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# Correspondent Evaluation of Anti-pyretic Activity by Using *Salacia fruticosa*

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**ABSTRACT**

*The present pharmacological research were carried out in anti pyretic activity of Salacia fruticosa formulation in rats against yeast induced and vaccine induced pyrexia methods was standardized. In this injecting yeast suspension (S.C, P.O) followed by recording the temperature at regular intervals. Then the evaluation of anti pyretic activity of Salacia fruticosa formulation was carried out by using standard procedure. Both the Salacia fruticosa samples including vehicle significantly turn down in the rise of temperature after 3 hours of yeast injection. After 19-23 hours of yeast injection of Salacia fruticosa samples minimize the rise in temperature at extremely significant manner in comparision to both yeast and vaccine control groups. The data initiated during studies show that both the Salacia fruticosa formulation having significant anti-pyretic activity.*

**Keywords:** Anti-pyretic; *Salacia fruticosa*; Suspension

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## INTRODUCTION

From former times, conventional frameworks of drug are of worldwide significance. Indeed, even today in many creating nations, larger part of populace depends enormously on conventional practioners and restorative plants to meet essential social insurance needs, in spite of accessibility of present day prescriptions. These home grown phytomedicines have turned out to be well known for authentic and social reasons. As of now numerous individuals in created nations have started to go to elective home grown medications.

Logical assessment of restorative herbs for their therapeutic worth and application is on rise. Wellbeing and adequacy of information of numerous herbs, their concentrates and dynamic fixings, and the arrangements containing them was settled. Anyway the market of home grown medications is inadequately managed and affirmation of security, viability and nature of such home grown items has now turned into a key issue in industrialized and creating countries [1]. Clinical and basic research are being carried out on the medicinal plants

and their formulations, with the state-of-the-art methods in a number of Universities and different institutions. Many Indian medicinal plants provide a abundant source for antioxidants that are known to cure different diseased states. The antioxidant protection is observed at different levels. These plants also have many other beneficial compounds like ingredients that are used for functional foods. In the traditional system of medicine, most of the remedies were taken from plants and they were proved to be useful through the rational behind their use is not well established through systemic pharmacological and clinical studies except for some composite herbal drugs and plants.

The plant kingdom still holds different variety of species of plants which contain many substances of medicinal value which are yet to be discovered in large number of plants are constantly being screened for their possible pharmacological effects (Figure 1) [2].

**Figure 1. *Salacia fruticosa***

**TAXONOMIC CLASSIFICATION**

Kingdom: Plantae

Subkingdom: tracheobionta

Division: Magnoliophyta

Class: Magnoliatae

Subclass: Rosidae

Order: Celastrales

Family: Hippocrateaceae

Genus: Salacia

Species: Fruticosa [3].

**Vernacular names**

English: Common willow

Malayalam: Ponkarandi, Ekanayakam

Unani: Bedmushk, Bedsaada

Ayrvedic: Saptachakra, Swarnmula [4].

**Description**

*Salacia fruticosa* grows from generally unbranched taproots and produces one to more than ten stems that are typically 5 to 40 cm tall but sometimes up to 70 cm tall. The stems can be tinted purplish, upright or lax, produced flower heads that are held as taller than the foliage. The foliage is upstanding developing or on a level plane orientated, with leaves having barely winged petioles or being unwinged. The stems can be glabrous or scantily secured with short hairs [5,6].

The 5-45 cm long and 1-10 cm wide leaves are oblanceolate, elongated fit as a fiddle with bases steadily narrowing to the petiole. The leaf edges are consistently shallowly lobed and profoundly lobed and regularly cut or toothed with sharp or dull teeth. The calyculi (the cup like bracts that hold the florets) is made out of 12 to 18 portions: each fragment is reflexed and once in a while glaucous. The lanceolate molded bractlets are in 2 arrangement with the apices taper fit as a fiddle. The 14 to 25 mm wide involucres are green to dim green orthey might be earthy green with dim dark or purplish tips. The florets number 40 to more than 100 for each head, having corollas that are yellow or orange-yellow in shading. The organic products, which are called cypselae, they extend in shading from olive-green or olive-dark colored to straw-hued to grayish for the most part they are oblanceoloid fit as a fiddle and 2 to 3 mm long with slim beaks. They are for the most part white to silver-white in shading and nearly around 6 mm wide. Plants for the most part have limit of 24 or 40 sets of chromosomes yet in certain plants they have 16 or 32 chromosomes. Plants for the most part have smooth sap and the leaves are altogether basal where each blooming stem needs bracts and has atleast one single blossom head.

**Distribution**

*Salacia fruticosa* is distributed in South-West India, Peninsula, Ceylon, Java, Thailand and Phelippines.

Within India, it is distributed in Karnataka (rare in semi evergreen forests of western Ghats of phanamthitta and Idukki districts, and southern Orissa.

**Medicinal uses and indications**

Traditionally *Salacia fruticosa* used as acrid, bitter, thermogenic, anti inflammatory, depurative, vulnary, livertonic, and stomachic, Analagesic.

*Salacia fruticosa* is useful in hemorrhoids, inflammation, leucorrhoea, leprosy, skin diseases, amenorrhoea, dysmenorrhoea, wounds, ulcers, hyperhydrosis, hepatopathy, dyspepsia, flatulence [7,8].

**Pyrexia**

Fever is also known as pyrexia or it is also called as controlled hyperthermia which is a common medical sign that is characterized by the action of elevated temperature which is above the normal range of 36.5–37.5 °C (98–100 °F) due to an increase in the body temperature which is the set point. This increase in set-point will make increased muscle tone and shivering [9].

Fever completely differs from uncontrolled hyperthermia which is that hyperthermia is an elevated in body temperature over the body's thermoregulatory set-point due to excessive heat production or an insufficient thermoregulation.

A pyrogen is a substance that induces fever. They can be moreover internal (endogenous) or external (exogenous) to the body. The bacterial substance lipopolysacharide (LPS), present in the cell wall of some bacteria is a best

example of an exogenous pyrogen. Pyrogenicity can vary In extreme examples some bacterial pyrogens known as super antigens that can cause rapid and dangerous fevers depyrogenation may be achieved through filtration, distillation, or inactivation.

Hyperthermia is an sample of a high temperature that not at all a fever. This occurs from more number of causes including heatstroke, neuroleptic malignant syndrome, malignant hyperthermia, malignant hyperthermia stimulants such as amphetamines and cocaine, and serotonin syndrome, idiosyncratic drug reactions

**Signs and Symptoms**

A fever is usually assisted by sickness behavior, which it usually consists of lethargy, depression, anorexia, sleepiness, hyperalgesia, and the inability to concentrate.

**Endogenous:** In essence, all endogenous pyrogens are cytokines, molecules that are a part of the innate immune system. They are mostly produced by the phagocytic cells and can cause the increase in the thermoregulatory set-point in the hypothalamus. Important endogenous pyrogens are interleukin1 (α and β), interleukin2 (IL-6) and tumor necrosis factor alpha. Minor endogenous pyrogens include interleukin8, tumor necrosis factor alphatumour necrosis factor beta, macrophage inflammatory protein-α and macrophage inflammatory protein-β

**Exogenous:** Mechanism of fever caused by exogenous pyrogens includes LPS, it is a cell wall component of the gram negative bacteria. An immunological protein that is known as lipopolysaccharide binding protein (LBP) binds to LPS. The LBP–LPS complex then later binds to the CD14 receptor which is nearby macrophage. This binding will results in the synthesis and release of different endogenous cytokine factors, such as interleukin 1 (IL-1), interleukin 6 (IL-6), and the tumor necrosis factor-alpha. Otherwise stated exogenous factors cause release of endogenous factor which in turn will activate the arachidonic acid pathway.

**Extraction**

Pharmaceutically extraction as the term that is used, involves in the separation of therapeutically active portions of plant or animal tissues from the inactive components by using different selective solvents in standard extraction procedures.

**Collection and Authentication of plant material:** The fresh leaves of Salacia fruticosa were collected from Thirupathi, Andhra pradesh, shade dried and ground powdered in a mechanical blender. The powdered is subjected to soxhlet extraction using methanol as solvent. A specimen of the plant is deposited in the herbarium of Vaageswari College of Pharmacy, Karimnagar identified and authenticated by Dr. K. Madhava Chetty, botanist of Sri Venkateswara University.

**Preparation of Extracts**

The dried and powdered leaves of Salacia *fruticosa* was extracted successively with of methanol and aqueous in soxhelt apparatus [10].

A greenish colored methanolic extract was obtained (5.6% with respect to dry powdered plant material), then, the same has been extracted with water to yield brownish green semisolid mass (yield 4.2% with respect to dry plant material). Two extraction procedures were carried out until the solvent system becomes a colorless. All the extracts were collected and concentrated by evaporating the solvent completely. These extracts were dried and stirred in refrigerator for the future use of various chemical group identification and pharmacological evaluation.

## PHARMACOLOGICAL INVESTIGATION

### Experimental Animals

Animals were procured from Central animal house, Vaageswari College of Pharmacy, Karimnagar (CPCSEA Reg. No: 1505/po/a/11). Male wister albino rats weighing between 150 and 2000 g were selected for the study. Female albino mice weighing between 25 g and 30 g were selected for the acute oral toxicity studies. The were maintained on 12 h/12 h light and dark cycle at ambient room temperature and relative humidity (50%). They were kept in propylene cages in a well-ventilated room under hygienic conditions through the study. The animals were fed with commercial rst feed pellets and were given water ad libitum. Maintenance of animals was as per CPCSEA guidelines. All animals were carried out only after approval of IAEC [11,12].

### Determination of LD50:

The herbal preparation *Salacia fruticosa* ***Wall*** have been subjected to toxicity studies according to OECD guidelines and no death was found up to 3 g/kg body weight, so 10% and 20% of it i.e. 300 mg/kg and 600 mg/kg are taken for carrying pharmacological activities.

### Acute Oral Toxicity Study (Acute Toxic Class Method)

A prilimenary pharmacological study was condected to assess the acute pharmacological effects and safety of the drug. Acute toxicity was conducted to determine the median lethal dose ($LD_{50}$) of the methanolic extracts of the leaves of *Salacia fruticosa*. The procedure was followed by OECD (organization for ethical and cooperative development) guidelines, 423(acute toxic class method). The acute toxic class method was step wise procedure with 3 animals of a single sex per step. This technique uses defined doses like (5, 50, 300, 2000 mg/kg body weight) (Table 1).

**Table 1. Acute toxic class method**

| Group | Dose (mg/kg) | Number of animals used | Number of dead animals |
|---|---|---|---|
| 1 | 5 | 3 | 0 |
| 2 | 50 | 3 | 0 |
| 3 | 300 | 3 | 0 |
| 4 | 2000 | 3 | 0 |

It was observed that the extract was not mortal for mice even at 2000 mg/kg dose. Hence one tenth $1/10^{th}$ of the dose (200 mg/kg) and one fifth $1/5^{th}$ of the dose (400 mg/kg) selected for further study, Anti-pyretic Activity, Yeast induced Pyrexia.

## MATERIAL AND METHODS

### Animals

Wistar albino rats weighing 180-200 gm of either sex were used in the study. Animals were procured from Laboratory Animal House of Vaageswari College of Pharmacy, Karimnagar, uru s (Reg. no.:/ac/CPCSEA). All animal experiments strictly complied with the approval of institutional animal ethical committee. The animals are kept in polyacrylic cages and they are maintained under high standard housing conditions of temperature (24-27°C)

and humidity (60-65%) with 12 h light–12 h dark cycle. They were acclimatized for seven days. Food was completely provided in the form of dry pellets and water [13].

**Equipment**

Digital Clinical Thermometer (Hartmann, Germany).

**Method**

Rectal temperature was measured by inserting a thermister probe 3-4 cm deep into the rectum. After measuring the basal temperature, animals were given a subcutaneous injection of 10 ml/kg of 15%w/v yeast suspended in normal saline solution. After 19 h of yeast injection, the animals were treated with their respective doses of test drugs and their rectal temperatures were recorded till 23rd hour per every day.

**Treatment protocol:** The animals were numbered, weighed and then divided into 6 groups with 6 animals in each as follows

Group I: Animals received yeast (10 ml/kg 15%w/v of yeast s.c.)

Group II: Animals received yeast and Paracetamol (150 mg/kg weight s.c.)

Group III: Animals received yeast and 200 mg/kg body weight, MESF (p.o.)

Group IV: Animals received yeast and 400 mg/kg body weight, MESF (p.o.)

Group V: Animals received yeast and 200 mg/kg body weight, AESF (p.o.)

Group VI: Animals received yeast and 400 mg/kg body weight, AESF (p.o).

**Vaccine induced pyrexia**

**Material & Methods**

**Animals:** Wistar albino rats weighing 180-200 gm of either sex were used in the study. Animals were procured from Laboratory Animal House of Vaageswari College of Pharmacy, Karimnagar, uru s (Reg. no.:/ac/CPCSEA).. All animal experiments strictly complied with the approval of institutional animal ethical committee. The animals are kept in polyacrylic cages and maintained under standard housing conditions of temperature (24-27°C) and humidity (60-65%) with 12 h light–12 h dark cycle. They were acclimatized for seven days. Food is provided in the form of dry pellets and water [14-20].

**Equipment:** Digital Clinical Thermometer (Hartmann, Germany)

**Method:** Animals were fasted and grouped. Basal rectal temperatures of all the animals were recorded. Pyrexia was induced by injecting typhoid-paratyphoid vaccine A and B (TAB) at a dose of 1 ml/kg body weight (i. p.). six hours after injection of TAB, the temperature was again recorded and the animals that did not show a minimum rise of 1.5°C in temperature were discarded. Thus 24 animals were selected and grouped accordingly. After 6 grs, the animals were treated with their respective test compounds and their rectal temperatures were recorded till $11^{th}$ h pert every 1 h [21-25].

**Treatment Protocol:** The animals were numbered, weighed and then divided into 4 groups with 5 animals in each as follows (Figures 2, 3, Tables 2 and 3).

- Group I: Animals received vaccine alone (1 ml/kg body weight i.p-intra peritoneal)
- Group II: Animals received vaccine and Paracetamol 150 mg/kg weight

( i.p: intra peritoneal )

- Group III: Animals received vaccine and 200 mg/kg body weight, MESF

(p.o-Per Oral)

- Group IV: Animals received vaccine and 400 mg/kg body weight,

MESF: Methanolic extract of *Salacia fruticosa* (p.o-Per Oral )

- Group V: Animals received vaccine and 200 mg/kg body weight,

AESF: Aqueous extract of *Salacia fruticosa* (p.o-Per Oral )

- Group VI: Animals received vaccine and 400 mg/kg body weight,

AESF: Aqueous extract of *Salacia fruticosa* (p.o-Per Oral).

## RESULTS

**Table 2. Yeast Induced Pyrexia**

| Treatment | 0 h | 19 h | 20 h | 21 h | 22 h | 23 h |
|---|---|---|---|---|---|---|
| Control | 37.21 ± 0.08 | 38.21 ± 0.11 | 38.41 ± 0.08 | 38.45 ± 0.06 | 38.56 ± 0.07 | 38.62 ± 0.06 |
| Paracetamol | 37.19 ± 0.17 | 38.19 ± 0.15 | 38.13 ± 0.14$^{*}$ | 38.05 ± 0.12$^{*}$ | 37.51 ± 0.15$^{**}$ | 37.21 ± 0.18$^{***}$ |
| MESF | 37.16 ± 0.10 | 38.20 ± 0.16 | 38.23 ± 0.16$^{*}$ | 38.13 ± 0.16$^{*}$ | 37.65 ± 0.16$^{**}$ | 37.42 ± 0.12$^{**}$ |
| MESF | 37.24 ± 0.01 | 38.21 ± 0.05 | 38.19 ± 0.02$^{*}$ | 38.11 ± 0.03$^{*}$ | 37.46 0.05$^{**}$ | 37.24 ± 0.01$^{***}$ |
| AESF | 37.30 ± 0.12 | 38.22 ± 0.14 | 38.28 ± 0.14$^{*}$ | 38.22 ± 0.16$^{*}$ | 38.00 ± 0.04$^{*}$ | 37.53 ± 0.16$^{**}$ |
| AESF | 37.27 ± 0.06 | 38.18 ± 0.05 | 38.25 ± 0.06$^{*}$ | 38.19 ± 0.02$^{*}$ | 37.61 ± 0.02$^{**}$ | 37.36 ± 0.02$^{**}$ |

Values are mean ± SEM of 6 animals per group ; (n=6); $^{*}$p<0.05, $^{**}$p<<0.01, $^{***}$p<0.001 Vs control (ANOVA) with Dunnet's t-test.

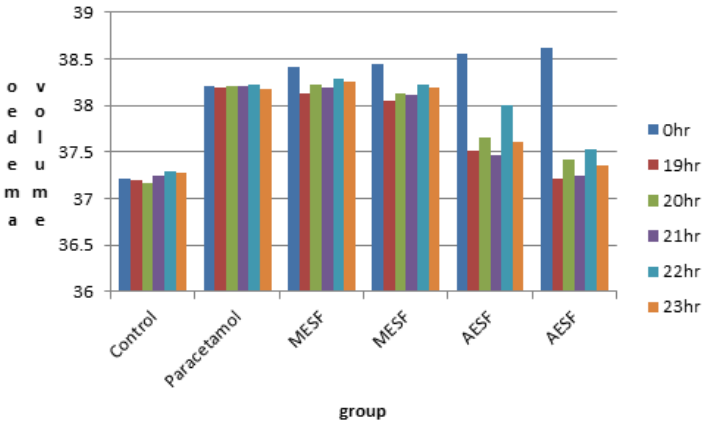


**Figure 2. Effect of different leaf extracts of *Salacia fruticosa* on reaction time of mice by Eddy's Hot plate method.**

**Table 3. Vaccine induced pyrexia**

| Treatment | 0 h | 7 h | 8 h | 9 h | 10 h | 11 h |
|---|---|---|---|---|---|---|
| Control | 37.23 ± 0.08 | 38.64 ± 0.11 | 38.78 ± 0.09 | 38.64 ± 0.06 | 38.52 ± 0.09 | 38.41 ± 0.06 |
| Paracetamol | 37.32 ± 0.10 | 38.63 ± 0.16 | 38.43 ± 0.12$^{*}$ | 38.31 ± 0.16$^{*}$ | 38.03 ± 0.15$^{**}$ | 37.29 ± 0.12$^{***}$ |
| MESF | 37.72 ± 0.09 | 38.73 ± 0.11 | 38.58 ± 0.06$^{*}$ | 38.39 ± 0.05$^{*}$ | 38.12 ± 0.09$^{**}$ | 37.69 ± 0.12$^{*}$ |

| | | | | | | |
|---|---|---|---|---|---|---|
| MESF | 37.29 ± 0.01 | 38.71 ± 0.02 | 38.52 ± 0.06* | 38.37 ± 0.06* | 38.09 ± 0.06** | 37.31 ± 0.09*** |
| AESF | 37.68 ± 0.16 | 38.71 ± 0.16 | 38.63 ± 0.23* | 38.51 ± 0.21* | 38.11 ± 0.20** | 37.69 ± 0.26** |
| AESF | 37.25 ± 0.06 | 38.78 ± 0.09 | 38.46 ± 0.08* | 38.33 ± 0.06* | 38.10 ± 0.06** | 37.32 ± 0.04*** |

Values are mean ± SEM of 6 animals per group; (n=6); *p<0.05, **p<<0.01, ***p<0.001 Vs control (ANOVA) with Dunnet's t-test.

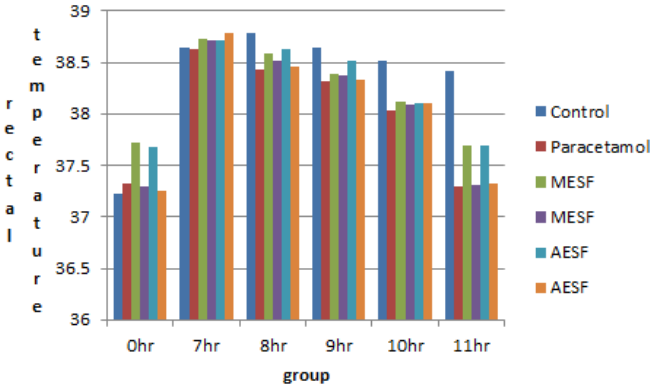


**Figure 3. Variation with stand drugs and leaf extractions.**

## DISCUSSION

### Anti Pyretic Activity

Subcutaneous injection of yeast suspension markedly increased the rectal temperature 19 h after injection. This type of fever, which is induced by yeast, is called pathogenic fever. Yeast releses high molecular weight lipopolysaccharides, which in turn cause sustainedrelease of leukocytic pyrogens. These endogenous pyrogens produce effect by activating prostaglandin synthase in the hypothalamus and the PGE1 produced cause a rise in body temperature. Since almost all anti pyretic agents act by inhibiting PG synthesis it is logical to presume that MESF and AESF also exerts their effects through the same. Some of the mutant strains of gram –ve rods are used in vaccine preparations (salmonella ty The cell wall of this type of bacteria consists of endotoxins (lipoplysaccharides), which activates the macrophages thereby releasing interleukin-1, which causes pyrexia. The antipyretic activity of MESF and AESF in vaccine induced pyrexia may be attributed to the inhibition of PGE2, which is synthesized fromIL-1.

## CONCLUSION

In anti-pyretic activity all the extracts have significant anti-pyretic activity and can be comparable with the standard drug paracetamol. In this activity it has been observed that there is no significant change in changing of body temperature in different dose.

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