

ANALGESIC, ANTI INFLAMMATORY AND ANTI PYRETIC ACTIVITY OF *TRICHO SANTHESDIOICA ROXB.* LEAF EXTRACTS

Ms. Mobina Begum, Ms. Safiya Begum, Mr. Rahul Chakraborty

Assistant professor^{1,3} Associate professor²

Department of Pharmaceutics,

Global College of Pharmacy, Hyderabad. Chilkur (V), Moinabad (M), Telangana- 501504.

ABSTRACT: **Aim of the study:** This work aims to offer experimental evidence for the analgesic, anti-inflammatory, and antipyretic effects of *Trichosanthes dioica Roxb.* by evaluating its aqueous, methanol, and n-hexane extracts. customary use, including the treatment of fever, discomfort, and inflammation. **Procedures and materials:** Researchers examined the analgesic effects of *Trichosanthes dioica Roxb.* by inducing writhing in rats with acetic acid and a standard of Aspirin. Edema of the hind paw of rats generated by carrageenin and treated with indomethacin as a standard allowed the anti-inflammatory action to be examined. Paracetamol was used as a reference to examine the antipyretic efficacy in rats induced by yeast. **Findings:** The writhing response in mice generated by acetic acid was considerably attenuated by the methanol and water extracts. The methanol and water extracts not only reduced the carrageenin-induced edema perimeter in rats, but they also dramatically reduced the acetic acid-induced increase in vascular permeability. In a rat model of yeast-induced pyrexia, both the methanol and water extracts bring the core temperature down. This study lends credence to the long-held belief that this plant may alleviate pain and inflammation by demonstrating that both the methanol and water extracts exhibit analgesic and anti-inflammatory properties. The results further demonstrate that the extracts in both methanol and water have mild antipyretic properties. When compared to the gold standard, the analgesic, anti-inflammatory, and antipyretic effects of the methanol extract are superior to those of the water extract.

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

INTRODUCTION: Throughout history, India has been renowned as a source of medicinal herbs. Medicinal compounds and traditional medical systems have relied on plants for their foundation and efficacy since ancient times. Since the beginning of time, people have been fighting for a way to alleviate suffering. Traditional medicines, such as herbs, are relied upon by the vast majority of the global population for the treatment of a wide range of illnesses.

Modern medicine has its roots in herbal practices. The International Association for the Study of Pain (IASP) defines pain as an unpleasant sensory and emotional experience that is either directly linked to or defined in terms of actual or prospective tissue damage.

While inflammation serves as a protective mechanism to eliminate harmful stimuli and start the healing process for tissues, it may cause the emergence of illnesses including atherosclerosis, rheumatoid arthritis, and vasomotor rhinorrhea if left uncontrolled. In certain cases, it may cause a loss of function in addition to redness, swelling, heat, and discomfort. A fever is characterized by an increase in core body temperature elevated temperature. An typical adult's mouth temperature is 37 degrees Celsius (98.6 degrees Fahrenheit). Infection, inflammation, tissue injury, or disease condition may all cause fever. It develops after an infection, cancer, or other illness has already taken hold. 1. Traditional Indian medical practices including Ayurveda, Siddha, and Amchi are still widely practiced today. Traditional Indian herbal remedies, which include plants utilized by indigenous communities, are effective in treating a broad range of medical conditions in India. Assam is home to many medicinal plants, one of which being *Trichosanthes dioica Roxb.*, a member of the Cucurbitaceae family. In India, *Trichosanthes dioica Roxb.* is a common ingredient in many traditional medicine prescriptions for the treatment of a broad range of conditions, including inflammation, pain, and fever, according to its historical use.

Trichosanthes dioica Roxb. leaves were used for this investigation. But modern medicine

(allopathy) has done a great deal over the years to improve our country's healthcare system. Traditional medications and treatments will always be at the core of advancement, nevertheless. According to a survey, ethnomedicinal research is the source of 75% of the herbal medicines used globally. In India, natural resources and various synthetic analogues made from plant prototype compounds account for about 70% of newer drugs.

According to sources, *Trichosanthes dioica* Roxb. contains carbs, alkaloids, glycosides, flavonoids, steroids, and tannins, the major components of which provide the plant its analgesic, anti-inflammatory, and antipyretic properties. The pharmacological effects of the aqueous and methanol extracts of *Trichosanthes dioica* Roxb. are little known, however traditional uses of the plant have focused on its analgesic, anti-inflammatory, and antipyretic properties. Our next step should be to assess its anti-inflammatory, antipyretic, and analgesic effects *in vivo*.

The current investigation compared the results of three different extracts: aqueous, methanol, and n-hexane. of *Trichosanthes dioica* Roxb. on rat and mouse tests for hyperpyrexia caused by yeast, tail immersion, carrageenin-induced swelling of the hind paw, and acetic acid-induced writhing.

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 °C 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:

$$\% \text{ Analgesic activity} = \frac{N_c - N_t}{N} \times 100$$

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 immersed 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:

$$\text{Percentage reduction} = \frac{V_o - V_t}{V_o} \times 100$$

Vo

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

Values are mean \pm 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.

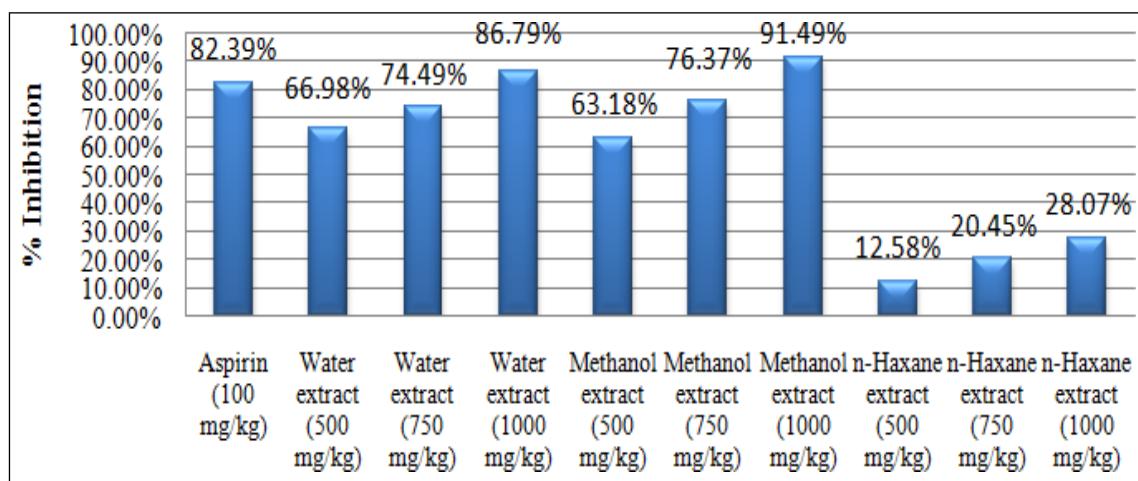


FIG. 1: GRAPH BETWEEN % INHIBITION OF WRITHING RESPONSE AND DOSE OF THE CONTROL, STANDARD AND EXTRACT

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 (150mg/kg) also inhibited paw edema in rat after carrageenin injection.

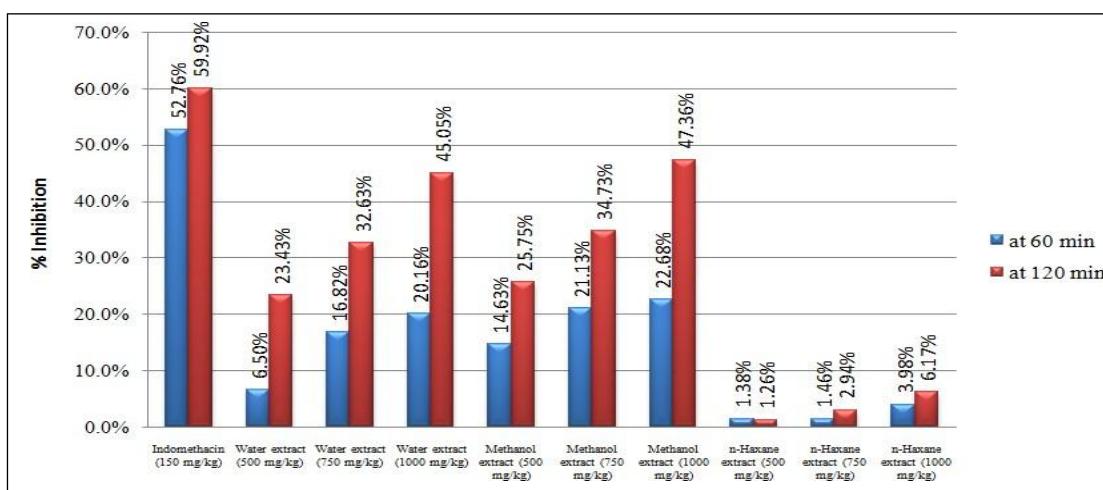
TABLE 2: INFLUENCE OF *TRICHOSANTHES DIOICA ROXB.* LEAVES EXTRACT ON CARRAGEENAN-INDUCED RAT HIND PAW OEDEMA

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***
Methanol extract	500	0.530±0.006	0.660±0.012***	0.825±0.012*	1.050±0.043*	1.058±0.037***
	750	0.572±0.005	0.628±0.010***	0.812±0.011***	0.970±0.031***	0.931±0.035***
n-Hexane extract	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
Methanol extract	500	14.63	25.75
	750	21.13	34.73
n-Hexane extract	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 \pm 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).

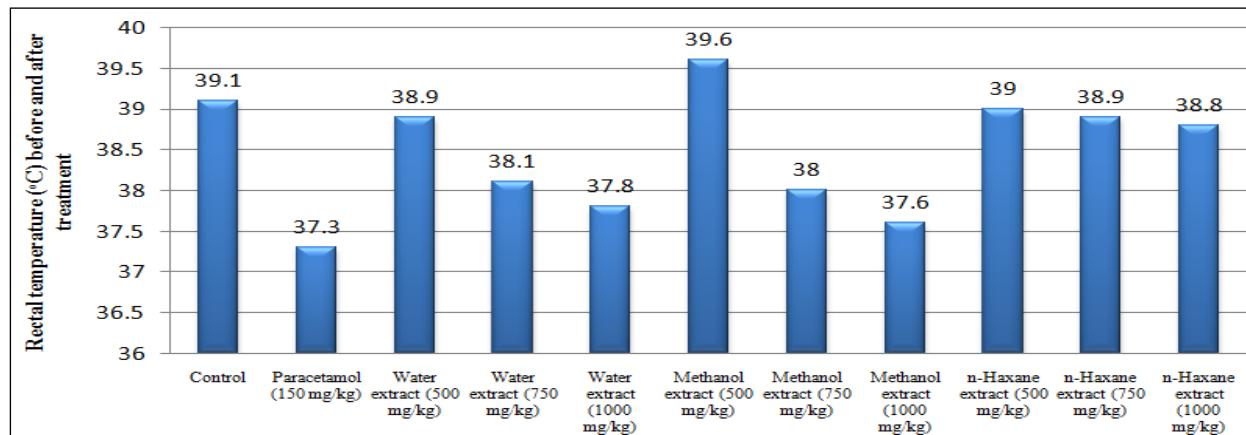


FIG. 3: GRAPH BETWEEN RECTAL TEMPERATURE (°C) AT 23 hr AND DOSE OF THE CONTROL, STANDARD AND EXTRACT

DISCUSSION: This research aimed to evaluate the analgesic, anti-inflammatory, and antipyretic properties of *Trichosanthes dioica* Roxb.'s aqueous, methanol, and n-Hexane extracts. Using two animal models, the analgesic actions were assessed. The central analgesic action was investigated using a tail immersion test. To examine the peripheral analgesic effects, the acetic acid-induced writhing reaction was used.

According to Table 1, the aqueous and methanol extracts showed a substantial analgesic effect in the acetic acid-induced writhing test. The doses of 500, 750, and 1000 mg/kg body weight inhibited pain by 66.98%, 74.49%, 86.79%, 63.18%, 76.37%, and 91.49%, respectively. Aspirin at 100 mg/kg reduced acetic acid-induced discomfort by 82.39% ($p < 0.001$). The presence of acetic acid in the peritoneal fluids increased the levels of PGE2 and PGF2 α , serotonin, and histamine 13. This suggests that the leaf extracts of *Trichosanthes dioica* Roxb. have a strong inhibitory effect on inflammation pain, which might be associated with the inhibition of the production and/or release of endogenous substances that promote inflammation.

A carrageenan-induced paw oedema test was used to determine the anti-inflammatory efficacy of an extract from the leaves of *Trichosanthes dioica* Roxb. One common model for studying the efficacy of drugs against acute inflammation is carrageenan-induced paw edema 14. Injuries caused by carrageenin lead to the production or release of inflammatory mediators, which in turn increase temperature and discomfort.

Injecting carrageenan into a rat's paw triggers plasma extravasation, which in turn induces inflammation. Inflammation is marked by increased exudation of tissue water and plasma proteins, as well as neutrophil extravasation and the metabolism of arachidonic acid via the cyclooxygenase and lipoxygenase enzyme pathways. There is a biphasic reaction to carrageenan-induced paw edema. The first phase, which starts right after injection and fades away within an hour, is regulated by histamine and serotonin 16. The second, or delayed, phase,

which starts at 1 hour and lasts for three hours, is regulated by neutrophil infiltration, eicosanoid release, free radical production, and release.

of additional mediators generated from neutrophils 17. Inflammatory exudates are caused by the release of a chemical similar to bradykinin, which is implicated in the formation of oedema between the early and late phases. This substance activates the manufacture of prostaglandin and other autocoids.

The body's primary defense mechanisms against inflammatory stimuli are fever and discomfort. Therefore, a medicine that reduces inflammation may also have anti-pyretic and analgesic effects. The rat model of brewer's yeast-induced hyperthermia was used to ascertain the antipyretic activity of *Trichosanthes dioica* Roxb. Useful antipyretic, analgesic, and anti-inflammatory doses of the plant's water, methanol, and n-hexane extract were administered in three doses: 500 mg/kg, 750 mg/kg, and 1000 mg/kg intraperitoneally. Comparable to Paracetamol's (150 mg/kg, i.p.) somewhat lowering rectal temperature was the methanol extract. Since prostaglandin is thought to regulate core body temperature, this finding suggested that the plant may have an effect on prostaglandin production.

The water and methanol extracts had encouraging analgesic, anti-inflammatory, and mild antipyretic efficacy at dosages of 500 mg/kg, 750 mg/kg, and 1000 mg/kg body weight, respectively, but the n-Hexane extract exhibited no activity at all. At 1000 mg/kg body weight, the methanol extract exhibited superior analgesic and anti-inflammatory action compared to the water extract and Standard Aspirin and Indomethacin, according to the results. Comparing the analgesic and anti-inflammatory effects of the water and methanol extracts, the methanol extract is superior.

Carbohydrates, alkaloids, glycosides, flavonoids, steroids, and tannins are the components that were identified in the phytochemical analysis. These findings provide light on the chemical components that could be accountable for the

wide range of pharmacological effects. *Trichosanthes dioica* Roxb's anti-inflammatory and analgesic benefits were attributed to those chemical ingredients, according to the study.

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.

REFERENCES:

1. "Analgesic, anti-inflammatory, and antipyretic activities of the methanol leaf extract of *Dalbergia saxatilis* Hook. F in rats and mice" (Hassan FI, Abdulkadir UZ, Yaro AH, Danmalam UH). Publication: 2015, Journal of Ethnopharmacology, 166: 74-78.
2. 2. Sen, S., Chakraborty, R., and De, B.: India's place and function in the world's herbal medicine advancements: challenges and prospects. The article is from the Journal of Herbal Medicine in 2011, volume 1, pages 67-75.
3. Wendakoon, Calderon, and Gagnon (2003) evaluated the antibacterial activity of medicinal plants extracted with varying amounts of ethanol against human infections. Page 60-68 of the 2012 edition of the Journal of Medicinally Active Plants.
4. Researchers Akter, Imam, Hasan, Hossain, Mazumder, and Rana found that the aerial portions of *Trichosanthes dioica* Roxb had antioxidant, antidiarrheal, and cytotoxic effects. Volume 3, Issue 1, pages 95-101, American Journal of Food and Nutrition, 2011.
5. 5. Research on the anti-nociceptive and locomotor properties of root extracts of *Trichosanthes dioica* in Swiss albino mice by Bhattacharya S and Haldar PK. This article appears in the 2012 edition of the Asian Pacific Journal of Tropical Biomedicine, volume 5, pages 1-5.
6. 6. OECD recommendations 423 (Annexure 2d) for chemical testing in 2001.
7. 7. Vogel HG: Springer Publishers, Germany, 2002 Second Edition: Drug Discovery and Evaluation.
8. Research on the Anti-Inflammatory, Antipyretic, and Analgesic Properties of the Stem Bark Extract of *Stachytarpheta indica* by Akuodor GC, Essien AD, Udia PM, David EO, Chilaka KC, Asika EC, and Nwadum SK. Citation: British Journal of Pharmacology and Toxicology 2015; 6(1): 16-21.
9. 9. Parayil VC, Teoh YX, Choong FK, Lim CL, Ng GF, Gai LY, Subramani P and Murugaiyah V: Study on the effects of aqueous and methanol extracts of *Polygonum minus* Huds. (Polygonaceae) leaves on rats: analgesic, anti-inflammatory, antipyretic, and antiulcer. Journal of the American Medical Association 2015, Volume 3, Issue 1, Pages 12-17.
10. 10. The analgesic and anti-inflammatory properties of *Pistacia integerrima* extract in mice were studied by Ahmad NS, Waheed A, Farmanc M, and Qayyum A. Publication date: 2010; volume: 129, pages 250-253.
11. 11. The influence of ethanol and water extracts of *Pterocephalus hookeri* (C.B. Clarke) Hoeck on inflammation and pain: a study by Zhang L, Hu JJ, Lin JW, Fang WS, and Dua GH. Publication date: 2009, volume 123, pages 510-514, Journal of Ethnopharmacology.
12. 12. Nirmal KS, Abdur SM, and Mohammad AA: *Schoenoplectus grossus* Root Methanol Extract and Its Fraction: Analgesic and Antipyretic Activities. Supplemental and Alternative Medicine Based on Evidence 2016; 3: 1-8
13. The suppression and release of prostaglandins E and F during an algogenic

response was studied by Deraedt, Jouguey, Delevallee, and Falhaut (2013). The article is published in the European Journal of Pharmacology in 1980 and spans pages 17 to 24.

14. 14. Masubuchi Y, Kano S, and Horie T: The hepatotoxicity of antidiabetic thiazolidinediones may be determined by mitochondrial permeability transition. The relevant section of the Toxicology journal is 222, pages 233-239, published in 2006.
15. 15. Alkaloids from Bulbus fritillariae cirrhosae with antitussive, expectorant, and anti-inflammatory properties were studied by Wang D, Zhu J, Wang S, Wang X, Ou Y, Wei D, and Li X. The article was published in Fitoterapia in 2011 and can be found in volume 82, pages 1290-1294.
16. The role of vinegar, Truax, Selph, Johnston, Venable, and McKenzie in the development of inflammation in the rat hind limbs caused by carrageenan. Proceedings of the Federation, 1987, vol. 46, pp. 118-126.