.

AIM AND OBJECTIVE

Study was aimed to evaluate the anti-inflammatory activity of Atorvastatin.

MATERIALS AND METHODS

Study Centre

Study was carried out in the Institute of Pharmacology, Madurai medical College, Madurai after getting clearance from the Institutional Animal ethical committee.

Study Design

Eighteen adult male Albino rats weighing about 150-200gms were used for this study. They were divided into 3 groups, each group consists of 6 rats. Animals were kept in cages and allowed to acclimatize at least 7 days prior to the study, when they were housed at ambient temperature of 21+1C with ad libitum access to food and water. On the day prior to study the animals were kept fasting overnight.

METHODOLOGY

Carrageenan Induced paw edema

Baseline paw edema of right hind paw was measured using mercury plethysmography. The animals were pretreated according to the group allocated with drugs orally one hour before the experiment. The rats were injected with subplantar injection of 0.1 ml of 1% solution of carrageenan into right hind paw. Paw of each animal was marked with ink at the level of lateral malleolus. Volume of the same paw was measured after 1hour, 2 hours, and 3 hours. Amount of edema was obtained by subtracting volume of right hind paw at base line before injecting carrageenan from volume of the same paw at 1 hour, 2 hours, and 3 hours. The percent inhibition of edema due to control and treatment was calculated using the following formula

Percent inhibition of edema = $100 \times (L - Vt / Vc)$

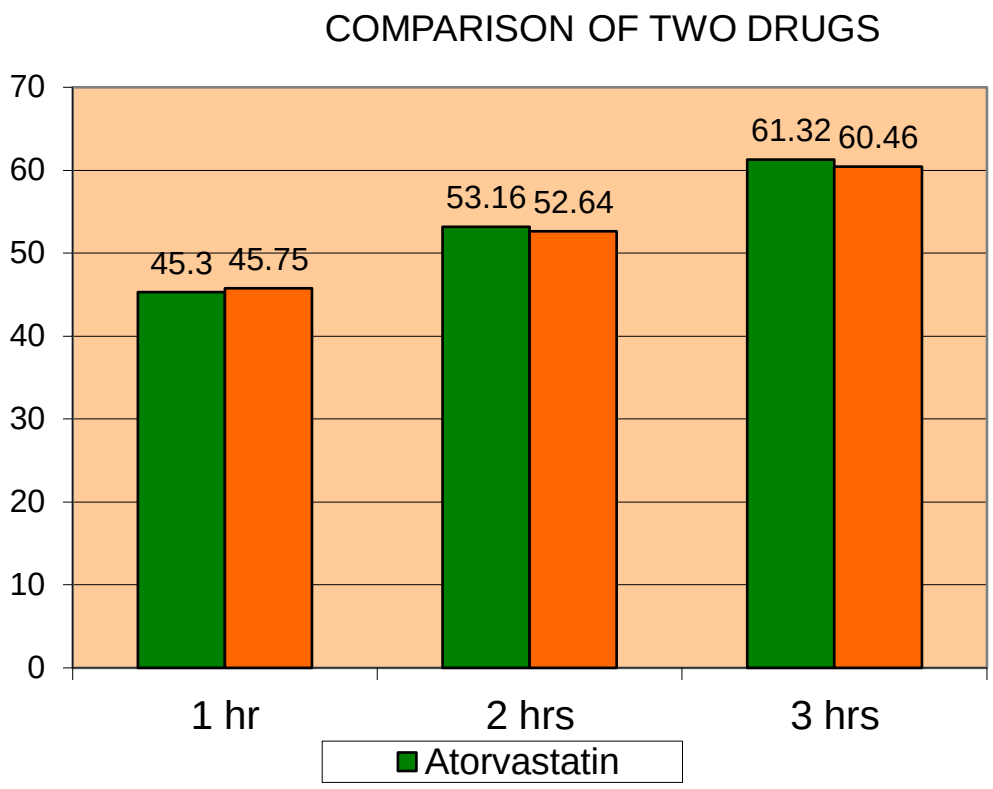
Vc - mean paw edema volume in control groups

Vt - mean paw edema volume in treated group.

Statistical Analysis

The information collected regarding all the selected cases were recorded in a master chart. Data analysis was done with the help of computer by using SPSS software and Sigma Stat 3.5 version (2012). Using this software, percentage, mean, standard deviation and ‘p’ value were calculated through Student ‘t’ test, One way ANOVA, and Chi square test and P value of < 0.05 was taken as significant.

DOI: 10.69605/ijlbpr_14.5.2025.11



RESULTS

Indomethacin was administered in a dose of 10mg / kg orally 1 hr before corrageenan challenge. All the 6 test groups showed significant reduction in paw edema (p value > o.oo1) Oral administration of Atorvastatin in a dose of 6 mg / kg orally 1 hr before corrageenan challenge produced an inhibition of foot pad swelling comparable to that of Indomethacin. (p value > o.oo1) No difference was observed in anti-inflammatory effect in standard and test groups.

DISCUSSION

Statins have been widely used in the treatment of dyslipidemia. More recently there has been an interest in the anti-inflammatory activities of statins following reports about their ability to relieve pain and inflammation. In model of acute inflammation, Atorvastatin showed anti-inflammatory activity comparable to Indomethacin. The carrageenan-induced paw edema is a well-defined model of acute inflammation that a variety of inflammatory mediators involve in its development and has wildly been used to evaluate the anti-inflammatory effect[8]

Carrageenan is a sulphated polysaccharide obtained from sea weed (Rhodophyceae) and is commonly used to induce acute inflammation and is believed to be bi-phasic.The first phase is due to release of histamine and serotonin.The second phase is caused by the release of bradykinin,protease, prostaglandin and lysosome. Based on this, it would be argued that suppression of Ist phase may be due to inhibition of release of early mediators, such as histamine, serotonin and action in IInd phase may be explained by inhibition of cyclo-oxygenase. These mediators take part in inflammatory response[9]

The anti inflammatory effect of atorvastatin similarly to indomethacin are probably related to inhibition of proinflammatory mediators, polymorphonuclear leucocyte infiltration as well as to inhibition of release polymorphonuclear leucocytes derived free radicals.

The results of this study support the hypothesis that atorvastatin has a potent anti-inflammatory effect in acute local inflammation which might be a consequence of its inhibitory effect on PMN leucocyte infiltration.

CONCLUSION

Statins have been proven to have a positive effect on the reduction of inflammation in patients with various diseases such as coronary artery disease, chronic renal disease, and diabetes mellitus. All statins examined were shown to lower the levels of inflammatory markers and especially CRP levels. Statins were arguably proven to be an effective treatment as far as the inhibition of inflammation is concerned[10] Atorvastatin has inflammatory activity which is comparable to Indomethacin. However for detailed elucidation of effects of atorvastatin on carrageenan induced acute inflammatory response further studies are required.

FUNDING: No funding sources

CONFLICT OF INTEREST: Nil

ETHICAL APPROVAL: The study was approved by the Institutional Animal Ethics Committee

DOI: 10.69605/ijlbpr_14.5.2025.11

REFERENCES

1. Chen L, Deng H, Cui H, Fang J, Zuo Z, Deng J, Li Y, Wang X, Zhao L. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget. 2017 Dec 14;9(6):7204.
2. Stone WL, Basit H, Zubair M, Burns B. Pathology, inflammation. InStatPearls [Internet] 2024 Aug 11. StatPearls Publishing4.
3. Goodman & Gilmon's, The pharmacological Basis of Therapeutics 14th edition, Laurene Brunton, Bruce chaloner, B. Jorn Knollman
4. Peng S, Xu LW, Che XY, Xiao QQ, Pu J, Shao Q, He B. Atorvastatin inhibits inflammatory response, attenuates lipid deposition, and improves the stability of vulnerable atherosclerotic plaques by modulating autophagy. Frontiers in Pharmacology. 2018 May 3;9:438.
5. Barsante MM, Roffê E, Yokoro CM, Tafuri WL, Souza DG, Pinho V, Castro MS, Teixeira MM. Anti-inflammatory and analgesic effects of atorvastatin in a rat model of adjuvant-induced arthritis. European journal of pharmacology. 2005 Jun 15;516(3):282-9.
6. Abbasifard M, Kandelouei T, Aslani S, Razi B, Imani D, Fasihi M, Cicero FG, Sahebkar A. Effect of statins on the plasma/serum levels of inflammatory markers in patients with cardiovascular disease; a systematic review and meta-analysis of randomized clinical trials. Inflammopharmacology. 2022 Apr;30(2):369-83.
7. Wahane VD, Kumar VL. Atorvastatin ameliorates inflammatory hyperalgesia in rat model of monoarticular arthritis. Pharmacological research. 2010 Apr 1;61(4):329-33. 11. Mansouri MT, Hemmati AA, Naghizadeh B, Mard SA, Rezaie A, Ghorbanzadeh B. A study of the mechanisms underlying the anti-inflammatory effect of ellagic acid in carrageenan-induced paw edema in rats. Indian journal of pharmacology. 2015 May 1;47(3):292-8. .
8. Mansouri MT, Hemmati AA, Naghizadeh B, Mard SA, Rezaie A, Ghorbanzadeh B. A study of the mechanisms underlying the anti-inflammatory effect of ellagic acid in carrageenan-induced paw edema in rats. Indian journal of pharmacology. 2015 May 1;47(3):292-8.
9. INDIA S. Research Article ISSN: 2230-7346. Journal of Global Trends in Pharmaceutical Science. 2012 Apr;3(2):677-858.
10. Mansouri MT, Hemmati AA, Naghizadeh B, Mard SA, Rezaie A, Ghorbanzadeh B. A study of the mechanisms underlying the anti-inflammatory effect of ellagic acid in carrageenan-induced paw edema in rats. Indian journal of pharmacology. 2015 May 1;47(3):292-8.