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Anti-Inflammatory Activity of Arthakure in Rats

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Abstract This study investigates the anti-inflammatory potential of poly herbal formulation Arthakure which contains *Asphaltum punibionm, Piper longum, Cinnamomum cassia, Boswellia carteru, Aloe barbadnsis, Rubia cordifolia, Argillia vilrlolutum, Myristica fragrans* and *Butea frondosa koen* by using Carrageenan induce paw edema and cotton pellets granuloma. Diclofenac was used as reference. The result of the study indicates that ARTHAKURE (500 and 1000 mg/kg, p.o.) play a crucial role as protective factors against the carrageenan-induced acute inflammation. In the cotton pellet- induced granuloma formation, ARTHAKURE was slightly effective in inhibiting the transudative phase and proliferative phase of inflammation. The dry weight of the pellets correlates with the amount of the granulomatous tissue. Administration of ARTHAKURE (500 and 750 $mgkg^{-1}$ p.o) and Diclofenec (5 $mgkg^{-1}$ p.o) appear to be effective in inhibiting the dry weight of cotton pellet.

Keywords Arthakure, Anti-Inflammatory Activity, Cotton pellets granuloma, Carrageenan induce paw edema

1. Introduction

Inflammation is a fundamental process that occurs in response to tissue damage and is responsible for repairing the injured area. It involves a series of cellular and microvascular reactions that aim to eliminate damaged tissue and promote the growth of new tissue. The process encompasses increased permeability in microvessels, adhesion of circulating cells to the vessels at the injury site, migration of various cell types, cell programmed cell death, and regeneration of new tissue and blood vessels. The classical medical indications of this condition consist of painful sensations, elevated temperature, redness, swelling, and eventually tissue repair accompanied by the production of scars [1-3].

There is a general agreement among stakeholders that modern drugs will be inaccessible to a significant portion of the population in future. Achieving universal health may only be possible through the utilization of thoroughly evaluated herbal products. Since the inception of human civilization, mankind has employed herbal medicine for therapeutic purposes. Western society, with the emergence of modern medicine, have tended to view herbal products unfavourably. However, there has been a consistent rise in the global utilization of herbal medicine for healthcare in recent years. Nevertheless, there are growing apprehensions over the safety, purported effectiveness, and quality of herbal items employed as herbal medicine, nutraceuticals, health food, and cosmetics. While herbal goods are commonly seen as safe due to their long-standing use, numerous herbal items, including herbal medicine, have been associated with notable adverse effects. The adverse effects are primarily attributed to accidental contamination and intentional adulteration [4-6].

Herbal remedies are a secure, efficient, and superior choice as anti-inflammatory medicines compared to their synthetic counterparts. The phytoconstituents have comparable efficacy and mode of action to synthetic compounds [7]. Anti-inflammatory herbs are effective in suppressing inflammatory responses that can cause significant

abnormalities in the body's systems. Inflammation is a defensive reaction to infection or damage, but it can become harmful or get severe and require prompt management for effective resolution. Medicinal plants or their components are seen as advantageous because of their desirable characteristics, such as high effectiveness, widespread accessibility, affordability, minimal or nonexistent adverse effects, and superior efficiency in comparison to synthetic alternatives. These medicinal plants contain phytoconstituents that have the ability to prevent unwanted inflammatory processes and also possess anti-inflammatory properties. The plants include a variety of phytoconstituents such as steroids, glycosides, phenolics, flavonoids, alkaloids, polysaccharides, terpenoids, cannabinoids, and fatty acids. Various mechanisms have been investigated to understand the anti-inflammatory effects of these active substances. They have the potential to enhance the functioning of enzymes, factors, and proteins involved in the anti-inflammatory system, or disrupt the activity of certain components in the inflammatory pathway such as lipooxygenases, cyclooxygenases, tumor necrosis factors, interleukins, prostaglandin, nitric oxide, mitogen-activated protein, nuclear factor, and others [7-11].

Anti-inflammatory agents are chemical compounds that have the ability to inhibit or prevent inflammation. They can be categorized as either synthetic or natural. Synthetic substances can be steroidal or non-steroidal and often have several adverse effects. The primary adverse effects and constraints of steroidal anti-inflammatory medicines are miscarriage, weakened immune system, increased body weight, hormonal imbalances, addiction, complications upon discontinuation, financial burden, and limited accessibility. Similarly, primary adverse effects and constraints of non-steroidal anti-inflammatory agents include headache, tinnitus, dizziness, blurred vision, irritability, hyperventilation, hypertension, edema, rarely coronary heart failure, abdominal pain, nausea, vomiting, peptic ulceration, bleeding, bronchial asthma, angioedema, rashes, thrombocytopenia, hypoprothrombinemia, and bleeding tendency. In addition to side effects, there are several contraindications that restrict the use of NSAIDs, such as peptic ulcer, esophageal varices, bronchial asthma, idiosyncrasy, allergy, viral infection (particularly in neonates), and bleeding tendency. On the other hand, natural substances are derived from plants and/or microbes and tend to have fewer or no negative effects [7,12-14]. Various countries, including India, China, Korea, Japan, Turkey, and Brazil, have utilized medicinal herbs to treat a range of inflammatory diseases and conditions such as rheumatic diseases, periodontal diseases, ulcerative colitis, colonic injuries, neurogenic pain, digestive and respiratory diseases, cardiovascular diseases, and bowel diseases. Additionally, these herbs have been used for healing wounds, burns, and injuries [15-20]. They were employed based on conventional knowledge or arbitrary experiments without understanding the phytoconstituents. Some examples of commonly used herbal plants with anti-inflammatory properties include *Curcuma longa, Zingiber officinale, Rosmarinus officinalis, Borago officinalis, Oenothera biennis, Harpagophytum procumbens, Urtica dioica, Uncaria tomentosa, Salvia officinalis, Ribes nigrum, Persea americana/Glycine max, Elaeagnus angustifolia, Vaccinium myrtillus,* and *Olea europaea* [7].

The Piper longum fruit has been utilized in traditional medicine, including the Ayurvedic system of medicine. While there are several evidence supporting its use, controlled trials are necessary to ascertain its efficacy. The main components extracted from different portions of *P. longum* include piperine, piperlongumine, sylvatin, sesamin, diaeudesmin piperlonguminine, pipermonaline, and piperundecalidine. It is primarily employed for the treatment of chronic bronchitis, asthma, constipation, gonorrhea, lingual paralysis, diarrhea, cholera, chronic malaria, viral hepatitis, respiratory infections, stomachache, bronchitis, splenic illnesses, cough, and tumors [21].

The plant Cinnamon cassia Blume is widely recognized as Chinese cinnamon. Primarily, the medicinal applications of this plant involve the utilization of its bark and leaves. C. cassia is considered safe when used in moderate quantities, such as in culinary applications and therapeutic dosages. The entire plant holds medicinal significance in the Indian traditional system of medicine, namely in Ayurveda. Cinnamon is a time-honored spice utilized in several places. The product is made from the dehydrated inner bark of Cinnamomum cassia Blume (Lauraceae). The substance comprises around 1-2% of a volatile oil known as cassia oil. The main components of the essential oil consist of 65–80% cinnamaldehyde and a smaller quantity of eugenol. Additionally, it includes mucilage, starch, and tannins. Bark is utilized for its carminative, stomachic, diarrhea, and antibacterial attributes. The pharmacological actions of Cinnamon cassia Blume encompass a range of beneficial effects, including as anti-inflammatory,

antioxidant, hepatoprotective, antiulcer, antimicrobial, antifungal, anticancer, anti-HIV, antidiabetic, and anti-gout properties [22-24].

The primary constituents of B. carterii are volatile oils and terpenes, including triterpenes and diterpenes. Nevertheless, numerous chemical constituents have been extracted and characterized from B. carterii. The many Boswellia extracts and components exhibited pharmacological capabilities, including anti-inflammatory, antitumour, and antioxidant actions. B. carterii demonstrated a beneficial impact on the management and prevention of various age-related ailments, including diabetes, cancer, cardiovascular disease, and neurological illnesses. Boswellia carterii was initially employed as a traditional Chinese medicinal remedy for the treatment of urticaria. Contemporary pharmacological research has verified that B. carterii possesses not only anti-inflammatory, antioxidant, antiviral, antimalarial, and antitumor properties, but also provides protection to the liver and nerves. The application of B. carterii resin has been utilized for the treatment of many inflammatory conditions, including rheumatoid arthritis. The anti-inflammatory activities of Boswellic acids, which are the primary active constituents of B. carterii resin, have been found. It also has antioxidant, antitumour, antiviral, antimicrobial, neuroprotective, hepatoprotective, kidney protective, and immunomodulatory effects [25,26].

Aloe barbadensis is presently the most extensively utilized species of Aloe and enjoys global recognition. The primary reason for this is the leaves' exceptional efficiency, resilience, and simplicity of processing into beverages or gels for external application. The active components of this renowned strain are incomparable, in terms of quantity, to other less common and underutilized smaller types from an industrial perspective. The advantageous impacts of A. barbadensis are widely acknowledged in contemporary times. The composition includes Malolyl glucans, Chromones, Anthraquinones, Tetrahydroanthracenones, Anthrones, Phenolic compounds, and Sterols. The aloe fractions included high levels of Ca, K, Na, and Mg, which were the most abundant mineral elements. The primary applications of this substance include antitumoral, anti-inflammatory, antibacterial, and laxative. It also possesses immunomodulatory properties. Application of undiluted gel topically facilitates the process of skin repair and regeneration. Multiple studies have demonstrated that extracts produced from aloe vera have a protective impact against insulin resistance and can lower lipid levels [27-29].

Rubia cordifolia, also referred to as Common Madder or Indian Madder, is a significant botanical species utilized in traditional and Ayurvedic medicine to treat many illnesses. According to numerous medical sources, Rubia plant roots have a well-established reputation for their effective treatment of various conditions such as malignancies, tuberculosis, rheumatism, hematemesis, metrorrhagia, epistaxis, contusion, and menoxenia in Chinese traditional medicine. In addition, Indian folk medicine also included several remedies using Genus Rubia to treat wounds, inflammation, and skin infections. Rubia cordifolia is a plant of great importance in the Ayurvedic system of medicine, where it is utilized for the treatment of several skin ailments. The internal usage of this plant's root is effective in treating conditions such as abnormal uterine bleeding, internal and external hemorrhage, bronchitis, rheumatism, kidney and gall bladder stones, diuretic, and dysentery. The roots are employed for the purpose of reducing blood pressure. It possesses numerous additional traditional therapeutic properties. The roots include various quinones, such as glycosides like rubiadin, 1-hydroxy-2-methoxy anthraquinone, and 3-dimethoxy-2-carboxy anthraquinone. Additionally, they contain rubiprasin A, B, and C, ruiearbonls, aborane triterpenoids, mangistin, alizarin, garancin, mollugin, and furomollugin. The plant's roots possess a combination of flavors, including sweetness, bitterness, and acridness. They are utilized for their various medicinal properties, such as anti-inflammatory, haemostatic, antidysentric, antipyretic, analgesic, and anthelmentic effects. Additionally, they are known to enhance vocal quality, improve complexion, and provide relief for Kapha-related ailments, as well as inflammation-related conditions affecting the uterus, vagina, eye, ear, and blood. Additionally, it is employed in the treatment of leucoderma, ulcers, urine discharges, jaundice, and piles. The pharmacological actions of this substance have been proven to include anti-inflammatory effects, neuroprotective properties, hepatoprotective activity, antibacterial activity, antidiabetic activity, anti-proliferating properties, radioprotective properties, anti-nephrotoxicity, anti-ulcer effects, antioxidant effects, anti-adipogenic activity, anti-HIV activity, wound healing effects, and anti-tumor activity [30-33].

Śilājatu, its primary constituents, and prospective applications derived from the qualities of fulvic acid. The phytocomplex called Śilājatu mostly consists of humic compounds. One of these substances, fulvic acid, is recognized for its characteristics as an antioxidant and anti-inflammatory agent. The Śilājatu preparations contain many additional compounds such as eldagic acid, fatty acids, resins, latex, gums, albumins, triterpenes, sterols, aromatic carboxylic acids, 3,4-benzocoumarins, amino acids, polyphenols, and phenolic lipids. Typical traditional applications encompass its efficacy in treating genitourinary problems, jaundice, digestive disorders, enlarged spleen, epilepsy, neurological disorders, chronic bronchitis, and anemia. Śilājatu has been shown beneficial in the treatment of renal calculi, edema, and hemorrhoids. It serves as an internal antiseptic and aids in reducing anorexia. Furthermore, it has been said in India that it can be utilized as Yogavāhi, meaning a substance that enhances the effects of other medications. Śilājatu holds significant prominence in Ayurvedic medicine due to its attributes as a Rasāyana. Within this particular framework, the consumption of this substance has been associated with several health advantages, including an extended lifespan, revitalization, and the prevention of aging processes [34,35].

The volatile oil in nutmeg and mace of Myristica fragrans contains several chemicals, with terpinen-4-ol, β-pinene, and limonene being the main ingredients found in all species. Various portions of Myristica fragrans have yielded several lignans and neolignans through isolation. M. fragrans has been shown to possess several pharmacological activities, such as anticancer, antidepressant, antidiabetic, antiobesity, antiinflammatory, analgesic, antibacterial, antioxidant, hepatoprotective, and memory-enhancing effects [36].

Butea frondosa koen contains a wide range of active components, including coreopsin, isocoreopsin, sulphurein, butein, butin, isobutrin, monospermoside, isomonospermoside, aurones, chalcones, flavonoids (palasitrin, prunetin), and steroids. Butea frondosa is rich in phytoconstituents including alkaloids, flavonoids, phenolic compounds, amino acids, glycosides, and steroids. The flowers, seeds, barks, fruits, leaves, and other plant parts primarily exhibit pharmacological activity. It possesses many pharmacological properties, such as astringent, aphrodisiac, antihelmintic, anti-inflammatory, antibacterial, antifungal, anti-asthmatic, hepatoprotective, antifertility, anti-filarial, antidiabetic, antiviral, anticonvulsant, antifungal, antimicrobial, antiestrogenic, anticancer, antioxidant, antiulcer, wound healing, antidiarrheal, anti-implantation, anti-dopaminergic, antimycobacterial, osteogenic, and osteoprotective activities [37,38].

Sen et al. (1991) studied and assessed the anti-inflammatory properties of the methanolic fraction of a chloroform extract derived from the roots of Pluchea indica [39]. Goldberg et al. examined the anti-inflammatory properties of an aqueous extract of Achillea millefolium using the mouse paw edema test. They observed a 35% decrease in swelling [40]. Lee et al. documented the anti-inflammatory properties of Hedera rhombea bean leaves [41]. The authors Chandra et al. demonstrated the anti-inflammatory effects of the ethanolic root extract of Swertia chirata (Gentianaceae) in a rat paw edema model induced by carrageenan [42]. Franzotti et al. examined the anti-inflammatory properties of Sida cordifolia L [43]. Ojewole observed the anti-inflammatory properties of the aqueous leaf extract of Bryophyllum pinnatum (Crassulaceae) [44]. Silva et al. investigated the anti-inflammatory properties of the extract, fractions, and amides derived from the leaves of Piper ovatum Vahl (Piperaceae) [45]. The anti-inflammatory properties of Cassia fistula (Leguminosae) leaf extract on rats were assessed by Mukherjee et al. [46]. Kumar et al. documented the anti-inflammatory properties of Piper longum fruit oil [47]. Chavan et al. observed the anti-inflammatory properties of Caryophyllene oxide derived from the bark of Annona squamosa L [48]. Sreejith et al. documented the anti-inflammatory properties of Cassia occidentalis Linn [49]. Shimoda et al. investigated the anti-inflammatory effects of red ginger extract (Zingiber officinale var. Rubra) utilizing both acute and chronic inflammation models [50]. Verma et al. observed the anti-inflammatory effects of Aconitum heterophyllum on cotton pellet-induced granuloma in rats [51]. Benni et al. investigated the anti-inflammatory properties of the root plant Aegle marmelos, commonly known as Bilwa [52]. Muthuraman et al. reported the anti-inflammatory properties of the extract, fractions, and amides derived from the leaves of Piper ovatum Vahl (Piperaceae) [53]. Ilavarasan et al. observed the anti-inflammatory properties of the aqueous and ethanol extracts derived from the leaves of Thespesia populnea [54]. The anti-inflammatory properties of the fruit skin extract of Azadirachta indica and its isolated compound, azadiradione, were assessed [15]. The herb Abutilon indicum is utilized as a demulcent and its aqueous extract also possesses antidiabetic properties [55]. The shrub Acacia arabica is highly beneficial for

treating gingivitis and reducing plaque buildup in the gums. The plant Acacia catechu includes a compound called flavocoxid, which is a mixture of baicalin and catechin. These compounds are responsible for the strong anti-inflammatory effects of the plant. Acacia farnesiana has been increasingly prominent in the field of traditional medicine. The plant contains compounds such as acasiane A and B, farnesirane A and B, and betulinic acid, which have anti-inflammatory activities [56-58]. The ethanolic extract of Sapindus trifoliatus seeds exhibits anti-inflammatory properties in Wistar rats [59]. Strychnos nuxvomica includes brucine and the N-oxide of brucine, which have the ability to decrease the release of prostaglandin E2. This action results in an anti-inflammatory effect [60]. The fruit skin of the Azadirachta indica plant includes a compound called azadiradione, which possesses both anti-nociceptive and anti-inflammatory effects. This plant possesses ethnomedicinal properties for the healing of wounds and burns [15, 61]. Morinda citrifolia, often known as Noni, has been discovered to have strong anti-inflammatory properties [62, 63].

This present study investigates the anti-inflammatory potential of poly herbal formulation Arthakure by using Carrageenan induce paw edema and cotton pellets granuloma.

2. Materials and Methods

2.1 Poly Herbal formulation constituents:

No	Botanical Name	Sanskrit Name	Formula /100 mg	Formula/600mg
1	*Asphaltum punibionm*	Sudha shalajtu	20	120
2	*Piper longum*	Pippili moolam	12	72
3	*Cinnamomum cassia*	Gudatvak	5	30
4	*Boswellia carteru*	Dev dhoom	20	120
5	*Aloe barbadnsis*	Kumari	10	60
6	*Rubia cordifolia*	Visaka	12	72
7	*Argillia vilrlolutum*	Sphatikari	3	18
8	*Myristica fragrans*	Malathi phalum	3	18
9	*Butea frondosa koen*	Kinsuka palasa	15	90

2.1 Preparation of Poly Herbal drug solution:

Poly Herbal formulation (Arthakure) was dissolved in 0.5 % CMC solution.

2.2 Animals:

Studies were carried out using Male Wistar Rats (150-170 gm). The animals were maintained under standard laboratory conditions (temperature 25 ±2ºC) with dark and light circle. They were allowed free access to standard dry pellet diet and water ad libitum. The rats were acclimatized to laboratory condition for 10 days before commencement of experiment. All procedures described were reviewed and approved by the M S university animal ethical committee.

2.3 Experimental Design:

2.3.1 Animal Models:

(A) Acute Inflammatory Model:

λ-Carrageenan induce paw edema in rats

Animal Groups: each group contains 6 animals

(1) Group 1: Control group, received saline & λ-carrageenan (0.1 ml of 1% in saline)

(2) Group 2: ARTHAKURE 100 mg p.o + λ-Carrageenan

(3) Group 3: ARTHAKURE 500 mg p.o + λ-Carrageenan

(4) Group 4: ARTHAKURE 1000 mg p.o+ λ-Carrageenan

(5) Group 5: Diclofenec Sodium 5 mg/kg p.o+ λ-carrageenan

The anti-inflammatory activity was evaluated by the λ-carrageenan- induced paw-edema test in the rats (Winter et al., 1962; Schapoval et al., 1998).

Paw edema was induced (Winter et al., 1962) by injecting 0.1 ml of 1% λ-carrageenan in physiological saline into the sub plantar region of the left hind paw of each rat. The contra lateral paw was injected with 0.1mL saline and used as a control.

The ARTHAKURE (100 mg, 500 mg, and 1000 mg) and Diclofenec sodium (5 mg/kg p.o.) as reference standard were administered orally 1 hour prior to λ-carrageenan administration. The paw volume was measured before and 1, 2, 3, 4, 5, 6 and 24 hr after the injection of λ- carrageenan into the sub-plantar region of the left hind paw. Paw volume was measured with the help of a Plethysmometer (model 7150, Ugo Basile).

The percentage inhibition of increase in paw volume in drug treated groups were compared with the carrageenan control group. Paw edema was expressed as the increase in paw volume (ml) after carrageenan injection with respect to the contra lateral paw volume.

(B) Chronic inflammatory animal models: (cotton pellets Granuloma)

Animal Groups: each group contains 6 animals

(1) Group 1: Control group received saline
(2) Group 2: ARTHAKURE (500 mg/kg, p.o)
(3) Group 3: ARTHAKURE (750 mg/kg p.o)
(4) Group 4: Diclofenec Sodium (5 mg/kg p.o)

Male Wistar rats with an average weight of (175-200 gm) were anaesthetized with ether. The back skin was shaved and disinfected with 70% ethanol. An incision was made in the lumbar region. By a blunted forceps subcutaneous tunnels were formed and a sterilized cotton pellet (20 mg) was placed on both sides in the scapular region. After placing the cotton pellets, incision was sealed by RESEAL (a tissue adhesive). The animals were treated for 7 days orally with ARTHAKURE (500, 750 mg/kg), Diclofenec (Reference standard), saline (control). On 8th day the animal were sacrificed, cotton pellets were removed, dried at 60ºC in hot air oven until the weight remains constant. The net dry weight, i.e. after subtracting the weight of the cotton pellet was determined.

The average weight of the pellets of the control group as well as of the treated group was calculated. The percentage inhibition of granuloma formation relative to vehicle control group was determined.

2.4 Statistical Analysis:

All the values are expressed as mean S.E.M. Statistical significance between more than two groups was tested using one-way ANOVA followed by the Bonferroni multiple comparisons test or unpaired two- tailed student's t-test as appropriate using computer-based fitting program (Prism, Graphpad 5). Differences were considered to be statistically significant when $p < 0.05$.

3. Results:

3.1 λ-Carrageenan induce paw edema in rats:

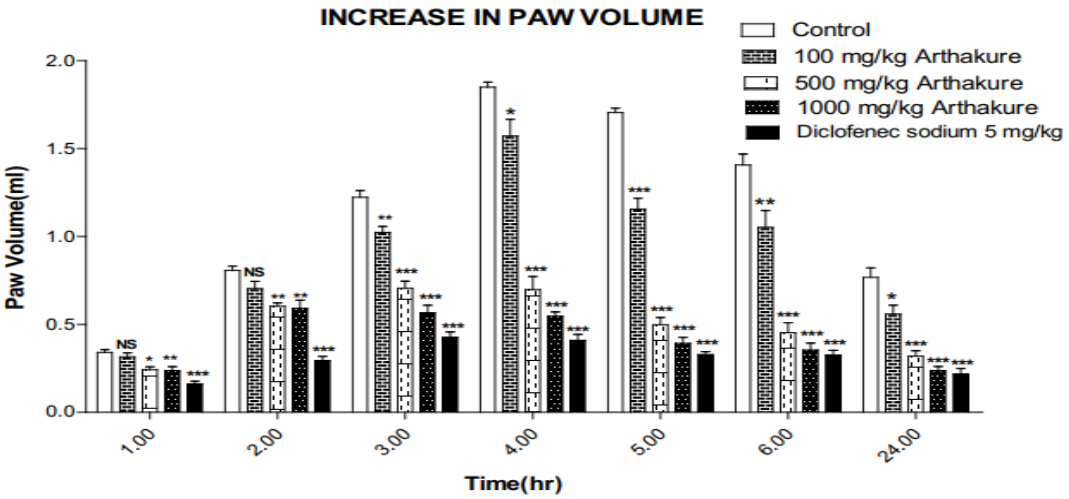

Figure 1: Effect of ARTHAKURE on paw volume after λ- Carrageenan administration

Each data represents the mean ± SEM of 6 rats. P value * p<0.05, ** p<0.01, ***p<0.001, NS- Non Significant

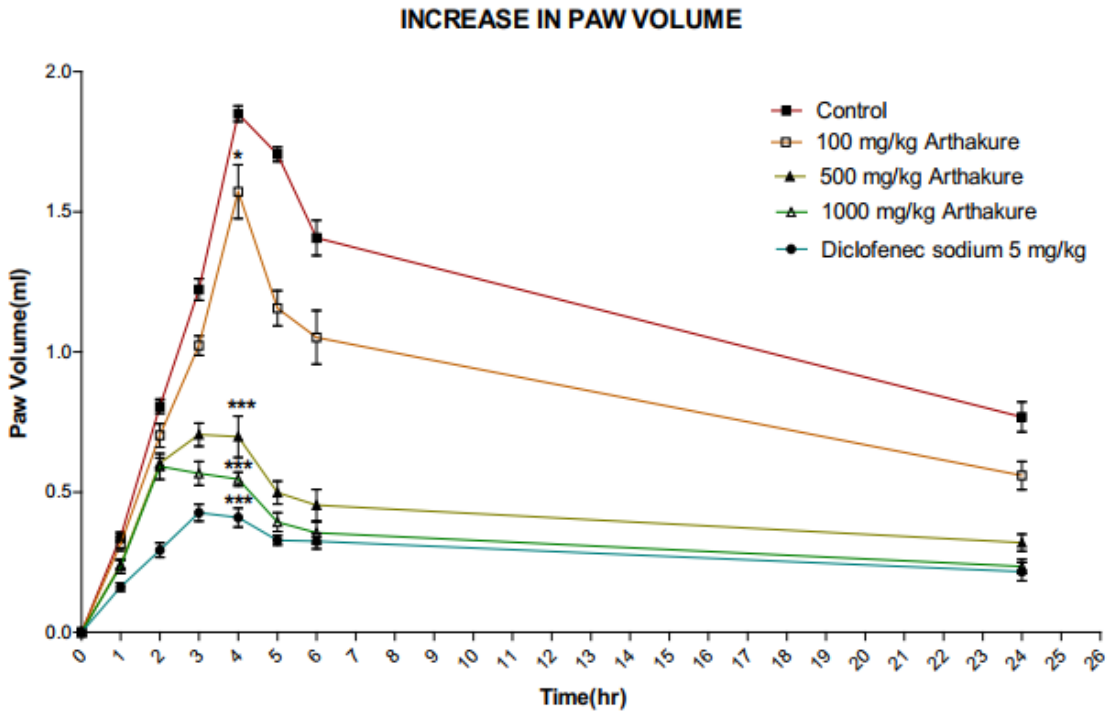

Figure 2: Effect of ARTHAKURE on paw volume after λ-Carrageenan administration

Each data represents the mean ± SEM of 6 rats. P value * p<0.05, ** p<0.01, ***p<0.001, NS- Non Significant

Table 1: Effect of ARTHAKURE on % inhibition of edema at 3 hr. after λ- Carrageenan administration.

Time	**Animal**			
	10 mg/kg	**500 mg/kg**	**1000 mg/kg**	**Diclofenac (5 mg/kg)**
% inhibition of edema (at 3 hr.)	16.35 %	42.35 %	53.66 %	65.11%

Subplantar injection of λ-carrageenan in rats showed a time dependent increase in paw volume (Fig. 1&2); this increase was observed at 1 h and was maximal at 4 h after administration of λ-carrageenan injection in the vehicle treated groups. However, carrageenan-induced inflammation was significantly ($P < 0.001$) reduced in all phases of the experiment by treatment with ARTHAKURE 500 and 1000 mg/kg.

The lower dose of ARTHAKURE (100 mg/kg, p.o.) did not show any considerable change in paw edema as compared with vehicle treated group. Diclofenac shows 65.11 % inhibition of paw edema, ARTHAKURE shows 42.35, 53.66 % inhibition of paw edema by 500 mg/kg, 1000 mg/kg ARTHAKURE respectively.

3.2 Cotton Pellets Granuloma Techniques:

The effects of ARTHAKURE and Diclofenac on the proliferative phase of inflammation are shown in table 2. there was a significant reduction in the weight of cotton pellets was observed with ARTHAKURE (500 and 750 mgkg- 1 p.o) compared to the vehicle treated rats. However, the degree of reduction was less than the effect caused by Diclofenac Sodium.

Table 2: Effect of ARTHAKURE & Diclofenec sodium on the formation of granulomas & % inhibition of granulomas formation in rats.

No	Groups	Dry Wt. of Granulomas	% Inhibition of Granuloma
1	CONTROL	157.5 ± 7.042	---------
2	500 mg/kg ARTHAKURE	134.0 ± 5.574 *	**14.92 %**
3	750 mg/kg ARTHAKURE	110.2 ± 4.285 ***	**30.03 %**
4	Diclofenac Sodium	87.67 ± 4.096 ***	44.33 %

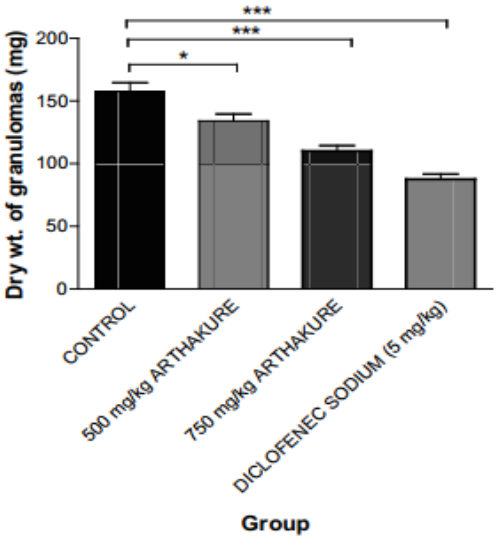

Figure 3: Effect of ARTHAKURE & Diclofenec sodium on the formation of granulomas in rats

4. Discussion:

Carrageenan-induced rat paw edema is suitable test for evaluating anti- inflammatory drugs, which has frequently been used to assess the anti- edematous effect of natural products. Development of edema in the paw of the rat after injection of carrageenan is a biphasic event. The initial phase observed during the first hour is attributed to the release of histamine and serotonin. The second phase of edema is due to the release of prostaglandins, protease and lysosome.

Based on this, it could be argued that the suppression of the first phase may be due to inhibition of the release of early mediators, such as histamine and serotonin, and the action in the second phase may be explained by an inhibition of cyclo-oxygenase. The result of the present study indicates that ARTHAKURE (500 and 1000 mg/kg, p.o.) and Diclofenec Sodium play a crucial role as protective factors against the carrageenan-induced acute inflammation

The cotton pellet method is widely used to evaluate the transudative and proliferative components of the chronic inflammation. In the cotton pellet- induced granuloma formation, ARTHAKURE was slightly effective in inhibiting the transudative phase and proliferative phase of inflammation.

The dry weight of the pellets correlates with the amount of the granulomatous tissue. Administration of ARTHAKURE (500 and 750 $mgkg^{-1}$ p.o) and Diclofenec (5 $mgkg^{-1}$ p.o) appear to be effective in inhibiting the dry weight of cotton pellet. These data support the hypothesis of the greater effect of the ARTHAKURE on the inflammation in rats.

5. Conclusion

The present study reveals the anti-inflammatory activities of ARTHAKURE.

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