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Research Article

Spatoglossum Asperum, J. Agarth, A Marine Brown Alga Mediated *In Vivo* Antipyretic Activity On Rat Model

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ABSTRACT

Marine algae is one of major source for novel natural products that recommended as a drug for alternative system of biomedicine for several treatments. With light of the above, we are intended to explore the antipyretic activity of a brown marine algae, *Spatoglossum asperum* using it's methanol extract. The antipyretic activity of *S. asperum* examined using Wistar albino rats in which pyrexia was induced by Brewer's yeast method and the results are compared with Paracetamol (150 mg/kg body weight) standard drug. The investigation revealed that the animals treated with the algal extract exhibited significant reduction in the body temperature. Further, the experimental algal extract at a dose of 10 mg/kg body weight caused significantly lowering the body temperature within 3 hrs as compared to that of standard drug (150 mg/kg bodyweight). Thus, the present investigation has been provided the evidence for the antipyretic activity of *S. asperum* could partly contribute to its ethno medical use.

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INTRODUCTION:

Any kind of infection, malignancy and other diseased states could trigger fever as a secondary impact. The fever also called as pyrexia is a body's natural defense system would be created an environment in which the infectious agent or damaged tissue cannot survive [1]. The drug which is used treat fever or pyrexia is classified as antipyretic agents act to lower the body temperature. It is also used to prevent or alleviate fever [2]. In many ethnobotanical cultural systems, the conventional drugs possessing antipyretic properties are mostly derived from plant source. In ethnobotany, plants with naturally occurring antipyretic properties are commonly referred to as febrifuges which is known as the drug or agent that reduce pain [3,4]. In the past two decades, the focus on biological activities of secondary metabolites derived from marine algal species, including antipyretic activities has created a enormous significance because of the low impact and more drug safety [5-10].

The infected or damaged tissue initiates the enhanced formation of pro-inflammatory mediator's (cytokines like interleukin 1a and TNF-a) which increase the synthesis of prostaglandin E2(PGE2) near peptic hypothalamus area and thereby triggering the hypothalamus to elevate the body temperature [11]. As the temperature regulatory system is governed by a nervous feedback mechanism, so when body temperature becomes very high, it dilates the blood vessels and increase sweating to reduce the temperature; but when the body temperature becomes very low hypothalamus protect the internal temperature by vasoconstriction [12].

The common complications in human beings are found to be pain, inflammation and fever. Wide spectrum of plants and their products are claimed and proved to possess antipyretic property [13]. In the quest for indentifing novel drugs, the marine algae are found to produce a great variety of secondary metabolites which characterized by a broad spectrum of biological activities [10, 14]. A exhaustive literature assessment suggested that the antipyretic activity of *Spatoglossum asperum* has not been clinically evaluated so far using animal model as well as by any other processes. Hence we interested to study effect on the antipyretic properties of the methanol extract of *Spatoglossum asperum.*

MATERIALS AND METHODS:

Sample collection and preparation

S. asperum was collected from the intertidal regions of the Mandapam coast (Lat. 09˚ 17.417'N; Long. 079˚ 08.558'E) of the Gulf of Mannar, Tamil nadu in a safe container along with sea water in order to prevent evaporation. The experimental alga was identified and authenticated by the monograph of Phaeophyceae [15]. After brought to the laboratory, the collected algal samples were completely washed with sterilized sea water to remove unnecessary materials trapped on the samples. The samples were shade dried until constant weight attained and ground well using a laboratory blender. The powdered samples were stored in an airtight container and the container kept in a desiccator for future use.

Preparation of algal extracts

About 50g of dried seaweed powder was stirred in the methanol solvent (150 mL) (1:3 w/v) at 60 ºC for 24 hrs and the extracts were filtered through a Buchner funnel with Whatman No.1 filter paper. The filtrate was collected and concentrated to get in solid form under pressure using a rotary vacuum evaporator at 50 ºC and the crude extract was weighed. The yield of powdered sample obtained was 5g (Yield: 10%) in methanol solvent. These crude extracts were then tested for their antipyretic activity.

Experimental animals

Wistar albino male rats were weighed in the range of 180 and 220 g obtained from K.M. College of Pharmacy, Madurai, India. The chosen animals were housed in the departmental animal house under standard conditions (25 ± 2°C and relative humidity 50 ± 5%) in 12 hours light and 12 hours dark cycle respectively for 1 week before and during the experiments. Animals were provided with standard rodent pellet diet and free access to water. The composition of diet is as follows: 10% protein, 4% Arachis oil, 1% fiber, 1% calcium, 1000 IU/gm vitamin A and 500 IU/gm vitamin-D. Prior to the experimentation, all the animals were acclimatized to the laboratory conditions. All the experiments were conducted between 08.00 and 16.00 hrs and were in accordance with the ethical guidelines of the

International Association for Study of Pain [16]. The above animal experiment was performed in accordance with the CPCSEA norms and are approved by the Institute of Animal Ethical Committee (IAEC) No: IAEC/KMCP/153/FT/9599/2013-2014.

Drugs and Chemicals **:** Injection of 20 % w/v of brewer's yeast (10 mL/kg) methanol extract of *S. asperum.*

Treatment protocol

Body weights of the animals were recorded and they were randomly divided into 4 groups of 6 animals each as follows:

Group I : Normal control rats, received 0.9% saline in a dose of 10 mL/kg/body weight/rat/day through orally.

Group II : Rats were treated with yeast (10 mL/kg/body weight/rat/day) via subcutaneous injection.

Group III : Rats were treated with yeast (10 mL/kg/body weight/rat/day) and the standard drug paracetamol (150 mg/kg body weight/rat/day) through orally.

Group IV : Rats were treated with yeast (10 mL/kg/body weight/rat/day) and the methanolic extract of *S. asperum* (10 mL/kg/body weight) with 2 mL of sterile water administered through orally.

Yeast induced pyrexia method

A suspension containing 15% of Brewer's yeast in 0.9% saline was prepared. Four groups, each containing 6 rats of either sex were taken. The pyrexia was induced by subcutaneous injection of 20% w/v of brewer's yeast (10 mL/kg) in distilled water. The basal rectal temperature was measured before the injection of yeast. The sight of injection was massaged in order to spread the suspension beneath the skin. For the measurement of body temperature, the sterile thermocouple was inserted about 2 cm into the rectum and the rectal temperature was recorded. The room temperature was kept at 22-24 °C, immediately after yeast administration, food was withdrawn and the rise in rectal temperature was recorded. The measurement was repeated after 30 minutes of the injection. The dose of the algal extract and standard drug was given orally. The rectal temperature was recorded again after 1, 2 and 4 hrs. Paracetamol (10 mL/kg) was selected as a standard drug. The methanolic extracts were dissolved in saline with the help of 2% w/v Gum acacia.

RESULTS AND DISCUSSION:

The antipyretic ability of *S. asperum* methanol extract was evaluated by determining its effect on yeast-induced pyrexia in albino rats. Table.1 shows that animals treated with methanol extract of *S. asperum* possess significant antipyretic property. In addition, the results showed that the drug, experimental alga at a dose of 10 mL/kg body weight was able to reduce body temperature from 41.58 to 39.13°C within 1 hr in the animals and maintained the tendency up to 3 hrs (37.73 °C). After 3 hrs, the algal drug treated animals exhibited a body temperature was 37.73 °C while, that of the normal control animals were 37.61 °C. The examination of the antipyretic activity of the algal control was found to be equal to that observed for the paracetamol (drug) control.

Table.1 Efficiency of methanolic extract of S. asperum on body temperature on yeast induced pyrexia in rats.

Group	Rectal Temperature (°C)			
	0 hr	1 hr	2 hr	3 hr
Normal control (Group I)	38.30 ± 0.8	37.50 ± 0.80	37.70 ± 0.80	37.61 ± 0.50
Pyrexia control (Yeast (Group II))	41.54 ± 0.23	42.18 ± 0.18	39.30 ± 0.15	39.19 ± 0.26

Positive control (Yeast+ paracetamol (Group III))	41.43 ± 0.19	39.70 ± 0.18	38.50 ± 0.23*	37.65 ± 0.38*
Treatment control (Yeast+ Methanol extract of *S. asperum* (Group IV)	41.58 ± 0.13	39.13 ± 0.13	38.30 ± 0.13*	37.73 ± 0.26*

Values are expressed as Mean ±SEM. n= 6 in each group.
**Values are significant ($p<0.01$) different from pyrexia control (Group II).*

In Indian medicine, Ayurveda, Siddha, Unani and Homeopathy, the plants are the major source of drugs [17], as well as other ancient systems in the world. This could be clearly evident from the description of the medicinal plants and their healing behavior in Rig-Veda, Charaka Samhita and Sushruta Samhita which give an exhaustive description about various medicinal herbs [18]. In the current scenario, the emerging interest in adopting and studying traditional systems and exploiting the potential based on different health care systems around the globe. The evaluation of the rich heritage of traditional medicine is necessary to overcome the side effects caused by the synthetic drugs. In this regard, an attempt was made in the present work to study detail pharmacological action, particular antipyretic activity of marine brown alga *S. asperum*.

The elevation in body temperature results from the pyrogen induced upward resetting of thermoregulatory set point. The exogenous substances, which are known to induce fever in animal models. These pyrogens, on injection into experimental animals, induce the production of pro-inflammatory cytokines (e.g., IL-1β, IL-6, IFN-α and TNF) which stimulate the release of local PG (produced by the activity of COX) that leads to elevation of body temperature [19]. Pyrexia induced by the yeast in rats is a well appropriate and sensitive model for evaluating antipyretic effects of compounds. Both TNF-α and prostaglandin synthesis are induced by the yeast. Antipyretics such as acetyl salicylic acid (ASA) and other NSAID reduce fever by suppressing inflammatory messages at both peripheral sites of tissue inflammation and within central nervous system thermoregulatory sites. The antipyretic drugs reduce pyrogenic cytokines such as TNF-α and IL-1β products, while lowering the thermoregulatory set-point by blocking COX production of PGE2 [20]. The extract administration resulted in lowering of temperature, but the decrease of temperature was not comparable with standard antipyretic which showed significant antipyretic effect similar results were also reported elsewhere [21-23].

The elevated body temperature could be reduced by employing the antipyretic drugs. Yeast-induced fever is also known as pathogenic fever. It is etiology includes production of prostaglandins which set the thermoregulatory center lower temperature [24]. There several earlier studies which highlights the antipyretic activities of various marine algae previously tested using *Ulva rigida* [25], *Gracilaria* dura [26], *Chaetomorpha litorea* [27] and *Lobophora variegata* [10]. Since antipyretic activity is commonly mentioned as a characteristic of drugs or compounds, which have an inhibitory activity on prostaglandins biosynthesis, the yeast induced hyperpyrexia in rat model was employed to investigate the antipyretic activity of the extract [28]. Yeast induced pyrexia tends to the production of prostaglandins (PGE2) which set the thermoregulatory center at a higher temperature [29].

The methanol extract of *S. asperum* showed significant antipyretic activity. The animals were also fevered by injection of Brewer's yeast suspension (10 mL/kg body weight) simultaneously in back below the nape of the neck for the antipyretic activity. The methanol extract of *S. asperum* showed significant decrease in elevated body temperature as compared to standard drug paracetamol. 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 [30]. For pyrexia and their inhibition, there are several mediators of which

any one of these could be responsible for the antipyretic effect [31].

Antipyretics have been shown to suppress fever by inhibiting prostaglandin synthetase, resulting in the blockade of the synthesis of prostaglandin in the brain or suppressing the rise of interleukin-1α production subsequent to interferon production. The intraperitoneal administration of methanol extract of *S. asperum* were significantly attenuated rectal temperature of yeast induced pyrexia in rats and comparable to that of standard drug paracetamol. Thus, preventing prostaglandin synthesis would be the potential mode of antipyretic action as that of paracetamol [32]. Thus, it can be postulated that the methanol extract of *S. asperum* contains pharmacologically active principles that interfere with the release of prostaglandins. This may be attributed to the presence of the various bioactive compound present in the methanol extract of *S. asperum* may be involved in inhibition of prostaglandin synthesis. Also, there are several mediators or multiprocessors underlining the pathogenesis of fever. Inhibition of any of these mediators may bring about antipyresis. Flavonoids like baicalin have been shown to exert antipyretic effect by suppressing TNF-α [33] and its related compounds also exhibit inhibition of arachidonic acid peroxidation, which results in reduction of prostaglandin levels thus reducing the fever and pains [34]. The present study also correlates with the study of Zakaria *et al.*, (2007)[35] that the compounds like flavonoids and saponins are suggested to act synergistically to exert the observed pharmacological activity. Flavonoids are known to target prostaglandins which are responsible for pyrexia [36]. The presence of flavonoids in the methanol extract of *S. asperum* may be contributory to its antipyretic activity. This potentiality supports the earlier traditional claims as a pediatric antipyretic remedy.

Herbal medicines derived from the algal extracts are being increasingly utilized to treat a wide variety of clinical diseases, though relatively little knowledge about their mode of action is available. In conclusion, the present study provides evidences for the methanolic extract of *S. asperum* shows significant antipyretic activity. However, further investigation is required for isolation of active components and its mode of action for the development of a new drug in the treatment of pyrexia and analgesia.

CONCLUSION:

The present study clearly highlights the antipyretic activity of methanol extract of *S. asperum*, which could partly contribute to its ethno medical use. Because of the interesting behavior of this algae, further investigation is required to isolate and indentification of the active constituents responsible for the antipyretic activities and to elucidate the exact mechanisms of action.

REFERENCES:

1. Chattopadhyay D, Arunachalam G, Ghosh L. Antipyretic activity of *Alstonia macrophylla* Wall ex A DC: An ethnomedicine of Andaman Islands. J Pharm Pharmaceutical Sci. 2005;8: 558-564.
2. Merriam S, Taylor E, Tisdell E, Taylor K, Lamoreaux A, Clark M. Beyond Andragogy: New Directions in Adult Learning Theory In Proceeding of the Adult Education Research Conference. 2009.
3. Biren N, Shah Pankaj B, Patel Ankit B, Patel Bhavesh S, Nayak, Dikshit C Modi. *Rehmannia glutinosa* – A Phyto-pharmacological review. Pharmacology Online, 2010;1:737-753.
4. Sullivan JE, Farrar HC. "Fever and Antipyretic Use in Children" Pediatrics. 2011;127(3):580–587.
5. Dang D, Hong H, Minh H, Hoang TLA. Studies on the analgesic and anti-inflammatory activities of *Sargassum swartzii* (Turner) C Agardh (Phaeophyta) and *Ulva reticulata* Forsskal (Chlorophyta) in experiment animal models. African J Biotech. 2011;10(12):2308-14.
6. Ji-Young K, Jae-Suk C, Nam Gyu P, Dong-Hyun A. In Vivo Antipyretic Analgesic and Anti-inflammatory Activities of the Brown Alga Ecklonia cava Extracts in Mice. Fisheries and Aquatic Sci. 2012;15(1):73-76.
7. Kanga MC, Kang SM, Kim KN, Lee SH, Ahna G, Chac SH, Kima AD, Yanga XD, Jeon YJ. Anti-inflammatory activity of polysaccharide purified from AMG-assistant extract of Ecklonia cava in LPS-stimulated RAW 2647 macrophages. Carbohydr Polym. 2011;85(1):80–85.

8. Kupferschmidt K. "Fight the Flu Hurt Society?" *Science Now*. 2014.
9. Sadish Kumar S, Kumar Y, Khan MSY, Anbu J, Sam KG. Acute Toxicity Study and Antipyretic Effect of the Brown Alga *Turbinaria Conoides* (J Agardh) Kuetz. Afr J Tradit Complement Altern Med. 2009;6(3):233–240.
10. Thennarasan S, Murugesan S, Chidambaranathan N, Sivamurugan V. Analgesic Anti-inflammatory and Antipyretic Activity of the Methanol Extracts of Brown Alga *Lobophora variegate* (JVLamouroux) Womersley ex ECOliveir. American J Phytomed Clinical Ther. 2016;042-045.
11. Spacer CB, Breder CD. The neurologic basis of fever. N Engl J Med. 1994;330:1880-1886.
12. Veugelers PJ, Kaldor JM, Strathdee SA, Page-Shafer KA, Schechter MT, Coutinho RA, Keet IP, Griensven GJ. Incidence and prognostic significance of symptomatic primary human immunodeficiency virus type 1 infection in homosexual men. J Infectious Dis. 1997;176:112 – 117.
13. Nanda BK, Jena J, Rath B, Behera BR. Analgesic and Antipyretic activity of whole parts of *Sphaeranthus indicus* Linn. J Chem Pharmaceutical Res. 2009;(1):207-212.
14. Newman DJ, Cragg GM, Snader KM. Natural products as sources of new drugs over the period 1981–2002. J Nat Prod. 2003;66:1022–1037.
15. Krishnamurthy V, Baluswami M. Phaeophyceae of India and neighbourhood Volume I *Ectocarpales Sphacelariales Dictyotales Chordariales and Scytosiphonales* pp [2] i-iv 1-193 308 figs pls I-VI Chennai: Krishnamurthy Institute of Algology. 2010.
16. Zimmermann M. Ethical guidelines for investigations of experimental pain in conscious animals *Pain* 1983;16(2):109-110.
17. Satyavati, Gupta AK. Medicinal Plants of India Indian council of Medical Research New Delhi: vol II, 1987.
18. Kirtikar KR, Basu BD. Indian medicinal plants Eds E Blatter Caius J F Lalit Maohan Basu Allahabad 2nd edn vol II, 1989.
19. Dalal S, Zhukovsky DS. Pathophysiology and Management of Fever. J Support Oncol. 2006;4:9–16
20. Chomchuen S, Singharachai C, Ruangrungsi N, Towiwat P. Antipyretic effect of the ethanolic extract of *Ficus racemosa* root in rats. J Health Res. 2010;24(1):23–28
21. Gautham SA, Onkarappa R. In vitro antioxidant activity of metabolite from Streptomyces fradiae strain GOS1 Int J Chem Sci. 2013;5(1):235-244
22. Gautham SA, Onkarappa R. Pharmacological activities of metabolite from Streptomyces fradiae strain GOS1. Int J Chem Sci. 2013;11(1):583-590
23. Prashith Kekuda TR, Pavithra GM, Rakesh KN, Dileep N, Syed J , Ramesh Kumar KA. Elemental analysis antimicrobial and radical scavenging activity of Lagerstroemia speciosa (L) flower. J Chem Pharm Res. 2013;5(6):215-222
24. Chandrashekaran NV, Dai H, Roos KL. COX-3 a cyclooxygenase-1 variant inhibited by acetaminophen and other analgesic/antipyretic drugs: cloning structure and expression. Proc Natl Acad Sci. 2002;99(21):13926-13931
25. Muthu Sheeba M, John Peter Paul J. Evaluation of antipyretic activity of methanol extract of *Ulva rigida* cag (green seaweed) in hare island Thoothukudi Tamil nadu India. Int J Exp Pharm. 2014;4(2):105-108
26. John Peter Paul J, Shri Devi SDK. Antipyretic activity of methanol extract of *G*racilaria dura (ag) jag (red seaweed) in hare island Thoothukudi Tamil nadu India. Acta Biomedica Scientia. 2014;1(2):80-83
27. Muthu Sheeba M, John Peter Paul J, Iniya Udhaya C. Antipyretic activity of methanol extract of *Chaetomorpha litorea* harvey in yeast induced pyrexia. Asian J Pharm Res. 2016;6(1):43-46
28. Ighodaro I, Raymond I, Ozolua S, Okpo O, Osahon O. Antipyretic and Analgesic Effects of the Aqueous Extract of the Fruit Pulp of *Hunteria umbellata* K Schum (Apocynaceae). Tropical J Pharm Res. 2009;8(4):331-336
29. Aman A, Alzubier, Patrick N Okechukwu. Investigation of anti-inflammatory antipyretic and analgesic effect of Yemeni Sid honey. World Academy of Science Eng Tech. 2011;80:47-52

30. Chandrasekharan NV, Simmons DL. The Cyclooxygenases *Genome Biology*. 2004;241
31. Rawlins MD, Karger AG. Mechanism of salicylate induced antipyresis. The Pharmacology of Thermoregulation San Francisco. 1973;311-324
32. Akio M, Tomoki N, Tatsuo W. Pattern difference in experimental fevers induced by endotoxin endogenous pyrogen and prostaglandins. Am J Physiol. 1998;254:633- 640
33. Adesokan AA, Yakubu MT, Owoyele BV, Akanji MA, Soladoye AO, Lawal O. Effect of administration of aqueous and ethanol extracts of *Enantia chlorantha* stem bark on brewer's yeast induced pyresis in rats. African J of Biochem. 2008;2(7):165-169
34. Germain S, Bum EN, Talla E, Dimo T, Weiss N, Sidiki N, Dawe A, Moto FC, Dzeufiet PD, De Waard M. Antipyretic and antinociceptive effects of Nauclealatifolia roots decoction and possible mechanisms of action. Pharm Biol. 2011;49(1):15-25
35. Zakaria Z, Loo Y, Nurul I, Abdul R, Abdul H, Abdul A, Roslan S, Hanan KG. Antinociceptive anti-Inflammatory and antipyretic properties of the aqueous extract of *Bauhinia purpurea* leaves in experimental animals. Medical Principles and Prac. 2007;16:443-449
36. Rajnarayanan RV, Rowley CW, Hopkins NE, Alworth WL. Regulation of phenobarbital-mediated induction of CYP102 (cytochrome P450 (BM-3)) in *Bacillus megaterium* by phytochemicals from soy and green tea. J Agric Food Chem. 2001;49:4930-4936

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