WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 24, 752-761. Research Article ISSN 2277–7105

ANTI-INFAMMATORY EFFECT OF *POLYGONUM AVICULARE* L. ETHANOLIC LEAF EXTRACT IN RODENT MODES OF ACUTE AND CHRONIC INFLAMMATION: INVOMENT OF POSSIBLE MECHANISMS

Avinash Joriya*, Jitendra Kumar and Anand Singh

School of Pharmaceutical Science, SINGHANIA UNIVERSITY, Pacheri Bari, Jhunjhunu (Raj.), India.

Article Received on
24 Oct. 2024,

Revised on 13 Nov. 2024,
Accepted on 03 Dec. 2024

DOI: 10.20959/wjpr202424-34671

***Corresponding Author**
Avinash Joriya
School of Pharmaceutical Science, SINGHANIA UNIVERSITY, Pacheri Bari, Jhunjhunu (Raj.), India.

ABSTRACT

Ethanolic extracts from the leaves of *Polygonum aviculare* L. were assessed at doses of 500 mg/kg for anti-inflammatory effects using both acute and chronic inflammatory models. It was found that the doses possessed inhibitory effects on the acute phase of inflammation as seen in carrageennan-induced paw edema. The anti-inflammatory activity elicited by plant ethanolic leaves extracts may be due to the influence of the active constituents such as beta-sitosterol and stigmasterol. A possible mechanism may also be due to the inhibition of prostaglandin synthesis which is also evidenced by the delay in the formation of wet faeces. Further study is required to postulate the exact molecular mechanism involved in this process of inhibition of inflammation by leaves extract.

KEYWORDS: *Polygonum aviculare* L, anti-inflammatory, paw edema.

INTRODUCTION

The inflammation term is taken from the Latin word “inflammare” (to burn) (*de oliveira*). Inflammation is one of the most central processes required in defense of animal cells against certain injuries or microbial infections.[1-2] Nevertheless, inflammation regularly progresses to acute.[3] Chronic inflammation is caused due to a variety of diseases including neurodegenerative disorders, cancer, and cardiovascular diseases.[4]

Mechanism of inflammation represents a chain of organized, dynamic responses including both cellular and vascular events with specific humoral secretions. These pathways involve changing physical location of white blood cells (monocytes, basophils, eosinophils, and neutrophils), plasma, and fluids at inflamed site.[5] A group of secreted mediators and other signaling molecules (e.g., histamine, prostaglandins, leukotrienes, oxygen- and nitrogen-derived free radicals, and serotonin) are released by immune defense cells principally in the mechanism which can contribute in the event of inflammation.[6]

Whatever, the inflammatory response is triggered through two phases: (a) acute and (b) chronic, and each is apparently mediated by a different mechanism. These immune responses which involved in acute inflammation can be divided into vascular and cellular.

The responses which occur in microvasculature normally appear in few minutes following tissue injury or microbial infection in the presence of other inflammatory stimuli named vascular events.[7] The occurrence of these processes is rapid and eventually will lead to vasodilatation and subsequently makes the vessels become more permeable. These processes will result in entry of inflammatory mediators and produces interstitial edema.[8-11]

Cellular events encompass the successive capture, trundling, and firming an adhesion to the microvascular endothelium.[15] These events in the mobilization pathway are arranged by cell adhesion molecules (CAMs). These CAMs include intracellular adhesion molecules (ICAM)-1, ICAM-2, integrins, and selectin. The selectin group of CAM contains three families; P-selectin and E-selectin produced by endothelial cells and L-selectin produced by white blood cells.[12-16]

The adhesion of high affinity presented on white blood cells in the endothelium is mediated by the interaction between integrins (CDII/CDI8), and adhesion molecules (CAM-l and CAM-2) expressed on white blood cells and endothelium cells, respectively.[17] Following a period of stationary adhesion, the white blood cells may leave the postcapillary venules extending pseudopodia between endothelial cells and reach into the subendothelial space. This complex event is often referred as white blood cell extravasations and transendothelial migration.[18]

The inflammations of chronic events are distinguished by mononuclear cell infiltration (e.g., monocyte and lymphocytes), fibroblasts proliferation, collagen fibers, and connective tissue

formation, which ultimately result in 2-mm granuloma.[19] With chronic inflammation, the tissue degeneration is normally mediated by nitrogen species, proteases, and other reactive oxygen species released from infiltrated inflammatory cells.[20] Certainly, genomic alterations in were approved as causes for many chronic inflammatory diseases (e.g., inflammatory bowel diseases and rheumatoid arthritis) in addition to cancers.[21]

MATERIAL AND METHODS

Plant name: *Polygonum aviculare L.*

Figure 1: *Polygonum aviculare*.

Polygonum aviculare or common knotgrass is a plant related to buckwheat and dock. It is also called prostrate knotweed, birdweed, pigweed and lowgrass.

It is an annual found in fields andwasteland, with white flowers from June to October. It is widespread across many countries in temperate regions, apparently native to Eurasia and North America, naturalized in temperate parts of the Southern Hemisphere.[22-23]

Botanical Name: It is derived from *Polygonum aviculare* and belonging from Polygonaceae (family).

Geographical Source: Widespread and common in North India, Great Britain, Ireland, and Scandinavia.

Description

Common knotgrass is an annual herb with a semi-erect stem that may grow from 10 to 40 cm (4 to 16 in) high. The leaves are hairless and short-stalked. They are longish-elliptical with short stalks and rounded bases; the upper ones are few and are linear and stalkless.

The stipules are fused into a stem-enclosing, translucent sheath known as an ochrea that is membranous and silvery. The flowers are regular, green with white or pink margins.[24-25]

Medicinal uses

The whole flowering plant is used to make medicine. Knotweed is used for bronchitis, cough, gum disease (gingivitis), and sore mouth and throat. It is also used for lung diseases, skin disorders, and fluid retention. Some people use it to reduce sweating associated with tuberculosis and to stop bleeding.[26]

Selection and Collection of plant material

The Plant leaves (*Polygonum aviculare)* were selected of the exhaustive literature survey and collected from nearby area Sonepat, (Haryana), India in the month of March 2021.

Authentication

The plant leaves of *Polygonum aviculare L.* leaves was authenticated by a senior Botanist Head of Department of Botany, Singhania University, Pacheri Bari, Jhunjhunu (Raj.), India.

Preparation of extract

The Plant leaves of *Polygonum aviculare L.* was collected reduced to small size after dried in shade for one month or till dry and crushed to form coarse powder. The powdered drug (250 gm) was subjected to continuous hot extraction with the help of soxhlet apparatus using a solvent ethanol. The plant material was dry in hot air oven at 50^0C for an hour. After the effective extraction, the solvent will distilled off, the extract will then concentrated on water bath to become dried. The obtained extract was weighing and stored in an air tight container. [Lin et al.,]

Anti-inflammatory activity

Carrageennan induced paw edema

The experiment model was based on various inflammatory mediator released by carragennen. Edema formation in the rat paw is a biphasic event. In the first phase is attributed to the release of histamine & serotonin while second phase is the release of prostaglandin, protease & lysosome. First phase begins after the injection (s.c) of carragennen and gets diminished in two hours while second phase continues up to five hours. The experiment method was performing by **winter 1962.**

Procedure

Anti-inflammatory evaluation of *Polygonum aviculare L.* Ethanolic leaves extract was used against carragennen induced paw edema model. Experimental animals were divided into following three groups. Each group contains six animals and weight approximately 180 to 200 gm.

Groups	**Treatments**
Group 1 (control**)**	Received vehicle
Group 2 (standard**)**	Received Diclofenac sodium dose of (50 mg/kg)
Group 3 (test-1**)**	Received *Polygonum aviculare* extract dose of (500 mg/kg)

All the groups were pretreated according to their treatments, 1 hour before the administration of 0.1 ml of 1% carrageennen (suspended in sterile 0.9% normal sterilized saline) in subplanter region of right hind paw of rat. The initial paw volume (IPV) and final paw volume (FPV) was measured after 60, 120, 180, 240 & 300 minutes of carragennen administration using plethysmometer.[27-28] The difference initial and final paw volume was used to calculate the percentage inhibition using following equation:-

$$\text{Percentage inhibition} = \frac{(X-Y)}{X} \times 100$$

Where,

X= increase in paw volume of rats in the control group

Y= increase in paw volume of rat in the drug treated group

Statistical Analysis

All data were entered into MS Excel 2010 and were analyzed using SPSS version 7.1. Final results were expressed in the form of mean ± SEM. One-way analysis of variance (ANOVA) was used to detect any statistical significance. Following ANOVA, Tukey's post hoc test was performed for inter-group comparisons. A $P < 0.05$ was considered to be statistically significant at a 95% confidence interval.

RESULT

Carrageenan induced paw oedema

The ethanolic extracts of leaves of *Polygonum aviculare* were evaluated for anti-inflammatory activities using the carrageenan induced paw oedema model. At the dose whole plant of *Polygonum aviculare* (500 mg/kg) was used as positive reference standard and the result were as shown below:

Table 1: Effects of ethanolic extract of leaves of *Polygonum aviculare* on carrageenan induced paw volume (in cm).

Paw oedema volume (cm) measured							
Mean± SEM							
Groups	0 hr	1 hr	2 hr	3 hr	4 hr	5 hr	6 hr
Control	1.205± .004	1.916± .026	2.241± .010	2.210± .007	2.443± .010	2.423± .016	2.423± .016
Standard (Diclofenac Sodium) 50 mg/kg	1.045±. 014	1.186±. 014***	1.290± .024***	1.191± .022***	1.339± .023***	1.279± .020***	1.161± .020***
***Polygonum aviculare* (500 mg/kg)**	1.198± .003*	1.381± .011*	1.466± .016*	1.883± .044*	1.961± .039*	1.925± .037*	1.533± .037*

Group I-Control; Group II-Indomethacin; Group III-Extract; Group Values are expressed as mean ± SEM for groups of six animals each, *P0.05 as compared to Group II

All valves were shown as mean ± sem n=6 by one way ANOVA, *P<0.05, **P<0.01, ***P<0.001 vs control.

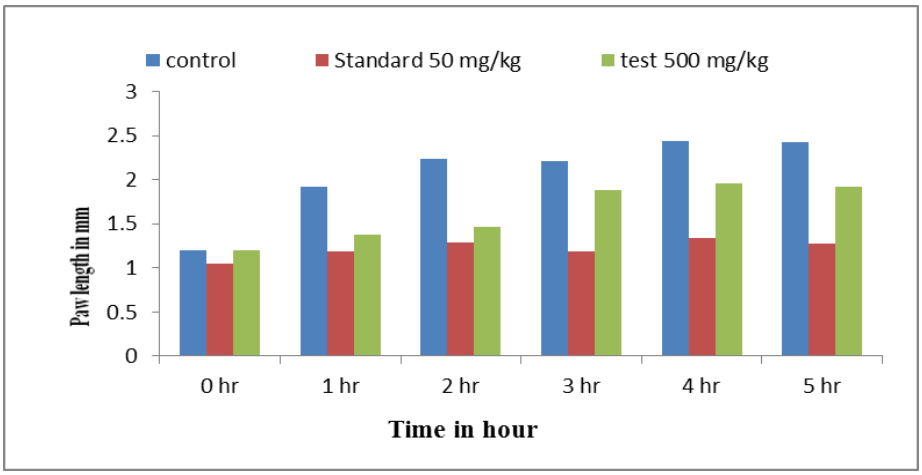

Figure 2: Graph representing mean increase in paw volume in mm at deferent time Intervals.

Tukey post hoc analysis clearly showed the reduction in the mean paw edema was significant in Group III at 1 and 6 h and highly significant at 5 and 6 hr compared to control. PI values were highest in the diclofenac sodium group at all measured hours of inflammation and lowest in the extract treated group. Taken together, the above results indicate that Group III reduced inflammation at all tested hours but showed high significance only at 4 and 5, 6 hr. At all hours of inflammation, Groups II and III did not significantly different indicating that their anti-inflammatory effect was comparable to one another.

DISCUSSION

In our study, we evaluated the anti-inflammatory property of ethanolic whole plant extract of *Polygonum aviculare* in Wistar rats. The anti-inflammatory activity of the extract was assessed by parameters namely mean paw edema volume and PI of inflammation. Anti-inflammatory activity was studied by carrageenan induced paw edema and we adopted the methodology of Winter et al. to produce acute edema. In our study, carrageenen produced inflammation in all the three groups of rats which was evident from increase in the right hind paw volume measured by plethysmometer. Group I (control) which received only vehicle and inflammation (carrageenan), exhibited significant inflammation. Inflammation steadily increased with time and reached its maximum at about 4 h following carrageenan administration. This inflammatory response elicited by carrageenan is classified into 3 phases. The early phase (0–2 h) is mediated by vasoactive amines (histamine, bradykinin, and serotonin). Cytokines and kinins are released at around 3 h contributing to the intermediate plateau phase and prostaglandins and oxygen free radicals mediate the final/late accelerating phase (4 h) of inflammation. Thereafter, inflammation is maintained by this phase.

Group II which was the standard group that received diclofanac sodium showed notable paw volume reduction at all the measured hours (1, 2, 4, 5 & 6) of inflammation when compared with the control group. It is a well-known fact that diclofanac sodium reduces inflammation by non-selective COX inhibition leading to the reduction of prostaglandin, one of the essential inflammatory mediators.

Group III which received 500 mg/kg of the ethanolic whole plant extract also offered a significant reduction in mean paw edema in comparison with the control group. This implies that the extract has significantly reduced acute inflammation. In a similar study by Arul et al., [29] in 2005, the anti-inflammatory effect of *Polygonum aviculare* whole plant were evaluated at a dose of 500 mg/kg which indicated that the extract reduced paw edema at 5th h of inflammation. The above study findings were also in accordance with our animal study.

Many studies that investigated the carrageenan-induced paw edema model have observed the paw volume changes only at 4, 5 & 6 hr after inducing inflammation. In our study, paw edema was measured and PI at 1, 2, 3, 4, and 5 & 6 hr of inflammation was calculated. This aided us in assessing the duration as well as the time of maximal extract activity. The anti-inflammatory effects of *Polygonum aviculare* lasted for hours with maximal activity at around 4 h of inflammation. This shows that the extract acts at all the inflammatory phases

and the most likely mechanism of action can be attributed to the inhibition of various inflammatory mediators, especially those of the late phase since the extract inhibited this phase maximally. The major phytochemical constituents present in our extract were coumarins, alkaloids, anthocyanins, and tannins which may have a role in reducing inflammation.

CONCLUSION

The obtained plant extract were subjected to pharmacological studies. *Polygonum aviculare* ethanolic leaves extract exhibited better anti-inflammatory activities using carrageenan induced paw edema comparable to standard diclofenac. Hence it was concluded that the extract revealed more significant effect for anti-inflammatory rather than individual ethanolic leaf extract when compared to the standard.

Therefore it seems worthy to develop the formulation extract optimized affects in acute & chronic inflammation condition.

ACKNOWLEDGEMENT

Author are in debt to research guide Dr. Anand Singh, School of Pharmaceutical Science, SINGHANIA UNIVERSITY, Pacheri Bari, Jhunjhunu (Raj.), India to be providing laboratory facilities for PhD research work.

AUTHOR CONTRIBUTION STATEMENT

Mr. Avinash Joriya conceptualized and gathered the data with regard to this work. Dr. Anand Singh analyzed these data and necessary inputs were given towards the designing of the manuscript. Both authors discussed the methodology and results and contributed to the final manuscript.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCE

1. Isailovic N, Daigo K, Mantovani A, Selmi C. Interleukin-17 and innate immunity in infections and chronic inflammation. *J. Autoimmun,* 2015; 60: 1–11.
2. Todd I, Spickett G, Fairclough L, editors. *Lecture Notes: Immunology*. New York: John Wiley & Sons, 2015.
3. Serhan C.N, Dalli J, Colas R.A, Winkler J.W, Chiang N. Protectins and maresins: New

pro-resolving families of mediators in acute inflammation and resolution bioactive metabolome. *Biochim Biophys. Acta (BBA) Mol. Cell Biol. Lipids*, 2015; 1851: 397–413.

4. Uttara B, Singh A.V, Zamboni P, Mahajan R.T. Oxidative stress and neurodegenerative diseases: A review of upstream and downstream antioxidant therapeutic options. *Curr. Neuropharmacol*, 2009; 7: 65–74.
5. Huether S.E, McCance K.L. *Understanding Pathophysiology*. Förlag: Elsevier Health Sciences, 2015.
6. Anwikar S, Bhitre M. Study of the synergistic anti-inflammatory activity of *Solanum xanthocarpum* Schrader and Wendl and *Cassia fistula* Linn. *Int. J. Ayurveda Res.*, 2010; 1(3): 167.
7. Nguyen T.T. *Systems Biology Approaches to Corticosteroid Pharmacogenomics and Systemic Inflammation (Doctoral dissertation, Rutgers University-Graduate School-New Brunswick)*, 2012.
8. Porter S. *Tidy's Physiotherapy*. Amsterdam: Elsevier Health Sciences, 2013.
9. Goljan E.F. *Rapid Review Pathology: With Student Consult Online Access*. Philadelphia, PA: Elsevier Health Sciences, 2014.
10. Kumar V, Abbas A.K, Aster J.C. *Robbins Basic Pathology*. Philadephia, United States: Elsevier Health Sciences, </AQ28>, 2013.
11. Kumar V, Abbas A.K, Aster J.C, Robbins S.L. *Inflammation and repair. Robbins Basic Pathology*. Philadelphia, London: Saunders, 2012; 29–74.
12. Bitencourt C.S, Bessi V.L, Huynh D.N, Ménard L, Lefebvre J.S, Lévesque T, Marleau S. Cooperative role of endogenous leucotrienes and platelet-activating factor in ischaemia–reperfusion-mediated tissue injury. *J. Cell Mol. Med.*, 2013; 17: 1554–1565.
13. Curcic S, Holzer M, Frei R, Pasterk L, effector responses are suppressed by secretory phospholipase A 2 modified HDL. *Biochim. Biophys. Acta (BBA) Mol. Cell Biol. Lipids*, 2015; 1851: 184–193.
14. McDonald B, Kubes P. *Leukocyte Trafficking. Inflammatory Diseases of Blood Vessels*. Canada: Department of Physiology and Pharmacology, Faculty of Medicine, University of Calgary, 2012; 28.
15. Nourshargh S, Hordijk P.L, Sixt M. Breaching multiple barriers: Leukocyte motility through venular walls and the interstitium. *Nat. Rev. Mol. Cell Biol.*, 2010; 11: 366–378.
16. Springer T.A, Anderson D.C, Rosenthal A.S, Rothlein R, editors. Leukocyte Adhesion Molecules: Proceedings of the First International Conference on: Structure, Function and Regulation of Molecules Involved in Leukocyte Adhesion, Held in Titisee, West

Germany, September 28-October 2, 1988. *Springer Science and Business Media*, 2012.

17. Ogra P.L, Mestecky J, Lamm M.E, Strober W, McGhee J.R, Bienenstock J. *Handbook of Mucosal Immunology.* San Diego: Academic Press, 2012.
18. Sies H, editor. *Oxidative Stress.* London: Elsevier, 2013.
19. Gleeson M, Bishop N.C, Stensel D.J, Lindley M.R, Mastana S.S, Nimmo M.A. The anti-inflammatory effects of exercise: Mechanisms and implications for the prevention and treatment of disease. *Nat. Rev. Immunol*, 2011; 11: 607.
20. Murakami M. *The Molecular Mechanisms of Chronic Inflammation Development.* Tokyo: Frontiers E-Books, 2012.
21. Ogrunc M, Di Micco R, Liontos M, Bombardelli L, di Fagagna F.D.A. Oncogene-induced reactive oxygen species fuel hyperproliferation and DNA damage response activation. *Cell Death Differ*, 2014; 21: 998–1012.
22. Kong A.N.T. *Inflammation, Oxidative Stress, and Cancer:Dietary Approaches for Cancer Prevention.* London, New York: CRC Press, 2013.
23. Niederhuber J.E. *Abeloff's Clinical Oncology.* Philadelphia, PA: Churchill Livingstone Elsevier, 2014.
24. Vetriselvan S., Subasini U., Velmurugan C., Muthuramu T., Shankar Jothi., Revathy *"anti-inflammatory activity of cucumis sativus seed in carrageenan and xylene induced edema model using albino wistar rats"* International Journal of Biopharmaceutics, 2020; 4(1): 34-37.
25. Neha Mohan P.V., Suganthi. V., Gowri. S., *"Evaluation of anti-inflammatory activity in ethanolic extract of Coriandrum sativum L. Using carrageenan induced paw oedema in albino rats"* Scholars Research Library, 2020; 5(2): 139-143.
26. Jian-Yu Su, Qing-Chan Li, Liang Zhu *"evaluation of the in vivo anti-inflammatory activity of a flavone glycoside from cancrinia discoidea (ledeb.) Poljak"* excli Journal, 2011; 10: 110-116.
27. T. Dimo, Agathe L. Fotio T.B. Nguelefack, E.A. Asongalem, P. Kamtchouing *"antiinflammatory activity of leaf extracts of Kalanchoe crenata andr"* Indian J Pharmacol, 2005; 38(2): 115-119.
28. R. Gupta1, M. Lohani, S. Arora *"anti-inflammatory activity of the leaf extracts/fractions of bryophyllum pinnatum saliv. syn"* International Journal of Pharmaceutical Sciences Review and Research, 2010; 3(1): 16-18.
29. Arul V, Miyazaki S, Dhananjayan R. Studies on the anti-inflammatory, antipyretic and analgesic properties of the leaves of *Aegle marmelos* Corr. J Ethnopharmacol, 2005; 96:

159-63.