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Research Article

ANTI-PYRETIC ACTION OF *CAULERPA LENTILLIFERA*, *HIBISCUS ROSA-SINENSIS*, AND *PIPER SARMENTOSUM* AQUEOUS EXTRACT IN MICE

DZULSUHAIMI DAUD[1,2,3]*, NUR FAZULIANA MOHD ARSAD[1,3], ASMIDA ISMAIL[3], ALENE TAWANG[4]

[1]Reproductive Biology & Toxicology Research Group, Universiti Teknologi MARA, 40450 Shah Alam, Selangor, Malaysia. [2]Pharmaceutical & Life Sciences Community of Research, Universiti Teknologi MARA, 40450 Shah Alam, Selangor, Malaysia. [3]School of Biology, Faculty of Applied Sciences, Universiti Teknologi MARA, 40450 Shah Alam, Selangor, Malaysia. [4]Department of Biology, Faculty of Science and Mathematics, Universiti Pendidikan Sultan Idris, 35900 Tanjong Malim, Perak, Malaysia. Email: dzuls990@salam.uitm.edu.my

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ABSTRACT

Objective: The present study was conducted to evaluate the anti-pyretic activity of *Caulerpa lentillifera*, *Hibiscus rosa-sinensis,* and *Piper sarmentosum* aqueous extracts.

Methods: The suspension of yeast was injected intraperitoneally (0.1 g/kg of bodyweight [BWT]) to induce fever in experimental animals. Rectal temperature was recorded every hour with a lubricated digital thermometer and animals with at least 0.7°C elevations in body core temperature were included in the experiment. The animals with fever were administered orally with aqueous extracts of *C. lentillifera*, *H. rosa-sinensis,* and *P. sarmentosum* (500 mg/kg of BWT). Another group was given the commercial drug, acetaminophen (10 mg/kg of BWT), to serve as a control.

Results: The result of the study showed that *C. lentillifera* and *H. rosa-sinensis* aqueous extracts significantly ($p<0.05$) effective in combating fever. However, *P. sarmentosum* aqueous extract has no potential as an anti-pyretic agent.

Conclusion: *H. rosa-sinensis* and *C. lentillifera* aqueous extracts have anti-pyretic potential but not *P. sarmentosum* aqueous extract.

Keywords: *Caulerpa lentillifera*, *Hibiscus rosa-sinensis*, *Piper sarmentosum*, Anti-pyretic, Fever, Pyrexia, Yeast.

INTRODUCTION

Fever is a common medical symptom characterized by an elevation of temperature above the 99°F and leads to the disturbance in human physiology [1,2]. This elevation in body temperature normally occurs as a result of infection or inflammation. Macrophages, in response to microbial invasion, release endogenous pyrogen which acts on the hypothalamic thermoregulatory center. Endogenous pyrogen raises the set point of the hypothalamic thermostat by triggering the local release of prostaglandins. This is the natural body's defense to create an environment where the infectious agent or damaged tissue unable to survive [3,4].

Anti-pyretic is a type of medication that will prevent or reduce fever by lowering body temperature from a raised state. Previously, herbal medicine is used as a source of anti-pyretic agent by almost all of the world population. However, due to the discovery of synthetic anti-pyretic, plant-based anti-pyretic were neglected [5]. Aspirin is one example of synthetic anti-pyretic, reduces fever by inhibiting the synthesis of prostaglandins. However, aspirin and other popular synthetic anti-pyretic drugs exhibited several side effects. Thus, there is a greater global interest in non-synthetic, natural drugs derived from herbal sources due to their better tolerance and minimum adverse drug reactions [6].

Caulerpa lentillifera is green algae that are naturally distributed in tropical regions and eaten fresh in Japan, Korea, Philippines, and Malaysia [7]. *C. lentillifera* and other green seaweeds have higher total phenol contents and free radical scavenging properties compared to other algae [8]. Matanjun and co-workers reported that *C. lentillifera* helped prevent coronary heart disease and hyperlipidemic artherosclerosis [9]. Meanwhile, *Hibiscus rosa-sinensis* is a large shrub that gets up to 15 ft tall in a frost-free climate with glossy leaves and brilliant flowers. The hypoglycemic activity [10] and wound healing property [11] of *H. rosa-sinensis* leaves ethanolic extract has been reported. Flowers of *H. rosa-sinensis* have been found to be effective in the treatment of arterial hypertension [12] and exhibited antifertility effect [13]. *Piper sarmentosum* is a herb that belongs to the Piperacea family and widely distributed in tropical countries in South East Asia [14]. A study has reported that *P. sarmentosum* is high with antioxidant compounds such as vitamin E, carotenoids, xanthophylls, tannins, and phenolics [15]. Hypoglycemic activity of *P. sarmentosum* whole plant aqueous extracted has been documented [16]. *P. sarmentosum* also demonstrated anti-nociceptive [17] and anti-atherosclerotic [18] activities.

Though reports are available to support the ethnic use of leaves of the *H. rosa-sinensis* [19], there are no reports on the efficacy of *C. lentillifera* and *P. sarmentosum* on pyrexia. The present study was conducted to evaluate the pharmacological significance of aqueous extracts of *C. lentillifera*, *H. rosa-sinensis,* and *P. sarmentosum* on yeast-induced pyrexia in mice.

METHODS

Plants material and aqueous extract preparation

Fresh *C. lentillifera* was collected from Tawau, Sabah in Eastern Malaysia. Fresh leaves of *H. rosa-sinensis* and *P. sarmentosum* were collected from Kota Bharu, Kelantan in Peninsular Malaysia. The plants were identified and authenticated by Ahmad Ismail, PhD of the Universiti Kebangsaan Malaysia. Herbarium specimens were deposited in Biology Laboratory, Universiti Teknologi MARA.

About 100 g of dried plant materials were added to 900 ml of distilled water and boiled for 3 hrs [20]. Then, the mixture was filtrated, and the filtrate was centrifuged at 3000 rpm for 15 minutes. The supernatant was collected and was freeze-dried to obtain powder form of the extract. The powder of extract was stored in a refrigerator at 4°C for later use. The extract was dissolved in distilled water for use on the day of the experiment.

Experimental animals and animal ethics

The study was carried out with a group of 24 adult male mice (*Mus musculus*) within a body weight (BWT) range of 24-30 g. The animals were maintained under suitable nutritional and environmental conditions. The protocols were observed by the Research Ethics Committee of The Faculty of Applied Sciences, Universiti Teknologi MARA.

Yeast-induced pyrexia

A stock solution of brewer's yeast was prepared in sterile saline and pyrexia was induced in the mice by the administration of brewer's yeast suspension at a dose of 0.1 g/kg of BWT [21]. 18 hrs following pyrexia induction, the body temperature of each mouse was measured as previously described by Kang *et al*. and Manikandar *et al.* [21,22]. The body temperature of each rat was measured by inserting a digital thermometer (MT16F1, Microlife AG, Switzerland) into their anal cavities. Mice which showed a rise in temperature of at least 0.7°C were included for the anti-pyretic study.

Anti-pyretic evaluation

Mice with fever were divided into four groups (n=6). The first group was treated with 10 mg/kg BWT of Acetaminophen and served as a control. Meanwhile, other groups were supplemented with 500 mg/kg BWT of aqueous extract of *C. lentillifera*, *H. rosa-sinensis,* and *Piper sarmentosum*, respectively. Anti-pyretic drugs were given orally. Then, the rectal temperatures were measured and recorded hourly for a maximum of 5 hrs.

Statistical analysis

Differences between control and treated groups were tested for statistical significance by ANOVA (SPSS for Windows). A probability of $p<0.05$ was chosen as the criterion of statistical significance. Data are presented as mean ± standard error.

RESULTS AND DISCUSSION

Acetaminophen, a classic anti-pyretic, significantly ($p<0.05$) reverted yeast-induced fever in mice and showed a greater anti-pyretic effect compared to another alternative anti-pyretic tested in this study (Fig. 1). Within 5 hrs, the rectal temperature of mice with fever decreased by 2°C following consumption of 10 mg/kg of acetaminophen.

H. rosa-sinensis and *C. lentillifera* aqueous extracts also significantly ($p<0.05$) demonstrated anti-pyretic activity (Fig. 1). Rectal temperatures of mice with fever decreased by 1.55°C, 5 hrs after *H. rosa-sinensis* aqueous extract consumption. Meanwhile, a rectal temperature of mice with fever decreased by 1.15°C, 5 hrs after consumption of *C. lentillifera* aqueous extract. On the other hand, *P. sarmentosum* aqueous extract unable to reverse yeast-induced fever in mice (Fig. 1).

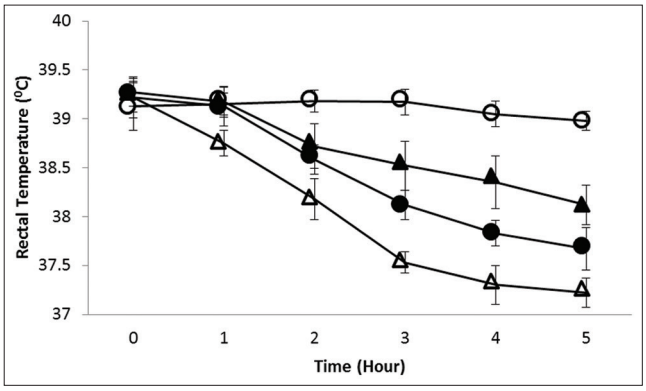

Fig. 1: Anti-pyretic effects of 10 mg/kg bodyweight (BWT) of Acetaminophen (Δ, served as a control), 500 mg/kg BWT of *Hibiscus rosa-sinensis* (●), 500 mg/kg BWT of *Caulerpa lentillifera* (▲), and 500 mg/kg BWT of *Piper sarmentosum* (○) on yeast-induced pyrexia in mice

Overall, the observed anti-pyretic effect of acetaminophen, *H. rosa-sinensis,* and *C. lentillifera* was found to be sustained and lasted up to at least 5 hrs after oral consumption of tested drugs. Acetaminophen is well-established synthetic anti-pyretic and works by inhibiting an enzyme known as cyclooxygenase (COX). COX is a catalyst for the conversion of arachidonic acid to prostaglandins [23]. In the current study, there is no attempt was made to ascertain the mechanism of the observed anti-pyretic activity in *H. rosa-sinensis* and *C. lentillifera* aqueous extracts. However, it can be suggested that it may be acting through either the peripheral or central mechanism by blocking the COX, and, therefore, the subsequent production of prostaglandins.

Previously, flavonoids have been found to inhibit COX production [24] and prostaglandins synthesis [25,26] which are involved in pyrexia. Plants, such as *Ocimum gratissum* [5], *Bombax malabaricum* [27], and *Viola betonicifolia* [28], contain flavonoids and have been found to possess anti-pyretic properties. Qualitative analysis demonstrated that *H. rosa-sinensis* [29] and *C. lentillifera* [8] rich with flavonoids. Hence, the present of flavonoids might accounts for the anti-pyretic effect that was observed in *H. rosa-sinensis* and *C. lentillifera* aqueous extracts.

Surprisingly, previous data were shown *P. sarmentosum* aqueous extract contained high total flavonoid content [15] but lacking anti-pyretic activity in the present study. A similar result was reported by previous authors that *P. sarmentosum* methanolic extract did not decrease yeast-induced pyrexia in rats [30]. We postulated that the flavonoids content in 500 mg/kg BWT of *P. sarmentosum* aqueous extract insufficient to inhibit COX activity and prostaglandins secretion.

CONCLUSION

H. rosa-sinensis and *C. lentillifera* aqueous extracts have anti-pyretic potential, and it's efficacious almost comparable to synthetic anti-pyretic, acetaminophen. However, we also concluded that *P. sarmentosum* aqueous extract was lacking anti-pyretic activity.

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