

## Evaluation of antipyretic activity of alcoholic extract of *Murraya koenigii* leaves in rabbits

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**Received:** 18 April 2019

**Accepted:** 30 May 2019

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### ABSTRACT

**Background:** The present study was carried out to evaluate the antipyretic activity of alcoholic extract of *Murraya koenigii* leaves in rabbits by using PGE1 induced hyperpyrexia method. We found that not much work has been done on the antipyretic effect of this plant.

**Methods:** Laboratory breed New Zealand strains of rabbits of either sex weighing 1000-1500 gm were used in the study. The animals were divided into five groups (n=6). The rabbits of all the groups were made febrile by injecting misoprostol (PGE1) subcutaneously in the dose of 100 mcg/kg. For group 1 and 2, normal saline 2ml/kg as control and aspirin 28mg/kg as standard were given respectively. Alcoholic extract of *Murraya koenigii* leaves in the doses of 200, 400 and 800mg/kg were administered in remaining three groups respectively. Rectal temperatures were recorded with help of digital thermometer for every 30 min after drug treatment.

**Results:** Alcoholic extract of *Murraya koenigii* produced highly significant (p<0.001) antipyretic effect in 400 and 800 mg/kg doses. But onset of action was fast with 800mg/kg dose.

**Conclusions:** This study concludes that Alcoholic extract of *Murraya koenigii* has fast onset of action and also exhibited sustained anti pyretic action in New Zealand rabbits.

**Keywords:** Anti pyretic, Digital thermometer, *Murraya koenigii*, PGE1 induced hyperpyrexia

### INTRODUCTION

Fever or pyrexia is one of the common signs of illness. It is defined as an increase in temperature over the normal (370° C) for a given individual at that particular time of day.<sup>1</sup> Antipyretics are the agents which reduce the increased body temperature. Currently, the drugs obtained from synthetic source like aspirin, acetaminophen and other non-steroidal anti-inflammatory drugs which are used as analgesics and antipyretics causes severe side effects and sometimes may exhibit toxic effects.<sup>2</sup> Hence, the synthesis of drugs from plant source is considered to be safe. Because they exhibit least or no side effects.

Several plants have been used as antipyretic agents traditionally. One of those medicinal plants that have been used is *Murraya koenigii*. It is commonly known as curry leaf or karipatha, is a native plant of India, Srilanka and other south asian countries.<sup>3</sup> *Murraya koenigii* is belonging to Family Rutaceae which represents more than 150 genera and 1600 species.<sup>4</sup> *Murraya koenigii* is a highly valuable plant for its characteristic medicinal values. The various pharmacological activities such as vasodilatation, antimicrobial, antidiabetic, antiulcer, analgesic, phagocytic and antioxidant activities of this plant were well studied.<sup>5-7</sup> Though the literature revealed antipyretic property of *Murraya koenigii* leaves, authors found that

not much work has been done on the antipyretic effect. In earlier studies, antipyretic action of different plant extracts was studied by using yeast induced hyperpyrexia method. PGE1 induced hyperpyrexia method is more convenient and reliable for inducing pyrexia. Hence, this method was adopted in the present study to investigate the antipyretic activity of alcoholic extract of leaves of *Murraya koenigii*.

## METHODS

This study was carried out in Mamata Medical College, Khammam, Telangana.

### Animals

New Zealand strains of rabbits of either sex, weighing 1000-1500g, were obtained from animal house of Mamata Medical College. They were maintained under standard housing conditions of 25°C, commercial pellet diet with water ad libitum and normal photo period (12hr dark/12hr light) was maintained throughout the study period. The experimental protocol has been approved by the Institutional Animal Ethics Committee (IAEC).

### Drugs and chemicals

Aspirin-Zydus cadila and Misoprostol-Misoprost, Cipla pharmaceuticals.

### Instruments

Medical digital thermometer-Sanitas, India

### Animal dose calculation from human dose

Aspirin (Human dose=600mg)

For rabbit =  $600 \times 0.07 = 42/1500$  gm rabbit = 28 mg/kg.<sup>8</sup>

### Plant material and extraction procedure

Fresh leaves of *Murraya koenigii* were collected locally from Khammam market. Collected leaves were washed and then dried under the shade for one month. The dried leaves were powdered and stored. The preparations of crude leaf extract of *Murraya koenigii* were done by continuous hot percolation process with the help of Soxhlet apparatus.<sup>9</sup>

### Acute toxicity study and establishment of dose of the extract

Acute toxicity study of alcoholic extract of *Murraya koenigii* was determined by acute toxic class method of OECD guidelines. Based on the results obtained from this study, the doses of alcoholic extracts of *Murraya koenigii* for antipyretic activity was fixed to be 200 mg/kg, 400 mg/kg and 800 mg/kg body weight.<sup>10,11</sup>

## Methodology and experimental design

Rabbits were used for the evaluation of antipyretic effect of alcoholic extract of *Murraya koenigii*. The animals were divided into five groups with six animals in each.

The five groups are as follows:

- Group I: served as control and treated with normal saline 25 ml/kg
- Group II: Standard group, ASPIRIN 28 mg/kg
- Group III: Alcoholic Extract of *Murraya koenigii* (AEMK) at a dose of 200 mg/kg
- Group IV: Alcoholic Extract of *Murraya koenigii* at a dose of 400 mg/kg
- Group V: Alcoholic Extract of *Murraya koenigii* at a dose of 800 mg/kg

Before starting the experiment, rectal temperatures of the rabbits were recorded using a digital thermometer. Care was taken to insert it to the same depth each time into the rectum.<sup>12</sup> The rabbits were made febrile by administering misoprostol (PGE<sub>1</sub>) subcutaneously in the dose of 100 mcg/kg and the temperatures were recorded.<sup>13</sup> Normal saline in a dose of 2 ml/kg was administered orally to control group and the standard drug aspirin was administered in the dose of 28 mg/kg orally and the temperatures were recorded. Then the test drug i.e. alcoholic extract of the plant was administered orally in 200, 400 and 800 mg/kg doses and the temperatures were recorded for every 30 minutes up to 240 minutes.

### Statistical analysis

Statistical significance was done by one-way analysis of variance (ANOVA) followed by Bonferroni test using Graph pad prism, software (version 5.01.) P value less than 0.05 was considered to be statistically significant.

## RESULTS

The different doses of alcoholic leaf extract of *Murraya koenigii* were tested for its antipyretic activity in New Zealand rabbits. In Control Group (Group-1), the normal mean rectal temperatures ( $38.4 \pm 0.10$ ) of rabbits were recorded before PGE<sub>1</sub> administration. The mean rectal temperature after 30 minutes of PGE<sub>1</sub> injection was  $40.32 \pm 0.2^\circ\text{C}$  and  $39.8 \pm 0.05^\circ\text{C}$  at the 240 minutes (4<sup>th</sup> hour). In Standard Group (Group-2), the mean rectal temperature after 30 minutes of PGE<sub>1</sub> injection was  $40.3 \pm 0.12^\circ\text{C}$ . After administration of standard drug aspirin, there was significant ( $P < 0.05$ ) decrease in temperature at 30 minutes and, there after there was a highly significant ( $P < 0.001$ ) reduction in temperature from 60 minutes to 240 minutes. In Test-1 (Group-3)/*Murraya koenigii* 200 mg/kg, the mean rectal temperature after 30 minutes of PGE<sub>1</sub> injection was  $40.4 \pm 0.12^\circ\text{C}$ . A significant reduction in body temperature was observed at 180 and 240 minutes (4 hr), in between temperature was maintained constantly above the set point.

**Table 1: The effect of AEMK on temperature at various time interval.**

Time Groups	0min/nor mal temp	30min after PGE1	30min after treatment	60 min	90 min	120 min	150 min	180 min	240 min
Group-I Control (NS 2 ml/kg)	38.4±0.10	40.32±0.2	40.2±0.05	40.1±0.02	40±0.04	40±0.04	40±0.16	39.9±0.01	39.8±0.05
Group-II Standard (Aspirin 28 mg/kg)	38.7±0.11	40.3±0.12	39.9±0.20 *	39.6±0.12 **	39.5±0.13 **	39.4±0.08 **	39.2±0.15 **	38.9±0.14 **	38.6±0.09**
Group-III Murraya Koenigii (200 mg/kg)	38.6±0.09	40.4±0.12	40.3±0.02	40.2±0.04	40.1±0.05	40±0.09	39.9±0.05	39.7±0.06 *	39.7±0.01*
Group-IV Murraya Koenigii (400 mg/kg)	38.6±0.15	40.39±0.1 4	40.2±0.10	40.1±0.06	39.7±0.15 *	39.7±0.06 *	39.6±0.10 *	39.5±0.20 *	39.3±0.13**
Group-V Murraya Koenigii (800 mg/kg)	38.7±0.08	40.4±0.00 4	40.1±0.05 *	40.0±0.04 *	39.6±0.12 *	39.6±0.01 *	39.3±0.10 **	39.2±0.15 **	38.8±0.12**

In Test-2 (Group-4)/*Murraya koenigii* 400 mg/kg, the initial mean rectal temperature after 30 minutes of PGE1 injection was 40.39±0.14°C. A significant (P=<0.05) reduction in body temperature was recorded from 90

minutes onwards and highly significant (P=<0.001) reduction was observed at 240 minutes (39.3±0.13°C). In Test-3 (Group-5)/*Murraya koenigii* 800 mg/kg, the initial mean rectal temperature after 30 minutes of PGE1

injection was  $40.4 \pm 0.004^\circ\text{C}$ . A significant ( $P < 0.05$ ) reduction in body temperature was observed at 30 minutes and continued up to 120 minutes and highly significant ( $P < 0.001$ ) reduction in body temperature was evident from 150 min onwards up to 240 min as depicted in Table 1.

## DISCUSSION

In the present study with Alcoholic extract of *Murraya koenigii* (AEMK) leaves a dose dependent antipyretic activity was observed. Significant antipyretic activity was started at 180 min, 90 min and 30 min after treatment with three graded and doubling doses respectively. Highly significant antipyretic activity was observed with group-III and group-IV doses, whereas with group-V it was observed early (Table 1). Hence onset of action is reduced with increased doses.

Normal body temperature is regulated by hypothalamus which balances heat loss and heat production. Fever occurs when there is a disturbance in this balance that leads to the set point of body temperature being raised.<sup>14</sup> The anterior hypothalamus, the posterior hypothalamus and the mid brain reticular formations are considered to be the PGE<sub>1</sub> febrile sensitive sites involved in the thermoregulatory function.<sup>15</sup> Milton and Wendlandt proposed that prostaglandins act as molecular transmitter of pyrogenic stimuli.<sup>16</sup> There is a remarkable similarity in the mode of action of PGE<sub>1</sub> and pyrogen in the production of fever except in the speed of onset. PGE<sub>1</sub> produces pyrexia early than pyrogen as the latency of several minutes reported after injection pyrogen was absent after the PGE<sub>1</sub> injection. Non-steroidal anti-inflammatory drugs show their antipyretic effect by inhibiting prostaglandin synthesis in the hypothalamus.<sup>14</sup> In one study, ethanolic extract of *Murraya koenigii* leaves showed significant antipyretic activity than aqueous extract by inhibiting prostaglandin synthesis.<sup>17</sup> One more study also proved significant antipyretic activity with ethanolic extract of *Murraya koenigii* leaves.<sup>18</sup> Considering the above-mentioned points and comparing all the other methods of producing pyrexia in rabbits, we have rightly and convincingly selected PGE<sub>1</sub> administration as the method for producing pyrexia in rabbits for our study

*Murraya koenigii* leaf extract consist of alkaloids, flavonoids, tannins, glycosides and diterpenes.<sup>19</sup> The presence of flavonoids was reported in Dalbergia species and flavonoids are known to inhibit prostaglandin synthase.<sup>20</sup> Therefore, it appears that the antipyretic action of Dalbergia species may be related to the inhibition of prostaglandin synthesis in hypothalamus.<sup>21</sup> The antipyretic property of Acacia catechu may be ascribed to the presence of flavonoids.<sup>22</sup> Some of the flavonoids are predominant inhibitors of cyclooxygenase or lipo-oxygenase. Thus, flavonoids have antipyretic effects.<sup>23</sup>

The results of the present study confirm the antipyretic effect of alcoholic extract of *Murraya koenigii* against

PGE<sub>1</sub> induced elevation of body temperature in rabbits. The onset of action for *Murraya koenigii* in high doses was very fast when compared to moderate doses.

## CONCLUSION

The present study concludes that alcoholic extract of *Murraya koenigii* possess fast onset of anti-pyretic action. The probable mechanism of antipyretic action may be attributed to the presence of flavonoids. The exact mechanisms responsible for the antipyretic activity and the lead compound responsible for such action may be revealed by conducting further studies in future.

## ACKNOWLEDGEMENTS

Authors would like to thank Department of Botany, Government Degree College, Khammam and Management of Mamata Medical College for their support.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Pokala N, Sayeli V, Jayasree T. Evaluation of antipyretic activity of alcoholic extract of *Murraya koenigii* leaves in rabbits. Int J Basic Clin Pharmacol 2019;8:1577-81.