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An experimental evaluation of anti-inflammatory activity of dashanga agada w.s.r. to keeta visha (insect bite)

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Abstract
Background: Inflammation is the self-protective reaction of tissues towards infection, irritants or foreign substances. The exogenous substance induced by the insect will trigger the inflammatory response in case of insect bite. Though it is a part of host defense mechanism it causes tissue damage and systemic reactions. Hence control of inflammation becomes necessary. Non-Steroidal Anti-Inflammatory Drugs are proven to be quick acting but are associated with many side effects like various organ damage. In Ayurvedic texts a number of medicinal preparations to combat inflammation have been found; among them Dashanga agada is also one which is said to be very significantly effective to combat inflammation due to insect bite. To revalidate this claim the present experimental study was undertaken.
Objectives: To prepare Dashanga agada as per classical reference and determine its quality standards. To induce & study acute inflammation. To evaluate the Anti-inflammatory activity of Dashanga agada.
Methods: Wisterstrain albino rats weighing 200±50 of either sex were used in the study. Pharmacologically validated Carrageenan Induced Anti-Inflammatory model was used to evaluate anti-inflammatory activity of test drug. Dashanga agada was administered at dose of 540mg/kg.
Results: Dashanga Agada moderately inhibited carrageenan induced paw edema at both three and six hours in comparison to control group. However the effect was found to be reduced in 24th hour, where it is not so significantly effective when compared to standard group.
Interpretation and Conclusion: Most of the ingredients of Dashanga Agada are having Shothahara, vedanasthapana, and vishagna action, drugs due to its ushna veerya acts as kaphavatahara and help in reducing inflammation due to insect bite. The results reveal that Dashanga Agada has Anti-Inflammatory activity. Hence it can be used in the management of inflammation produced due to keeta damsha and also for other inflammatory conditions.

Keywords: Inflammation, dashanga agada, carrageenan, shothahara, vedanasthapana, vishagna

Introduction
Ayurveda is an Indian traditional system of medicine, which was practiced since many years. The science of *ayurveda* includes eight branches (*Ashtanga ayurveda*) of treatment specialization and *Agadatantra* is one among the eight branches. *Gada* literally means disease and *agada* means any agent which makes the body free from disease [1].
Agadatantra has got wide range of scope as it deals with the different types of envenomation like snake bite, Spider bite, insect bite and other organic and inorganic poisoning along with their antidotes their effects on humans, prevention and management of poisoning. There is also explanation about different formulations which are indicated in different conditions of envenomation [2].
The effects of poisons of both *sthavara* and *jangama visha* were studied extensively by the ancient Indian physicians. Among the *jangama vishas* there are several references available about the different, *keeta, loota, vrishchika etc* symptoms produced by envenomation and treatment procedures and formulations used for the treatment. *Dashanga agada* is one such formulation which is mentioned in *keeta visha adhikara* [3] for the treatment of all types of *keeta damsha* (Insect bite).
Irrespective of the triggering etiology, inflammation is the initial response of the host defence mechanism towards any infection, irritants, or foreign substances [4]. When it becomes severe it turns out to be a condition which causes tissue damage. It involves a complex array of enzyme activation, mediator release, extravasation of fluid, cell migration, tissue breakdown and repair [5]. Sometimes it may also evoke systemic signs and symptoms such as fever, malaise, loss of appetite and so on. Therefore control of inflammation becomes essential.

Modern anti-inflammatory drugs are extremely quick acting and efficient. However, long term use of such drugs can induce serious adverse reactions affecting various organs. For e.g. long term use of Diclofenac causes nephrotoxicity [6]. In this regard, *Ayurveda* has explained the formulations that are safe and effective. Specifically, there are numerous medicinal formulations described in *Agadatantra* (*Ayurvedic* toxicology) which may have potential to use as anti-inflammatory agents in general clinical practice, other than *visha* also.

One such herbal formulation is *Dashanga agada*, which has got ten components among which nine are herbal and one is mineral. The first reference of *Dashanga agada* is available in *Kashyapa samhita* as noted in *Sanskrit* quotation which says *Acharya Kashyapa* prepared this formulation and the actual literature of which is not available. The same formulation is mentioned in *Astanga hridaya* [7], Chakradatta [8], *Bhaishajya ratnavali* [9] and *Yoga ratnakara* [10] and is followed till now.

This *yoga* is highly practiced by most of the traditional *visha vaidhyas* in kerala for the treatment of *keeta visha,* where inflammation is the first symptom seen clinically. Hence to assess the rationality present behind the action of *Dashanga agada* in reduction of inflammation the following study has been undertaken with the title "an experimental evaluation of anti-inflammatory activity of dashanga agada W.S.R. To keeta visha (insect bite)"

Aims and Objectives

- To prepare *Dashanga agada* as per classical reference and determine its quality standards [11].
- To induce & study acute inflammation.
- To evaluate the Anti-inflammatory activity of *Dashanga agada.*

Materials and Methods

Raw materials for preparation of Dashanga agada were procured from SDM Ayurveda Pharmacy Udupi and Identified by the authenticated sources. The formulation was prepared in the practical hall of Dept of RSBK SDMCA Udupi.

Animals; in bread wistar strainalbino rats of either sex of body weight ranging from 200-250g were obtained from Central animal house of SDM Center for Research in Ayurveda and Allied sciences Udupi. They were maintained at standard housing conditions and fed with standard animal pillet and provided with tap water ad libitum during the experiment. The institutional animal ethical committee (49/AEC27/15-16) permitted the study.

The dose was decided as 6gm a day as the human dose. The human dose of Dashanga agada was converted to animal dose by using standard conversion formula as Human dose x 0.018 x 5 /kg body weight of albino rats. It was about 0.54mg/g and the dose for each rat was calculated on the basis of its body weight.

Carrageenan was used to induce inflammation in sub-plantar region of left hind paw. As it is study on acute inflammation the study was conducted for 7 days using the following mentioned groups with 6 rats in each group.

Group I Water control, fed with distilled water by oral route.

Group II Standard control, Diclofenac 5mg/kg body weight of albino rats by oral route.

Group III Test group, Dashanga agada 540mg/kg body weight of albino rats by oral route

Duration; for 7 days on 7th day carrageenan was injected in the subplantar region of left hind \paw of the animals of all the groups

Assesment of Anti Inflammatory Activity of Dashanga Agada

Assessment of anti-inflammatory activity was made on the basis of change in the paw volume at basal followed by 1st, 3rd, 6th, and 24th hour after carrageenan injection.

And the results were assessed with One Way ANOVA test.

Observation and Results

Table 1Shows the effect of Dashanga agada on change in paw volume at 1st, 3rd, 6th and 24th hour. Table 2 shows the effect of dashanga agada on % change in paw volume in 1st hour. Table3 shows the effect of dashanga agada on % change in paw volume in 3rd hour, Table 4 shows the effect of Dashanga agada on % change in paw volume in 6th hour, Table6 shows the effect of Dashanga agada on % change in paw volume in 24th hour.

Anti-Inflammatory Effect

Table 1: The effect of dashanga agada on change in paw volume in 1st, 3rd, 6th and 24th hour.

Group	Basal	1ST Hour	3RD Hour	6TH Hour	24TH Hour
Control	0.93±0.07	1.33±0.068**	1.37±0.035**	1.34±0.093**	1.04±0.047
Standard	0.885±0.026	1.035±0.035*	1.115±0.044**	0.08±0.056**	0.976±0.049
Test	0.81±0.02	1.13±0.04**	1.11±0.05**	1.016±0.05**	0.90±0.01

Data: MEAN±SEM * $p<0.01$ ** $p<0.001$

Table 2: The effect of dashanga agada on % change in paw volume in 1st hour

Group	% Change In Paw Volume	% Change
Control	45.50±8.49	-
Standard	17.18±3.73**	62.2↓
Test	39.90±4.29	12.3↓

Data: Mean ± SEM **$P<0.01$,

Table 3: The Effect of Dashanga Agada on % Change in Paw Volume In 3rd Hour

Group	% Change In Paw Volume	% Change
Control	50.29±7.93	-
Standard	26.55±6.23	47.20↓
TEST	38.05±8.65	24.33↓

Data: Mean ± SEM $P>0.05$

Table 4: The Effect of Dashanga Agada on % Change In Paw Volume In 6th Hour

Group	% Change In Paw Volume	% Change
Control	44.55±7.83	-
Standard	21.78±3.77*	51.11↓
Test	25.06±5.38	43.74↓

Data: Mean ± SEM *P<0.05

Table 5: The Effect of Dashanga Agada on % Change in Paw Volume in 24th Hour

Group	% Change In Paw Volume	% Change
Control	13.84±6.63	-
Standard	7.09±2.076	48.77↓
Test	12.3±4.233	11.1↓

Data: Mean ± SEM P>0.05

Discussion

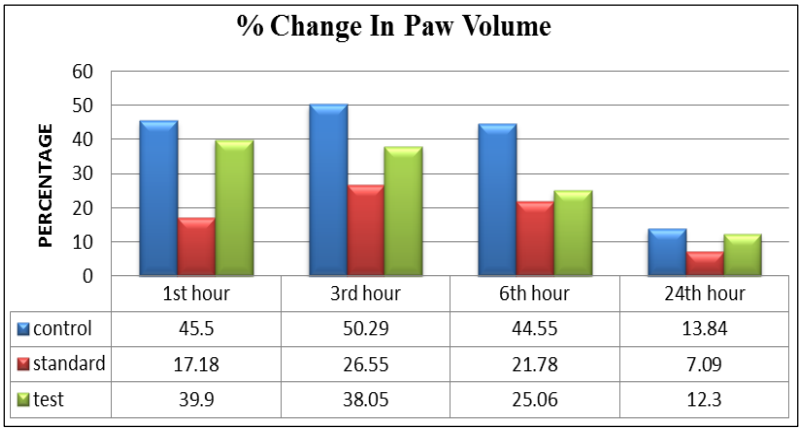
It is a timeless tradition to use the plant based medicine to fulfil the basic health needs of the mankind. The scientists all over the world are striving hard to develop newer drugs which are optimally safe and effective within the dose recommended for human. Hence search for effective therapy for inflammatory condition in other system of medicine vigorously pursued. One of the most widely used compound formulation is Dashanga agada, with proven clinical efficacy. This prompt us to initiate the present study to evaluate the effect of Dashanga agada in experimental models of inflammation to provide pharmacological basis for observed clinical efficacy.

Evaluation for Anti-Inflammatory Activity against Acute Inflammation

Inflammation comprises of three phases namely Acute, Subacute chronic. In acute inflammation, due to change in small blood vessels, fluid and granulocyte cell accumulate at the site of injury. This reaction obtain triggers a systemic response such as fever, leucocytosis, protein catabolism, and altered hepatic synthesis of acute phase proteins such as C Reactive Protein. In condition where inflammation is inappropriate acute inflammation can cause considerable morbidity hence drugs with anti-inflammatory activity would be required to meet the contingencies such situations. The test formulation was evaluated against carrageenan paw oedema to assess its effect on acute inflammation.

Effect of Dashanga agada on Carrageenan induced Paw oedema

Carrageenan induced inflammation is the most commonly used experimental model for evaluating the anti-inflammatory potency of compounds of natural products. This model exhibits a high degree of reproducibility. According to Vinegar *et al*. (1969) the carrageenan induced paw oedema is a basic event. The first phase occurs within an hour and is partly due to trauma of injection and also is attributed to the release of histamine, serotonin and kinins. The second phase of oedema is due to release of prostaglandins (PG), protease and lysosome. The second phase is sensitive to the most clinically effective anti-inflammatory drugs. Prostaglandins play a major role in the development of the second phase of the reaction, which is measured around 3h (Di Rosa, 1970). The presence of PGE2 in the inflammatory exudates from the injected foot paw can be demonstrated at 3 h and thereafter. The results obtained while screening the formulation against carrageenan induced paw oedema are provided in the form of consolidated statement in Diagram-



Standard-Diclofenac sodium Test-Dashanga agada

Analytical

- Organoleptic Characters; Dashanga Agada was soft in touch, Grey in colour, Pungent bitter in taste, and characteristic in odour.
- The Physicochemical constants of Dashanga agada
    - Loss on drying 11.60
    - Total Ash 14.98
    - Acid Insoluble Ash 0.90
    - Water Soluble Ash 12.67
    - Alcohol Soluble Extractive Value 17.36
    - Water Soluble Extractive value 26.20
- Loss on drying indicates the moisture content, in DA it was 11.60%w/w. Presence of inorganic substances in the formulation is indicated by determination of Ash value, which plays important role in standardization, more ash vale denotes higher inorganic substances, in present sample Ash value was 14.98%w/w. Various components have different solubility media, DA solubility was seen in water and methanol, water and methanol soluble extractive value of DA was 26.20% & 17.36%, respectively which shows that DA having more bioavailability in water media than methanol
- HPTLC Analysis of Ethanolic extract of Dashanga agada was done and scanned under UV at 254nm, 366nm and 620nm to visualize different bands of components of Dashnga agada also the densitometric scan was recorded. Hence the formulation was said to be according to the standard protocol.

Anti-inflammatory study

- Dashanga Agada inhibited increase in paw volume at 1st hour after carrageenan injection to 39.90 compared to control which was 45.50.
- At 3rd hour Dashanga Agada moderately inhibited paw edema to 38.05, compared to control which was 50.29.
- At 6th hour the test drug showed its highest activity in inhibiting paw oedema to 25.06, compared to control which was 44.55.
- At 24th hour Dashanga agada moderately inhibited paw oedema to 12.3 compared to control which was 13.84.
- Hence Dshanga Agada has mild to moderate anti-inflammatory activity against carrageenan induced paw oedema.
- As Dashanga Agada has showen mild to moderate anti-inflammatory activity it can be recommended in the treatment of keeta visha to treat inflammatory conditions.

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