Research Article

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SYST PRECLINICAL INVESTIGATION OF ANTI-INFLAMMATORY POTENTIAL OF SIDDHA DRUG PASUNEER KADUKKAI CHOORANAM USING CARAGEENAN INDUCED PAW OEDEMA MODEL IN RATS

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ABSTRACT

Inflammation is a biological process characterized by the orchestration of vascular and cellular processes, facilitated by mediators such as prostaglandin, leukotrienes, cytokines, and thromboxanes. This process serves as a crucial and protective mechanism employed by organisms in response to damage, infection, and trauma. Nevertheless, the persistence of inflammation can result in the development of chronic conditions such as rheumatoid arthritis and periodontitis, which are characterized by tissue damage and the loss of bone structure. Conventional drugs used for clinical management of inflammation impose life threatening side effects, hence there is dire need of exploring the traditional system of medicine. Siddha system of medicine has a holistic approach on treating inflammatory condition. The main objective of the present research work is to evaluate the analgesic and anti-inflammatory activity of siddha preparation Pasuneer Kadukkai Chooranam (PKC) in rats. Acute inflammation in rats was induced by carrageenan-induced rat paw edema. Result analysis of carrageenan induced paw edema reveals that treatment with PKC at the dose of 100 and 200 mg/kg shown significant reduction in paw volume with the percentage protection of 31.42 to 65.45 % when compared to that of the standard indomethacin with 120.7 % which reveals the significant anti-inflammatory potential of the drug PKC. Based on the findings, it can be inferred that the siddha medication PKC exhibits considerable potential as an anti-inflammatory agent. This effect is likely attributed to the presence of bioactive compounds within the drug. Consequently, the utilisation of these alternative traditional medicines demonstrates significant efficacy in the clinical treatment of acute inflammation.

KEY WORDS: ***Inflammation, Anti-inflammatory, Siddha, Pasuneer Kadukkai Chooranam, Carrageenan, Paw edema.***

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1. Introduction

Inflammation is a transient physiological reaction of the tissues to detrimental stimuli, such as damage, external and endogenous antigens. Its purpose is to remove the stimulus, promote tissue repair, and eventually restore homeostasis [1]. While inflammation serves as a beneficial defence mechanism in the body, it is well acknowledged that an imbalanced and protracted inflammatory response is implicated as the root cause of several illnesses, including diabetes, allergies, atherosclerosis, obesity, cancer, and pain. In addition, the presence of inflammatory dysfunction, which is a significant factor in the development of chronic illnesses, is contributing to a rise in healthcare expenses within society [2, 3].

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely prescribed pharmaceutical agents for the management of pain and inflammation [4]. According to literature around 5-10% of the total annual prescriptions for pharmaceuticals. The use rate of NSAIDs among individuals aged 65 and above reaches a substantial proportion of 96% within the general practise environment [5,6]. In a given one-year timeframe, it was observed that around 7.3% of individuals aged 60 years and above, who fall under the category of senior patients, obtained at least one prescription for NSAIDs [7]. In addition to their anti-inflammatory capabilities, NSAIDs possess analgesic and antipyretic effects. The drugs in question exert an inhibitory effect on the enzymes known as Cyclooxygenases (COXs). These enzymes play a crucial role in the manufacture of prostaglandins and other prostanoids, including thromboxanes, by acting as rate-determining factors. Professional groups such as the American Geriatric Society, American College of Rheumatology, and the European League Against Rheumatism advocate for the cautious utilisation of NSAIDs, emphasising the need of restricting their administration to the minimal effective dosage and shortest possible timeframe. It is recommended that frequent monitoring be conducted for common gastrointestinal, renal, and cardiovascular adverse effects when they are utilised [8,9].

The superior safety and therapeutic indices of herbal medicine have led to its significant prominence among consumers worldwide. The Siddha system of medicine is a time-honored practise that has effectively addressed the healthcare needs of individuals for many generations [10]. The fundamental idea of siddha therapy is primarily centred upon the identification of the underlying factors that contribute to the onset of an illness, which is determined by the condition of vata, pitha, and kaba. The philosophy of traditional medicine highlights the significance of modifying or adjusting the tridosha, which in turn leads to metabolic transformations inside the body, potentially resulting in various ailments [11]. Chooranam refers to dry formulations that are produced by pulverising herbal substances in certain proportions. These substances fall within the category of internal medicine and are commonly provided with appropriate carriers such as honey, ghee, buttermilk and coconut water. The main aim of the present investigation is to evaluate the anti-inflammatory potential of siddha drug Pasuneer Kadukkai Chooranam using carrageenan induced paw edema model in wistar rats.

2. Materials and Methods

2.1. Source of raw drugs

The Required raw materials were procured from a well reputed indigenous drug shop from, Chennai, Tamil Nadu, India. All raw drugs were authenticated by respective authorities before utilizing the same for the preparing the formulation Pasuneer Kadukkai Chooranam.

2.2. Preparation of the formulation PKC

Trial drug PKC was formulated based on the procedure listed in the Pharmacooeia of siddha medicine [12]. The exocarp of the herb Terminalia Chebula, commonly referred to as kadukkai, undergoes an initial purification process followed by pulverisation into a fine powder. Subsequently, the substance is amalgamated with bovine (Cow) urine and allowed to immerse for a duration of twenty-four hours. On the subsequent day, the concoction is subjected to boiling until its volume is diminished by half compared to its initial

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quantity. Subsequently, the resultant mixture is extracted from the heat source and amalgamated with Zingiber officinale (commonly known as chukka) powder and panamkarkandu. The mixture is further heated by boiling until it attains a dense consistency. It is then its transferred into a glass container and afterwards buried beneath a paddy heap for a period of around 10 days.

Dosage: 1 teaspoon twice a day

Adjuvant: Luke warm water

Duration: 48 days

2.3. Animal

Healthy adult Wistar albino rats were used for the study. The animals were housed in poly propylene cages and were kept in well ventilated with 100% fresh air. A 12 light / dark cycle were maintained. Room temperature was maintained between 22 ¬+ 20 C and relative humidity 50–65%. They were provided with food (Sai feeds, Bangalore, India) and water ad libitum. All the animals were acclimatized to the laboratory for 7 days prior to the start of the study. The experimental protocol was approved by The Institutional Animal Ethics Committee of C.L.Baid Metha College of Pharmacy, Chennai, Tamil Nadu, India. 06/31/PO/Re/S/01/CPCSEA/dated 06/04/2022.

2.4. Carageenan Induced Paw Oedema [13,14]

Anti-inflammatory activity was measured using carrageenan-induced rat paw edema assay Edema was induced by subplantar injection of 100 µL of 1% freshly prepared solution of carrageenan in distilled water into the right-hind paws of each rat. Paw thickness were measured just before the carrageenan injection, that is, at “0 hour” and then at 1, 2, 3, 4, and 5th hour after carrageenan injection. Increase in paw thickness was measured as the difference in paw thickness at “0 hour” and paw thickness at respective hours. The paw volume was measured using Plethysmometer (Model 7150 UGO Basile, Italy) Edema was expressed as the mean increase in paw volume relative to control animals. Percentage protection is calculated by the formulae: (T2-T1/ T2) x 100 , T 1- Normal control and T2 - Drug treated test

2.5. Grouping for Anti-Inflammatory Activity

For the experiment, the animals were divided into 5 groups with 6 animals in each group.

•Group-I (control) received 3% gum acacia 10 ml/kg p.o.

•Group-II (Carrageenan) received 0.1ml of 1% w/v suspension of carrageenan sub-plantar injection

•Group-III (standard) received Indomethacin 40 mg/kg p.o.

•Group-IV (Test group I) received PKC 100mg/kg p.o.

•Group-V (Test group II) received PKC 200mg/kg p.o.

2.6. Statistical analysis

The statistical analysis will be carried by one-way ANOVA (GRAPH PAD PRISM 5 computer program). Results were expressed as mean ± standard error. A statistical comparison was carried out using the Dunnet’s test for the control and treatment group. P-values less than 0.05 were set as the level of significance.

3. Results

3.1.Effect of Pasuneer Kadukkai Chooranam on paw edema volume in carrageenan induced edematous rats

Result analysis of carrageenan induced paw edema reveals that treatment with PKC at the dose of 100 and 200 mg/kg shown significant reduction in paw volume with the percentage protection of 31.42 to 65.45 % when compared to that of the standard indomethacin with 120.7 %. As shown in table 1 and 2.

Table 1: Effect of Pasuneer Kadukkai Chooranam on paw edema volume in carrageenan induced edematous rats

Group	Dose	Initial paw volume	Change in paw edema mm at different time intervals				
		0hr	1 hr	2hr	3hr	4hr	5hr
I	Control	1.20 ± 0.14	1.20± 0.14	1.20± 0.14	1.20± 0.14	1.20±. 14	1.20±0.14
II	Carrageenan, subplantar injection	1.23± 0.19	1.98 ± 0.22	2.32 ± 0.12	2.37 ± 0.24	2.49 ± 0.28	2.65 ± 0.21
III	Indomethacin 40 mg/kg, p.o.	1.31± 0.16	2.23 ± 0.27	1.87 ± 0.12	1.50 ± 0.15	1.31 ± 0.28	1.21 ± 0.27
IV	PKC 100mg/kg, p.o.	1.44 ± 0.13	1.66 ± 0.32	1.76 ± 0.26	1.68 ± 0.18	1.62 ± 0.12	1.58 ± 0.54
V	PKC 200mg/kg, p.o.	1.28±0.22	1.66 ± 0.31	1.74 ± 0.14	1.66 ± 0.41	1.58 ± 0.40	1.31 ± 0.32

- The paw volume up to the tribiotural articulation was measured at 0, 1, 2, 3, 4, 5 hrs
- Statistical analysis one way ANOVA followed by Dunnett t-test with n = 6 per group

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Table 2: Effect of Pasuneer Kadukkai Chooranam on percentage protection in carrageenan induced edematous rats

Group	Treatment	Initial paw volume	5 hr in mm	Difference in paw volume	Percentage protection
I	Control	1.20 ± 0.14	1.20±0.14	00	-
II	Carrageenan	1.23± 0.19	2.65 ± 0.21	2.18	23.76
III	Indomethacin, 40mg/kg	1.31±0.16	1.21±0.27	0.1	120.7
IV	PKC 100 mg/kg	1.44 ± 0.13	1.58 ± 0.54	0.68	32.14
V	PKC 200 mg/kg	1.28±0.22	1.31 ± 0.32	0.35	67.02

- Statistical analysis one-way ANOVA followed by Dunnett t-test with n = 6 per group

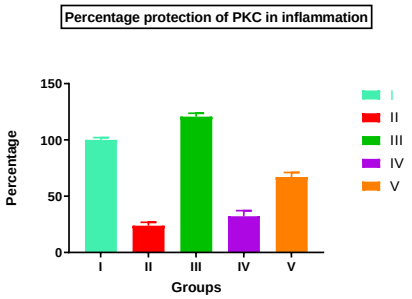

Figure 1: Percentage protection of PKC and standard drug in carrageenan induced edematous rats

4. Discussion

Inflammation is a complex biological response initiated by the body in response to harmful stimuli, such as injury, infection, or irritation. It is an essential part of the body's defense mechanism, aimed at protecting tissues and promoting healing [15]. When the body detects a harmful stimulus, the immune system responds by releasing chemicals and immune cells to the affected area, leading to characteristic signs of inflammation like redness, swelling, heat, and pain [16]. Throughout history, the predominant strategy for addressing inflammation has revolved on the management of pro-inflammatory mediators and/or the modulation of adhesion molecule expression [17,18]. However, it has been recognised in recent years that the resolution of inflammation may depend on the use of multi-target drugs [19]. Previous studies have demonstrated that the utilisation of many signalling pathways can augment the pro-inflammatory, immunomodulatory, and pro-resolving cascades that are indicative of different facets of inflammation [20].

The carrageenan-induced rat paw edoema model is a widely employed method for testing the efficacy of anti-inflammatory medicines, specifically in assessing their antiedematous properties. Carrageenan is a potent chemical compound employed for the induction of inflammatory and proinflammatory mediators, such as prostaglandins, leukotrienes, histamine, bradykinin, TNF-α, among others [21].

The progression of acute inflammation follows a biphasic pattern. The initial stage commences with the liberation of histamine, serotonin, and kinins subsequent to the administration of a phlogistic agent within the initial hours [22]. The second phase is characterised by the subsequent release of prostaglandin-like compounds within a time frame of 2 to 3 hours. The second phase is responsive to both steroidal and nonsteroidal anti-inflammatory agents that are clinically beneficial [23]. Prostaglandins are the primary causative agents accountable for the onset of acute inflammation.

Siddha medicines comprise a wide range of components, including herbs, minerals, metals, animal products, and seaweed [24]. The siddha guidelines govern the protocols pertaining to the purification, detoxification, processing, and quality assurance of siddha medications. Each formulation comprises many phytotherapeutics that has the capacity to exhibit advantageous pharmacological actions inside the biological system [25]. The Siddha way of medicine is a well-regarded ancient approach that has persisted and thrived for millennia. The recognition of the interplay between the physiological aspects of biological systems and their implications for human well-being has been extensively acknowledged, owing to the extensive understanding of medicinal herbs and associated supplements. There remain several facets of siddha that have yet to be thoroughly examined and comprehended. Result analysis of carrageenan induced paw edema reveals that treatment with PKC at the dose of 100 and 200 mg/kg shown significant reduction in paw volume with the percentage protection of 31.42 to 65.45 % when compared to that of the standard indomethacin with 120.7%.

5. Conclusion

In conclusion, the findings of the current study revealed that the siddha medicine PKC exhibit strong anti-inflammatory action in carrageenan-induced rat paw edoema, which is equivalent to indomethacin. This was determined by comparing the drug's effect on the edoema to that of indomethacin. It is possible that the anti-inflammatory mechanism of PKC is connected to

the lowering of inflammatory cytokines, which might result in a percentage inhibition given by PKC towards the production of inflammation by carrageenan. These recent discoveries open up fresh avenues of inquiry about the therapeutic application of the siddha formulation Pasuneer Kadukkai Chooranam in the treatment of inflammatory illnesses.

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6. References

1. Huang SS, Chiu CS, Chen HJ. Antinociceptive activities and the mechanisms of anti-inflammation of asiatic acid in mice. Evidence-Based Complementary and Alternative Medicine. 2011;2011:10 pages. Article ID 895857.
2. Chang HY, Sheu MJ, Yang CH, et al. Analgesic effects and the mechanisms of anti-inflammation of hispolon in mice. Evidence-Based Complementary and Alternative Medicine. 2011;2011:8 pages. Article ID 478246.
3. Fang SC, Hsu CL, Yen GC. Anti-inflammatory effects of phenolic compounds isolated from the fruits of Artocarpus heterophyllus . Journal of Agricultural and Food Chemistry. 2008;56(12):4463–4468.
4. Abdulla A, Adams N, Bone M, Elliott AM, Gaffin J, Jones D, et al. (2013). Guidance on the management of pain in older people. Age Ageing, 42 Suppl 1: i1–-57.
5. Onder G, Pellicciotti F, Gambassi G, Bernabei R (2004). NSAID-related psychiatric adverse events: who is at risk? Drugs, 64: 2619-2627
6. Pilotto A, Franceschi M, Leandro G, Di Mario F (2003). NSAID and aspirin use by the elderly in general practice: effect on gastrointestinal symptoms and therapies. Drugs Aging, 20: 701-710.
7. Vandraas KF, Spigset O, Mahic M, Slordal L (2010). Non-steroidal anti-inflammatory drugs: use and co-treatment with potentially interacting medications in the elderly. Eur J Clin Pharmacol, 66: 823-829
8. Gnjidic D, Blyth FM, Le Couteur DG, Cumming RG, McLachlan AJ, Handelsman DJ, et al. (2014). Nonsteroidal anti-inflammatory drugs (NSAIDs) in older people: prescribing patterns according to pain prevalence and adherence to clinical guidelines. Pain, 155: 1814-1820.
9. Meara AS, Simon LS (2013). Advice from professional societies: appropriate use of NSAIDs. Pain Med, 14 Suppl 1: S3-10
10. A.Lavanya , W.Zafiroon Nisa , U.Chitra , N.Anbu , D.Sivaraman .Evaluation of Anti-ulcer potential of Siddha formulation Agasthiyar Elathy Chooranam in Aspirin-Induced ulcerated rats. Int J Trans Res Ind Med 2019, 1(3): (P):19-24.
11. Shanmugapriya P, Sivaraman D, Christian GJ, Rajalakshmi K, Jeeva Gladys R .Hepatoprotective Potential of Novel Siddha Formulation Santha Santhrodhaya Mathirai against Paracetamol and Methotrexate Induced Hepatotoxicity in Chang liver Cell line Model. Journal of Pharmaceutical Sciences and Research (JPSR).2019;11(6): 2379-2384.
12. The Pharmacooeia of siddha medicine, Page 127.
13. C. A. Winter, E. A. Risley, and G. W. Nuss, “Carrageenan-induced edema in the hind paw of rat as an assay for anti-inflammatory activity,” Proceedings of the Society for Experimental Biology and Medicine, vol. 111, pp. 544–547, 1962. View at Google Scholar
14. O. O. Adeyemi, S. O. Okpo, and O. O. Ogunti, “Analgesic and anti-inflammatory effects of the aqueous extract of leaves of Persea americana Mill (Lauraceae),” Fitoterapia, vol. 73, no. 5, pp. 375–380, 2002.
15. Chen, L., Deng, H., Cui, H., Fang, J., Zuo, Z., Deng, J., Li, Y., Wang, X., & Zhao, L. (2017). Inflammatory responses and inflammation-associated diseases in organs. Oncotarget, 9(6), 7204–7218. https://doi.org/10.18632/oncotarget.23208.
16. HY, Sheu MJ, Yang CH, et al. Analgesic effects and the mechanisms of anti-inflammation of hispolon in mice. Evidence-Based

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Complementary and Alternative Medicine. 2011;2011:8 pages. Article ID 478246.
17. Rainsford KD. Anti-inflammatory drugs in the 21st century. Subcell Biochem. 2007;42: 3–27.
18. Georgakopoulou EA, Scully C. Systemic use of non-biologic corticosteroids in orofacial diseases. Oral Dis. 2014;20: 127–35. 10.1111/odi.12132
19. Koeberle A, Werz O. Multi-target approach for natural products in inflammation. Drug Discov Today. 2014;19: 1871–82. 10.1016/j.drudis.2014.08.006
20. Kohli P, Levy BD. Resolvins and protectins: mediating solutions to inflammation. Br J Pharmacol. 2009;158: 960–71. 10.1111/j.1476-5381.2009.00290.x
21. Fuller RW. Serotonergic stimulation of pituitary-adrenocortical function in rats. Neuroendocrinology. 1981;32:118–127.
22. Hesketh S, Jessop DS, Hogg Sand Harbuz MS. Differential actions of acute and chronic citalopram on the rodent hypothalamic-pituitary-adrenal axis response to acute restraint stress. J. Endocrinol. 2005;185:373–382.
23. Raap DK, Van de Kar LD. Selective serotonin reuptake inhibitors and neuroendocrine function. Life Sci. 1999;65:1217–1235.
24. S. Arul Jothi , K.Dhivyalakshmi , N. Anbu , D.Sivaraman. Systematic Toxicity Profiling of Siddha Formulation Thoothula Pazha Chooranam by Acute and 28-Day Subacute Toxicity Studies in Swiss albino mice. International Journal of Advanced Research in Biological Sciences. Int. J. Adv. Res. Biol. Sci. (2019). 6(10): 11-22
25. D.Sivaraman, N.Anbu, N.Kabilan, M.Pitchiah Kumar, P.Shanmugapriya , G.J.Christian. Exploration of Anti-Urolithiasis Potential of Traditional Siddha formulations Amukkara Chooranam and Karisalai Karpam Chooranam by Struvite Crystal Growth Inhibition Assay. Pharmacognosy Journal.2019;11(4) :683-688.

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