Ind. J. Pharm. Edu. Res., 2025; 59(1):252-263.
https://www.ijper.org

Original Article

Evaluation of Antipyretic and Antioxidant Activities of Ten Indigenous Medicinal Plants of Tirtajaya, Karawang Regency, West Java, Indonesia

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ABSTRACT

Aim: This research aimed to explore the antipyretic and antioxidant activity of infusions of *Chromolaena odorata* (COI), *Abelmoschus manihot* (AMI), *Annona muricata* (AMCI), *Allium ascalonicum* (AAI), *Carica papaya* (CPI), *Tamarindus indica* (TII), *Zingiber officinale* (ZOI), *Abrus precatorius* (API), *Momordica charantia* (MCI) and *Strobilanthes crispus* (SCI). **Materials and Methods:** The antipyretic activity of plant infusions was tested using a peptone-induced rat model. The male rat used were divided into 32 groups for each test. Each group consisted of four rats, including a negative control, a positive control (paracetamol 150 mg/kg) and groups COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI, each administered doses of 100, 200 and 400 mg/kg. Initial rectal temperature was recorded using a rectal thermometer at a depth of 1.5 cm in the rat rectum. Fever induction was confirmed by a temperature rise of more than 0.5°C. After drug administration, rectal temperature was recorded periodically at 1, 2, 3 and 4 hr. Furthermore, antioxidant activity was tested using the DPPH method. **Results:** The results showed that administration of COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI was able to significantly reduce the rectal temperature of febrile rat which depended on dose and time. The antioxidant test results indicated that AAI exhibited very strong antioxidant intensity, while AMCI, CPI, ZOI, API and SCI showed strong antioxidant intensity, COI and MCI had medium antioxidant intensity, AMI had weak antioxidant intensity and TII displayed very weak antioxidant intensity. **Conclusion:** Based on the results, it can be concluded that COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI exhibit antipyretic and antioxidant activity.

Keywords: Antipyretic, Antioxidant, Medicinal plants, Peptone-induced rat model, DPPH.

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Received: 08-02-2024;
Revised: 18-07-2024;
Accepted: 07-10-2024.

INTRODUCTION

Fever is a common medical sign that often occurs due to infection, tissue damage, inflammation, malignancy, graft rejection and other inflammatory disease conditions, leading to an elevation in body temperature beyond the normal range of 36.5-37.5°C.[1] This natural response creates an environment conducive to the body's defense mechanisms, aiding in tissue repair and rendering it inhospitable for infectious agents. Infected or damaged tissue produces different inflammatory mediators such as Interleukin (IL-1β), Interferon (IFN-α and β), Tumor Necrosis Factor (TNF-α), thereby increasing the synthesis of Prostaglandin E (PGE-2) in the hypothalamus.[2] Additionally, PGE-2 binds to the PGE-2 type 3 receptor on glial cells, leading to the generation and release of cyclic Adenosine Monophosphate (cAMP). This serves as a neurotransmitter and simultaneously triggers thermosensitive neurons, elevating the thermostatic set point from normothermic levels to induce fever.[3] Subsequently, when having a fever, sufferers often feel discomfort such as pain (myalgia), chills, anorexia, inability to concentrate, increased muscle tone and lethargy,[4] thereby drugs are needed in order to reduce fever and its effects.[5]

Presently, nearly all antipyretic medications, including Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), function by inhibiting the synthesis of PGE-2 through irreversible blocking of the Cyclooxygenase-2 (COX-2) enzyme with high selectivity.

DOI: 10.5530/ijper.20256381

This mechanism can lead to toxicity in brain cortex, glomeruli, liver cells and heart muscle.[6,7] Moreover, NSAIDs also cannot neutralize the side effects of inflammation in the form of excessive production of free radicals during fever. Hence, it is important to explore alternative medicines with safer and more effective antipyretic and antioxidant effects, particularly derived from natural products, which are necessary to mitigate side effects.[8,9] Globally, there are at least 80% of people depend on herbal medicine and food supplements for their basic health, which is a very significant increase over the last three decades.[10,11] This is inseparable from tribes and indigenous peoples who still have a strong belief in medicinal plants to cure illnesses. In general, each ethnic group has extensive ethnomedicinal knowledge to identify medicinal plants and also has unique and different techniques for using these medicinal plants for the treatment of various diseases.[12] Subsequently, Indonesia is one country where tribes and traditional communities continue to rely on medicinal plants for various health needs.[13,14]

Indonesia is known to have the second largest forest biodiversity in the world, with twenty-eight thousand plant species, of which two thousand five hundred species are included as medicinal plants.[15,16] These diverse medicinal plant species are distributed across different provinces, including Tirtajaya, Karawang Regency, West Java, Indonesia. Traditionally, people in Tirtajaya often use medicinal plants from generation to generation to treat various diseases, one of which is to treat fever. Ten types of plants are often used by local people to treat fever, including balakacida (*Chromolaena odorata*), mustajab (*Abelmoschus manihot*), soursop (*Annona muricata*), shallots (*Allium ascalonicum*), papaya (*Carica papaya*), tamarind (*Tamarindus indica*), ginger (*Zingiber officinale*), saga (*Abrus precatorius*), bitter melon (*Momordica charantia*) and kejibeling (*Strobilanthes crispus*). The medicinal plants are typically utilized by boiling them and consuming the resulting infusion or boiled water.[17] Therefore, this research aimed to evaluate the antipyretic activity *in vivo* in the rat model of peptone-induced fever and the antioxidant activity *in vitro* in the DPPH model from infusions of ten medicinal plants originating from Tirtajaya, Karawang Regency, West Java, Indonesia.

MATERIALS AND METHODS

Research area

Tirtajaya, situated in Karawang Regency, West Java, Indonesia, is positioned 8 km from the north coast of Java Island. Covering an area of 92.25 km², it consists of land, rice fields and pond areas. The population of Tirtajaya is 70,002, comprising 34,940 men and 35,062 women. Additionally, its average height is 3 meters above sea level. Meanwhile, the maximum average air temperature is 27°C. Tirtajaya is positioned between 06°3′39″ S latitude and 107°17′18″E longitude. It experiences a humid tropical climate and is predominantly inhabited by Sundanese, constituting 98% of the population, with the remaining 2% representing other ethnic groups. The research area location map is presented in Figure 1.

Data collection

An extensive field survey was conducted to obtain information about various plants used as fever treatments by local communities in the Tirtajaya Region, Karawang, West Java, Indonesia. To compile information about these plants, the research conducted multiple field visits spanning from January to December 2022. During the field survey, ethnomedicinal information was collected from local communities in their local language (Sundanese) through direct interviews and discussions.

Botanical identification

After obtaining information about different plants utilized by the Tirtajaya community for fever treatment, the research proceeded by analyzing these plants at the UPT. Herbal Materia Medica Batu Laboratory, East Java, Indonesia (No. 074/764/102.20-A/2022).

Chemicals and drugs

Paracetamol, ascorbic acid (Sigma Chemical Company, USA), 1,1, Dipheny-2-Picrylhydrazyl (DPPH), aquadest, zinc powder, magnesium powder, ferric chloride, gelatin, pulvis gummi arabicum and peptone (EMSURE® ACS Merck, Darmstadt, Germany) of analytical grade.

Sample collection and plant extraction

A total of 5 kg of each fresh leaves of *C. odorata, A. manihot, A. muricata, A. ascalonicum, C. papaya, T. indica, Z. officinale, A. precatorius, M. charantia* and *S. crispus* were obtained in January 2023 from Tirtajaya, Karawang Regency, West Java, Indonesia. The leaves obtained were cleaned and taken to the Pharmacognosy Laboratory at Universitas Buana Perjuangan Karawang, for the extraction process. In this research, the extraction method used was the infusion method. The infusion was prepared by weighing 100 g of each plant leaves simplicia, placing it in the infusion pot, adding 1000 mL of distilled water and heating at 90°C for 15 min. Furthermore, the filtering process was carried out using filter paper and filled to 1000 mL. The infusion obtained was frozen using a deep freezer with a temperature of -50°C for 2 days and dried using a freeze dryer with a vacuum pressure of 0.250 mbar and a chamber temperature of -50°C for 2x48 hr.[18] The percentage yield of the extracts was determined using the following formula:

$$\text{Yield (\%)} = \frac{\text{Extract dried weight}}{\text{Simplicia weight}} x\ 100\%$$

Phytochemical screening

The phytochemical screening was performed to determine the presence of secondary metabolites such as flavonoids, polyphenols, saponins and tannins.

A

B

Figure 1: Location of the research area. A) Map of West Java, Indonesia, B) Map of Tirtajaya Region, Karawang, West Java, Indonesia.

Experimental animals

In this research, a total of 128 male Wistar rats weighing 150 to 250 g were used for antipyretic testing. The rats were obtained from Animal House, CV. Mitra Putra Animal, Bandung, Indonesia and well maintained at the Pharmacology Laboratory, Universitas Buana Perjuangan Karawang, under 12 hr light and dark cycle conditions, as well as given free access to standard pellets and water *ad libitum*. The rats were placed in plastic cages with softwood shavings.

Protocol for antipyretic activity

In this research, testing of antipyretic activity was carried out using a rat model of peptone-induced fever. Subsequently, rat were randomly into 32 groups with each group consisting of four. Group 1 acted as a negative control which was given 1%w/v PGA suspension and group 2 as a positive control was given a standard drug (paracetamol) at a dose of 150 mg/kg. Meanwhile, this research provided treatment using COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI in groups 3-32 with various doses, namely 100, 200 and 400 mg/kg respectively orally. Before experimenting, measurements of the initial rectal temperature were carried out using a rectal thermometer with a depth of 1.5 cm in the rectum of each rat. Furthermore, 0.5 mL of peptone (5%w/v) in aqua pro injection was injected intra-peritoneally into each experimental mouse. Fever induction was confirmed by increasing the temperature of the rat by more than 0.5°C.[19] The rectal temperature of the rat was measured again periodically at 1, 2, 3 and 4 hr after administering the plant infusion. The percentage reduction in fever was calculated using the following formula:

$$\% \text{ Inhibition} = \frac{Z - Xn}{Z - N} \; x \; 100\%$$

Where,

Z: rectal temperature of rat after fever induction.

Xn: rectal temperature of rat at 1, 2, 3 and 4 hr after administration of plant infusion.

N: rectal temperature of rat before fever induction (normal temperature).

Protocol for antioxidant activity

In this research, antioxidant activity testing was carried out using the 1,1-Diphenyl-2-Picrylhydrazyl (DPPH) method.[20] A total of 5 mg DPPH was dissolved in 100 mL methanol to obtain a stock solution with a concentration of 50 µg/mL. Furthermore, 250 mg each of COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI were dissolved in 25 mL of methanol, after which dilution was carried out to obtain various test concentrations including 25, 50, 100, 200 and 400 µg/mL, as well as 2 mL of each solution, was mixed with 2 mL of DPPH stock solution until homogeneous and incubated at 30°C for 30 min. Determination of antioxidant activity was carried out using a UV-Vis spectrophotometer at a wavelength of 515.50 nanometers and repeated three times. On the other hand, ascorbic acid with various concentrations (2, 4, 6, 8 and 10 µg/mL) was used as a standard drug. The % of DPPH radical scavenging activity was calculated using the formula below:

$$\text{Inhibition rate (\%)} = \frac{Db - Ds}{Db} \text{ x } 100\%$$

Where:

Db= absorbance of the blank.

Ds= absorbance of the sample.

Statistical analysis

The results are presented in the form of mean±SEM with $p<0.05$ considered significantly different. Furthermore, statistical analysis was carried out using a one-way Analysis of Variance (ANOVA) test and continued with a *post hoc* Tukey test using GraphPad Prism version 9.

RESULTS

The yield of the extract

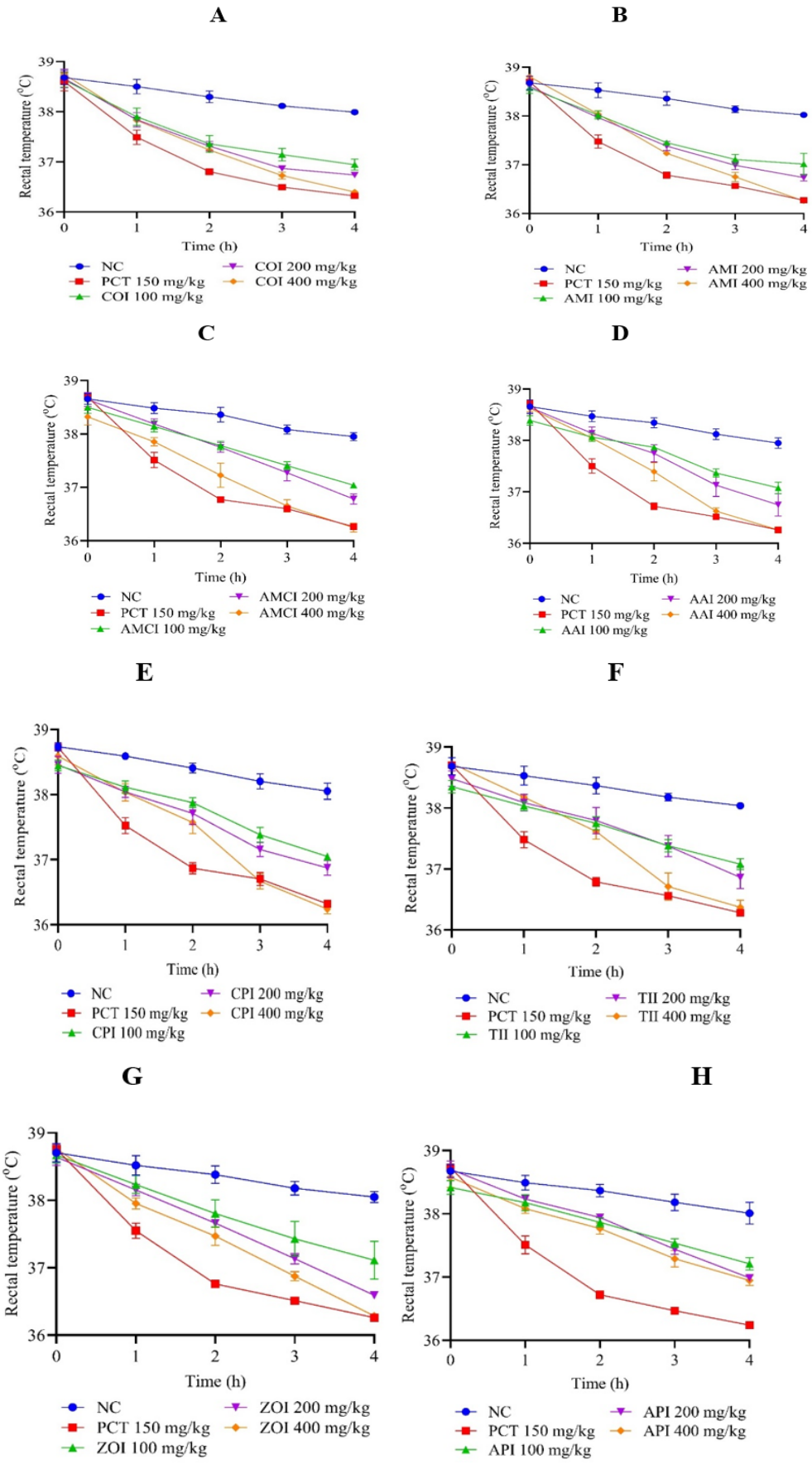
According to Table 1, AAI showed the highest yield percentage with an actual yield of 31.52 g (31.52%).

Phytochemical screening

The phytochemical screening of COI, AMI, AMCI, CPI, TII, ZOI, API, MCI and SCI revealed the presence of chemical constituents such as, flavonoids, phenolics, saponins and tannins, whereas AAI contained flavonoids, phenolics and tannins (Table 2).

Antipyretic activity

In this research, the potential antipyretic effect of ten medicinal plants originating from Tirtajaya was carried out using a rats model of peptone-induced fever. These medicinal plants are administered orally in the form of infusions (COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI) with various doses, respectively 100, 200 and 400 mg/kg. Additionally, paracetamol at a dose of 150 mg/kg was used as a positive control. The rectal temperature of the rats was recorded immediately at 0 hr, after 45 min, all rats injected with peptone experienced fever with rectal temperatures ranging from 38.59±0.12 to 38.72±0.06°C. Moreover, this research proceeded to monitor the rectal temperature of rats at 1, 2, 3 and 4 hr following the administration of the plant infusion. The results showed that COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI at various doses (100, 200 and 400 mg/kg) were able to reduce the rectal temperature of peptone-induced fever rats significant (Figure 2). The results also showed that there was a significant percentage of fever inhibition in the treatment group given COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI when compared with the Negative


A
Rectal temperature (°C)
Time (h)
NC
PCT 150 mg/kg
COI 100 mg/kg
COI 200 mg/kg
COI 400 mg/kg
B
Rectal temperature (°C)
Time (h)
NC
PCT 150 mg/kg
AMI 100 mg/kg
AMI 200 mg/kg
AMI 400 mg/kg
C
Rectal temperature (°C)
Time (h)
NC
PCT 150 mg/kg
AMCI 100 mg/kg
AMCI 200 mg/kg
AMCI 400 mg/kg
D
Rectal temperature (°C)
Time (h)
NC
PCT 150 mg/kg
AAI 100 mg/kg
AAI 200 mg/kg
AAI 400 mg/kg
E
Rectal temperature (°C)
Time (h)
NC
PCT 150 mg/kg
CPI 100 mg/kg
CPI 200 mg/kg
CPI 400 mg/kg
F
Rectal temperature (°C)
Time (h)
NC
PCT 150 mg/kg
TII 100 mg/kg
TII 200 mg/kg
TII 400 mg/kg
G
Rectal temperature (°C)
Time (h)
NC
PCT 150 mg/kg
ZOI 100 mg/kg
ZOI 200 mg/kg
ZOI 400 mg/kg
H
Rectal temperature (°C)
Time (h)
NC
PCT 150 mg/kg
API 100 mg/kg
API 200 mg/kg
API 400 mg/kg

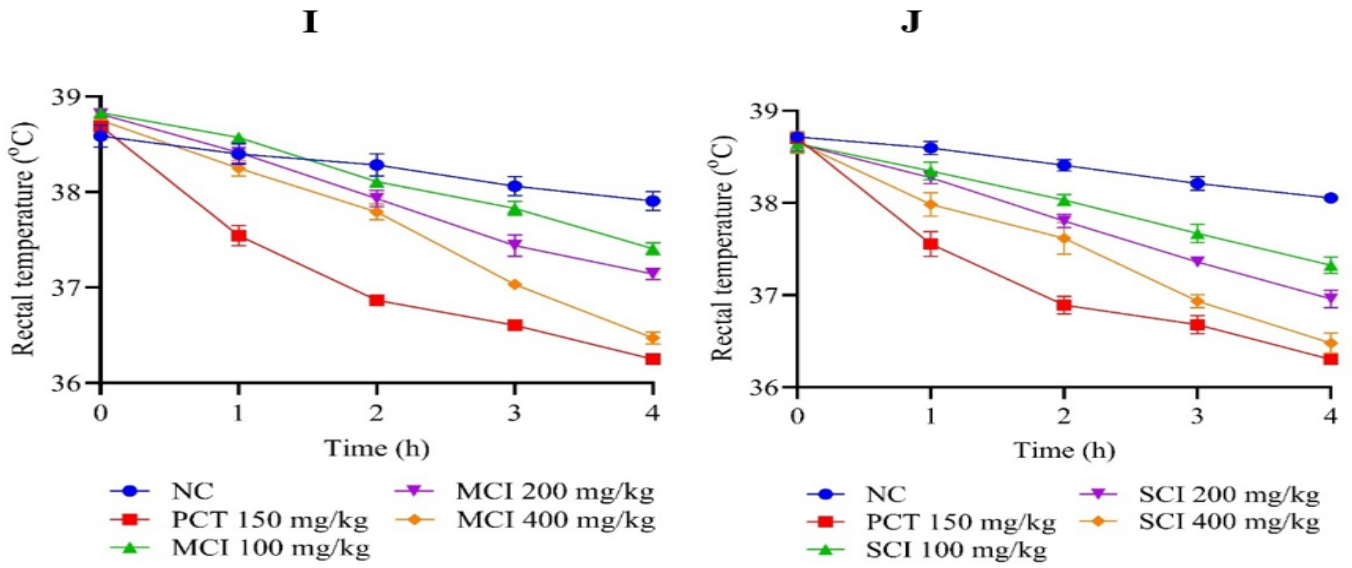


Figure 2: Effect of COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI on peptone-induced pyrexia in rats. A) COI; B) AMI; C) AMCI; D) AAI; E) CPI; F) TII; G) ZOI; H) API; I) MCI; J) SCI with doses for each plant of 100, 200 and 400 mg/kg. Data are presented as mean±SEM of 4 animals in each group. NC: Negative control; PCT 150 mg/kg: Paracetamol dose 150 mg/kg.

Table 1: Yields of COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI.

Extract	Actual yield (g)	Yields (%)
COI	11.10	11.10
AMI	12.26	12.26
AMCI	12.83	12.83
AAI	31.52	31.52
CPI	25.00	25.00
TII	20.70	20.70
ZOI	19.60	19.60
API	13.90	13.90
MCI	18.30	18.30
SCI	13.50	13.50

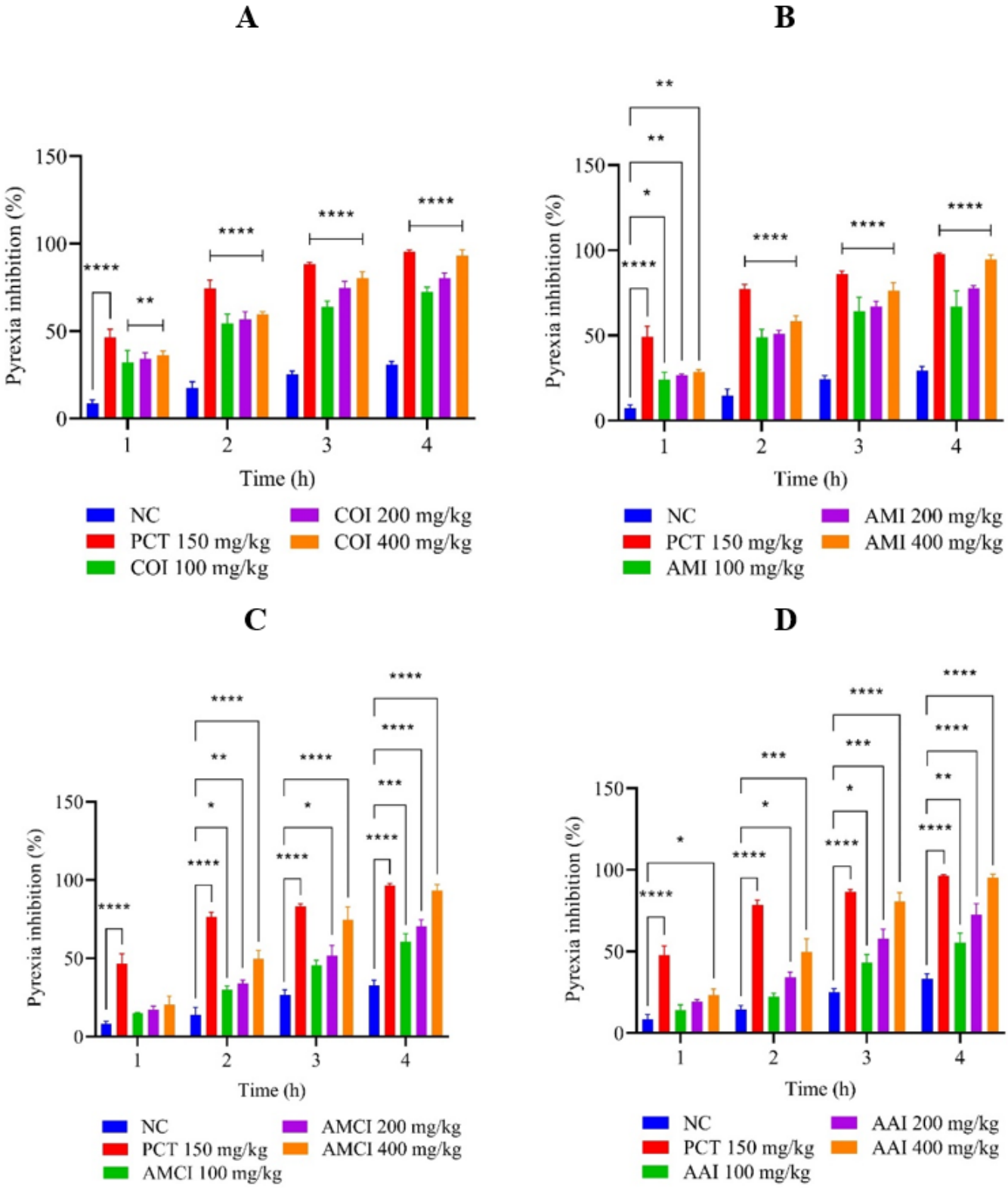
Control group (NC). Meanwhile, the standard drug paracetamol at a dose of 150 mg/kg showed a significant percentage of fever inhibition from 1-4 hr (Figure 3). This research showed that administration of COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI was able to reduce the rectal temperature of febrile rats induced by peptone which depends on dose and time.

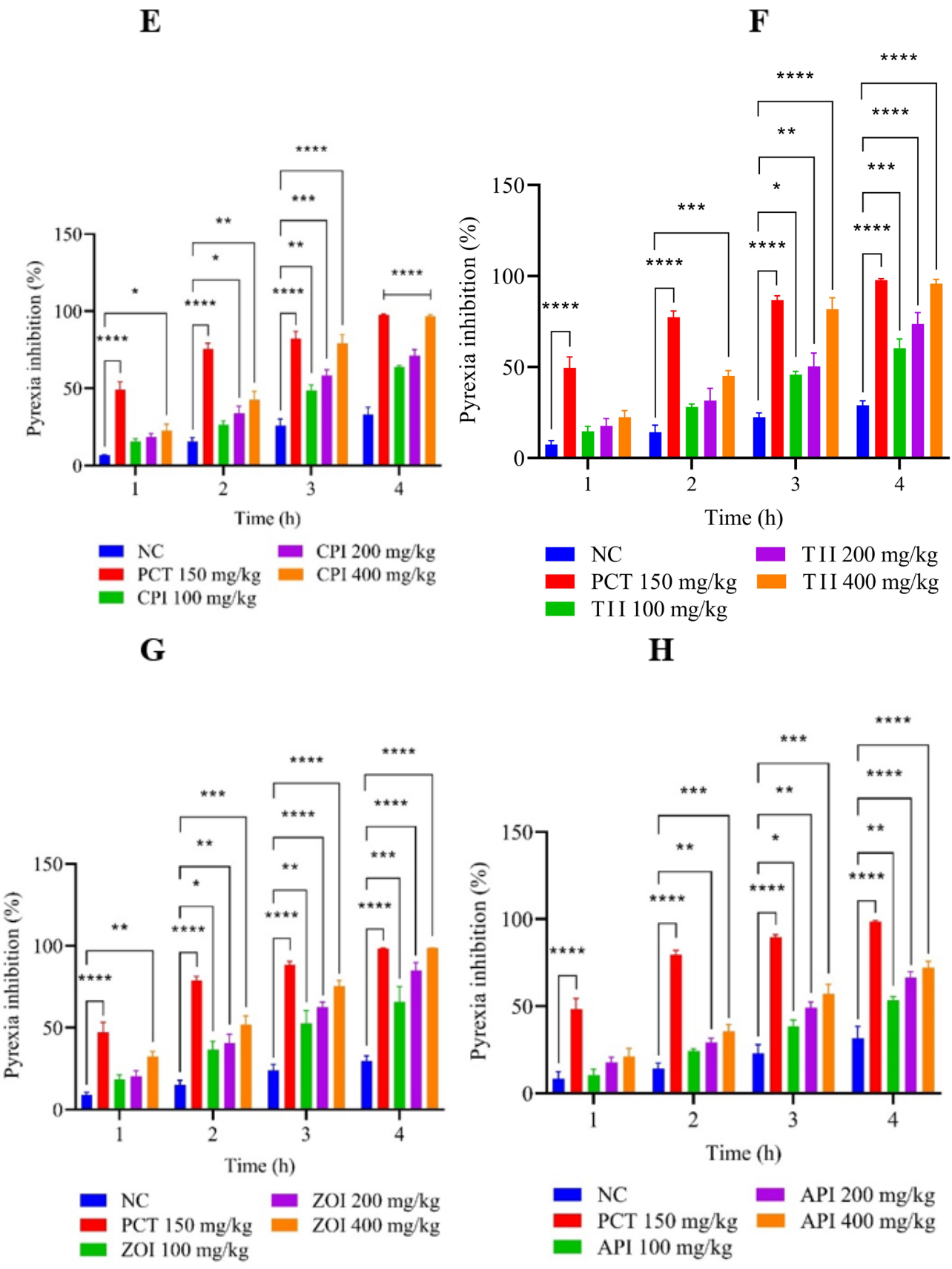
Antioxidant activity

In this research, quantitative determination of antioxidant activity was carried out using the DPPH method, expressed as IC_{50}, namely the concentration needed to inhibit fifty percent of DPPH free radicals.[20] The antioxidant activities of COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI were carried out at different concentrations. Additionally, it was found that the higher the extract concentration, the higher the percentage value of inhibition of DPPH. The findings indicate that one plant exhibits very strong Antioxidant Intensity (AAI), five plants show strong antioxidant intensity (AMCI, CPI, ZOI, API and SCI), two plants have medium antioxidant intensity (COI and MCI), one plant displayed weak antioxidant intensity (AMI) and one plant demonstrated very weak antioxidant intensity (TII). Notably, ascorbic acid exhibited very strong antioxidant intensity (Table 3).

DISCUSSION

The hypothalamus regulates body temperature by maintaining a balance between heat production and heat loss through set-point control. However, under conditions such as infection, tissue damage, inflammation and various health issues, an elevated set-point may occur.[21] When the set point increases, there is an increase in body temperature through active generation and retention of heat. Vasoconstriction also plays a role in helping reduce heat loss through the skin. In this way, the body matches the brain's blood temperature with the new set-point created by the hypothalamus.[22] Moreover, during fever, there is also an increase in the formation of cytokines such as IL-(1β, 2, 6) and TNF-α.[23] These cytokines will cause an increase in the thermoregulatory set point in the hypothalamus. In the early phase, the thermoregulatory response to these cytokines is believed to be mediated by the release of ceramide in the preoptic neuron area in the anterior hypothalamus.[24] Meanwhile, in the slow response, PGE-2 formation occurs which is mediated by COX-2 and microsomal Prostaglandin E Synthase-1 (mPGES-1) in the arachidonic acid pathway in the endothelium of blood


A
Pyrexia inhibition (%)
Time (h)
NC
PCT 150 mg/kg
COI 100 mg/kg
COI 200 mg/kg
COI 400 mg/kg
B
Pyrexia inhibition (%)
Time (h)
NC
PCT 150 mg/kg
AMI 100 mg/kg
AMI 200 mg/kg
AMI 400 mg/kg
C
Pyrexia inhibition (%)
Time (h)
NC
PCT 150 mg/kg
AMCI 100 mg/kg
AMCI 200 mg/kg
AMCI 400 mg/kg
D
Pyrexia inhibition (%)
Time (h)
NC
PCT 150 mg/kg
AAI 100 mg/kg
AAI 200 mg/kg
AAI 400 mg/kg


E
F
G
H
Pyrexia inhibition (%)
Time (h)
NC
PCT 150 mg/kg
CPI 100 mg/kg
CPI 200 mg/kg
CPI 400 mg/kg
TII 100 mg/kg
TII 200 mg/kg
TII 400 mg/kg
ZOI 100 mg/kg
ZOI 200 mg/kg
ZOI 400 mg/kg
API 100 mg/kg
API 200 mg/kg
API 400 mg/kg

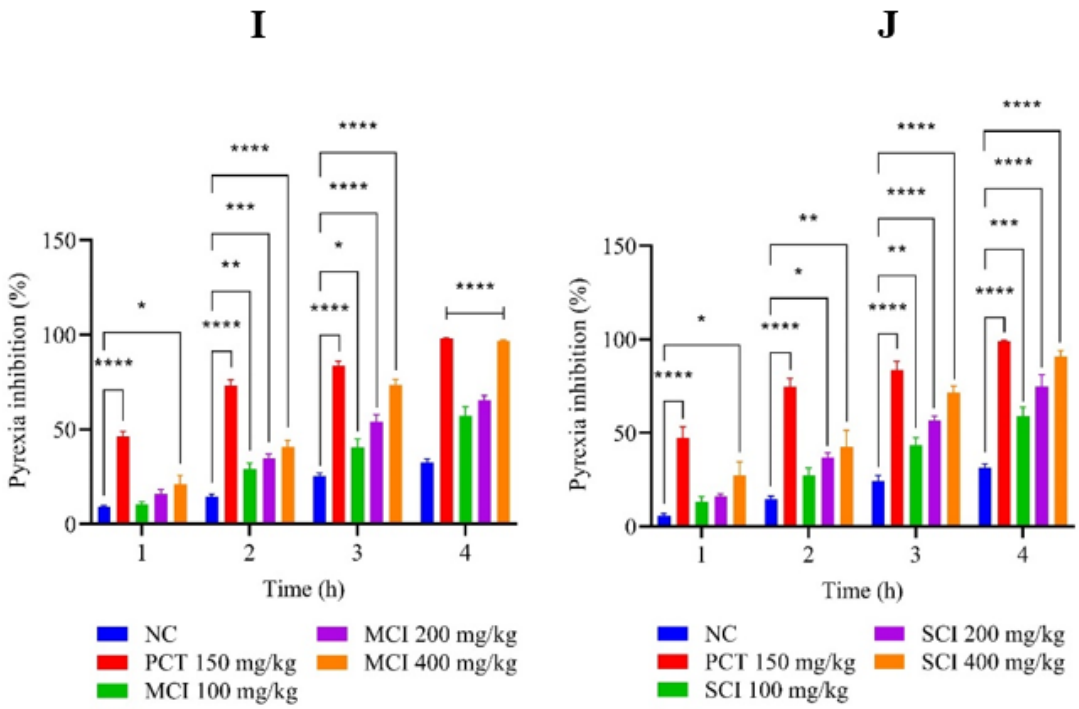


Figure 3: Antipyretic effect of COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI in rats model. A) COI; B) AMI; C) AMCI; D) AAI; E) CPI; F) TII; G) ZOI; H) API; I) MCI; J) SCI with doses for each plant of 100, 200 and 400 mg/kg. Data are presented as mean±SEM of 4 animals in each group. **p*<0.05; ***p*<0.01; ****p*<0.001; *****p*<0.0001 compared to the Negative Control (NC). PCT 150 mg/kg: Paracetamol dose 150 mg/kg.

Table 2: Phytochemical screening of COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI.

Phytochemical compounds	Reagents	Observation	Results								
			COI	AMI	AMCI	AAI	CPI	TII	ZOI	API	MCI	SCI
Flavonoids	Zn+HCl (p)	(+) Red	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)
	Mg+HCl (p)											
Polyphenols	1% $FeCl_3$	(+) Dark blue	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)
Saponins	Hot water+HCl	(+) Bubble	(+)	(+)	(+)	(-)	(+)	(+)	(+)	(+)	(+)	(+)
Tannins	1% Gelatin	(+) White sediment	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)

vessels in the preoptic hypothalamus area.[25] PGE-2 can cross the blood-brain barrier and act on EP-3 and EP-1 receptors on thermosensitive neurons, thereby triggering the hypothalamus to increase body temperature by encouraging increased heat generation and minimizing heat loss through the cAMP pathway.[3,26,27]

The induction of fever in rat through intra-peritoneal injection of peptone is associated with an elevation in prostaglandin production, specifically PGE-2. This subsequently leads to an increased set-point of the thermoregulation center in the hypothalamus.[28] This is considered a useful experiment for the initial screening of plants as well as synthetic drugs to test their antipyretic effects.[29,30] Based on the results, COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI have antipyretic activity in rat models of peptone-induced fever. This is believed to be caused by the content of secondary metabolite compounds contained in the infusions of these plants, including flavonoids, tannins and saponins (Table 2). Subsequently, flavonoid and tannin compounds are reported to inhibit pro-inflammatory mediators that cause fever, including IL-1β and 6 and TNF-α.[31,32] This compound is also reported to strongly inhibit the COX-2 and 5-Lipoxygenase (5-LOX) enzymes which are involved in the production of eicosanoids in the arachidonic acid pathway.[33,34] By inhibiting the COX-2 enzyme, PGE-2 synthesis will be reduced, which ultimately causes a decrease in fever temperature.[35] On the other hand, saponin compounds are also reported to be able to

Table 3: Percentage of inhibition of DPPH, IC_{50} and classification of antioxidants based on IC_{50} values for COI, AMI, AMCI, AAI, CPI, TII, ZOI, API, MCI and SCI at different concentrations compared with Ascorbic Acid (AA).

Sample	Inhibition (%)					IC_{50} (µg/mL)	Antioxidant intensity
	25 (µg/mL)	50 (µg/mL)	100 (µg/mL)	200 (µg/mL)	400 (µg/mL)		
COI	45.26±1.52	46.64±0.74	48.80±1.25	51.83±1.24	58.30±0.68	149.88±1.41	Medium
AMI	19.19±1.47	23.92±0.71	30.30±1.04	37.78±0.88	51.23±0.73	369.57±1.66	Weak
AMCI	40.80±0.98	45.75±1.36	59.31±1.10	70.99±1.03	86.89±0.82	65.05±1.22	Strong
AAI	49.23±1.45	50.77±0.97	52.31±0.43	55.64±0.34	60.37±1.15	28.17±1.11	Very strong
CPI	47.80±0.80	48.05±0.62	53.30±0.71	56.14±0.73	60.42±0.73	61.75±1.19	Strong
TII	29.65±0.81	30.70±0.79	31.47±0.91	33.06±0.51	34.77±0.82	1555.43±1.19	Very weak
ZOI	47.47±0.61	49.32±0.70	52.30±0.82	56.53±0.84	63.43±0.81	63.06±1.29	Strong
API	47.67±0.60	48.57±0.88	50.40±0.86	56.20±1.33	65.90±0.98	79.31±1.40	Strong
MCI	42.58±0.78	47.00±0.83	48.85±0.88	52.88±0.30	60.81±0.35	145.35±1.22	Medium
SCI	46.61±0.79	49.35±0.84	51.88±0.57	55.22±0.86	64.74±0.64	77.09±1.00	Strong
Sample	**Inhibition (%)**					**IC_{50} (µg/mL)**	**Antioxidant intensity**
	2 (µg/mL)	**4 (µg/mL)**	**6 (µg/mL)**	**8 (µg/mL)**	**10 (µg/mL)**		
AA	28.29±0.37	42.44±0.71	56.59±0.89	68.30±0.75	83.17±0.84	5.15±0.72	Very strong

inhibit arachidonic acid metabolism, which ultimately causes a decrease in PGE-2 synthesis.[36]

During fever caused by inflammation, immune cells consume substantial oxygen for energy production, leading to the generation of excessive free radicals by mitochondria in the form of Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS).[37,38] At high concentrations, these free radicals can cause oxidative stress which can damage all cell structures, hence causing even more serious diseases such as cancer, cardiovascular disease, aging, neurodegenerative and autoimmune disorders.[37] The human body possesses various mechanisms to counteract free radicals by generating antioxidants (free radical scavengers) but, during inflammation, the natural antioxidant production decreases.[38] Therefore, antioxidants are needed from outside the body, one of which comes from food or medicinal plants.[39] Based on this research, it appears that several plant infusions tested showed antioxidant activity *in vitro*, either with very strong (AAI), strong (AMCI, CPI, ZOI, API and SCI), medium (COI and MCI) antioxidant intensity, weak (AMI) and very weak (TII). The antioxidant activity of these plant infusions is attributed to their flavonoid, tannin and saponin content. These components are reported to activate antioxidant enzymes, catalyze metal chelation, transfer free electrons, reduce α-tocopherol radicals and inhibit oxidase.[40-43]

CONCLUSION

In conclusion, the traditional use of infusions from *Chromolaena odorata, Abelmoschus manihot, Annona muricata, Allium ascalonicum, Carica papaya, Tamarindus indica, Zingiber officinale, Abrus precatorius, Momordica charantia* and *Strobilanthes crispus* to treat fever gained scientific validation for the first time, as shown by this research. The results showed that the infusion of ten medicinal plants exhibited antipyretic and antioxidant activity. The medicinal plants exhibited potential as novel antipyretic agents, offering an alternative to synthetic drugs with numerous hazardous side effects. Additionally, they have the potential to neutralize the excessive production of free radicals that occur during fever due to their antioxidant properties. However, there is a need for further research to find out the mechanism of action of the active compounds contained in these plants which act as antipyretics and antioxidants. Therefore, the results support the claim of the traditional use of ten medicinal plant infusions by the Tirtajaya people for the treatment of fever.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

COI: *Chromolaena odorata* infusion; **AMI:** *Abelmoschus manihot* infusion; **AMCI:** *Annona muricata* infusion; **AAI:** *Allium ascalonicum* infusion; **CPI:** *Carica papaya* infusion; **TII:** *Tamarindus indica* infusion; **ZOI:** *Zingiber officinale* infusion;

API: *Abrus precatorius* infusion; **MCI:** *Momordica charantia* infusion; **SCI:** *Strobilanthes crispus* infusion.

ETHICAL APPROVAL

This study protocol was approved by the Research Ethics Commission, Universitas Padjadjaran, Indonesia, with the following numbers: 1392/UN6.KEP/EC/2022 and 27/UN6.KEP/EC/2023.

SUMMARY

This study aims to evaluate the antipyretic and antioxidant activity of ten indigenous medicinal plants of Tirtajaya, Karawang Regency, West Java, Indonesia. Antipyretic activity testing was carried out using the peptone-induced rat model, while antioxidant activity testing was carried out using the DPPH model. The results showed that the infusion of ten medicinal plants exhibited antipyretic and antioxidant activity. The results support the claim of the traditional use of ten medicinal plant infusions by the Tirtajaya people for the treatment of fever.

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Cite this article: Gunarti NS, Alkandahri MY, Wahyuningsih ES, Agustina P, Mursal ILP, Hidayah H, Nurviana V. Evaluation of Antipyretic and Antioxidant Activities of Ten Indigenous Medicinal Plants of Tirtajaya, Karawang Regency, West Java, Indonesia. Indian J of Pharmaceutical Education and Research. 2025;59(1):252-63.