



PHARMACOLOGY SCREENING OF *SCUTIA MYRTINA* FOR ANTIPYRETIC ACTIVITY

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ABSTRACT

Herbal medicines continue to be a major market in US pharmaceuticals and constitute a multi-billion-dollar business. Approximately 1500 botanicals are sold as dietary supplements; formulations are not subject to Food and Drug Administration (FDA) clinical toxicity testing to assure their safety and efficacy. Fever is managed using synthetic drugs such as aspirin, paracetamol among others. Synthetic drugs are associated with many side effects. Herbal medicines form alternative therapy since they possess fewer side effects and are readily available. This study aimed to determine antipyretic potential of Hydroalcoholic leaves extract of *Scutia myrtina* in albino rats. The present study indicates us with the fact that the plant extracts have noteworthy antipyretic activity due to the presence of potentially bioactive compounds in them. Our investigations also showed that the hydroalcoholic extract of leaves of *Scutia myrtina* exerted significant antipyretic effects in a dose dependent manner.

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INTRODUCTION:

Ayurvedic medicines mainly based on plants enjoy a respective position today, especially in the developing countries, where modern health services are limited. Safe effective and inexpensive indigenous remedies are gaining popularity among the people of both urban and rural areas especially in India and China. Information from ethnic groups or indigenous traditional medicines has played vital role in the discovery of novel products from plants as chemotherapeutic agents. Herbal medicines

have been main source of primary healthcare in all over the world. From ancient times, plants have been catering as rich source of effective and safe medicines. About 80 % of world populations are still dependent on traditional medicines. Herbal medicines are finished, labeled medicinal products that contain as active ingredients, aerial or underground part of plants or other plant materials, or combination thereof, whether in the crude state or as plant preparations. Medicines containing plant materials

combined with chemically defined active substances, including chemically defined isolated constituents of plants are not considered to be herbal medicines (WHO, 1998).

Herbal medicines continue to be a major market in US pharmaceuticals and constitute a multi-billion dollar business. Approximately 1500 botanicals are sold as dietary supplements; formulations are not subject to Food and Drug Administration (FDA) clinical toxicity testing to assure their safety and efficacy. The Indian herbal drug market size is about \$1 billion and the export of plant based crude drug is around \$100 million. The current market potential of herbal medicine is estimated about \$ 80-250 billion in Europe and USA (Nehir and Karakaya, 2004).

The current market size of the herbs and natural health products in China is about USD 650 million, of which imported herbal medicines account for USD 15 million. In response to the expected improvement in modern herbal medicine and reflective of their growing demand for natural medicines, 73 % of the respondents to a consumer survey indicated they would depend more on herbal medicine in the future. Imports of herbs into Hong Kong in 2003 amounted to USD 166.4 million, a 6.8 % decrease over the 2002's

imports. This reflects less imports of licorice roots of USD 0.2 (-23.8 %) and ginseng root of USD 123.2 (-8.8 %) (samy et al., 2008).

Knowledge of plants used for Ayurvedic preparations in relation to their use as therapeutic agents, pharmacological properties, medicinal plants being imported; medicinal plant parts being exported, endangered medicinal plants and availability of medicinal plants in different biogeographical zones of India. The authors have tried to put all these classes of plants at a common platform so that the data and information of this review could be utilized in drawing strategies for use of medicinal plants in a way that can be extended for future scientific investigation in different aspects. The Ayurvedic concept appeared and developed between 2500 and 500 BC in India. The literal meaning of Ayurveda is "science of life," because ancient Indian system of health care focused views of man and his illness. It is pointed out that the positive health means metabolically well-balanced human beings. The practice of Ayurveda therapeutics consisted of 8 sections divided into 180 chapters and listed 314 plants, which are used as medicines in India (Subhose, et al., 2005).

Four thousand years ago, the medical knowledge of the Indian subcontinent was

termed as Ayurveda. Ayurveda remains an important system of medicine and drug therapy in India. Plant alkaloids are the primary active ingredients of Ayurvedic drugs. Today the pharmacologically active ingredients of many Ayurvedic medicines are being identified and their usefulness in drug therapy being determined. As mentioned in the introduction only a certain percentage of plants are used in traditional medicines. The Indian subcontinent is a vast repository of medicinal plants that are used in traditional medical treatments (Chaurasia *et al.*, 2012).

Pyrexia or fever is caused as a secondary impact of infection, malignancy or other diseased states. It is the body's natural defense to create an environment where infectious agent or damaged tissue cannot survive¹⁷. Normally the infected or damaged tissue initiates the enhanced formation of proinflammatory mediator's (Cytokines like interleukin 1β , α , β and TNF- α), which increase the synthesis of prostaglandin E₂ (PGE₂) near peptic hypothalamus area and thereby triggering the hypothalamus to elevate the body temperature (Spacer and Breder; 1994).

Pyrexia or Fever is defined as an elevation of body temperature. It is a response due to tissue damage, inflammation, malignancy or graft rejection. Cytokines, interleukin, interferon

and Tumor Necrosis Factor α (TNF- α) are formed in large amount under this condition, which increase PGE₂ which in turn triggers hypothalamus to elevate body temperature²⁴. Fever is associated with symptoms of sickness behavior which consist of lethargy, depression, anorexia, sleepiness, & inability to concentrate. This increase in set point triggers increased muscle tone & shivering. However antipyretic medication can be effective at lowering the temperature which may include the affected person's comfort (Duraikanar and Ravichandran; 2012).

According to Ayurveda, pyrexia originates from a combination of indigestion, seasonal variations and significant alterations in daily routine (Gupta *et al.*, 2008). Due to poor hygiene practices and malnutrition, children in developing countries frequently suffer from various forms of infections which present as fevers. These fevers are often accompanied by aches and pains which all lead to morbidity and mortality (Igbe *et al.*, 2009).

Causes of fever include infections caused by parasites, viruses, bacteria, rickettsia, Chlamydia, immune reactions (including the defects in collagen, immunological abnormalities and acquired immunodeficiency. Other causes of fever are destruction of tissues, such as trauma, local

necrosis (infarction), and inflammatory reaction in tissues and vessels (flebitis, arthritis), pulmonary infarction, and rhabdomyolysis.

Scutia myrtina is an erect, glabrous or minutely pubescent branched ever green herb which grows up to 75 – 80 cm height. Stem is striate, leaves are distant, and serrate margin and ovate. Flowers are white in color. The seeds are small and yellowish brown in color. The present study is designed to evaluate the biological properties including antipyretic activity of extract of *Scutia myrtina*.

MATERIAL AND METHODS

Collection of plant material

Leaves of *Scutia myrtina* was collected from Vindhya Herbal, Bhopal in the month of December, 2020.

Extraction procedure

Following procedure was adopted for the preparation of extract from the shade dried and powdered herbs (Mohan et al., 2021):

Defatting of plant material

Leaves of *Scutia myrtina* was shade dried at room temperature. The shade dried plant material was coarsely powdered and subjected to extraction with petroleum ether by soxhlet

extraction. The extraction was continued till the defatting of the material had taken place.

Extraction by soxhlet extraction

56.4 gm of dried powdered leaves of *Scutia myrtina* has been extracted with hydroalcoholic solvent (ethanol : water, 80:20 v/v) using soxhlet extraction process for 24-48 hrs, filtered and dried using vacuum evaporator at 40°C.

Determination of percentage yield

The percentage yield of each extract was calculated by using following formula:

$$\text{Percentage yield} = \frac{\text{Weight of Extract}}{\text{Weight of powder drug Taken}} \times 100$$

Phytochemical Screening

Phytochemical screening: Phytochemical examinations were carried out for all the extracts as per the standard methods.

1. Detection of alkaloids: Extracts were dissolved individually in dilute Hydrochloric acid and filtered.

Mayer's Test: Filtrates were treated with Mayer's reagent (Potassium Mercuric Iodide). Formation of a yellow coloured precipitate indicates the presence of alkaloids.

Wagner's Test: Filtrates were treated with Wagner's reagent (Iodine in Potassium Iodide). Formation of brown/reddish precipitate indicates the presence of alkaloids.

Dragendroff's Test: Filtrates were treated with Dragendroff's reagent (solution of Potassium Bismuth Iodide). Formation of red precipitate indicates the presence of alkaloids.

Hager's Test: Filtrates were treated with Hager's reagent (saturated picric acid solution). Presence of alkaloids confirmed by the formation of yellow coloured precipitate.

2. Detection of carbohydrates: Extracts were dissolved individually in 5 ml distilled water and filtered. The filtrates were used to test for the presence of carbohydrates.

Molisch's Test: Filtrates were treated with 2 drops of alcoholic α -naphthol solution in a test tube. Formation of the violet ring at the junction indicates the presence of Carbohydrates.

Benedict's Test: Filtrates were treated with Benedict's reagent and heated gently. Orange red precipitate indicates the presence of reducing sugars.

Fehling's Test: Filtrates were hydrolysed with dil. HCl, neutralized with alkali and heated with Fehling's A & B solutions. Formation of red precipitate indicates the presence of reducing sugars.

3. Detection of glycosides: Extracts were hydrolysed with dil. HCl, and then subjected to test for glycosides.

Legal's Test: Extracts were treated with sodium nitropruside in pyridine and sodium

hydroxide. Formation of pink to blood red colour indicates the presence of cardiac glycosides.

4. Detection of saponins

Froth Test: Extracts were diluted with distilled water to 20ml and this was shaken in a graduated cylinder for 15 minutes. Formation of 1 cm layer of foam indicates the presence of saponins.

Foam Test: 0.5 gm of extract was shaken with 2 ml of water. If foam produced persists for ten minutes it indicates the presence of saponins.

5. Detection of phenols

Ferric Chloride Test: Extracts were treated with 3-4 drops of ferric chloride solution. Formation of bluish black colour indicates the presence of phenols.

6. Detection of tannins

Gelatin Test: To the extract 1% gelatin solution containing sodium chloride was added. Formation of white precipitate indicates the presence of tannins.

7. Detection of flavonoids

Alkaline Reagent Test: Extracts were treated with few drops of sodium hydroxide solution. Formation of intense yellow colour, which becomes colourless on addition of dilute acid, indicates the presence of flavonoids.

Lead acetate Test: Extracts were treated with few drops of lead acetate solution. Formation

of yellow colour precipitate indicates the presence of flavonoids.

8. Detection of proteins

Xanthoproteic Test: The extracts were treated with few drops of conc. Nitric acid. Formation of yellow colour indicates the presence of proteins.

9. Detection of diterpenes

Copper acetate Test: Extracts were dissolved in water and treated with 3-4 drops of copper acetate solution. Formation of emerald green colour indicates the presence of diterpenes (Salhan et al., 2011).

Estimation of total phenolic content

The total phenolic content of the extract was determined by the modified Folin-Ciocalteu method (Olufunmiso et al., 2011).

Preparation of Standard: 10 mg Gallic acid was dissolved in 10 ml methanol, various aliquots of 5- 25µg/ml was prepared in methanol.

Preparation of Extract: 10mg of dried extracts of were dissolved in 10 ml methanol and filter. Two ml (1mg/ml) of this solution was used for the estimation of phenol.

Procedure: 2 ml of each extract or standard was mixed with 1 ml of Folin-Ciocalteu reagent (previously diluted with distilled water 1:10 v/v) and 1 ml (7.5g/l) of sodium carbonate. The mixture was vortexed for 15s

and allowed to stand for 15 min for colour development. The absorbance was measured at 765 nm using a spectrophotometer.

In vivo antipyretic activity of *Scutia myrtina*

Animals:-

Albino Wistar rats of either sex (150–200 g) were group housed (n= 6) under a standard 12 h light/dark cycle and controlled conditions of temperature and humidity (25±2 °C, 55–65%). Rats received standard rodent chow and water *ad libitum*. Animals were acclimatized to laboratory conditions for 7 days before carrying out the experiments. All the experiments were carried in a noise-free room between 08.00 to 15.00 h. Separate group (n=6) of rat was used for each set of experiments. The animal studies were approved by the Institutional Animal Ethics Committee (IAEC), constituted for the purpose of control and supervision of experimental animals by Ministry of Environment and Forests, Government of India, New Delhi, India.

Acute oral toxicity study

Acute oral toxicity was conducted according to the method of Organisation for Economic Co-operation and Development. Hydroalcoholic extract of leaves of *Scutia myrtina* (5, 50, 300, and 2000 mg/kg) was administered orally for 4 days of six groups of rats (n=6) and the animals were kept under observation for mortality as

well as any behavioral changes for evaluation of a possible anti-pyretic activity (OECD; 2000).

On the basis of acute toxicity study, two test were selected for the pharmacological screening on the basis of maximum tolerated dose limit (MTD), as there was no lethality observed up to 2000 mg/Kg. Finally, selected doses (2000 mg/kg) were chosen for further pharmacological studies.

Body weights of the animals were recorded and they were randomly divided into 5 groups of 6 animals each as follows:

Group I served as normal saline

Group II served as control- animals were treated with yeast via subcutaneous injection (10ml/kg).

Group III animals were administered with yeast (10ml/kg) and the standard drug paracetamol (150mg/kg b.w.), orally

Group IV animals were administered with yeast (10ml/kg,) and with hydroalcoholic extract of leaves of *Scutia myrtina* (100mg/kg b.w.), orally

Group V animals were administered with yeast (10ml/kg,) and with hydroalcoholic extract of leaves of *Scutia myrtina* (200mg/kg b.w.), orally.

Yeast induced pyrexia

Pyrexia was induced by subcutaneous injection of 20 % w/v of brewer's yeast (10ml/kg) in

distilled water. Basal rectal temperature was measured before the injection of yeast, by inserting digital clinical thermometer to a depth of 2 cm into the rectum. The rise in rectal temperature was recorded 18 h after yeast injection. Paracetamol 150mg/kg body weight was used as the standard antipyretic drug. Rectal temperature of animals was noted at regular intervals following the respective treatments. The temperature was measured at 1st, 2nd, and 3rd hour after drug administration (Nazi et al., 2010).

Statistical analysis

The values were expressed as mean \pm SEM (n=6). The statistical significance was assessed using one-way analysis of variance (ANOVA) followed by Tukey's test and P<0.05 were considered to be statistically significant.

RESULTS AND DISCUSSION

The effect of hydroalcoholic extract of leaves of *Scutia myrtina* on yeast induced pyrexia has been shown in Table 7.9. Treatment with hydroalcoholic extract of leaves of *Scutia myrtina* at dose of 100 and 200 mg/kg body weight and paracetamol at dose of, 150mg/kg decreased body temperature of yeast induced mice in a dose-dependent manner. The antipyretic effect started as from the first hour and the effect was maintained for 3 h, after administration of the extract. The results obtained from both standards and extracts

treated groups were compared with the control group. A significant reduction in the yeast elevated rectal temperature was observed in the test drug.

Fever may be due to infection or one of the sequels of tissue damage, graft rejection and/or other disease states. Fever can be induced in experimental animals by intravenous or subcutaneous injection of pyrogens. To evaluate the antipyretic activity of test drugs, the most commonly employed method to induce fever involves injection of lipopolysaccharides (LPS) or brewer's yeast in rabbits or rats. Antipyretic are the agents, which reduce the elevated body temperature. Regulation of body temperature requires a delicate balance between production and loss of heat, and the hypothalamus regulates the set point at which body temperature is maintained. In fever this set point elevates and a drug like aspirin does not influence body temperature when it is elevated by the factors such as exercise or increase in ambient temperature. Yeast induced fever is called pathogenic fever. Its etiology includes production of prostaglandins, which set the thermoregulatory center at a lower temperature.

The present results show that both extract possesses a significant antipyretic effect in yeast- provoked elevation of body temperature

in mice and its effect is comparable to that of aspirin (standard drug). So inhibition of prostaglandin synthesis could be the possible mechanism of antipyretic action as that of aspirin. Also, there are several mediators or multiprocesses underlining the pathogenesis of fever. Inhibition of any of these mediators may bring about antipyretic effect. Fever (pyrexia) is defined as a complicated physiologic response caused by infection or aseptic stimuli. The body temperature elevation occurs when PGE₂ accumulate in the hypothalamus pre-optic region. The neurons firing rate in the hypothalamus control thermoregulation and is usually altered by increased synthesis of PGE₂. Research has reported that most antipyretic drugs exert their action by inhibiting cyclooxygenase enzymatic activity and consequently reducing PGE₂ levels within the hypothalamic region. However, other different mechanisms in the management of pyrexia cannot be ruled out⁶¹⁻⁶². Antipyretics are the agents which reduce the elevated body temperature. Regulation of body temperature requires a delicate balance between the production and loss of heat, and the hypothalamus regulates the set point at which body temperature is maintained.

Yeast induced or other pathogen-induced fever presents an economical and suitable method for investigating new antipyretic drugs. The

presence of proteins in pathogens, yeast in this method is linked to fever via inflammatory reactions. Paracetamol, the antipyretic drug used in this study act through numerous ways by reducing prostaglandins level. In the management of fever, it acts on cyclooxygenase enzymes and exerts antipyretic message within the brain and thereby stimulates anti-inflammatory signals at injury site. Phytochemical compounds were found to be present in the hydroalcoholic extract of leaves of *Scutia myrtina*. It showed a very potential antipyretic action which sustained for a longer duration.

The antipyretic effect of steroids and flavonoids has been proved in various studies. Herbal medications produced from plant extracts are rapidly being used to treat a wide range of clinical illnesses, despite the fact that little is known about their mechanism of action. The hydroalcoholic extract of leaves of *Scutia myrtina* had a more dramatic impact in reducing hyperthermia than the aqueous extract, but after the 3 hr of treatment, it was shown to have a similar effect as the conventional medication Paracetamol. The extracts are likely to reduce pyrexia by reducing brain concentration of prostaglandin E2 especially in the hypothalamus through its action on COX-3 or by enhancement of the

production of the body's own antipyretic substances like vasopressin and arginine.

The outcomes of the present study indicate us with the fact that the plant extracts have noteworthy antipyretic activity due to the presence of potentially bioactive compounds in them. Our investigations also showed that the hydroalcoholic extract of leaves of *Scutia myrtina* exerted significant antipyretic effects in a dose dependent manner. Since this plant parts are used as traditional medicines, the extracts should be discovered scientifically for their phytochemical profiles so that the identification and isolation of active components that are responsible for the exerted pharmacological activities can be possible in future study.

Table 1: % Yield of leaves of *Scutia myrtina*

S. No.	Extract	% Yield (w/w)
1.	Hydroalcoholic	6.52%

Table 2: Phytochemical screening of extract of *Scutia myrtina*

S. No.	Constituents	Hydroalcoholic extract	Observation
1.	Alkaloids Mayer's Test: Wagner's Test: Dragendroff's Test: Hager's Test:	-ve -ve -ve +ve	Green coloured Green coloured Light Green coloured Yellow coloured precipitate.
2.	Glycosides Legal's test	+ve	Red coloured
3.	Flavonoids Lead acetate Alkaline Reagent Test:	+ve -ve	Yellow coloured precipitate Yellow coloured
4.	Phenolics Ferric Chloride Test	+ve	Black coloured
5.	Proteins Xanthoproteic test	-ve	Green coloured
6.	Carbohydrates Molisch's Test: Benedict's Test: Fehling's Test:	-ve -ve +ve	Yellow coloured Yellow coloured Red precipitate
7.	Saponins Froth Test: Foam Test:	+ve -ve	Layer of foam No foam
8.	Diterpins Copper acetate test	-ve	Green coloured
9.	Tannins Gelatin Test:	+ve	White precipitate

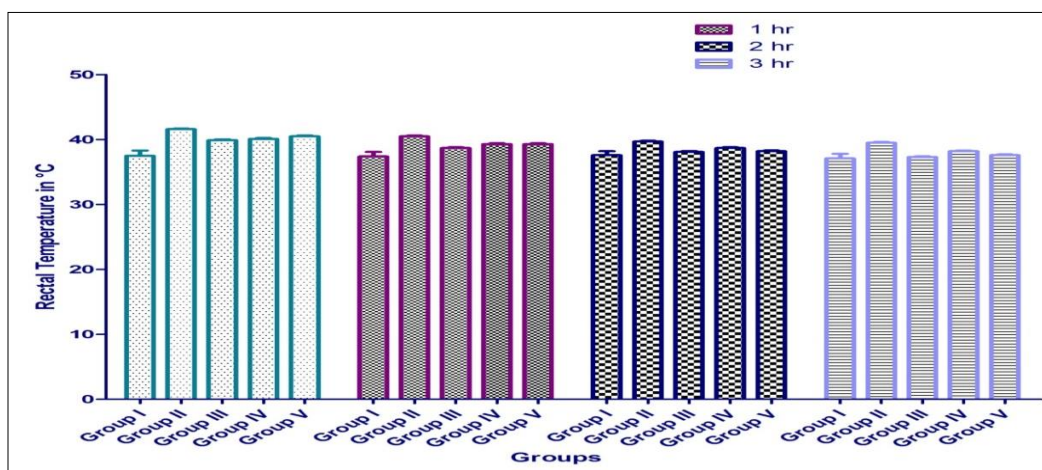
Table 3: Total phenolic and total flavonoid content of *Scutia myrtina*

S. No.	Total Phenol content	Total flavonoid content
1.	0.671 mg/100mg	0.923 mg/100mg

Table 4: Antipyretic activity of hydroalcoholic extract of leaves of *Scutia myrtina* against yeast induced pyrexia in rats

Rectal Temperature in °C after 18hrs of Yeast Injection				
Group	0 hr	1 hr	2 hr	3 hr
Group I (Normal Control)	37.50±0.80	37.40±0.70	37.60±0.6	37.10±0.70
Group II (Control yeast via subcutaneous injection (10ml/kg))	41.60±0.10	40.50±0.10	39.70±0.11	39.50±0.11
Group III Standard drug paracetamol (150mg/kg b.w.)	39.90±0.12	38.70±0.12	38.10±0.12*	37.30±0.11*
Group IV (Hydroalcoholic extract of leaves of <i>Scutia myrtina</i> (100mg/kg b.w.))	40.10±0.12	39.30±0.12	38.70±0.11	38.20±0.11*
Group V (Hydroalcoholic extract of leaves of <i>Scutia myrtina</i> (200mg/kg b.w.))	40.50±0.12	39.30±0.12	38.20±0.12*	37.60±0.11*

Values expressed as mean ± SEM (n=6) *P<0.05as compared to arthritis Control

**Figure 1: Antipyretic activity of hydroalcoholic extract of leaves of *Scutia myrtina* against yeast induced pyrexia in rats**

CONCLUSION

The present investigation it may be concluded that the hydroalcoholic extract of leaves of *Scutia myrtina* has antipyretic activity. All these biological activities may be said to be a promising findings brought out by the present study. These contributions can be used as parameters for the authentication of plant as well as for developing newer drugs based on their activity. In this study no attempt was made to ascertain the mechanism of the observed antipyretic activity. However, it can be suggested that it may be acting through either the peripheral or central mechanism enumerated above. It is also possible that both the mechanisms may be involved. Further, study regarding isolation and characterization of active principle responsible for antipyretic activity are under planning in our laboratory.

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