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ANTIINFLAMMATORY ACTIVITY OF ERANDA PAKA AGAINST CARRAGEENAN INDUCED PAW OEDEMA IN ALBINO RATS

Barman Kamal Kr.[1] Suresh Parimi[2] Ahmad Ayaz[3]

[1]Rasashala Assistant Govt. Ayurvedic College, Guwahati, Assam, India

[2]Associate Professor, PG Department of Rasashastra & B.K. National Institute of Ayurveda, Jaipur, Rajasthan, India

[3]Associate Professor NIMS Institute of Pharmacy, NIMS University, Rajasthan, India

ABSTRACT

Introduction: *Amavata* still remains a formidable disease, as it causes severe crippling deformities and functional disabilities. Therefore there is need to identify an antiinflammatory compound which can be effective and prevents the deformity. *Eranda Paka* is used extensively in Ayurveda for treatment of *Amavata* and so we aimed to study the antiinflammatory effect of the combination. **Material and Methods:** The granules of Eranda paka were prepared and antiinflammatory effect was investigated by using Carrageenan induced paw oedema model in different doses. **Results**: The result showed significant antiinflammatory activity. **Conclusion**: The study reveals that *Eranda Paka* has a potent antiinflammatory activity.

Key words: *Amavata, Eranda Paka*, Antiinflammatory, Carrageenan.

INTRODUCTION:

Ayurveda is an age old science of life, was not merely to cure the diseases but to preserve the health. It is the oldest and most holistic medical system available on the planet today. The medicinal herbs are moving to mainstream as it is used by a greater number of people seeking remedies and health approaches free from side effects caused by synthetic chemicals[1]. *Amavata* is such type of disease, which is associated with inflammation of joints causing severe crippling deformities and functional disabilities, where people are fed up with modern treatment due to their side effect. The disease *Amavata* is compared with Rheumatoid arthritis(RA) where *angamarda, aruchi* and *sunyata* in different body parts are the symptoms observed generally.

The disease draws attention for the consideration of research firstly due to the gravity of the problem and secondly due to adverse effect from the modern drugs for the treatment. Therefore the development of newer and more potent antiinflammatory drugs with lesser side effect is necessary which can safely used on *Amavata* (RA).

Inflammation is considered as a primary physiologic defence mechanism that helps body to protect itself against infection, burn, toxic chemicals, allergens or other noxious stimuli. An uncontrolled and persistent inflammation may act as an etiologic factor for many of these chronic illnesses[2]. Although it is a defence mechanism, the complex events and mediators involved the inflammatory reaction can induce, maintain or aggravate many diseases[3]. Currently used anti-inflammatory drugs are associated with some severe side effects. Therefore, the development of potent anti-inflammatory drugs with fewer side effects is necessary.

So, the present study is designed to evaluate the antiinflammatory effect of a compound formulation namely *Eranda Paka*.

MATERIAL AND METHODS:

***Eranda Paka*- An overview:**

Eranda Paka, which is a classical polyherbal formulation as described in *Yogaratnakara*, it is also available in *Brighat Nighantu Ratnakar* under the name of *Vatari-paka.* The formula mentioned in *Yogaratnakara* has been adopted in the Official formulary i.e. Ayurvedic Formulary of India[4]. Though the *Eranda* and its various forms are

in vogue to treat the *vata* disorders in general and *Amavata* in particular but this *Eranda Paka* has not got its due recognition. Hence, it is planned to prepare this drug following the formula and method mentioned in Ayurvedic Formulary to fix the standards on one hand and on the other to verify the claims of the classics by experimentation of the prepared drug.

Latest research also shows that the effect of petroleum ether extract of root of *Ricinus communis* exhibited significant anti-inflammatory activity against Carrageenan, 5-Hydroxytryptamin, Dextran, Bradykinin induced rat's hind paw oedema[5]. The ethanolic extract of *Ricinus communis* root bark also found anti inflammatory properties[6].

There are various dosage form are available in Ayurvedic classics. *Paka* is one of them which comes under *Avaleha Kalpana*, which should come in semisolid form. But looking to durability it was prepared in granule form which can be stored for a long period of time. It consist of total 39 ingredients as mentioned below-

1. *Eranda* (*Ricinus communis*): 1 part
2. *Godugdha* (Cow's milk) : 8 part
3. *Goghrita* (Cow's ghee) : ½ part
4. *Khanda* (Sugar) : 2 part
5. *Sunthi (Zingiber officinale*):1/64 part
6. *Marich (Piper nigrum)* :1/64 part
7. *Pippali (Piper longum)* : 1/64 part
8. *Elachi (Elettaria cardamomum)*:1/64 part
9. *Twak (Cinnamomum zeylanicum)*:1/64 part
10. *Patra (Cinnamomum tamala)*: 1/64 part
11. *Nagkesar (Mesua ferrea)* : 1/64 part
12. *Granthi (Piper longum)* : 1/64 part
13. *Chitrak (Plumbago zeylanica)*: 1/64 part
14. *Cavya (Piper chaba)* :1/64 part
15. *Dhanyak (Coriandrum sativum)* :1/64 part
16. *Misreya (Foeniculum vulgare)*:1/64 part
17. *Sathi (Hedychium spicatum)*: 1/64 part
18. *Bilva (Aegle marmelos)* : 1/64 part
19. *Yavani (Trachyspermum ammi)* :1/64 part
20. *Sweta jirak (Cuminum cyminum)* :1/64 part
21. *Krishna jirak (Carum carvi)*: 1/64 part
22. *Haridra (Curcuma longa)*: 1/64 part
23. *Daruharidra (Berberis aristata)* :1/64 part
24. *Ashwagandh(Withania somnifera)* : 1/64 part
25. *Bala (Sida cordifolia)*: 1/64 part
26. *Patha (Cissampelos pareira)*: 1/64 part
27. *Hapusa (Juniperus communis)*: 1/64 part
28. *Vidanga (Embelia ribes)* : 1/64 part
29. *Puskarmul (Inula racemosa)*: 1/64 part
30. *Gokshur (Tribulus terrestris)*: 1/64 part
31. *Kustha (Saussurea costus)*: 1/64 part
32. *Haritaki (Terminalia chebula)*: 1/64 part
33. *Bibhitak (Terminalia bellerica)*: 1/64 part
34. *Amalaki (Phyllanthus emblica)*: 1/64 part
35. *Devadaru (Cedrus deodara):* 1/64 part
36. *Vellari (Callicarpa macrophylla)* :1/64 part
37. *Abha (Acacia nilotica)*: 1/64 part
38. *Aluka (Dioscorea bulbifera)*: 1/64 part
39. *Shatavari (Asperagus racemosus)*:1/64 part

The drug *Eranda Paka* has been selected for the study and prepared following the guidelines mentioned in the Ayurvedic Formulary of India. All the raw materials were procured from the Pharmacy attached to the National Institute of Ayurveda, Jaipur.

EXPERIMENTAL STUDY:

Anti inflammatory study:

Following the Institutional Animal Ethical Committee clearance of NIMS University Medical College, Jaipur, (Regd. No. 1302/ac/09/CPCSEA) the selected Wister strain Albino rats of either sex, weighting between 150-200 g. were selected for the study. They were maintained in the Animal house of NIMS University Medical College and care of laboratory animals was taken as per CPCSEA guidelines before the experiment. The animals were housed in polypropylene cages in the adequately ventilated room in 12 hours light/dark cycle at temperature $25^0 \pm 2^0$C. They were fed with pellets of Hindustan Lever Ltd., Mumbai and water given *ad libitum* throughout the course of the study.

Calculation of dose:

According to the Ayurvedic Formulary of India, the human dose of *Eranda Paka* is 5-15 g./day. The present study was designed in two dosage form i.e. 10 g./day and 15 g./day. The dose calculation for the animal was done on the basis of body surface area ratio by referring the Table of Paget and Barnes (1969)[6]. Thus the dose conversion formula in animals, is human dose multiplied by 0.018 (conversion factor for rats) and the resulting product will be further multiplied by 5 to obtain the dose per kg body weight. In this way the Rat dose will be 900 mg (rounded to

1 g.) in relation to human dose 10 g./day. And for human dose 15g./day, rat dose will be 1350 mg (rounded to 1.5g.). Indomethacin a known drug of modern system of medicine has also been given in the dose 10 mg/kg body weight. All the drugs were given in suspension form with 2% CMC sodium solution.

Method: Method of Winter et al. (1962) was adopted to screen the antiinflammatory activity of *Eranda Paka* against Carrageenan induced paw oedema in rats[8].

Plan of Study: Animals were fasted overnight before administering the study drugs. Total 30 Rats of either sex were selected for the study and divided into 5 groups i.e. 6 rats in each group.

- **Group 1** : 2% CMC Sodium solution
- **Group 2** : *Eranda Paka*- 1.0 g./kg b.w.
- **Group 3** : *Eranda Paka*- 1.5 g./kg. b.w.
- **Group 4** : Indomethacin- 10 mg./kg. b.w.
- **Group 5** : *Eranda Paka*- 1. 0 g./kg. and Indomethacin- 10 mg./kg.

The prepared suspension was administered orally with the help of Rubber catheter attached to a disposable syringe. Subsequently after 30 minutes of the drug administration, 0.1 ml of 1% (w/v) Carrageenan solution was injected subcutaneously in to the sub planter aponeurosis of the left hind limb to induce oedema. The paw volume was recorded initially and at ½, 1, 2 and 3 hour after Carrageenan injection by using a Plethysmograph upto the tibiotarsal articulation.

Statistical analysis:

The data obtained from investigations was analysed for statistical significance with the help of One way analysis of variance (ANOVA) followed by Dunnett Multiple Comparisons Test. The value of $p<0.05$ was regarded as significant.

The average percent increase in paw volume with time was calculated and compared against the control group. Percentage of inhibition was calculated using the formula-

$$\% \text{ Inhibition} = 100\left[1 - \frac{a - x}{b - y}\right]$$

Where, 'a' and 'b' denotes the mean paw volume of treated and control group after Carrageenan injection and 'x' and 'y' denotes the mean paw volume of treated and control group before Carrageenan injection respectively[9].

OBSERVATION AND RESULTS:

Table 1: Showing The Mean Increase In Paw Volume.

Treatment group (n=6)	Dose /kg b.w.	Mean increase in paw volume Mean ±SEM (ml)				
		0 hr.	½ hr.	1 hr.	2 hr.	3 hr.
CMC	-	0.887 ±0.081	0.320 ±0.015	0.510 ±0.036	0.793 ±0.091	0.975 ±0.112
Eranda Paka	1.0 g.	0.847 ±0.074	0.292 ±0.016	0.453 ±0.020	0.590 * ±0.032	0.542 ** ±0.031
Eranda Paka	1.5 g.	0.873 ±0.034	0.285 ±0.030	0.438 ±0.019	0.497 ** ±0.034	0.393 ** ±0.029
Indomethacin	10 mg.	0.830 ±0.089	0.262 ±0.009	0.372 ** ±0.025	0.352 ** ±0.014	0.325 ** ±0.013
***Eranda Paka* & Indomethacin**	1.0 g. 10 mg.	0.930 ±0.063	0.272 ±0.020	0.367 ** ±0.023	0.317 ** ±0.030	0.255 ** ±0.031

* Values are significantly different from control ($P< 0.05$). ** Values are significantly different from control ($P<0.01$). (One way ANOVA followed by Dunnet Multiple comparison test.)

Table 2: Showing the Percentage of Inhibition of oedema in Respect to Control Group.

Treatment group (n=6)	Dose /kg b.w.	% of Inhibition in oedema				
		0 hr.	½ hr.	1 hr.	2 hr.	3 hr.
CMC		-	-	-	-	-
Eranda Paka	1.0 g.	-	8.75	11.18	25.60	44.41
Eranda Paka	1.5 g.	-	10.94	14.12	37.33	59.69
Indomethacin	10 mg.	-	18.18	27.06	55.61	66.67
***Eranda Paka* & Indomethacin**	1.0 g. 10 mg.	-	15.00	28.04	60.03	73.85

Table 3: PERCENTAGE OF INCREASE IN PAW VOLUME

Treatment group (n=6)	Dose /kg b.w.	½ hr.	1 hr.	2 hr.	3 hr.
CMC	-	36.07	57.50	49.40	110.00
Eranda Paka	1.0 g.	34.47	53.48	69.66	63.99
Eranda Paka	1.5 g.	32.65	50.17	59.93	45.02
Indomethacin	10 mg.	31.57	44.82	42.41	39.16
***Eranda Paka* & Indomethacin**	1.0 g. 10 mg.	29.25	39.46	34.09	27.42

RESULTS:

The anti inflammatory activity was expressed as mean increased in paw volume ± SEM in terms of ml. and as percentage of inhibition. The *Eranda Paka* in the dose of 1.0 g./kg. caused significant inhibition of paw oedema 25.6% ($p<0.05$) and 44.41 ($p<0.01$) in 2nd and 3rd hour respectively and in case of 1.5 g./kg. the inhibition of paw oedema was 37.33%($p<0.01$) and 59.69%($p<0.01$) in 2nd and 3rd hour respectively. But the Indomethacin at the dose 10 mg./kg. was showed significant inhibition of paw volume from 1st hour onwards. The percentage of inhibition was 27.06%($p<0.01$), 55.61%($p<0.01$) and 66.67% ($p<0.01$) for 1st, 2nd and 3rd hour respectively.

In the group treated with *Eranda Paka* along with Indomethacin the significant inhibition of paw oedema was noticed and in 1st, 2nd and 3rd hour the 'p' value was <0.01 and percent of inhibition was 28.04%, 60.03% and 73.85% respectively.

DISCUSSION:

The experimental study was planned to reassess the anti inflammatory effect claimed in the texts and to assess the rodents have been selected for the study because of various reasons viz. ready availability, economical feasibility and wide applicability for such studies. The drug dose was calculated following the normal procedures and the effect was evaluated in two different doses i.e. 1.0 g. and 1.5 g. doses and the results were compared with that of the known NSAID drug Indomethacin. In the present study, it was also planned to evaluate for synergistic potential if any when given along with known drug. The statistical analysis has showed significant in all the groups tried. In control group the mean volume was 0.887ml. and the maximum reached after 3rd hour of induction where as in *Eranda Paka* and known treated groups initially the paw volume was quite comparable with that of the control group. But 2nd hour onwards the paw volume was decreased in comparison to that of control group.

From the results of the experimental study reveals that the animals in control group have showed continuous increase in the volume of the paw oedema whereas the trial group animals in the dose of 1.5 g./kg b.w. dose showed a great reduction 50.17%($p>0.05$), 59.93%($p<0.01$) & 45.02%($p<0.01$) in 1st, 2nd & 3rd hour respectively in the paw volume from the 1st hour onwards and showed maximum reduction in the 3rd hour. However the reduction in the paw volume is marginal in the dose in 1 g./kg b.w 53.48%($p>0.05$), 69.66%($p<0.05$) & 63.99 %($p<0.01$) in 1st, 2nd & 3rd hour respectively. The animals in the Indomethacin treated group has showed a great reduction in the paw volume right from the beginning and maintained till the end of the experiment 44.82%($p<0.01$), 42.41%($p<0.01$) & 39.16 %($p<0.01$) in 1st, 2nd & 3rd hour respectively. The trial drug when given along with known drug Indomethacin it is noticed that the trial drug potentiated the effect of Indomethacin as the reduction in the paw volume is very less 39.6%($p<0.01$), 34.09%($p<0.01$) & 27.42%($p<0.01$) in 1st, 2nd &3rd hour respectively throughout the study.

Thus it has been proved that the trial drug is having anti-inflammatory potential in the dose of 1.5g./kg. b.w. Apart from this it also showed potentiating effect on the known drug. In self control observations too the results showed same findings. The recent researches of all the ingredients also support the

above contention as the studies carried out on anti inflammatory effect.

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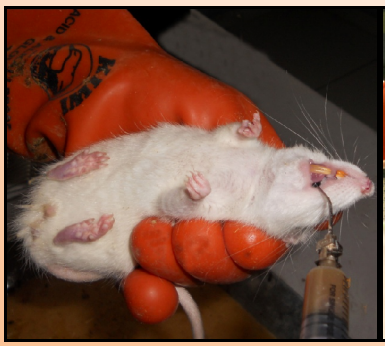
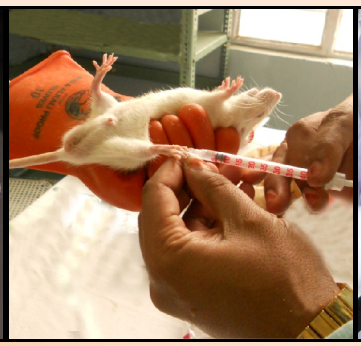
Housing of Albino Rats

RRESPONDING AUTHOR

Dr. Kamal Kr. Barman
Rasashala Assistant Govt.
Ayurvedic College, Guwahati,
Assam, India
Email:kamalkb31@rediffmail.com



Feeding of Drug



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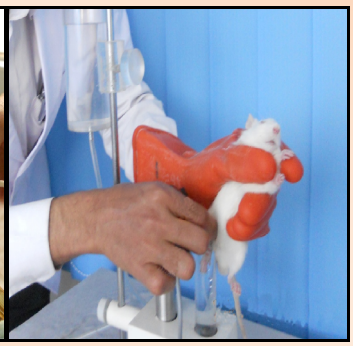

Measurement of Inflammation