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ANALGESIC, ANTIINFLAMMATORY AND ANTIPYRETIC ACTIVITY OF *TRICHOSANTHES DIOICA* ROXB. LEAF EXTRACTS

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Keywords:

Trichosanthes dioica Roxb., Methanol, n-hexane, Analgesic, Anti-inflammatory, Antipyretic activity

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ABSTRACT: Aim of the study: This study evaluates the analgesic, anti-inflammatory and antipyretic activities of the aqueous, methanol and n-hexane extracts of *Trichosanthes dioica* Roxb. to provide experimental evidence for its traditional use such as fever, pain and inflammation. **Materials and methods:** Investigations on the analgesic effects of *Trichosanthes dioica* Roxb. was carried out by acetic acid-induced writhing using Aspirin as standard. The anti-inflammatory activity was observed by carrageenin-induced edema of the hind paw of rats using indomethacin as standard. The antipyretic activity was observed by yeast induced pyrexia in rat using Paracetamol as standard. **Results:** It has been shown that the methanol and aqueous extracts significantly reduced acetic acid-induced writhing response in mice. The methanol and aqueous extracts remarkably inhibited the increase in vascular permeability induced by acetic acid and also significantly decreased the carrageenin-induced rat paw edema perimeter. The methanol and aqueous extracts also shows reduction of body temperature in yeast induced pyrexia in rat model. **Conclusion:** The results show that the methanol and aqueous extracts have analgesic activity and as anti-inflammatory effects, supporting the traditional application of this herb in treating various diseases associated with inflammation and pain. The result also shows that the methanol and aqueous extracts have moderate antipyretic activity. Out of methanol and water extract, methanol extract shows better analgesic, anti-inflammatory and antipyretic activity with respect to the standard used.

INTRODUCTION: India is known as the land of medicines from the starting of this world. Plants since ancient times have been the basis of traditional medicine systems and key source of medicinal agents. The struggle to relieve pain began with the origin of humanity. Majority of the world population depend on Traditional Medicine such as herbs for treatment of various ailments.

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Present day medicine was derived from herbal traditions. Pain according to the International Association for the Study of Pain (IASP) is an unpleasant, sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

Inflammation is a defensive mechanism of the body to remove injurious stimuli and initiate healing process for the tissue, but if it runs unchecked, it can lead to onset of certain diseases as vasomotor rhinnorrhoea, rheumatoid arthritis, and atherosclerosis. It is characterised by redness, swelling, heat and pain and a times loss of function. Fever is defined as the elevation of core body

temperature above normal. In normal adults, average oral temperature is 37 °C (98.6 °F). Fever may be due to infection, inflammation, or any tissue damage and disease state. It arises as a secondary impact of infection, malignancy or other diseased states [1]. The conventional traditional medicinal systems such as Ayurveda, siddha and amchi which were developed in India are still used by the common people. Traditional Indian herbal medicines, including tribal herbs, are used in the treatment of wide variety of clinical diseases in India. *Trichosanthes dioica* Roxb. of family Cucurbitaceae is one of the popular herbs of Assam having medicinal value. *Trichosanthes dioica* Roxb. has been widely applied in many Indian traditional medicine prescriptions and based on its traditional uses, it has been used for the treatment of variety of diseases like inflammation, pain and fever in India.

For our current study we have selected the leaves of the plant *Trichosanthes dioica* Roxb. However, over the decades the use of modern medicines (allopathy) has made a tremendous endeavour in enhancing the healthcare of our nation. But, we should always keep in mind that the basis of progress remains rooted to traditional medicines and therapies. Survey results shows that 75% of the herbal medicines used worldwide were derived from ethnomedicinal study and in India, approximately 70% of newer drugs are derived from natural resources and numerous other synthetic analogues which have been prepared from prototype compounds isolated from plants [2].

Recent phytochemical studies reveals that carbohydrates, alkaloids, glycosides, flavonoids, steroids and Tannins were the principal constituents of *Trichosanthes dioica* Roxb., as per the reports they found to have analgesic, anti-inflammatory and antipyretic effects. Traditional use are mostly related to the herb's analgesic, anti-inflammatory and antipyretic actions, and still few are reported on the pharmacological action of the aqueous and methanol extracts of *Trichosanthes dioica* Roxb. are available. Thus it is logical for us to evaluate its *in-vivo* analgesic, anti-inflammatory and antipyretic activities.

In the present study, the authors examined the effects of aqueous, methanol and n-hexane extracts of *Trichosanthes dioica* Roxb. on acetic acid-induced writhing, tail immersion test, carrageenin-induced edema of the hind paw, and yeast induced hyperpyrexia tests in rats and mice.

METHODS AND MATERIALS:

Plant Material: The plant specimen was collected from Nalbari District of Assam. The plant was collected in the month of March 2012. The plant identified as *Trichosanthes dioica* Roxb. was confirmed by Prof. Gajen Sharma of Department of Botany, Gauhati University, Assam, India. (Acct. no: 004328 on dated 27th April 2012)

Chemicals: Methanol, Ethanol, n-Hexane, Chloroform were procured from RANKEM (Ranbaxy Fine Chemicals Ltd.,) New Delhi, India, Ethyl acetate from Sisco Research Laboratories Pvt. Ltd., India. Carboxy Methyl Cellulose (Rankem Ranbaxy fine chemicals Ltd., New Delhi, India), Sodium Chloride (Rankem Ranbaxy fine chemicals Ltd., New Delhi, India) Aspirin, Indomethacin, Paracetamol (Novartis India Pvt. Ltd.,) Acetic acid was procured from (Rankem Ranbaxy fine chemicals Ltd., New Delhi, India), carrageenan and brewer's yeast was procured from Hi Media Laboratories Pvt. Ltd., Mumbai, India.

Preparation of Extract by Hot Continuous Extraction: The leaves of the *Trichosanthes dioica* Roxb. were collected and dried under shade. Dried leaves were powdered by using mechanical grinder. Powdered leaves (200 g) were extracted with methanol using Soxhlet apparatus. The extract was concentrated to dryness under reduced pressure to yield a dried crude methanol extract [3, 4, 5]. Similarly, the protocol was repeated with n-hexane and water to obtain crude n-hexane and water extracts respectively. The extracts were then stored at 4 ºC till the time of use. The % Yield of water, methanol and n-Hexane leaves extract of *Trichosanthes dioica* Roxb. were 15.22% w/w, 17.67% w/w and 12.82% w/w.

Animals: Male and female Wistar mice (20 - 22 g) and male and female rats (180 - 200 g) were purchased from the Pasteur Institute, Shillong, India Animal welfare and experimental procedures complied with Indian regulations, specifically the approved protocols of the Animal Ethics Committee of the Gauhati Medical College and

Hospital, Guwahati for experimental purpose. All animals were kept in a room maintained under environmentally controlled conditions of 25 ± 10 °C relative humidity 45 - 55% and a 12:12 hrs light / dark cycle. All animals had free access to water and standard diet. They were acclimatized at least 1 week before the experiments were started. The mice were fasted for 10 h prior to the experiments, and the test substances were given orally with free access to water.

Drug Administration: The aqueous extract (500, 750 and 1000 mg/kg), methanol extract (500, 750 and 1000 mg/kg), n-hexane extract (500, 750 and 1000 mg/kg), aspirin (100 mg/kg, reference drug) Indomethacin (150 mg/kg, reference drug) and Paracetamol (150 mg/kg, reference drug) were given orally to mice and rat. The primary experiments showed that these doses selected are suitable for the study. The control group received the same volume of 0.5% CMC, distilled water, and 0.9% sodium chloride.

Acute Toxicity Study: The acute toxicity for samples (*Trichosanthes dioica* Roxb. leaves extract) was determined in Albino mice. The animals were fasted overnight prior to the experiment. Fixed dose [Organisation for Economic Co-operation and Development (OECD) Guideline no. 423, Annexure 2d] [6] method of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) was adopted for toxicity studies. The tested extracts suspended in 0.5% w/v sodium carboxy methyl cellulose (CMC) and were administrated orally (1 ml/100 g) in 3 animals. The presence or absence of any signs of toxicity or mortality was monitored at 2000 mg/kg in the all cases for 14 days. Approval from the Institutional Animal Ethical Committee (IAEC) of Gauhati Medical College and Hospital, Guwahati, [Registration No.: 351/ CPCSEA on dated: 03/01/2001] was taken prior to the experiments [Reference No. MC/ 05/2015/11, date, 17/02/2015].

Writhing Reflex Induced by Acetic Acid in Mice: Analgesic activity was evaluated on the acetic acid induced writhing according to Koster *et al.*, 1959. Albino mice weighing between 20 to 25 gm were divided into 11 groups each comprising of six animals. 60 minutes after administration of extracts (orally), 0.1 ml 1% acetic acid (dose: 0.1 ml /10 gm of mice) was injected intraperitoneally. The number of abdominal contractions for the period of 20 minutes was counted. The response consisted of abdominal wall contractions, pelvic rotation, followed by hind limb stretches. A significant reduction in the number of abdominal contraction compared to the control was considered as an antinociceptive response [7, 8].

The percentage analgesic activity was calculated as follows:

$$\% \text{ Analgesic activity} = \frac{Nc - Nt}{Nc} \times 100$$

Where Nc is the average number of stretches of the control group, and Nt is the average number of stretches of the test drug group.

Tail Immersion Test: In hot water (temperature was maintained at 55 ± 0.5 °C) extreme 3 cm of the Albino mouse tail immerged in that water. Within a time period each mouse was reacted by withdrawing the tail, and the reaction time was recorded with a stopwatch. The standard drug and extract were given orally to the respective groups as described above. The experiment was repeated at 0, 0.5, 1, 2, 3, 5 h after administration of extracts and standard drug. Morphine was used as standard at a dose of 10 mg/kg [7, 9].

Rat Paw Edema Induced by Carrageenin: Male or female wistar rats with a body weight between 150 - 200 g were used. The animals were starved overnight. Rats were divided into 11 groups each comprising of six animals. To ensure uniform hydration, the rats received 5 ml/kg of water by stomach tube (controls) or the test drug dissolved or suspended in the same volume. The vehicle / Indomethacin / extracts were administered orally.

Thirty minutes later the rats were challenged by injection of 0.1 ml of 1% carrageenan into the plantar region of the left hind paw. The paw was marked with ink at the level of the lateral malleolus and immersed in mercury up to this mark. The paw volume was measured plethysmographically immediately after injection, and again at 15, 30, 60, 120 min after challenge. Mean percent change in paw volume was compared [10, 11].

Percentage reduction in edema volume was calculated by using the formula:

$$\text{Percentage reduction} = \frac{Vo - Vt}{Vo} \times 100$$

Where, Vo = Volume of the paw of control at time't'; Vt = Volume of the paw of drug treated at time't'.

From the data obtained, the mean edema volume and percentage reduction in edema was calculated.

Pyrexia in Rat Induced by Yeast: A 15% suspension of Brewer's yeast in 0.9% saline was prepared. Male albino Rats weighing between 150 - 200 g were divided into 11 groups each comprising of six animals. By insertion of a thermocouple to a depth of 2 cm into the rectum the initial rectal temperatures were recorded. The animals were fevered by injection of 10 ml/kg of Brewer's yeast suspension subcutaneously in the back below the nape of the neck. The site of injection was selected in order to spread the suspension beneath the skin. Immediately after yeast administration, food is withdrawn. 18 h post challenge, the rise in rectal temperature was recorded. The measurement was repeated after 60 min. Only animals with a body temperature of at least 38 °C were taken into the test. The animals received the test compound or the standard drug by oral administration. Rectal temperatures were recorded again 60, 120, 180, 240, 300 min post dosing. Standard drug used was Paracetamol 150 mg/kg body weight [7, 12].

Statistical Analysis: Data were presented as mean ± S.E.M. Statistical differences between the control and treated groups were tested by one-way ANOVA followed by Tukey's test. The differences were considered to be significant at $p < 0.05$.

RESULTS:

Effects of *Trichosanthes dioica* Roxb. on Acetic Acid-induced Writhing Reflex in Mice: The water, methanol and n-hexane extract at a dose of 500, 750 and 1000 mg/kg body weight were subjected for the study. The standard drug used was Aspirin at a dose of 100 mg/kg body weight. The number of writhing were observed and noted down. The methanol extract at a dose of 1000 mg/kg shows promising analgesic activity with comparison to the standard Aspirin used. The results are tabulated in **Table 1** and a graph in **Fig. 1**.

TABLE 1: EFFECT OF THE WATER, METHANOL AND n-HEXANE EXTRACTS OF *TRICHOSANTHES DIOICA* ROXB. ON ACETIC ACID INDUCED WRITHING RESPONSE AND TAIL IMMERSION TEST IN MICE

Groups	Dose (mg/ kg)	Writhing test		Tail immersion method Latency period (s)					
		Number of writhing	Inhibition ratio (%)	0min	30min	1h	2h	3h	5h
Control (0.5% CMC)	-	53.00±1.291	-	1.53±0.361	1.62±0.410	1.68±0.932	1.68±0.552	1.62±0.331	1.64±0.362
Aspirin	100	9.33±0.494***	82.39	-	-	-	-	-	-
Morphine	10	-	-	1.67±0.361	2.66±0.541	5.20±0.340*	9.83±0.540**	10.23±0.821***	10.73±0.321*
Water extract	500	17.50±0.671***	66.98	1.71±0.461	2.56±0.492	3.42±0.362	4.37±0.562	6.92±0.551**	6.38±0.452
	750	13.52±0.671***	74.49	1.63±0.661	2.22±0.421*	3.62±0.841**	5.68±0.462*	8.73±0.412*	7.01±0.593
	1000	7.00±0.730***	86.79	1.72±0.465	2.33±0.763	4.76±0.552***	8.81±0.921**	9.92±0.411*	7.45±0.452
Methanol extract	500	19.51±1.147***	63.18	1.71±0.371	2.13±0.452*	3.16±0.592*	4.32±0.571**	4.43±0.651	4.52±0.754
	750	12.52±0.764***	76.37	1.63±0.321	2.35±0.492*	3.62±0.225*	5.23±0.641**	6.37±0.442*	5.82±0.642
	1000	4.51±0.428***	91.49	1.63±0.352	1.95±0.641*	5.62±0.851*	9.30±0.731**	10.22±0.351***	10.41±0.324
n-Hexane extract	500	46.33±1.116***	12.58	1.58±0.672	1.68±0.551	1.73±0.341	2.21±0.532	1.92±0.912	1.74±0.824
	750	42.16±1.014***	20.45	1.62±0.124	1.88±0.364	1.97±0.451	1.99±0.441	2.32±0.642	2.03±0.361
	1000	38.12±0.777***	28.07	1.71±0.642	1.92±0.542	2.01±0.341	4.25±0.652	3.72±0.582	3.68±0.942

Values are mean ± S.E.M. (n = 6). *P < 0.05, **P < 0.01, ***P < 0.001 significantly different from control group (ANOVA followed by Tukey's test).

Effects of *Trichosanthes dioica* Roxb. on Tail Immersion Test in Mice: After a latency period of 0.5 h following oral administration of the extracts at a dose of 500, 750 and 1000 mg/kg, reduction of painful impression was observed against tail immersion test and the effect was observed to be dose dependent. The significant inhibition was of painful reaction, noted 1 h after drug administration. The analgesic effects of the extracts became evident between 1 and 3 h post-dosing and but activity decreased or remain same after 3 h. At higher dose of aqueous and methanol extract had nearly similar activity to that of morphine between 1 - 3 h. but methanol extract showed little more

effect compared to aqueous extract **Table 1**. Results symbolize significant activity of extracts though the duration of analgesic activity was less than the standard.

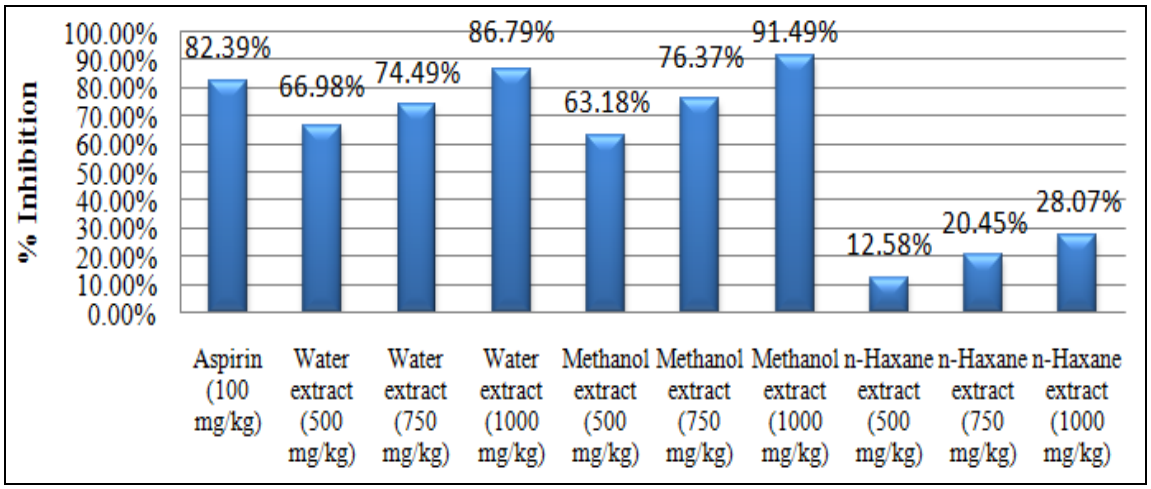

FIG. 1: GRAPH BETWEEN % INHIBITION OF WRITHING RESPONSE AND DOSE OF THE CONTROL, STANDARD AND EXTRACT

Effects of *Trichosanthes dioica* Roxb. on Carrageenin-induced Paw Edema in Rats: The results are presented in **Table 2** and **3**. The water extract (750 mg/kg and 1000 mg/kg) and methanol extract (750 mg/kg and 1000 mg/kg) showed reduction in the carrageenin-induced paw edema in rats at 60 min and 120 min. Indomethacin (150 mg/kg) also inhibited paw edema in rat after carrageenin injection.

TABLE 2: INFLUENCE OF *TRICHOSANTHES DIOICA* ROXB. LEAVES EXTRACT ON CARRAGEENAN-INDUCED RAT HIND PAW OEDEMA

Treatment	Dose (mg/kg)	Paw edema after carrageenan injection at				
		0 min	15 min	30 min	60 min	120 min
Control	-	0.513±0.005	0.748±0.008	0.892±0.008	1.230±0.031	1.425±0.018
Indomethacin	150	0.515±0.006	0.602±0.011***	0.618±0.010***	0.581±0.006***	0.571±0.008***
	500	0.602±0.005	0.762±0.007	0.870±0.011	1.150±0.043	1.091±0.027***
Water extract	750	0.550±0.005	0.700±0.008	0.842±0.012	1.023±0.044**	0.960±0.011***
	1000	0.580±0.006	0.702±0.011	0.803±0.012***	0.982±0.031***	0.783±0.033***
	500	0.530±0.006	0.660±0.012***	0.825±0.012*	1.050±0.043*	1.058±0.037***
Methanol extract	750	0.572±0.005	0.628±0.010***	0.812±0.011***	0.970±0.031***	0.931±0.035***
	1000	0.523±0.008	0.625±0.013***	0.793±0.011***	0.951±0.037***	0.752±0.018***
	500	0.537±0.007	0.765±0.013	0.877±0.010	1.213±0.029	1.407±0.028
n-Hexane extract	750	0.575±0.007	0.757±0.014	0.885±0.015	1.212±0.028	1.383±0.028
	1000	0.522±0.009	0.745±0.010	0.867±0.017	1.181±0.018	1.337±0.016

Values are mean ± S.E.M. (n = 6). *P < 0.05, **P < 0.01, ***P < 0.001 significantly different from control group (ANOVA followed by Tukey's test).

TABLE 3: % INHIBITION OF PAW EDEMA AFTER CARRAGEENAN INJECTION AT 60 min AND 120 min

Treatment	Dose (mg/kg)	% Inhibition of Paw edema after carrageenan injection at	
		60 min (%)	120 min (%)
Control	-	-	-
Indomethacin	150	52.76	59.92
	500	6.50	23.43
Water extract	750	16.82	32.63
	1000	20.16	45.05
	500	14.63	25.75
Methanol extract	750	21.13	34.73
	1000	22.68	47.36
	500	1.38	1.26
n-Hexane extract	750	1.46	2.94
	1000	3.98	6.17

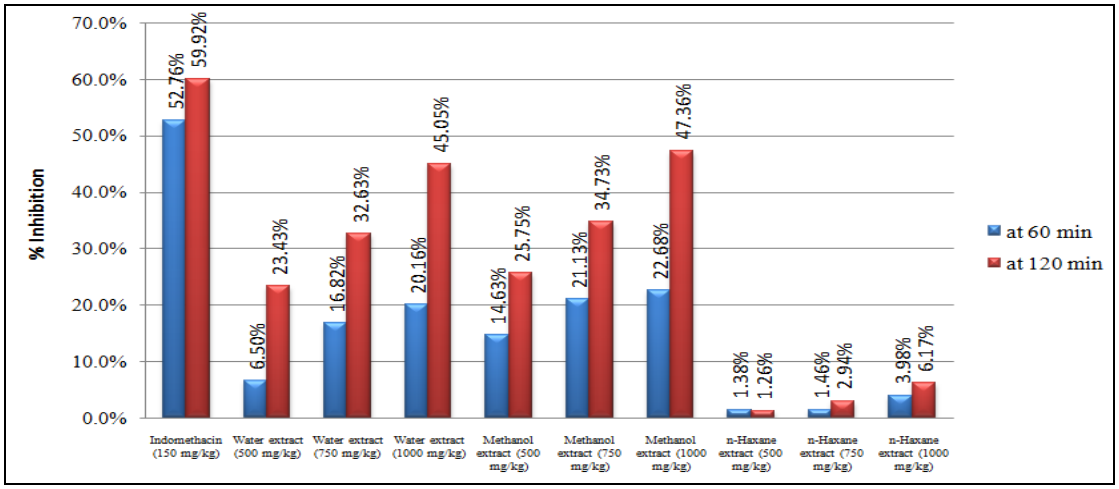

FIG. 2: GRAPH OF COMPARATIVE STUDY BETWEEN % INHIBITION OF PAW EDEMA AFTER CARRAGEENAN INJECTION AND DOSE OF THE CONTROL, STANDARD AND EXTRACT AT 60 min AND 120 min

Effects of *Trichosanthes dioica* Roxb. on Yeast Induced Pyrexia in Rats: The methanol extract at a dose of 1000 mg/kg body weight shows moderate antipyretic activity at 23 h, but water and n-hexane extracts do not show antipyretic activity at any dose with respect to the standard drug Paracetamol 150 mg/kg. The reduction of rectal temperature is tabulated in **Table 4** and graphically represented in **Fig. 3**.

TABLE 3: INFLUENCE OF *TRICHOSANTHES DIOICA* ROXB. LEAVES EXTRACT ON BREWER'S YEAST (15% w/v) INDUCED HYPERPYREXIA IN RAT

Treatment	Dose (mg/kg)	Rectal temperature (°C) before and after treatment					
		0 h	19 h	20 h	21 h	22 h	23 h
Control (0.9% NaCl)	-	37.4±0.034	39.8±0.038	39.4±0.041	39.2±0.038	39.1±0.032	39.1±0.032
Paracetamol	150	37.4±0.030	39.6±0.037	38.1±0.038*	37.5±0.034**	37.4±0.030**	37.3±0.030***
Water extract	500	37.3±0.031	39.5±0.040	39.4±0.039	39.3±0.033	39.0±0.033	38.9±0.029
	750	37.2±0.030	39.7±0.032	39.3±0.041	38.6±0.033	38.3±0.032*	38.1±0.038*
	1000	37.2±0.029	39.7±0.034	39.0±0.040	38.7±0.030*	38.2±0.037*	37.8±0.033**
Methanol extract	500	37.3±0.032	39.6±0.036	39.5±0.039	39.3±0.033	38.9±0.030	39.6±0.037
	750	37.1±0.034	39.7±0.035	39.0±0.037	38.3±0.031*	38.2±0.037*	38.0±0.038*
	1000	37.2±0.033	39.5±0.035	38.7±0.038*	38.0±0.033*	37.8±0.039**	37.6±0.039**
n-Hexane extract	500	37.3±0.035	39.5±0.030	39.5±0.032	39.2±0.041	39.2±0.039	39.0±0.040
	750	37.4±0.030	39.5±0.034	39.4±0.031	39.1±0.044	39.0±0.038	38.9±0.041
	1000	37.3±0.031	39.7±0.039	39.6±0.031	39.2±0.038	39.0±0.040	38.8±0.028

Values are mean ± S.E.M. (n = 6). *P < 0.05, **P < 0.01, ***P < 0.001 significantly different from control group (ANOVA followed by Tukey's test).

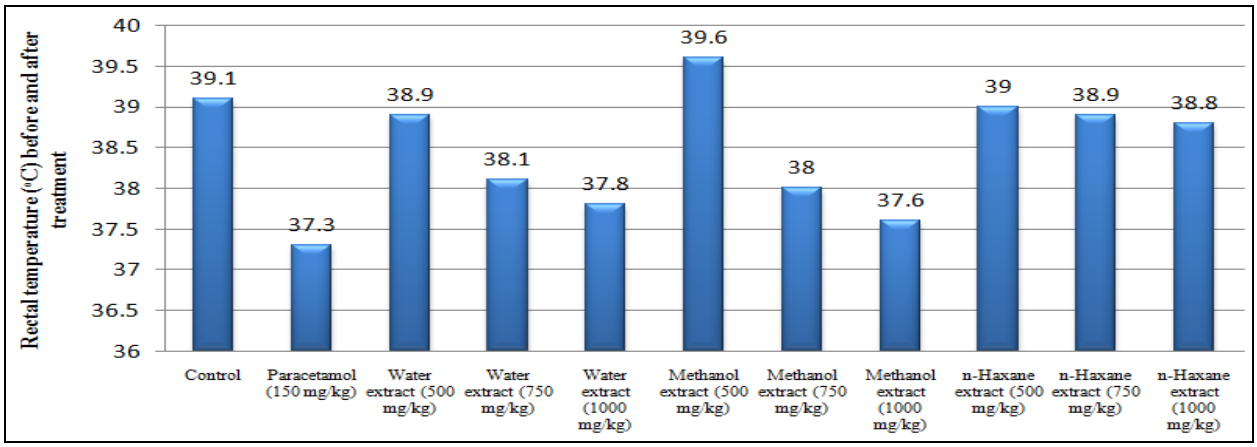

FIG. 3: GRAPH BETWEEN RECTAL TEMPERATURE (°C) AT 23 hr AND DOSE OF THE CONTROL, STANDARD AND EXTRACT

DISCUSSION: The analgesic, anti-inflammatory and antipyretic effects of the aqueous, methanol and n-Hexane extracts of *Trichosanthes dioica* Roxb. were investigated in this study. The analgesic activities were evaluated using two animal models. Tail immersion test was selected to investigate central analgesic activity. Acetic acid-induced writhing response was selected to observe peripheral analgesic effects.

In the acetic acid-induced writhing test, the aqueous and methanol extracts at a dose of 500, 750 and 1000 mg/kg body weight demonstrated a significant analgesic effect, inhibiting pain by 66.98%, 74.49%, 86.79%, 63.18%, 76.37% and 91.49% as compared to the control, respectively **Table 1**. A comparison done on acetic acid-induced pain showed that aspirin at 100mg/kg had 82.39% ($p < 0.001$). Acetic acid caused an increase in the peritoneal fluids of PGE2 and PGF2α, serotonin, and histamine [13], so the results show that the *Trichosanthes dioica* Roxb. leaves extracts have a significant inhibitory activity in inflammation pain, and this activity may be related with the suppression of synthesis and / or release of endogenous pro-inflammatory substances.

The anti-inflammatory activity of *Trichosanthes dioica* Roxb. leaves extract was evaluated by use of the carrageenan induced paw oedema method. The carrageenan induced paw oedema is recurrently used as an experimental model to find the effectiveness of investigated drug against acute inflammation [14]. Carrageenin involves in the synthesis or release of inflammatory mediators at the injured site which further cause pain and fever.

Carrageenan injection in rat paw causes plasma extravasation, and responsible for inflammation which is characterized by amplified tissue water and plasma protein exudation with neutrophil extravasation and cyclooxygenase and lipoxygenase enzyme pathways mediated metabolism of arachidonic acid [15]. Carrageenan induced paw oedema represent a biphasic response. First phase (begins immediatelly after injection and diminishes within 1 hr) is mediated by release of histamine and serotonin [16], while the second or delayed phase (begins at 1 hr and remains through 3 hr) is mediated by neutrophil infiltration, release of eicosanoid, production of free radicals and release of other neutrophil derived mediators [17]. The discharge of bradykinin like substance is involved in oedema formed in between early and late phase, which activate the biosynthesis of prostaglandin and other autocoids, and cause inflammatory exudates.

Increased body temperature and pain are known as the main symptoms of the body against an inflammatory stimulation. Hence, a drug possessing anti-inflammatory activity may also exhibit anti-pyretic and analgesic properties. In order to determine the antipyretic effect of *Trichosanthes dioica* Roxb., the brewer's yeast induced hyperthermia in rat model was used. Three dosages of water, methanol and n-hexane extract (500 mg/kg, 750 mg/kg and 1000 mg/kg i.p.) of the plant in the effective antipyretic, analgesic and anti-inflammatory dose were used. Methanol extract showed a moderate decrease in rectal temperature similar to that of Paracetamol (150 mg/kg, i.p.). This result suggested that the plant has some influence on prostaglandin biosynthesis because prostaglandin is believed to be a regulator of body temperature.

A dose of 500 mg/kg, 750 mg/kg and 1000 mg/kg body weight was considered as the dose and at those doses the water and methanol extract shows promising analgesic and anti-inflammatory activity and moderate antipyretic activity but n-Hexane extract does not shows any one activity. From the result it was also observed that amongst water and methanol extract, the methanol extract shows better analgesic and anti-inflammatory activity at 1000 mg/kg body weight with compare to the Standard Aspirin and Indomethacin. Out of water and methanol extract, methanol extract shows better analgesic and anti-inflammatory activity.

In the phytochemical investigation, we have found that, the extract contains carbohydrates, alkaloids, glycosides, flavonoids, steroids and tannins as constituents. These results expose that the chemical constituents, which may be responsible for the many pharmacological actions. It suggested that those chemical constituents were responsible for the anti-inflammatory and analgesic effects of the aqueous and methanol extracts of *Trichosanthes dioica* Roxb.

But it is noted that active components in such extracts are remained to be isolated in the further studies.

CONCLUSION: The results obtained in present work clearly support the traditional application of *Trichosanthes dioica* Roxb. in the treatments of fever, pain and inflammatory illness. From the result of *in-vivo* Pharmacological activity study it can be concluded that the water and methanol extracts of the leaves of the plant *Trichosanthes dioica* Roxb. at a dose of 1000 mg/ kg body weight has shown potent analgesic and anti-inflammatory activity and moderate antipyretic activity with comparison to the standard drug Aspirin, Indomethacin and Paracetamol used respectively.

But n-Hexane extract does not show any activity at the selected dose. Amongst water and methanol extract, methanol extract has shown better analgesic activity and hence methanol extract at a dose of 1000 mg/kg body weight was considered for the formulation of oral dosage form. Preliminary phytochemical screening of water and methanol extract of the leaves of the plant gave positive test for alkaloids, carbohydrates, glycosides, tannins, flavonoids and steroids, which might be in part responsible for analgesic and anti-inflammatory activities.

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