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EVALUATION OF CARRAGEENAN INDUCED ANTI-INFLAMMATORY ACTIVITY OF KADUKKAI PODI *TERMINELIA CHEBULA* (Retz). IN ALBINO WISTAR RATS

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ABSTRACT

The Inflammation is a complex biological response of vascular tissues against aggressive agents such as pathogens, irritants, or damaged cells. Acute inflammation is the initial response and is characterized by the increased movement of plasma and innate immune system cells, such as neutrophils and macrophages, from the blood into the injured tissues. The anti-inflammatory activity of the kadukkai Podi was evaluated by carrageenan-induced rat paw oedema method. Male albino rats (180 ± 5 g). The results obtained indicate that the kadukkai Podi had significant anti-inflammatory activity in rats. It reduced the edema induced by carrageenan by 55.30% and 57.53% on oral administration of 100 and 200 mg/kg, as compared to the untreated control group. The inhibitor of leukocyte migration and the formation of pleural exudates when given orally. Thus it can be concluded that the siddha single drug kadukkai Podi possess significant anti-inflammatory activity in rats.

KEYWORDS: Siddha Single Drug Kadukkai Podi, Anti-inflammatory, carrageenan-induced rat paw oedema method.

INTRODUCTION

The Inflammation is a complex biological response of vascular tissues against aggressive agents such as pathogens, irritants, or damaged cells. Acute inflammation is the initial response and is characterized by the increased movement of plasma and innate immune system cells, such as neutrophils and macrophages, from the blood into the injured tissues. The standard signs of inflammation are expressed by increased blood flow, elevated cellular metabolism, vasodilatation, release of soluble mediators, extravasation of fluids and cellular influx.[1] Upon the presence of the inflammatory agent, cell mem-branes induce the activation of phospholipase A2 followed by release of arachidonic acid and inflammatory mediators such as cytokines, serotonin, histamine, prostaglandin and leukotrienes that increase vascular permeability, thus facilitating the migration of leukocytes to the site of inflammation.[2] Inflammation induced by carrageenan is acute, nonimmune, well-researched, and highly reproducible. Cardinal signs of inflammation—edema, hyperalgesia, and erythema—develop immediately. Many saponins tested have displayed significant antinociceptive, anti-inflammatory and antipyretic activities possibly due to their non-glycosidic moiety, the sapogenin, but also many diverse activities have also been reported such as anti-allergic, antifungal, analgesic and others.[3–6] Moreover a variety of siddha single drug preparation have proved to be useful in animal models of inflammation.[7–10]

Paw swelling, or footpad edema, is a convenient method for assessing inflammatory responses to antigenic challenges and irritants. Typically, test compounds are assessed for acute anti-inflammatory activity by examining their ability to reduce or prevent the development of carrageenan-induced paw swelling. In the present study attempts are made to validate the claims of kadukkai Podi regarding the anti-inflammatory activities of this siddha preparation.

METHODS AND MATERIALS

Animals

Male albino rats (180 ± 5 g) were obtained from animal house, K.M.College of pharmacy, maduarai and maintained in standard laboratory conditions. They were given standard laboratory diet and water ad libitum. All animal experiments are approved by the Institutional Animal Ethics Committee, and were in accordance with the guidelines of the committee for the purpose of Control and Supervision of Experiments on Animal (CPCSEA), Government of India.

Acute inflammation

Carrageenan-induced rat paw oedema is used widely as a working model of inflammation in the search for new anti-inflammatory drug. The anti inflammatory activity of the siddha single drug kadukkai Podi was evaluated by carrageenan-induced rat paw oedema method.[11] Albino Wistar rats (180 ± 5 g) were used. Anti inflammatory activity was measured using carrageenan induced rat paw oedema assay. The rats were divided into 5 groups of 5 animals each. Group I. were given normal saline and treated as negative control. Rats of Group II was treated with carragenan (1%w/v) in saline in the subplanter region of the right hind paw Rats in Group III were administered Indomethacin(10 mg/kg, bw) and considered as standard. Rats from Group IV and V were given two doses siddha formulation(100 and 200 mg/kg bw). Acute paw edema was induced by injecting 0.1 ml of 1% (w/v) carrageenan solution, pre-pared in normal saline. After 1 h, 0.1 ml, 1% carrageenan suspension in 0.9% NaCl solution was injected into the sub-plantar tissue of the right hind paw. The linear paw circumference will be measured at hourly interval for 4 h. The perimeter of paw was measured by using vernier callipers. Measurements were taken at 0–4 h after the administration of the carrageenan.

The anti-inflammatory activity was calculated by using the relation

$$\%\text{inhibition of edema} = \frac{T - T0}{T} \times 100$$

T, Thickness of paw in control group; T0, Thickness of paw edema in the test compound treated group.

Carrageenan Induced Pleurisy in Rats

The animals were divided into five groups of five rats each as described in the carrageenan induced paw edema model[12, 13] and each were pretreated with siddha single drug (100 and 200 mg/kg, p.o.), Indomethacin (10 mg/kg, p.o.) or normal saline (0.1 ml).One hour later all the animals were received 0.25 ml of an intrapleural injection of 1 % carrageenan on the right side of the thorax. The animals were sacrificed 3 h after carrageenan injection by ether inhalation. One ml of heparinized Hank's solution was injected into the pleural cavity and gently massaged to mix its contents. The fluid was aspirated out of the cavity and the exudates were collected. The number of migrating leukocytes in the exudates was determined with Neubauer chamber. The values of each experimental group were expressed as mean ± SEM and compared with the control group.

RESULTS

The results of anti-inflammatory activity were expressed as Mean increase in paw diameter ± SD. Results were analyzed using one way ANOVA. Differences were considered as statistically significant at $P < 0.05$ are compared to control.

Table 1: Effect of siddha single drug kadukkai Podi on Carrageenan Induced Rat Paw Edema.

Treatment	Dose (mg/kg, p.o.)	Mean increase in paw volume (ml)	% Decrease in paw volume
Normal control	10ml/kg saline	0.90 ± 0.06	
Toxic control	0.1 ml, 1% carrageenan	3.25 ± 0.18*a	
Standard control	10mg/kg Indomethacin	1.32 ± 0.10*b	59.38%
Treatment control	100mg/kg kadukkai Podi	1.45 ± 0.14*b	55.30%
Treatment control	200mg/kg Kadukkai Podi	1.38 ± 0.12*b	57.53%

- Values are expressed as mean ± SEM.
- Values were compared by using analysis of variance (ANOVA) followed by Newman-Keul's multiple range tests.
- * (a) Values are significantly different from normal control G1 at P<0.01.
  * (b) Values are significantly different from Toxic control G2 at P<0.01.

Table 2: Effect of siddha single drug kadukkai Podi on Carrageenan Induced Pleurisy in Rats.

Treatment	Dose (mg/kg, p.o.)	Pleural exudates (ml)	Leukocytes (×103 cells/ml)
Normal control	10ml/kg saline	0.10±0.02	0.34±0.02
Toxic control	0.1 ml, 1% carrageenan	0.36±0.09*a	4.15±0.35*a
Standard control	10mg/kg Indomethacin	0.14±0.03*b	0.46±0.04*b
Treatment control	100mg/kg kadukkai Podi	0.19±0.06*b	0.54±0.06*b
Treatment control	200mg/kg Kadukkai Podi	0.16±0.04*b	0.52±0.05*b

- Values are expressed as mean ± SEM.
- Values were compared by using analysis of variance (ANOVA) followed by Newman-Keul's multiple range tests.
- * (a) Values are significantly different from normal control G1 at P<0.01.
  * (b) Values are significantly different from Toxic control G2 at P<0.01.

CONCLUSION

The effect of kadukkai Podi on carrageenan-induced edema in rats is shown in Table 1. The results obtained indicate that the siddha kadukkai Podi had significant anti-inflammatory activity in rats. The kadukkai Podi reduced the edema induced by carrageenan by 55.30% and 57.53% on oral administration of 100 and 200 mg/kg, as compared to the untreated control group. Indomethacin at 10 mg/kg inhibited the edema volume by 59.38%.

The effect of kadukkai Podi on carrageenan-induced pleurisy in rats is shown in Table 2. The volume of pleural exudates in the toxic control group was 0.36±0.09 ml. Animals treated with the kadukkai Podi (100 and 200 mg/kg, p.o.) decreased the pleural exudates to 0.19±0.06 ml and 0.16±0.04.Treatment with Indomethacin (10 mg/kg, p.o.) produced the exudates of 0.14±0.03 ml. The leukocyte count for the control group was found to be 4.15±0.35×103 cells/ml. Animals treated with the kadukkai Podi and standard produced a leukocyte migration of $0.54\pm0.06\times10^3$, 0.52 ± 0.0510^3 and $0.43\pm0.08\times10^3$ cells/ml, respectively.

DISCUSSION AND CONCULSION

The increasing frequency of intake of NSAID's and their reported common side effects, there is need to focus on the scientific exploration of siddha drugs having fewer side effects. So, there is a continuous search for indigenous drugs, which can provide relief to inflammation. Carrageenan induced inflammation is a biphasic phenomenon.[14] The first phase of edema is attributed to release of histamine and 5-hydroxytryptamine. Plateau phase is maintained by kinin like substances and second accelerating phase of swelling is attributed to prostaglandin like substances. The knowledge of these mediators involved in different phases is important for interpreting mode of drug action. The tests performed with the kadukkai Podi in the pleurisy model showed that the kadukkai Podi behaves as an inhibitor of leukocyte migration and the formation of pleural exudates when given orally, as reported earlier.[15] Thus it can be concluded that the kadukkai Podi possess significant anti-inflammatory activity in rats. Further studies involving the purification of the preparation and the investigations in the biochemical pathways may result in the development of a potent anti-inflammatory agent with a low toxicity and better therapeutic index.

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