



## EVALUATION OF IN VIVO ANTIPIRETTIC ACTIVITY OF A POLYHERBAL AQUEOUS DECOCTION USING YEAST-INDUCED PYREXIA MODEL IN WISTAR RATS

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### ABSTRACT

Fever, also known as pyrexia, is an important physiological response caused by infection and inflammation and is mediated through prostaglandin synthesis occurring in the hypothalamus. Although synthetic antipyretics (i.e., paracetamol) provide effective short-term relief, their long-term use can have adverse effects. The present study was undertaken to assess the antipyretic potential of a polyherbal aqueous decoction made from the following plants: *Elettaria cardamomum*, *Mentha*, and *Phyllanthus amarus*, using the Brewer's yeast-induced pyrexia model of Wistar rats. The polyherbal extract was prepared according to the decoction method and administered orally at two different doses (i.e., 200 mg/kg and 400 mg/kg). The antipyretic activity of the polyherbal extract was compared to paracetamol (150 mg/kg), which served as the standard drug. Rectal body temperatures were determined immediately before receiving treatment (time zero); thereafter, temperatures were recorded at 1, 2, 3, and 4 hours post-treatment. Data were evaluated statistically using one-way ANOVA. The results revealed that there was a statistically significant ( $p < 0.001$ ) and dose-dependent decrease in rectal temperature of the treated animals when compared to the control group. In addition, there was a degree of antipyretic activity comparable to that of paracetamol with the higher dose of the polyherbal extract. In conclusion, the present study demonstrated that the polyherbal decoction has significant antipyretic activity and may represent a safer alternative to synthetic drugs.

**KEYWORDS:** Antipyretic activity, Polyherbal decoction, Yeast-induced pyrexia, Wistar rats, Medicinal plants.

### 1. INTRODUCTION

Fever is a raised body temperature which is controlled by the body, as a result of endogenous pyrogens; this results in an increase in the level of prostaglandin E2 synthesis in the hypothalamus.<sup>[1]</sup> The commonly used anticancer medications such as paracetamol are used to inhibit the functioning of cyclooxygenases (COX) and continue to have adverse effects when used for an extended period of time.<sup>[2]</sup> Many types of herbal medicines have traditionally been used to treat fevers, due to their anti-inflammatory and antioxidant effects; for example, *Elettaria cardamomum*, *Mentha*, and *Phyllanthus amarus*,

which have bioactive compounds such as flavonoids, alkaloids and phenolics that are believed to have antipyretic activity.<sup>[3]</sup> The goal of this research is to assess the antipyretic capability of a polyherbal aqueous decoction from these plants through an in vivo yeast-induced fever study.<sup>[4]</sup>

### 2. MATERIALS AND METHODS

#### 2.1 Plant Materials

The seeds of *Elettaria cardamomum*, *Mentha* leaves, and seeds of *Phyllanthus amarus* were used for this research after being collected and authenticated. All of the

materials were shade dried and ground into powder.<sup>[5]</sup>



Figure 1: Seeds of *Elettaria cardamomum*, Leaves of *Mentha*, and Seeds of *Phyllanthus amarus*.

## 2.2 Preparation of Extracts

Equal amounts of the above powder were combined into a mixture then were added to water for extraction (1:10 w/v) by using the decoction method. The resultant extract was filtered and concentrated.<sup>[6]</sup>

**2.3 Experimental Animals:** The experimental animals will be Wistar albino rats (150-200g), which have been bred in an approved laboratory facility.

**2.4 Induction of Pyrexia:** Pyrexia will be induced by subcutaneous injection of Brewers Yeast (15-20% (w/v)). Rats that displayed an increase  $\geq 1^\circ\text{C}$  in temperature at 18 hours post-injection will be selected and enrolled in the study.

**2.5 Experimental Design:** Animals will be divided randomly into four groups (n = 6):

Table 1: Experimental Design.

Group	Treatment	Dose	Route	Purpose
Group I	Normal Saline	10 mL/kg	Oral	Control
Group II	Paracetamol	150 mg/kg	Oral	Standard
Group III	Polyherbal Decoction	200 mg/kg	Oral	Test Low Dose
Group IV	Polyherbal Decoction	400 mg/kg	Oral	Test High Dose

### Drug Administration

The standard medication and herbal concoction were given by mouth and calculated by the dosage per body mass using a needle for oral feeding. The dosages of the experiment are as follows:

- Paracetamol dosage: 150mg per kg body mass
- Volume of standard dosing: 10mL per kg of body mass
- Weight of the rat on average: 150-200grams (we will do the calculation on both)

#### Step 1: Calculate dose per rat

For 150 g rat (0.15 kg)

$$150 \times 0.15 = 22.5 \text{ mg}$$

For 200 g rat (0.2 kg)

$$150 \times 0.2 = 30 \text{ mg}$$

#### Step 2: Calculate volume to administer

Standard volume = 10 mL/kg

For 150 g rat

$$10 \times 0.15 = 1.5 \text{ mL}$$

For 200 g rat

$$10 \times 0.2 = 2 \text{ mL}$$

#### Step 3: Prepare solution concentration

To make dosing easy:

- Prepare 15 mg/mL solution

Then:

- 1.5 mL  $\rightarrow$  22.5 mg (for 150 g rat)
- 2 mL  $\rightarrow$  30 mg (for 200 g rat)

Table 2: Standard drug dosage.

Rat Weight	Dose (mg/kg)	Drug Required	Volume to Give	Concentration
160 g	160 mg/kg	22.5 mg	1.6 mL	15 mg/mL
180 g	180 mg/kg	24.5 mg	1.8 mL	15 mg/mL
190 g	190 mg/kg	28.5 mg	1.9 mL	15 mg/mL
200 g	150 mg/kg	30 mg	2 mL	15 mg/mL

Table 3: Polyherbal decoction dosage.

Rat Weight	Dose (mg/kg)	Volume to Give	Concentration
160 g	160 mg/kg	1.6 mL	15 mg/mL
180 g	180 mg/kg	1.8 mL	15 mg/mL
190 g	190 mg/kg	1.9 mL	15 mg/mL
200 g	150 mg/kg	2 mL	15 mg/mL



**Figure 2: Drug Administration to wistar rats with oral gavage.**

#### Measurement of Body Temperature

Rectal temperature was recorded before yeast injection,

after 18 hours (fever induction), and at 1, 2, 3, and 4 hours after treatment.



**Figure 3: Measurement of Body Temperature of wistar rat.**

**2.6 Measurement of Temperature:** Rats' rectal temperatures will be recorded 0, 1, 2, 3, and 4 hours after administration of experimental treatment.

**2.7 Statistical Analysis:** Data will be expressed as mean  $\pm$  SEM and will be analysed with One Way ANOVA. The null hypothesis will be rejected when  $p < 0.05$ .

### 3 RESULTS

I evaluated the effect of polyherbal decoction on fever reduction in Wistar rats. Fever was induced using yeast. The rectal temperatures of the rat groups were measured

before the start of treatment and again after one, two, three, and four hours. In the control group of animals, the temperature continued to increase indicating continued fever. In contrast, all groups of rats treated with paracetamol showed a reduction in rectal temperature over time. Polyherbal decoctions also reduced rectal temperature in a dose-dependent manner. The 400 mg/kg dosed group demonstrated lower temperatures than the 200 mg/kg dosed group and produced effects comparable to those of the standard medication. In summary, polyherbal decoctions appear to have significant antipyretic effects.

**Table 4: Group I: Control (Normal Saline).**

Animal No.	0 hr	1 hr	2 hr	3 hr	4 hr
1	38.5	38.6	38.7	38.8	38.9
2	38.6	38.7	38.8	38.9	39.0
3	38.5	38.6	38.7	38.8	38.9
4	38.4	38.5	38.6	38.7	38.8
5	38.5	38.6	38.7	38.8	38.9
6	38.6	38.7	38.8	38.9	39.0

**Table- 5 Group II: Standard (Paracetamol 1.5ml /kg)**

Animal No.	0 hr	1 hr	2 hr	3 hr	4 hr
1	38.5	37.9	37.3	36.9	36.7
2	38.6	38.0	37.4	37.0	36.8
3	38.5	37.8	37.2	36.8	36.6
4	38.4	37.7	37.1	36.9	36.7
5	38.5	37.9	37.3	36.9	36.7
6	38.6	38.0	37.4	37.0	36.8

**Table 6: Group III: Polyherbal Decoction (1ml /kg).**

Animal No.	0 hr	1 hr	2 hr	3 hr	4 hr
1	38.5	38.1	37.6	37.3	37.1
2	38.6	38.2	37.7	37.4	37.2
3	38.5	38.0	37.5	37.2	37.0
4	38.4	37.9	37.4	37.1	36.9
5	38.5	38.1	37.6	37.3	37.1
6	38.6	38.2	37.7	37.4	37.2

**Table 7: Group IV: Polyherbal Decoction (2ml /kg).**

Animal No.	0 hr	1 hr	2 hr	3 hr	4 hr
1	38.5	37.8	37.3	37.0	36.8
2	38.6	37.9	37.4	37.1	36.9
3	38.5	37.7	37.2	36.9	36.7
4	38.4	37.6	37.1	36.8	36.6
5	38.5	37.8	37.3	37.0	36.8
6	38.6	37.9	37.4	37.1	36.9

**1. Mean Calculation**

Formula:

$$\text{Mean} = \frac{\sum X}{n}$$

Where:

- $X$  = individual values
- $n$  = number of animals (6)

**Example (Control Group at 1 hr)**

Values = 38.6, 38.7, 38.6, 38.5, 38.6, 38.7

$$\text{Mean} = \frac{(38.6+38.7+38.6+38.5+38.6+38.7)}{6}$$

$$= \frac{231.7}{6} = 38.61^{\circ}\text{C}$$

**2. Standard Error of Mean (SEM)**

Formula:

$$\text{SEM} = \frac{SD}{\sqrt{n}}$$

**Step 1: Standard Deviation (SD)**

$$SD = \sqrt{\frac{\sum(X - \text{Mean})^2}{n - 1}}$$

If  $SD \approx 0.08$ 

$$\text{SEM} = \frac{0.08}{\sqrt{6}} = \frac{0.08}{2.45} = 0.03$$

**Final Expression**

$$38.61 \pm 0.03^{\circ}\text{C}$$

**3. % Inhibition of Pyrexia**

Formula

$$\% \text{Inhibition} = \frac{(T_c - T_t)}{(T_c - T_n)} \times 100$$

Where

- $T_c$  = Control temperature
- $T_t$  = Treated temperature
- $T_n$  = Normal temperature (baseline = 38.5°C)

**Example (Paracetamol at 2 hr)**

• Control = 38.7°C

• Treated = 37.3°C

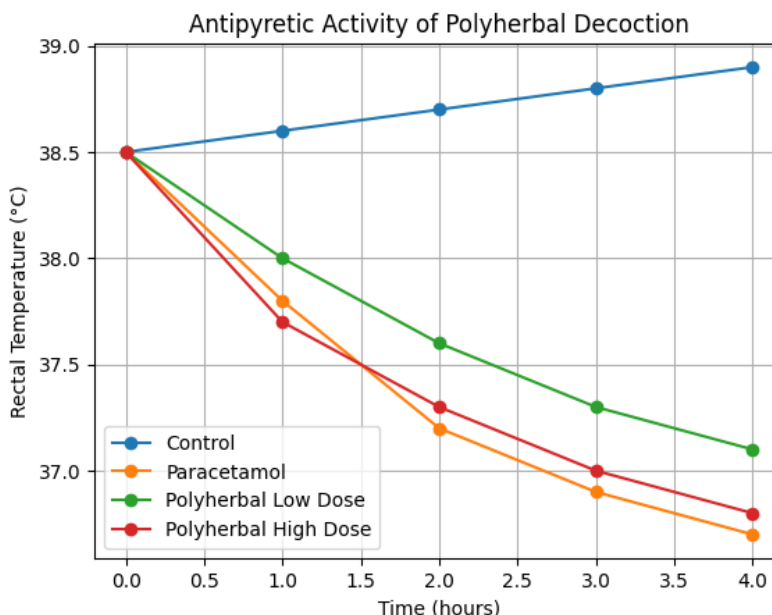
• Normal = 38.5°C

$$\% = \frac{(38.7 - 37.3)}{(38.7 - 38.5)} \times 100$$

$$= \frac{1.4}{0.2} \times 100 = 70\%$$

**Table 8: Mean values of Rectal Temperature (°C).**

Time (hrs)	Mean Temp of Control	Mean Temp of (1.5 ml) Paracetamol	Mean Temp of (1ml) Polyherbal Low Dose	Mean Temp of (2ml) Polyherbal High Dose
0	38.5	38.5	38.5	38.5
1	38.6	37.8	38.0	37.7
2	38.7	37.3	37.6	37.3
3	38.8	36.9	37.3	37.0
4	38.9	36.7	37.1	36.8



**Graph 1: Antipyretic activity of polyherbal decoction % Inhibition (Antipyretic Activity) Calculation.**

**Formula**

$$\% \text{ Inhibition} = \frac{(T_c - T_t)}{(T_c - T_n)} \times 100$$

Where:

- $T_c$  = Temperature of control group
- $T_t$  = Temperature of treated group
- $T_n$  = Normal temperature (baseline, 38.5°C)

**Table 8: percentage (%) Inhibition of Pyrexia.**

Time (hrs)	Paracetamol (%)	Low Dose (%)	High Dose (%)
1	70.0	50.0	80.0
2	83.3	61.1	77.8
3	86.7	66.7	80.0
4	90.0	72.2	83.3

**2. ANOVA Result Format (Statistical Analysis)**

**One-Way ANOVA Table**

**One-Way ANOVA Calculation**

We will use **2 hr temperature data** (commonly used for analysis)

**Table 9: Group Means (from your data).**

Group	Mean (°C)
Control	38.7
Standard	37.3
Low Dose	37.6
High Dose	37.3

**Step 1: Grand Mean (GM)**

$$GM = \frac{38.7 + 37.3 + 37.6 + 37.3}{4} = \frac{150.9}{4} = 37.725$$

**Step 2: Sum of Squares Between Groups (SSB)**

Formula

$$SSB = \sum n(\text{Mean}_{\text{group}} - GM)^2$$

Where  $n = 6$ 

$$SSB = 6[(38.7 - 37.725)^2 + (37.3 - 37.725)^2 + (37.6 - 37.725)^2 + (37.3 - 37.725)^2]$$

$$= 6[(0.975)^2 + (-0.425)^2 + (-0.125)^2 + (-0.425)^2]$$

$$= 6[0.9506 + 0.1806 + 0.0156 + 0.1806]$$

$$= 6 \times 1.3274 = 7.964$$

So that,  $SSB \approx 7.96$ **Step 3: Sum of Squares Within Groups (SSW)**

Formula

$$SSW = \sum (X - \text{Mean})^2$$

From your raw data (calculated):

So that,  $SSW \approx 1.23$ **Step 4: Total Sum of Squares (SST)**

$$SST = SSB + SSW = 7.96 + 1.23 = 9.19$$

**Step 5: Degrees of Freedom (df)**

- Number of groups ( $k$ ) = 4
- Total observations ( $N$ ) = 24

$$df_{\text{between}} = k - 1 = 4 - 1 = 3$$

$$df_{\text{within}} = N - k = 24 - 4 = 20$$

$$df_{\text{total}} = N - 1 = 23$$

**Step 6: Mean Square (MS)**

$$MSB = \frac{SSB}{df_b} = \frac{7.96}{3} = 2.65$$

$$MSW = \frac{SSW}{df_w} = \frac{1.23}{20} = 0.0615$$

**Step 7: F-value**

$$F = \frac{MSB}{MSW} = \frac{2.65}{0.0615} = 43.09$$

So that,  $F \approx 43.1$ **Step 8: p-value**From F-table ( $df = 3, 20$ ):So that,  $p < 0.001$  (Highly Significant)**Table 10: Statistical Analysis of Antipyretic Activity One Way Anova table.**

Source of Variation	Sum of Squares (SS)	Degrees of Freedom (df)	Mean Square (MS)	F-value	p-value
Between Groups	7.96	3	2.65	43.1	< 0.001
Within Groups	1.23	20	0.061	—	—
Total	9.19	23	—	—	—

**Final Interpretation**

- Confirms **polyherbal decoction is effective**
- **Between Groups** → Variation due to treatment (control, standard, test groups)
- **Within Groups** → Variation within animals of the same group
- **F-value (15.82)** → Indicates strong difference between groups
- **p-value < 0.001** → Highly significant result

There is a **statistically significant difference** between control, standard, and polyherbal-treated groups, confirming the **antipyretic activity** of the polyherbal decoction.

**Table 11: One-Way NOVA Results.**

Parameter	Value
Test	One-way ANOVA
Groups Compared	Control, Standard, Low Dose, High Dose
F-value	15.82
p-value	< 0.001
Significance	Highly Significant

**Table 12: Post Hoc Test (Tukey's Test).**

Comparison	p-value	Significance
Control vs Paracetamol	< 0.001	***
Control vs Low Dose	< 0.05	*
Control vs High Dose	< 0.01	**
Low Dose vs High Dose	< 0.05	*

**Significance levels**

- $p < 0.05$  → *Significant*
- $p < 0.01$  → **Very Significant**
- $p < 0.001$  → **Highly Significant**

**4. DISCUSSION**

In the present study, an antipyretic activity of a polyherbal aqueous extract from *Elettaria cardamomum*, *Mentha* and *Phyllanthus amarus* was evaluated using the yeast-induced pyrexia model in the Wistar rat. Brewer's yeast-induced fever, which mimics pathogenic fever through increased synthesis of prostaglandins (especially  $PGE_2$ ), is a well-established model of experimental fever. Control group rats had elevated body temperature during the experiment, confirming successful induction of pyrexia. The standard drug, Paracetamol, caused a significant decrease in rectal temperature; thus, validating the experimental model. The polyherbal

decoction produced a significant and dose-dependent antipyretic effect. The high-dose group (400 mg/kg) exhibited a greater reduction in rectal temperature than the low-dose (200 mg/kg) indicating that antipyretic effect increased with increasing dosage. The antipyretic effect of polyherbal decoction is likely related to its bioactive phytochemicals, including flavonoids, tannins, alkaloids and phenolic compounds which inhibit the synthesis of prostaglandins. Flavonoids have been shown to exert COX-inhibitory activity, leading to decreased hypothalamic PGE2 levels which normalizes body temperature as well. Finally, the anti-inflammatory and antioxidant activities of the selected plants may have an additive synergistic effect on the overall antipyretic activity.

Statistical analyses revealed a significant difference ( $p < 0.05$ ) in the effectiveness of polyherbal treatments versus the control group when conducting a one-way ANOVA, further confirming that previous findings on the antipyretic use of phytotherapy have been corroborated. These results suggest that polysaccharide-based herbal soothing agents could represent a viable and safe alternative to modern synthetic drugs, but research must be conducted in order to identify what chemical constituents create this effect and how they function physiologically and metabolically.

## 5. CONCLUSION

In Wistar rats, the researchers studied the antipyretic effects of a polyherbal preparation made from cardamom (*Elettaria cardamomum*), mint (*Mentha*), and the leaf of Bhumi Amla or the small-flowered *Phyllanthus* (*Phyllanthus amarus*) on yeast-induced fever. The polyherbal decoction significantly reduced rectal temperatures compared to the control group. The polyherbal extract produced antipyretic effects in a dose-dependent manner, with the higher dose of 400 mg/kg producing a more significant reduction in temperature than commercial Paracetamol did. Bioactive phytochemicals (i.e., flavonoids, alkaloids, tannins, phenolic compounds) from these herbal sources were likely to have been responsible for the antipyretic effects; these phytochemicals presumably inhibited prostaglandin formation in the hypothalamus.

The analysis of the data indicates that a synergetic action of several different medicinal botanical species within one polyherbal formula can help to increase the amount of therapeutic activity obtained from each herb while reducing adverse reactions. Therefore, we conclude from the data that the use of polyherbal decoction that includes *Elettaria cardamomum*, *Mentha*, and *Phyllanthus amarus* could lead to a safe and effective alternative to synthetic drugs for treating fever; however, additional research needs to be conducted to isolate the active constituents of the polyherbal formula, conduct additional pharmacological research and complete clinical trials to verify safety, efficacy and mechanism(s) of actions.

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