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ANTIPYRETIC AND ANALGESIC ACTIVITY OF P*HALLUSIA ARABICA* SAVIGNY, 1816

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ABSTRACT

Ethanolic extract of simple ascidian, *Phallusia arabica* Savigny, 1816 was subjected to antipyretic and analgesic activity on albino rats by Brewer's yeast induced pyrexia, Eddy's hot plate and Heat conduction methods respectively. The extract, when administered at a dose of 400 mg/kg body weight caused significant antipyretic activity by lowering the body temperature at sixth hour compared to the standard drug paracetamol (10 mg/kg bw). Results of analgesic activity showed that the groups treated with 200 mg/kg and 400 mg/kg bw had highly significant analgesic activity in both the methods compared to that of the standard drug, diclofenac sodium (9 mg/kg bw).

Keywords: *Phallusia arabica*, Antipyretic, Paracetamol, Analgesic, Diclofenac sodium.

INTRODUCTION

Pain is a protective mechanism occurring whenever tissues are being damaged and it causes the individual to react and remove the pain stimulus. Nature acts as a good source of salvation for human being by providing different remedies from its plants, animals and other sources to cure ailments [1]. The marine environment is considered as a very rich source of biologically active compounds. *Phallusia arabica* is a simple ascidian. Studies on the distribution, seasonal variation in the occurrence, chemical screening, antibacterial, antimitotic and antimicrobial activity have been reported from Phallusia Arabica [2-6]. Analgesic compounds selectively releive pain as a symptom by acting in the CNS or on the peripheral pain mechanism without affecting its cause [7].

Pyrexia or fever is a condition wherein there is abrupt increase the core temperature above the normal level [8], caused as a secondary impact of infection, malignancy or other diseased states. It is the body's natural defense to create an environment where infectious agent or damaged tissue cannot survive. A natural antipyretic agent with reduced or no toxicity is essential. Further as health care costs continue to escalate, the attraction for low cost remedies has stimulated consumers to re-evaluate the potential of alternatives [9-12]. Hence the present study was designed.

MATERIALS AND METHODS

Collection of animal

Collection of *Phallusia arabica* was carried out from Tuticorin coast by SCUBA diving. They were identified, authenticated and a voucher specimen AS 2276 has been deposited in the National Collections of Ascidians in the Museum of the Department of Zoology, A.P.C. Mahalaxmi College for Women, Tuticorin-628 002. (Figure 1).

Preparation of extract

The species *phallusia arabica* was dried in shade, homogenized to get a coarse powder which was stored in an airtight container and used for further investigations. 100 g of powdered animal material was extracted with

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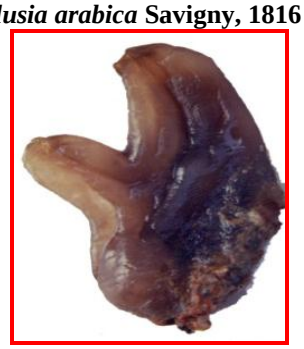
ethanol using soxhlet apparatus. The extract was cooled to room temperature, evaporated in a rotary evaporator under reduced pressure and a brown sticky residue was obtained (10 g).

Figure 1. *Phallusia arabica* Savigny, 1816



Experimental animal

Mature adult male Wistar albino rats weighing 180 - 200 gm were selected for the study. They were maintained in a well ventilated animal house with constant 12 hours of darkness and 12 hours light schedule, room temperature (24 ± 2^0 C) and humidity (60-70%). Clean water and standard pellet diet "ad Libitum" (Hindustan Lever Ltd., India) were given to them. The animals were kept under fasting for 16 hours before the experiment.

Antipyretic activity

Antipyretic activity was measured by Brewer's yeast induced pyrexia in rats [13]. Pyrexia was induced by subcutaneously injecting 20% w/v brewer's yeast suspension (10 ml/kg bw) into the dorsum region of the animal. Eighteen hours after the injection, the rectal temperature of each rat was measured using a digital thermometer. Temperature was measured in entire experimental groups 18 hr before pyrexia induction (-18 hr) and rise in temperature after 18 hr (0 hr). Only those rats which showed an increase in temperature of at least 0.7^0 C were used for the experiments. The animals were divided into five groups of six animals each. Group I was given 1% saline and considered as control, group II received the standard drug paracetamol (10 mg) and III, IV & V were treated with 100, 200 and 400 mg/kg bw of ethanolic extract in 1% vanillin respectively. All the treatments were administered orally using Intra Gastric Catheter. The temperature was recorded at an interval of 1 hr up to 6 hr.

Analgesic activity

Hot plate method

Animals were divided into five groups of six each. Group I which received 1% saline solution (10 mg/kg bw), acted as the control. Standard drug diclofenac sodium (9 mg/kg) was administered to group II. 100, 200 and 400 mg/kg bw of the ethanolic extract were given to group III, IV and V respectively. The animals were positioned on Eddy's hot plate kept at a temperature of $55^0\pm0.5^0$ C. A cut off period of 15 s was observed to avoid damage to the paw. Reaction time was recorded when animals flicked their fore or hind paws, or jumped prior to 0, 30, 60 and 90 minutes after oral administration of the extract [14].

Heat conduction method

The animals were divided into five groups of six each. Group I (control) received 1% saline solution (10 mg/kg bw). Group II was treated with the standard drug diclofenac sodium (9 mg/kg bw) and Group III, IV and V with 100, 200 and 400 mg/kg bw of ethanolic extract respectively. After 1 h the tip of the tail was dipped up to 5 cm into hot water maintained at 58^0 C. The response time was noted as the sudden withdrawal of the tail from the hot water. Cut off time of 10 s was maintained to avoid damage to the tail for all groups. The time required for flicking of the tail was recorded to assess response to noxious stimulus [15].

Statistical analysis

The data were statistically analyzed using one-way ANOVA for individual comparison of group with control. All values are expressed as mean ±SEM. 'p' values were considered moderately significant statistically when *$p<0.05$, significant when **$p<0.01$ and highly significant when ***$p<0.001$.

RESULTS AND DISCUSSION

Antipyretic activity

The ethanolic extract of *Phallusia arabica* at a dose of 200 and 400 mg/kg bw decreased the body temperature induced by injection of Brewer's yeast in the experimental animals significantly from 1h to 6 h (Table - 1). The antipyretic activity was equal to that of the standard drug paracetamol. Results of the present study showed that *Phallusia arabica* extract has marked antipyretic activity. The possible mechanism of antipyretic action may be due to the inhibition of prostaglandin as that of paracetamol by blocking the cyclo-oxygenase enzyme activity [16]. There are several mediators for pyrexia and the inhibition of any one of these can be responsible for the antipyretic effect [17].

The intraperitoneal administration of *Phallusia arabica* extract significantly attenuated rectal temperature of yeast induced pyrexia in rats. Thus it can be postulated that *Phallusia arabica* contains pharmacologically active principles that interfere with the release of prostaglandins. Flavonoids are known to target prostaglandins which is responsible for pyrexia [18]. The presence of flavonoids in the ethanolic extract of *Phallusia arabica* may be contributory to its antipyretic activity.

Analgesic activity

Observations on the analgesic activity using Eddy's hot plate and Heat conduction methods indicated a

highly significant response in the group treated with 100 mg/kg bw of ethanolic extract of *Phallusia arabica* (Table - 2). A very highly significant activity was noted in group IV (200 mg/kg) and V (400 mg/kg) when compared to the standard drug diclofenac sodium (9 mg/kg). Group V showed analgesic effect greater than that of the standard. Oral administration significantly (P<0.001) increased the response time of the animals to thermal stimuli in a dose dependent manner. Eddy's hot plate and heat conduction method induced thermal stimulation are models of pain that mainly involve peripheral and central mechanism, respectively. Analgesic effect observed in these two models with 200 mg/kg and 400 mg/kg doses of ethanolic extracts of *Phallusia arabica* indicates the involvement of both peripheral and central mechanisms. In the present study, administration of the extract led to significant increase in the latency to thermal stimulus and also a significant reduction in flicking time. Analgesics work by involving in the peripheral action by inhibiting pain mediating auticoids like prostaglandins [19]. A comparison of the results noted on treatment with the extract to that of the standard diclofenac sodium shows a similar mechanism of action. Like other non steroidal antiinflammatory analgesic agents, diclofenac sodium acts by inhibiting the synthesis of prostaglandins that are responsible for pain and pyrexia [20]. The analgesic activity of ethanolic extract of *Phallusia arabica* may be due to inhibition of phospolipase A2 or even blocking cyclooxygenase (COX-1 and/or COX-2) [21]. Flavonoids and terpenoids are also known to inhibit prostaglandins [22]. Preliminary chemical screening and GC-MS studies of the ethanolic extract of *Phallusia arabica* has shown the presence of alkaloids, terpenoids, flavonoids, quinones, anthraquinones and steroids [23].

Table 1. Antipyretic activity of the ethanolic extract of *Phallusia arabica*

Groups/Dose mg/kg	Rectal Temperature in ^{0}C after 18 hrs of Yeast Injection (Mean± SEM)					
	-18 hr	0 hr	1 hr	2 hr	3 hr	6 hr
I-Saline 1%	37.52±1.20	39.30±0.13	39.65±0.11	39.81±0.65	39.54±0.81	39.95±0.12
II- Paracetamol 10	37.08±0.90	39.68±0.13	37.91±0.21* (4.39)	37.66±0.16* (5.40)	36.16±0.25** (8.55)	35.05±0.18** (12.26)
III-PA extract 100	37.55±0.80	39.20±0.11	38.02±0.05* (4.11)	37.45±0.05** (5.93)	37.21±0.31* (5.89)	36.13±0.54** (9.56)
IV-PA extract 200	37.54±0.60	39.81±0.06	37.43±0.15** (5.60)	36.96±0.18** (7.16)	36.44±0.54** (7.84)	35.82±0.36** (10.34)
V-PA extract 400	37.91±0.80	39.74±0.13	37.12±0.16** (6.38)	36.11±0.21** (9.29)	35.62±0.33** (9.91)	35.13±0.16** (12.07)

Data represented as mean ±SEM, (N=6). Significance between control and extract treated groups.
*p <0.05; **p <0.01

Table 2. Analgesic activity of ethanolic extract of Phallusia arabica

Groups/Dose mg/kg	Response Time in sec (Mean ± SEM)	
	Eddy Hot Plate Method	Heat Conduction Method
I-Saline 1%	2.81±0.264	1.87±0.184
II-Diclofenac – 9	13.16±0.415***	11.24±0.265***
III-PA extract – 100	5.24±0.265**	4.39±0.246**
IV-PA extract – 200	9.34±0.516***	8.88±0.184***
V-PA extract – 400	14.88±0.348***	11.16±0.292***

Data represented as mean ±SEM, (N=6). Significance between control and extract treated groups.
*p <0.05; **p <0.01; ***p < 0.001

CONCLUSION

Thus it can be concluded that the ethanolic extract of *Phallusia arabica* shows significant antipyretic and analgesic activities. Further studies on the isolation and its mode of action are suggested for the development of a new drug candidate in the treatment of pyrexia and analgesia.

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