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Comparison of Antipyretic Activity in Rats by using Ethanolic Extraction of Premna Species

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Abstract
Fever is managed using synthetic drugs such as aspirin, paracetamol and other drugs has more adverse effects. Traditional medicine employing a plant-based system treatment from an important part of human medicine system. It has less side effects, adverse effects when compared with synthetic drugs. The present study is aimed to investigate the comparison of anti- pyretic activity of ethanolic extract of *Premna latifolia* species.
The present study is aimed to investigate the antipyretic activity of ethanolic leaf extract of *Premna latifolia* in Wistar albino rats. Pyrexia was induced in rats by Brewer's yeast suspension. The animals were divided in to 4 groups, 6 of each as following Group I received normal saline water (control); Group II received standard paracetamol 150 mg/kg; Group III, IV received ethanolic leaf extract of *Premna latifolia* at doses 100, 200 & 300 mg/kg respectively. In all experiments, rats were orally administered. The temperature of all the rats in each group was measured at the start of study, at 18 h after yeast injection and every hourly for 4 h thereafter. The mean temperature was found out for each group and was compared with the control group and standard drug group. The leaf extract at doses 200 and 300 mg/kg significantly reduced the body temperature on yeast induced pyrexia and was comparable with standard.

Keywords: Antipyretic Activity, Ethanolic Extraction, *Premna latifolia*.

Introduction
Medicinal plants are the part and parcel of human society to combat against different diseases from the dawn of human civilization. According to World Health Organization, approximately 80% population of the developing countries are facing difficulties to afford synthetic drugs and are relying on traditional medicines mainly of plant origin to maintain their primary health care needs. Plants are being Medicinal plants are the part and parcel of human society to combat against different diseases used in various disorders e.g., gastrointestinal disorders, genitourinary problems, and psychological and respiratory problems through time immemorial and people in western countries and people in western countries are now reverting back towards herbal medicines because of their extensive biological and medicinal activities, higher safety and lesser costs.

Pyrexia:
Fever may be defined as a complex physiologic response to a disease, mediated by pyrogenic cytokines and characterized by a rise in core temperature, generation of acute phase reactants and activation of immune systems. Regulation of body temperature requires a delicate balance between production and loss of heat, the hypothalamus regulates the set-point at which the body temperature is maintained. Alexander *et al*. reported the fever this hypothalamus thermostat set point is elevate and body temperature increases over normal values. The normal range of body temperature is 36.5*-37.5*C.

Fever or pyrexia is the elevation of an individual's body temperature above a set point regulated by the body's thermoregulatory centre in the hypothalamus. This increase in the body's temperature is often due to a physiological process brought by infectious cause or non- infectious causes such as inflammation malignancy, or autoimmune processes. These processes involve the release of immunological medicators, which trigger the thermoregulatory centre of the hypothalamus leading to the increase in body's core temperature. The fever is usually measured based on temperature and duration of time.

The types of fever

1. **Intermittent fever:** It has a fluctuating baseline between normal temperature and fever levels over the course of the day.
2. **Remittent fever:** It may come and go and the temperature fluctuates.
3. **Hectic fever:** It is a either an intermittent or a remittent fever. The temperature range swings widely throughout of at least 1.4 degrees Celsius between the highest and lowest temperature.
4. **Continuous fever /sustained fever:** It is prolonged fever with no change in temperature.
5. **Relapsing:** It is a type of intermittent fever that spikes up again after days /week.

The normal temperature of the human body is approximately 370 C or 98.60F and varies by about 0.5 C throughout the day.

The variation in the core body temperature results from the normal physiological processes throughout the human body, including metabolic changes, sleep-wake cycles, hormone variability and changing activity levels.

In case of a fever, the increase in the case body temperature is often greater than 0.5C and attributed to a fever- inducing substance.

The categories of fever:

Low-grade: 37.3 to 38.0 C (99.1 to 100.4 F)
Moderate-grade: 38.1- 39.0 C (100.6 to 102.2 F)
High-grade: 39.1 to 41 °C (102.4 to 105.8 F)
Hyperthermia: greater than 41C (105.8 F)

Signs and Symptoms of Fever

A fever is not an illness but a symptom or sign of an illness or infection in our body. However, a fever is commonly accompanied by other symptoms, including:

1. Sweats or chills
2. Headache
3. Achy muscles
4. Lack of appetite
5. Rash
6. Restlessness

Common causes of fever:

Our body will create a fever for a variety of issues. Some of the most common issues include:

1. Infections
2. Environmental Factors: such as heat stroke, heat exhaustion, and extreme sunburn
3. Inflammatory conditions
4. Hormone disorders
5. Cancer

Methodology

- A fever is a body temperature that is higher than natural body temperature. WISTAR ALBINO Rats were used for screening anti-pyretic activity, as descried by Bhalla *et al*. (1971) method.
- The pyrexia was induced by a suspension of Brewer's yeast, and the ethanolic extract of *Premna latifolia* species used to determine the antipyretic activity.
- The Premna species contains the following phytochemicals: Iridoids, Glycosides, Diterpenes, and Saponins, Alkaloids, and it has the pharmacological activity of Anti- Anti-Inflammatory, Antibacterial, Antioxidant, Antihyperlipidemic, and Antifeedant.

Methodology

Preparation of Brewer's yeast suspension:

- The 15% w/v brewer's yeast suspension was prepared.

Dry Yeast

Dry yeast can be sprinkled right into the cooled wort if we want. We do not need to rehydrate, but some people still like to get the yeast going before they pitch it. This is what we need to do if we plan on rehydrating it:

1. Add 1 cup of 800 F water to sanitized container.
2. Add 1 package of dry yeast to the water.
3. Stir the water and yeast mixture for 30 seconds. Do not stir vigorously.
4. Let the yeast sit for 15-30 minutes until we notice a light foam forming on top of the liquid.
5. Pitch (add) the yeast to our fermenter.

Maceration

- Powdered plant material (10g) was taken in a conical flask and extracted with organic solvents (100ml) such as n-hexane, ethyl acetate, methanol and ethanol in a mechanical shanker with temperature control (Room temperature) at constant stirring rate at 200rpm.
- It was left for 24h and solids were filtered using Whatman No.1 filter (Raaman, 2006). The extraction was repeated three times until complete extraction.

Successive Soxhlet Extraction

Soxhlet equipment was used in this study. Powdered plant material (60g) was extracted with organic solvents (300ml) such as n-hexane, ethyl acetate, methanol and ethanol in Soxhlet apparatus (Raaman, 2006).

Evaluation of antipyretic activity:

- The animals were divided into six groups (n=6). Fever was induced by administration of 15% w/v Brewer's yeast suspension subcutaneously below the nape of the neck.
- The rectal temperature was recorded using a digital thermometer immediately before and 18h after Brewer's yeast injection.
- After 18h of yeast injection different groups received vehicle (1% v/v Tween in distilled water), aqueous and ethanol extracts (200 and 300mg/kg body weight) and reference drug (paracetamol, 150 mg/kg body weight) through oral route.
- The rectal temperature was then periodically recorded for an observation period of 4h.

Fig 1

Statistical Analysis

The results are expressed as mean ± SEM of six independent experiments. Statistical significance between groups was evaluated by one-way analysis of variance (ANOVA) followed by Turkey's multiple comparison test. P≤ 0.05 value was considered statistically significant.

Results and Discussion

The experimental animals showed a marked increase in rectal temperature after 18 hours of Brewer's yeast injection. The Group III & IV showed a decrease in rectal temperature when compared to the control group after 1h. The decrease in temperature is statistically significant and is comparable to that of the standard group. In the present study, the antipyretic activity of ethanolic leaf extract of *Premna latifolia* in rats was evaluated. The ethanolic leaf extract and aqueous extract of *Premna latifolia* significantly reduced the yeast-induced elevated body temperature in a dose-dependent manner, and their effect is comparable to that of the standard antipyretic drug, Paracetamol.

Table 1

S.NO	Group Names	Dose	Normal temperature [^{0}C]	Rectal temperature [0c] 18 hrs after yeast induced pyrexia	Rectal temperature [0c] after treatment with extract			
					1hr	2hr	3hr	4hr
1	Yeast induced	150mg/kg	98.58 ± 0.36	99.61 ± 0.43	99.86 ± 0.36	99.80± 0.36	100.62± 0.31	102.2± 0.25
2	Paracetamol	100mg/kg	98.46 ± 0.47	99.54 ± 0.47	99.30 ± 0.87	98.76± 0.33	96.92± 0.38	94.06± 0.14
3	Ethanolic extract	200mg/kg	98.68 ± 0.64	99.60 ± 0.63	99.52 ± 0.43	98.24± 0.37	96.16± 0.62	94.86± 0.28
4	Aqueous extract	300mg/kg	98.58 ± 0.41	99.58 ± 0.45	99.42 ± 0.66	98.81± 0.18	97.26± 0.72	95.72± 0.21

Conclusion

In conclusion, ethanolic leaf extract and aqueous extract of *Premna latifolia* is having antipyretic activity. The underlying mechanism may be inhibition of prostaglandin synthesis within the hypothalamus. The active constituents such as alkaloids, flavonoids and sterols of ethanolic leaf extract and aqueous extract of *Premna latifolia* may be responsible for this antipyretic activity. Further studies at molecular levels are required to establish the exact mechanism of action.

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