Analgesic and antipyretic activities of *Momordica charantia* Linn. fruits

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**Abstract**

Plant *Momordica charantia* Linn. belongs to family *Cucurbitaceae*. It is known as bitter gourd in English and *karela* in Hindi. Earlier claims show that the plant is used in stomachic ailments as a carminative tonic; as an antipyretic and antidiabetic agent; and in rheumatoid arthritis and gout. The fruit has been claimed to contain charantin, steroidal saponin, momordium, carbohydrates, mineral matters, ascorbic acid, alkaloids, glucosides, etc. The ethanolic extract of the fruit showed the presence of alkaloids, tannins, glycosides, steroids, proteins, and carbohydrates. The present study was carried out using acetic acid-induced writhing and tail-immersion tests in mice, while yeast-induced pyrexia in rats. The ethanolic extracts (250 and 500 mg/kg, po.) showed an analgesic and antipyretic effect, which was significantly higher than that in the control rats. The observed pharmacological activities provide the scientific basis to support traditional claims as well as explore some new and promising leads.

**Key words:** Analgesic, antipyretic, *Momordica charantia*

**INTRODUCTION**

Pain is an ill-defined, unpleasant, sensation usually evoked by an external or internal noxious stimulus. It is a warning signal and primarily protective in nature, but causes discomfort. Analgesics are the drugs that selectively relieve pain by acting on the CNS (central nervous system) or on peripheral pain mechanisms, without significantly altering consciousness. Plant *Momordica charantia* Linn., known as bitter gourd in English, belongs to family *Cucurbitaceae*. It is cultivated throughout India, Malaya, China, Tropical Africa, and America. Earlier claims showed that its bitter fruits have carminative, aphrodisiac, and anthelmintic properties, and are used in syphilis, rheumatism, troubles of spleen, and ophthalmia. It is also useful in piles, leprosy, jaundice, and also used as a vermifuge.[1] Upon a literature review, it was found that the plant contains moisture (83.2%), proteins (2.9%), fat (1.0%), carbon (9.8%), fibers (1.7%), mineral matters (1.4%), calcium, phosphorus, iron, carotene, thiamine, nicotinic acid, riboflavin, ascorbic acid (88 mg/100 g), copper, and potassium.[2] Charantin, β-sitosterol-glucoside, stigmast-5, 25-dien-3 β-O-glucoside, stigmast-7,25-dien-3 β-ol, and stigmast-7, 22,25-trien-3 β-ol are isolated from the fruit.[3] Many pharmacological properties have been reported including antioxidant,[4] adipogenesis-reducing,[5] antilipolytic,[6] hypoglycemic,[7] antidiabetic,[8] anticancer,[9] antifertility,[10] antigenotoxic,[11] antimicrobial,[12] antiviral,[13] and hepatoprotective activity.[14] However, there are no reports to our knowledge on its analgesic and antipyretic activities. Hence, the present study was undertaken to investigate the analgesic and antipyretic potential of the ethanolic and aqueous fruit extract of *M. charantia* Linn. in experimental animal models.

**MATERIALS AND METHODS**

All the ingredients and chemicals were of analytical grade and purchased from Loba Chemie Pvt. Ltd., Mumbai.

**Collection of Plant Materials**

A healthy fruit was purchased from a medicinal plant supplier, Hakimm’s Brother, Savarkundala (Gujarat) in the month of July 2009. It was identified and authenticated by Dr. A. S. Reddy, taxonomist, Bioscience Department, S. P. University, Vallabh Vidyanaagar, Gujarat, India.
Preparation of the Plant Extract
The powdered fruit was extracted with ethanol by the Soxhlet apparatus. The solvent was concentrated by evaporating ethanol using a rotary evaporator.[16] The M. charantia ethanol extract (MC-EE) was further concentrated by allowing it to stand overnight in an oven at 30°C.

Phytochemical Tests
The MC-EE was subjected to preliminary, qualitative, phytochemical investigation.[17]

Animals Used
Wistar rats, weighing 200–220 g, and Swiss albino mice, weighing 18–25 g, of either sex were procured from the animal house of the Shree Leuva Patel Trust Pharmacy Mahila College, Amreli, Gujarat, India. All the animals were kept in standard polypropylene cages under standard conditions: temperature (24±1°C), relative humidity (45–55%), and a 12:12 light:dark cycle. The animals were fed a standard rodent diet, and water was given ad libitum. The animals were allowed to acclimatize to laboratory conditions 48 h before the start of the experiment. The experimental protocol is duly approved by the institutional ethical committee (reg. no. 949/a/06/ CPCSEA).

Acute Toxicity Study
Six Wistar rats (200–220 g) and six albino mice (18–25 g) of either sex were dosed with MC-EE extracts in different concentrations and were observed for any symptoms of toxicity for 48 h as per guideline no. 425 (OECD 2001), and LD\textsubscript{50} was estimated to be >5000 mg/kg. Based on the results obtained from this study, the doses of further pharmacological studies were fixed to be 250 and 500 mg/kg.[18]

Analgescic Activities
Acetic acid-induced writhing
Mice were divided into four groups each consisting of six mice. They were starved for 18 h. The treatment regimen was as follows:
1. Group I (control): Vehicle (3 ml/kg, po.), 1% suspension of Tween-80
2. Group II (standard): Aspirin (150 mg/kg, po.)
3. Group III (test 1): Ethanolic fruit extract (500 mg/kg, po.)
4. Group IV (test 2): Ethanolic fruit extract (250 mg/kg, po.)

After half an hour, all mice received a 0.7% aqueous solution of acetic acid 10 mg/kg, ip., and writhings were counted for 10 min after the acid injection.[19]

Acetic acid-induced writhing test
\[
\text{% Inhibition} = \left( \frac{\text{Mean no. of writhing in the control group} - \text{Mean no. of writhing in the test group}}{\text{Mean no. of writhing in the control group}} \right) \times 100
\]

Tail-immersion method
Mice were divided into four groups each consisting of six mice. The treatment regimen was as follows:
1. Group I (control): Vehicle (3 ml/kg, po.), 1% suspension of Tween-80
2. Group II (standard): Pentazocine (30 mg/kg, po.)
3. Group III (test 1): Ethanolic fruit extract (500 mg/kg, po.)
4. Group IV (test 2): Ethanolic fruit extract (250 mg/kg, po.)

The distal part of the tails of the animals was immersed in hot water maintained at 55.0±1.0°C. The time taken to withdraw the tail was noted as the reaction time. A cut-off time of 10 s was maintained at 55°C to prevent tissue damage. The reaction time was checked at 0, 15, 30, 45 and 60 min, respectively, after treatment.[19]

Antipyretic Activity
Rats were divided into four groups each consisting of six rats. The test was performed in rats by injecting 10 ml/kg sc. of the 15% aqueous solution of Brewer’s yeast to induce pyrexia. The rectal temperature of each animal was taken before and 24 h after the yeast injection using a digital clinical thermometer. Animals that did not show a minimum increase of 0.7°C in the temperature 24 h after the yeast injection were discarded. The selected animals were divided into four groups and treated as follows:
1. Group I (control): Vehicle (3 ml/kg, po.), 1% suspension of Tween-80
2. Group II (standard): Paracetamol (20 mg/kg, ip.)
3. Group III (test 1): Ethanolic fruit extract (500 mg/kg, po.)
4. Group IV (test 2): Ethanolic fruit extract (250 mg/kg, po.)

The rectal temperature of each animal was again recorded at 0.5, 1, 1.5, and 2 h after treatment.[20]

Statistical Analysis
Data were subjected to statistical analysis using ANOVA, and statistical comparison was done using the Tukey–Kramer multiple comparison test. Values of P<0.01 were considered statistically significant.

RESULTS
Phytochemical Tests
The crude extract was found to be positive for the presence of alkaloids, tannins, glycosides, steroids, proteins, and carbohydrates.

Acute Toxicity Study
After 48 h of the study with different concentrations of the extract, the LD\textsubscript{50} was estimated to be >5000 mg/kg.

Effect on acetic acid writhing
The ethanolic extracts (500 and 250 mg/kg, po.) significantly reduced the acetic acid-induced writhing by 59.99% and 51.22%, respectively [Table 1].
Effect on the tail-immersion test
Ethanolic extracts (500 and 250 mg/kg, po.) induced significant protection [Table 2] in rats in tail-immersion tests, with the ethanolic extracts (500 mg/kg) being more active compared to the standard drug pentazocine (30 mg/kg, po.).

Antipyretic Effect
Both the extracts showed a marked antipyretic effect [Table 3] by causing a reduction in yeast-induced fever. The ethanolic extract (500 mg/kg) showed the effect to the same degree as paracetamol (20 mg/kg, ip.).

DISCUSSION
Several experimentally induced laboratory models were employed in evaluating the analgesic and antipyretic activities of ethanolic extracts of *M. charantia*. It is necessary to apply tests which differ with respect to stimulus quality, intensity, and duration, to obtain as complete a picture as possible of the analgesic properties of a substance using behavioural nociceptive tests. The results obtained showed that the ethanolic extracts possess a significant analgesic effect on the various pain models used. A significant inhibitory effect was shown by both the extracts in the writhing test (a test useful for evaluating mild analgesic, nonsteroidal, anti-inflammatory agents). This suggests that the analgesic effect of the extract may be peripherally mediated. The extracts also showed a significant effect in the tail-immersion tests (centrally acting analgesic drugs elevate the pain threshold of animals toward heat and pressure). The effect of the extracts on this pain model indicates that it might be centrally acting.[20]

Table 1: Effect of ethanolic extracts of the *Momordica charantia* fruit in acetic acid-induced writhing in mice

| Group | Treatment               | Writhing count | Inhibition (%) |
|-------|-------------------------|----------------|----------------|
| I     | Control (3 ml/kg, po.)  | 35.69±1.32     | –              |
| II    | Aspirin (150 mg/kg, po.)| 09.65±0.13*    | 72.96          |
| III   | Ethanolic extract (500 mg/kg, po.) | 14.28±0.29* | 59.99          |
| IV    | Ethanolic extract (250 mg/kg, po.) | 17.41±0.20* | 51.22          |

Values are expressed as mean±SEM (standard error mean); *P<0.01 when compared to control rats

Table 2: Effect of ethanolic and aqueous extracts of the *Plectranthus amboinicus* leaf on tail-immersion tests in mice

| Group | Treatment               | Reaction time (s) | Latency (%) |
|-------|-------------------------|-------------------|-------------|
| I     | Control (3 ml/kg, po.)  | 2.73±0.63         | –           |
| II    | Pentazocine (30 mg/kg, po.) | 4.85±0.23* | 77.66       |
| III   | Ethanolic extract (500 mg/kg, po.) | 4.02±0.62* | 47.25       |
| IV    | Ethanolic extract (250 mg/kg, po.) | 3.76±0.46* | 37.77       |

Values are expressed as mean±SEM (standard error mean); *P<0.01 when compared to control rats

Table 3: Effect of ethanolic and aqueous extracts of the *Plectranthus amboinicus* leaf on yeast-induced pyrexia in rats

| Group | Treatment               | Rectal temperature (°C) | –24 h | 0 h | 0.5 h | 1 h | 1.5 h | 2 h |
|-------|-------------------------|--------------------------|-------|-----|-------|-----|-------|-----|
| I     | Control (3 ml/kg, po.)  |                          | 37.4±0.1 | 39.2±0.2 | 39.4±0.2 | 39.3±0.4 | 38.7±0.4 | 38.5±0.1 |
| II    | Paracetamol (20 mg/kg, ip.) |                         | 37.6±0.3 | 39.6±0.1 | 37.3±0.4** | 36.2±0.2** | 36.2±0.3** | 36.1±0.3** |
| III   | Ethanolic extract (500 mg/kg, po.) |                   | 37.8±0.1 | 40.1±0.3 | 38.6±0.2* | 37.7±0.2** | 37.5±0.1** | 37.2±0.3** |
| IV    | Ethanolic extract (250 mg/kg, po.) |                     | 37.3±0.2 | 38.8±0.2 | 37.3±0.6* | 37.2±0.2** | 37.1±0.5** | 37.1±0.2* |

Values are expressed as mean±SEM (standard error mean); *P<0.05 and **P<0.01 when compared to control rats

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