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**EXPERIMENTAL EVALUATION OF ANTIPYRETIC ACTIVITY OF
SEBASTIANIA CHAMAELEA (L.) MULL.ARG. (MALAYALAM NAME –
KODIYA AVANAKKU)**

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Abstract:

The drug *Sebastiania chamaelea* (L.) Mull.Arg of the family Euphorbiaceae is mentioned as Kodiyaavanakku in Van Rheede's Hortus Malabaricus along with its medicinal uses. Presently there is a need to validate the local flora to meet the rising need for herbal medicines. As an initial step for the purpose the drug *Sebastiania chamaelea* (L.) Mull.Arg was subjected to preliminary pharmacological evaluation which includes the evaluation of antipyretic activity. Detailed literary review regarding the subject had been done. In pharmacological study, in vivo analysis of antipyretic (Brewer's Yeast induced pyrexia) activity was done in Wistar albino rats. Animals were divided into a control group and three dose groups (effective dose, half the effective dose and double the effective dose). The choorna (powder) form of the whole plant *Sebastiania chamaelea* (L.) Mull.Arg (Kodiyaavanakku) was given orally to test dose groups. On statistical analysis, significant antipyretic activity was observed in each study group at $p < 0.05$. But this antipyretic effect was not statistically significant when compared between groups. From the statistical analysis, it can be concluded that the drug *Sebastiania chamaelea* (L.) Mull.Arg possess antipyretic activity.

Keywords: *Sebastiania chamaelea* (L.) Mull.Arg, Antipyretic activity, Brewer's yeast injection

INTRODUCTION

Herbal medicines have long played important role in the health care strategies of living beings. Due to the ill effects of the main stream medicines man have turned back to the time immemorial science so called Ayurveda. Thus the needs for the herbal medicines have risen rapidly. At the same time due to over exploitation of the Mother Nature many medicinal plants disappeared or are facing the extinction. This results in lack of raw materials for the Ayurvedic herbal preparations and paved the way for adulteration. To face these all issues local flora those are used in the folklore medicinal practices should be validated and bring them to the frontline of Ayurvedic medicinal practice.

Sebastiania chamaelea (L.) Mull.Arg. is one such medicinal plant that needs validation before the scientific community (Figure 1). The drug is known as *Kodiyaavanakku* in Malayalam and its medicinal uses have been described in the Van Rheedee's Hortus Malabaricus. [1] The drug was used in earlier days to treat diarrhoea and also to restore the strength. In the Malayalam textbook *Yogamrutham*, an ancient Malayalam textbook details the application of *Kodiyaavanakku* in *Swasa Chikitsa*, [2] *Antravidhi Chikitsa* [3] and *Vayukshobha Chikitsa*. [4] But the drug failed to occupy a stagnant position in the Ayurvedic formulations and clinical practices. Presently validating the pharmacological efficacy of the drug can open a way to explore the drug therapeutically in the Ayurvedic medicinal practices.



Figure 1. *Sebastiania chamaelea* (L.) Mull.Arg.



Figure 2: Subcutaneous injection of Brewer's Yeast

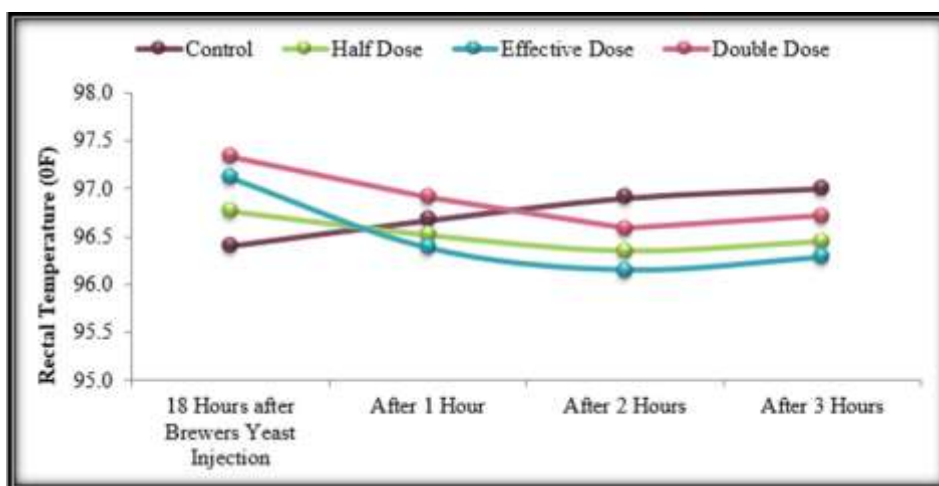


Figure 3: Line diagram showing the Mean value of rectal temperature - in Group A (Control), Group B (Half Dose), Group C (effective Dose) and Group D (Double Dose) at 1 hour interval

The drug is endowed with the chemical constituents like flavonoids, phenols, glycosides, tannins, steroids and terpenoids.[5] Also 0.5 % of the weight of the dried whole plant *Sebastiania chamaelea* (L.) Mull.Arg. is free amino acids. Of this free amino acids 77.5% were human necessary amino acids. Arginine holds the highest percentage i.e. 60% of the free amino acids obtained.[6] Prior research works have proven the antibacterial,[5] antifungal,[7] antiplasmodial,[8] antioxidant,[9] analgesic,[10] antidiabetic[11] activities of the drug. Also the drug was found to be nontoxic in its acute toxicity study.[11]

The present study aims to assess the antipyretic activity of *choorna* (powder) of the whole plant *Sebastiania chamaelea* (L.) Mull.Arg. experimentally in Wistar albino rats.

Materials and methods

A. Materials

1. Animal procurement

The animals were purchased from the proposed source, College of Veterinary and Animal Sciences, Mannuthy, Thrissur, Kerala.

2. Preparation of drug for the study

The suspension of the drug powder is prepared by mixing 12 gm powder in 100 ml distilled water (considering 12 gm as the human dose). It was shaken uniformly so that

1 ml of the solution contains 0.12 gm of test drug. This is administered according to the body weight of the animals by oral route with the help of feeding cannula.

3. Dose of the test drug

There was no available classical reference regarding the dose of *Sebastiania chamaelea* (L). Mull.Arg. Considered 12 gm human adult dose of *choorna*, the effective dose of the test drug for rats was calculated using the formula given by M. N. Ghosh in Fundamentals of experimental pharmacology. The doses of the drug was calculated by extrapolating the therapeutic dose to rat dose on the basis of body surface area ratio (conversion factor 0.018 for rats)

Animal dose = Human dose x 0.018 for 200 gm of animal:

= 12 gm x 0.018 = 0.216 gm / 200 gm of animal:

= 216 mg / 200 gm of animal

The drug was given in the following doses (1/2) X, X and 2X where 'X' represents the calculated effective dose of the test drug (0.216 gm/200gm b. wt.)

Dose of Brewer's yeast:

Dose for 150 gm rat = 1.5 ml

Dose for 200 g rat = 2 ml

4. Grouping of animals

The animals were divided into 4 groups of 6 rats (3 males, 3 females) each. Group A (Control) received standard diet and water. Treatment groups received calculated effective dose, half the calculated dose and double the calculated dose of the test drug. (Table 1)

Table 1: Grouping of animals

Groups	Drug Dose
Group A (Control)	Standard Diet And Water
Group B (Half Dose)	1/2 X (0.108gm/200gm b. Wt.)
Group C (Effective Dose)	X (0.216gm/200gm b. Wt.)
Group D (Double Dose)	2x (0.432gm/200gm b. Wt.)

B. Methods

Antipyretic activity was assessed using the Brewer's Yeast induced pyrexia method.

Preparation of yeast solution - 1.5 gm of yeast mixed with 10 ml of 5% Dextrose so as to prepare 15 % of yeast solution. 5% Dextrose was prepared by adding 5 gm of Dextrose in 100 ml distilled water. The solution was activated by keeping it closed for 15 min.

Design of animal experiment:

The study was conducted in 24 (12 male, 12 female) Wistar albino rats of about 150-200 gm. After induction of pyrexia, only the rats with raised rectal temperatures were selected for the study. The room temperature was maintained between 22^o C and 26^o C. Animals were marked and kept in separate cages for observation. The test drug was administered after the induction of pyrexia.

The grouped animals were kept in separate cages and marked for their easier observation. Rectal temperature of each animal was noted by inserting the thermosensitive end of digital thermometer into the rectum of animal for 1 min. After noting the initial temperature the animals were injected with 15% of Brewer's yeast solution in doses of 10 ml/kg body weight subcutaneously in the back below the nape of neck. (Figure 2) Then the site of injection was massaged in order to spread the suspension beneath the skin and rise in temperature was noted hourly. The peak pyrexia usually occurs at the 18th hour after yeast administration. Food was withdrawn immediately after yeast administration. After 18 hrs, animals with 1^oC rise in the basal temperature were selected for the study. These readings were taken as initial rectal temperature. Then the respective doses were administered to all the groups. After the administration of drug, rectal temperature was noted hourly for 3 hrs. Single time administration was done for all the groups through oral route.

Ethics -

Ethical clearance has been obtained from Institutional Animal Ethical Committee. Ethical clearance number is B4/2601/2017/AVC

RESULTS

The data obtained was statistically analyzed using repeated measures ANOVA with Tukey's post hoc analysis. Rectal temperatures were compared separately in Group A

(Control group), Group B (half dose group), Group C (effective dose group) and Group D (Double dose group). The comparison was done between rectal temperatures after Brewer's Yeast injection i.e. before treatment (BT), one hour after medicine induction (1st hr), two hours after medicine induction (2nd hr) and three hours after medicine induction (3rd hr) of each group separately. (Figure 3)

Also the rectal temperature was compared between Group A, Group B, Group C and Group D at BT, 1st hr, 2nd hr and 3rd hr.

Comparison between the groups at 1 hour interval during the treatment period showed that there was no statistically significant decrease in rectal temperature. Whereas the comparison within each group showed statistically significant antipyretic effect.

The rise in temperature in the Group A (control) at 1sthr, 2ndhr and 3rdhr was highly significant when compared to the rectal temperature before treatment. (Table 2).

Table 2: Comparison of rectal temperature within Group A (control)

Group A	Mean Difference	q	Significance	Summary	95% CI of diff
BT Vs 1 st hr	-0.2667	11.31	Yes	***	-0.3627 to -0.1706
BT Vs 2 nd hr	-0.5000	21.21	Yes	***	-0.5961 to -0.4039
BT Vs 3 rd hr	-0.6000	25.46	Yes	***	-0.6961 to -0.5039
1 st hr Vs 2 nd hr	-0.2333	9.900	Yes	***	-0.3294 to -0.1373
1 st hr Vs 3 rd hr	-0.3333	14.14	Yes	***	-0.4294 to -0.2373
2 nd hr Vs 3 rd hr	-0.1000	4.243	Yes	*	-0.1961 to -0.003929

In Group B (half dose) the rectal temperature tends to decrease after the medicine induction and this difference in the temperature was highly significant when compared to the rectal temperature before treatment. The group showed maximum antipyretic activity at the 2nd hr. (Table 3)

Table 3: Comparison of rectal temperature within Group B (Half dose)

Group B	Mean Difference	q	Significance	Summary	95% CI of diff
BT Vs 1 st hr	0.2500	12.75	Yes	***	0.1701 to 0.3299
BT Vs 2 nd hr	0.4167	21.25	Yes	***	0.3368 to 0.4966
BT Vs 3 rd hr	0.3167	16.15	Yes	***	0.2368 to 0.3966
1 st hr Vs 2 nd hr	0.1667	8.502	Yes	***	0.08676 to 0.2466
1 st hr Vs 3 rd hr	0.06667	3.401	No	ns	-0.01323 to 0.1466
2 nd hr Vs 3 rd hr	-0.1000	5.101	Yes	*	-0.1799 to -0.02009

The comparison within Group C (effective dose) showed that the group have highly significant antipyretic activity after the medicine induction and the maximum antipyretic effect was found at the 2ndhr after medicine induction. (Table 4)

The Group D (double dose) have also shown a highly significant antipyretic activity after the medicine induction when compared to the rectal temperature before treatment. And the group showed maximum antipyretic effect at the 2nd hr. (Table 5)

The difference in rectal temperature at 1sthr, 2ndhr and 3rdhr after the medicine induction was compared between groups and found that the antipyretic activity shown by each test group was not statistically significant with respect to other groups. (Table 6, 7& 8)

Table 4: Comparison of rectal temperature within Group C (Effective dose)

Group C	Mean Difference	q	Significance	Summary	95% CI of diff
BT Vs 1 st hr	0.7333	16.32	Yes	***	0.5502 to 0.9164
BT Vs 2 nd hr	0.9667	21.52	Yes	***	0.7836 to 1.150
BT Vs 3 rd hr	0.8333	18.55	Yes	***	0.6502 to 1.016
1 st hr Vs 2 nd hr	0.2333	5.194	Yes	*	0.05022 to 0.4164
1 st hr Vs 3 rd hr	0.1000	2.226	No	ns	-0.08311 to 0.2831
2 nd hr Vs 3 rd hr	-0.1333	2.968	No	ns	-0.3164 to 0.04978

Table 5: Comparison of rectal temperature within Group D (Double dose)

Group D	Mean Difference	q	Significance	Summary	95% CI of diff
BT Vs 1 st hr	0.4167	8.076	Yes	***	0.2064 to 0.6270
BT Vs 2 nd hr	0.7500	14.54	Yes	***	0.5397 to 0.9603
BT Vs 3 rd hr	0.6167	11.95	Yes	***	0.4064 to 0.8270
1 st hr Vs 2 nd hr	0.3333	6.460	Yes	**	0.1230 to 0.5436
1 st hr Vs 3 rd hr	0.2000	3.876	No	ns	-0.01030 to 0.4103
2 nd hr Vs 3 rd hr	-0.1333	2.584	No	ns	-0.3436 to 0.07697

Table 6: Comparison of rectal temperature between Groups 1 hr after medicine administration

Groups	Mean Difference	Q	Significance	Summary	95% CI of diff
Group A vs Group B	0.1500	0.5843	No	ns	-0.8964 to 1.196
Group A vs Group C	0.2833	1.104	No	ns	-0.7630 to 1.330
Group A vs Group D	-0.2500	0.9738	No	ns	-1.296 to 0.7964
Group B vs Group C	0.1333	0.5194	No	ns	-0.9130 to 1.180
Group B vs Group D	-0.4000	1.558	No	ns	-1.446 to 0.6464
Group C vs Group D	-0.5333	2.078	No	ns	-1.580 to 0.5130

Table 7: Comparison of rectal temperature between Groups 2 hrs after medicine administration

Groups	Mean Difference	Q	Significance	Summary	95% CI of diff
Group A vs Group B	0.5500	2.113	No	ns	-0.5108 to 1.611
Group A vs Group C	0.7500	2.882	No	ns	-0.3108 to 1.811
Group A vs Group D	0.3167	1.217	No	ns	-0.7442 to 1.377
Group B vs Group C	0.2000	0.7684	No	ns	-0.8608 to 1.261
Group B vs Group D	-0.2333	0.8965	No	ns	-1.294 to 0.8275
Group C vs Group D	-0.4333	1.665	No	ns	-1.494 to 0.6275

Table 8: Comparison of rectal temperature between Groups 3 hrs after medicine administration

Groups	Mean Difference	Q	Significance	Summary	95% CI of diff
Group A vs Group B	0.5500	2.038	No	ns	-0.5498 to 1.650
Group A vs Group C	0.7167	2.656	No	ns	-0.3832 to 1.817
Group A vs Group D	0.2833	1.050	No	ns	-0.8165 to 1.383
Group B vs Group C	0.1667	0.6177	No	ns	-0.9332 to 1.267
Group B vs Group D	-0.2667	0.9883	No	ns	-1.367 to 0.8332
Group C vs Group D	-0.4333	1.606	No	ns	-1.533 to 0.6665

Discussion

The antipyretic activity of the *choorna*(powder)of whole plant *Sebastiania chamaelea* (L.)Mull.Arg. in three different dose groups (half dose, effective dose and double dose) were assessed using the Brewer's yeast induced pyrexia method in Wistar albino rats. Obtained data were statistically analyzed using the repeated measure ANOVA with Tukey's post hoc test. When the difference in rectal temperature was compared within the group, each group, including the control group, showed statistically significant difference in the rectal temperature at $p < 0.05$. But when the difference were compared between groups, the difference in rectal temperature was not statistically significant. Even though the half dose, effective dose and double dose groups were not able to prove the significance of their antipyretic effect with respect to the control group, they showed a marked decrease in the rectal temperature during the treatment period where as the control group showed a subsequent increase in the rectal temperature. All the three test dose groups started to exhibit the antipyretic effect by the 1sthr after medicine administration and showed their maximum effect by the 2ndhr and then by 3rdhr the effect started to reduce.

The drug contains phytochemical constituents like flavonoids, saponins, tannins, steroids and phenols.[12] Flavonoids are known to have anti-inflammatory and antipyretic activities.[13] And these all phytoconstituents can be the reason behind the pharmacological action of the drug.

CONCLUSION

From the study, it can be summarized that *choorna* of the whole plant *Sebastiania chamaelea* (L.) Mull.Arg. possess significant antipyretic activity.

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