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Original Article

The Potential Antipyretic Activity of *Ficus septica* Leaf Extract in ICR Mice

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ABSTRACT

Ficus septica is a tree or shrub that is endemic in the Philippines. In this study, the potential antipyretic activity of the ethanol leaf extract of *F. septica* was evaluated. Initially, qualitative phytochemical screening was performed to evaluate the presence of active constituents in the extract. In the experiment, a total of 21 ICR mice was used [divided into three equal groups: negative (distilled water), positive (Paracetamol) and experimental (*F. septica*)] and pyrexia was induced using yeast. *F. septica* extract, and Paracetamol were given at a dose of 150 mg/kg. Animals were acclimatized for seven days. Before induction of pyrexia, basal body temperature was obtained. After induction, corresponding treatments were given, and the body temperature was monitored hourly for five times. Data were analyzed using one-way analysis of variance (ANOVA). Results revealed that *F. septica* extract had a significant anti-pyretic activity similar to paracetamol at the onset of action on the first hour and the third hour ($p < 0.05$). A mean reduction of temperature of 0.3 centigrade was observed. The present study showed that the *F. septica* extract had a potential anti-pyretic effect. Further studies must be made on the varying doses and toxicity of the *T. septica* extract.

KEYWORDS: *anti-pyretic, ethanol extract, Ficus septica, mice*

1 INTRODUCTION

Fever or pyrexia is a condition where body temperature is higher than normal (Kluger, 1986) as a result of the elevation of the thermostatic set point threshold. It is associated with bacterial infections and several pathological conditions and can be non-specific. While having a fever may not necessarily always require intervention, its treatment is necessary especially in critically ill patients (Henker *et al*., 2001).

Common treatment of fever includes synthetic drugs like paracetamol and ibuprofen. While these drugs have been known to be safe, some reports have shown that these drugs can be toxic (Prescott, 2000; Ulukol *et al.*, 1999). Thus, alternatives have been sought, especially the traditional medicine. The World Health Organization has expressed its high interest in traditional medicine because of its safety and effectiveness. Among the plants which may have potential anti-pyretic is *Ficus septica*.

F. septica, locally known as 'Lagnob', is an erect, small tree, growing 3 to 8 meters high, smooth, with more or less hairy young shoots (Berg, 2005). It has been used as a traditional treatment for several conditions, including fever (Morilla *et al*., 2014). However, studies documenting the anti-pyretic potential of *F. septica* have been limited.

The present study aimed to qualitatively evaluate the phytochemical properties of *F. septica*, and assess its anti-pyretic potential in mice. This study can provide valuable information on the potential of *F. septica* as a herbal treatment for fever, and as a baseline study to further investigate its properties.

2 MATERIALS AND METHODS

Research Design

The study is an experimental type. The potential anti-antipyretic property of *F. septica* extract was evaluated in ICR mice. Animals were acclimatized for seven days prior to experimentation and were randomly assigned into three equal groups: 1) negative control (no treatment), 2) positive control (Paracetamol), and experimental extract (*F. septica*).

Research subjects and plant sources

A total of 21 ICR mice (10-12 weeks old) were used. On the other hand, *F. septica* leaves were collected from a single source in Lapu Lapu City, Cebu, Philippines. Leaves were collected from plants with full-blown flowers when it starts to cover the plant. Species identification was confirmed by an expert

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botanist from the Biology Department of the University of San Carlos, Cebu City, Philippines.

Research Procedure

Preparation of samples and extract

Two hundred grams of finely cut fresh *F. septica* leaves were macerated with 95% ethanol for 72 hours. The mixture was then filtered, and the marc was discarded. The filtrate was evaporated using rotary evaporator until reaching a syrupy consistency. Excess solvent was removed by placing the remaining volume in a hot air oven (at 40 ˚C). The residue was re-macerated twice using the same strength and volume of ethyl alcohol. All filtrate was collected and evaporated. The compacted extract was liquefied by adding 20% tween surfactant and distilled water. Flammability and iodoform test was performed to determine any traces of the solvent. All extracts were placed in a tightly closed container and kept refrigerated at 2-8 degree Celsius until further use. One percent w/v solution of an extract of *F. septica* was subjected to phytochemical screening for the detection of various classes of constituents.

Animal marking and assignment to groups and cages

Upon arrival to the animal facility, the animals were randomly assigned to cages and marked at the base of the tail using permanent markers for identification. Cages were also randomly assigned to the different treatment groups. The health of animals was assessed by physical examination.

Animal acclimatization, monitoring, and maintenance

The mice were acclimatized for seven days. Commercial feeds and water were provided ad libitum. Lighting was on a 12-hour dark-light cycle, and ambient temperature was maintained between 24 to 26 degree Celsius. Beddings were changed every three days. Body score, appearance and attitude (Lillma-Cullere and Foltz, 1999; Bekkevold *et al*., 2013) were monitored.

Test solution, bioassay, and phytochemical analysis

The experimental test solution was prepared by dissolving the solid extract in sufficient amount of distilled water and of 2% v/v Polyoxyethylene (20) sorbitan monolaurate (tween 20) to make 100 ml of the solution. Also, phytochemical tests were performed on the solid extract.

Evaluating the anti-pyretic potential of the extract in mice were performed similarly as previously described (Okokon and Nwafor, 2010). Briefly, after the acclimatization period, mice were fasted overnight. The body temperature was recorded using digital thermometer via rectal route. Before pyrexia induction, basal body temperature was obtained. Pyrexia was induced in mice by subcutaneous injection of 20% Brewer's Yeast suspension (20 g of brewer's yeast mixed in 100 ml distilled water). The volume of the experimental solution administered to each mice was based on a predetermined dosage at 10 ml/kg (Diehl *et al*., 2001). For the controls, distilled water (negative) was administered at a dose of 10 ml/kg (Diehl *et al*., 2001) while Paracetamol (250mg/5 ml) (positive) was administered at a dose of 150 mg/kg (Coen *et al*., 2003). All treatments were administered orally. After 30 minutes, the temperature was rechecked, and those that showed a minimum increase of 0.5°C from its baseline body temperature were subjected to the corresponding treatment in their group. Those with elevated temperatures were considered to have a fever. The body temperature of mice was recorded hourly for five times.

Data processing and analysis

Observations were manually recorded on a tally sheet. Gathered data were encoded in Microsoft Excel and imported to a statistical software. Data were analyzed using one-way analysis of variance (ANOVA) with post-hoc analysis by Tukey's method. ANOVA by repeated measures was also performed. The significance level was set at 5%.

Ethical Consideration

The procedures performed in this study were guided by the principles of animal welfare, Animal Welfare Act of the Philippines (RA 8485) and AO 45 of the Bureau of the Animal Industry. The protocol was reviewed and approved by the Institutional Animal Care and Use Committee of the University of the Visayas.

3 RESULTS AND DISCUSSION

Comparing the body temperatures (BT) at baseline and 1 hour after brewer's yeast administration, results showed an increase in BT (more than 1 ˚C) which indicated that pyrexia induction was successful. After administration of the corresponding treatments in the different groups, BT (Table 1) in the positive control and experimental groups were observed to have lowered in the first to fifth hour of observation. Mean BT in the negative control group did not reduce. On the other hand, the phytochemical analysis revealed that the *F. septica* extract contained alkaloids, terpenoids, tannins, glycosides, carbohydrates, flavanoids and phenolic compounds (Table 2).

ANOVA by repeated measures showed a significant difference (Wilks' Lambda <0.001), with post-hoc analysis revealing the positive ($p <0.001$) and experimental ($p=0.01$) groups to be significantly different with the negative control. Hence, this implies that time has an effect on the resulting temperature of the different groups. Moreover, positive and experimental groups may have comparable results within the given observed periods.

Results indicate that the *F. septica* extract may have an anti-pyretic property. This may due to some phytochemicals like flavonoids and phenolic compounds found in the extract. Flavonoids and phenolic compounds target prostaglandins, which are involved in the pyrexia. These compounds have

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antipyretic action by inhibiting arachidonic acid peroxidation and subduing TNF-α, which results in the reduction of prostaglandin levels and consequently pyrexia (Qu *et al*., 2015). On the other hand, other components like the alkaloid (Damu *et al*., 2009), terpenoids (Bhaskar and Balakrishnan, 2015) and tannins (Hossain *et al*., 2011) have been reported to have anti-pyretic properties (Damu *et al*., 2009). Further studies testing the specific components of *F. septica* for its anti-pyretic properties must be explored.

A related species, *Ficus nota*, has also been reported to have anti-pyretic potential (Arquion *et al*., 2015). Another report also discussed the anti-pyretic property of *Ficus* spp. (Araujo, 2012). Hence, it is not surprising that *F. septica* extract will also show an anti-pyretic potential.

Table 1. Body temperature (rectal) of mice (n=21) given paracetamol and *F. septica*

Group	Baseline		1 hour after induction		Post Treatment Administration (hour) 1		2		3		4		5	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Positive control (Paracetamol) (n=7)	35.5	0.9	37.0	0.7	35.9	0.7	35.7	0.6	35.5	0.6	36.6	0.4	36.7	0.4
Negative control (Distilled water) (n=7)	36.1	0.6	37.4	0.5	37.4	0.3	37.8	0.4	37.8	0.2	37.8	0.2	37.9	0.2
Experimental (*Ficus septica* extract) (n=7)	35.8	0.6	37.3	0.6	36.7	0.5	36.5	0.6	36.7	0.9	36.7	0.9	36.6	0.9

Legend: SD= standard deviation

Table 2: Phytochemical analyses results of *F. septica* leaf extract

Active Constituents	Chemical Test	Indicator of Presence	Results
Alkaloids	Meyer's Test	White precipitate	Positive
Terpenoids	Salkowski Test	Red colour in the interface of the solution	Positive
Tannins	Ferric Chloride test	White precipitate	Positive
Reducing sugar	Benedict's Test	Orange red precipitate	Negative
Glycosides	Mohlisch's Test,	Dark green colouration	Positive
Carbohydrates	Molisch's Test	Violet junction between 2 layers	Positive
Flavonoids	Lead acetate Test	Bulky white precipitate	Positive
Saponins	Foam Test	Foam formation	Negative
Phenolic compounds	Ferric chloride Test	bluish black	Positive

4 CONCLUSION

F. septica leaf extract lowered the body temperature of mice after pyrexia induction. The present study showed the anti-pyretic potential of *F. septica* leaf extract. Further studies on varying doses, toxicity and specific fractions or components of *F. septica* that might have contributed to its anti-pyretic potential must be explored.

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