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Pharmacological Evaluation of Ethanolic Extract of *Duranta Erecta* Leaves for Anti-Pyretic Activity using Wistar Rats

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ABSTRACT:

This study investigates the ethanolic extract of *Duranta erecta* for its phytochemical properties and evaluates its antipyretic activity using yeast-induced and vaccine-induced hyperpyrexia models. The extract was also assessed for its effects on behavior, specifically ambulation and rearing frequency, as well as white blood cell (WBC) count. Phytochemical analysis revealed the presence of alkaloids, flavonoids, terpenoids, saponins, steroids, tannins, and phenolics. The ethanolic extract exhibited significant antipyretic activity, reducing fever in both experimental models, with a dose-dependent effect. Behavioral studies showed increased ambulation and rearing frequencies, while WBC count was significantly decreased after treatment. These results suggest the potential therapeutic benefits of *Duranta erecta* as an antipyretic and anti-inflammatory agent.

Keywords: *Duranta erecta*, Ethanolic extract, Phytochemical screening, Antipyretic activity, Behavioral effects, WBC count, Hyperpyrexia.

1. Introduction:

Duranta erecta, commonly known as golden dew drop or sky flower, is a perennial shrub native to the Americas, particularly in tropical and subtropical regions. It is widely recognized for its ornamental value due to its vibrant blue or purple flowers. Beyond its aesthetic appeal, *Duranta erecta* has a long history of use in traditional medicine across various cultures, where it is believed to possess several pharmacological properties. The plant has been used in folk medicine to treat a variety of ailments, including fever, inflammation, pain, and gastrointestinal disturbances. Different parts of the plant, such as the leaves, roots, and flowers, have been utilized for their purported therapeutic benefits.

The pharmacological potential of *Duranta erecta* is attributed to its rich chemical composition, which includes a wide array of secondary metabolites. Phytochemical studies have revealed the presence of alkaloids, flavonoids, terpenoids, saponins, tannins, phenolics, and steroids. These bioactive compounds are thought to contribute to the plant's antipyretic, anti-inflammatory, analgesic, antimicrobial, and antioxidant properties. However, despite its widespread use in traditional medicine, there is a lack of comprehensive scientific evidence that thoroughly investigates the mechanisms behind its purported therapeutic effects[7].

Among the many potential uses of *Duranta erecta*, one of the most significant is its application in treating fever, a common symptom of many infectious and inflammatory conditions. Traditionally, the plant has been employed as a remedy for fever, but scientific studies focusing on its antipyretic activity are limited. Fever, often caused by pyrogens, is an elevation in body temperature above the normal range, which is usually a sign of an underlying infection or inflammatory response. Non-steroidal anti-inflammatory drugs (NSAIDs) like paracetamol are commonly used to reduce fever by inhibiting the production of prostaglandins, which play a key role in the regulation of body temperature. However, due to concerns over side effects and long-term use, there is a growing interest in identifying alternative natural remedies with fewer adverse effects.

In addition to its antipyretic potential, *Duranta erecta* has been traditionally recognized for its ability to reduce inflammation and alleviate pain. Inflammation, a complex biological response to harmful stimuli, is characterized by swelling, redness, and pain, and it often accompanies fever. The plant's reported analgesic and anti-inflammatory effects have prompted interest in its therapeutic utility, especially considering the increasing global burden of inflammatory diseases and the limitations of current pharmaceutical treatments[8].

Behavioral effects are another critical area of investigation for medicinal plants. The impact of a substance on behavior, such as changes in locomotor activity, anxiety, or stress responses, can provide valuable insight into its central nervous system effects. While there is some evidence suggesting that *Duranta erecta* might influence the central nervous system, detailed studies exploring its behavioral effects are scarce. Understanding how the plant affects behavior can offer a more comprehensive understanding of its pharmacological profile and possible therapeutic uses beyond its antipyretic and anti-inflammatory properties.

The primary aim of this study is to explore the chemical composition of *Duranta erecta* ethanolic extract and assess its potential pharmacological effects, focusing on its antipyretic and behavioral activities. Specifically, the study evaluates the antipyretic effect of the extract in two experimental fever models—yeast-induced hyperpyrexia and vaccine-induced hyperpyrexia in rats. In addition, the study investigates the plant's effects on behavioral parameters such as ambulation frequency and rearing frequency, which are indicative of locomotor and exploratory behavior. The findings of this research will contribute to a deeper understanding of the therapeutic potential of *Duranta erecta* and provide scientific validation for its traditional use in the treatment of fever and related conditions.

Through this study, we hope to establish a foundation for the future development of *Duranta erecta* as a natural alternative to conventional antipyretic and anti-inflammatory agents, with potential applications in both clinical and traditional medicine[1-8]

2. Materials and Methods:

Plant selection:

Drug discovery from medicinal plants involves a wide range of fields of study and analytical techniques. According to the intensive literature survey, *Duranta erecta* was used for the present study[9].

Collection and Identification:

Collection and identification of plant include the plant material of leaves of *duranta erecta* was collected from local areas of Indore and the plant samples were authenticated by Dr. S.N. Dwivedi A.P.S. College Rewa. Voucher Specimen Number: J/Bot./2024-045. The plant specimen was washed thoroughly under the tape water to discard dust and other unwanted materials. Then plant part was dried under shade with usual sun- air drying.

Preparation of Extract:

The leaves of *duranta erecta* were thoroughly washed under the tap water and then with distilled water to remove any physical impurities. The cleaned leaves were allowed to dry in the shade. After drying, grind it into fine powder using an grinder. Then fine powder stored in an airtight container for further investigation [9].

- **Principle:-**In cold maceration process of extraction crude drug and ethanol are mix togather and keep a side for 48 hours at room temperature in a shaker.

Extraction Procedure:

The leaves of D. erecta was washed under running tap water to remove dust and other extraneous substances. They were subsequently dried under shade for 4 weeks. The shade-dried parts of the plant were coarsely powdered using a grinder. 60 g of the pulverized samples were extracted with 50% ethanol by cold maceration for 48 hours at room temperature on a shaker. The mixture was separated by centrifugation, and each supernatant was evaporated under reduced pressure using a rotary evaporator. The extracts was dried using a water bath to obtain the respective crude extracts which included D. erecta leaves[9].

Figure 1:- Cold Maceration

Preliminary Phytochemical Screening of Ethanolic Extract of *Duranta erecta*[10]

Extract was subjected to preliminary phytochemical investigation for detection of alkaloids, flavonoids, saponins, tannins, steroids, phenols and terpenoids etc. Phytochemical screening was carried out according to protocol.

- **Test for Terpenoids (Salkowski's Test):** To 0.5 g of each extract, 2 ml of chloroform was added. Concentrated H_2SO_4 (3 ml) was then carefully added to form a separate layer. A reddish-brown color at the interface indicates the presence of terpenoids.
- **Test for Flavonoids:** Dilute ammonia (5 ml) was added to a portion of the aqueous filtrate of the extract. Concentrated sulfuric acid (1 ml) was then added. A yellow coloration that disappears upon standing indicates the presence of flavonoids.
- **Test for Saponins:** To 0.5 g of the extract, 5 ml of distilled water was added in a test tube. The solution was shaken vigorously and observed for stable, persistent froth. The froth was mixed with 3 drops of olive oil and shaken vigorously again. Formation of an emulsion indicates the presence of saponins.
- **Test for Tannins:** About 0.5 g of the extract was boiled in 10 ml of water in a test tube, then filtered. A few drops of 0.1% ferric chloride were added, and the solution was observed for brownish-green or blue-black coloration.
- **Test for Alkaloids:** 0.5 g of the extract was diluted to 10 ml with acid alcohol, boiled, and filtered. To 5 ml of the filtrate, 2 ml of dilute ammonia was added. 5 ml of chloroform was added and shaken gently to extract the alkaloidal base. The chloroform layer was then extracted with 10 ml of acetic acid. This was divided into two portions. Mayer's reagent was added to one portion and Dragendorff's reagent to the other. Formation of a cream (with Mayer's reagent) or a reddish-brown precipitate (with Dragendorff's reagent) indicates the presence of alkaloids.
- **Test for Phenols:** To estimate total phenols, the protocol of Bray and Thorpe was followed. A standard curve of caffeic acid (a phenol) was prepared. A stock solution (100 µg/ml) of caffeic acid was prepared in 80% ethanol. From this, 0.1 to 0.9 ml was transferred into test tubes separately, and the volume in each case was adjusted to 1 ml with 80% ethanol. To each tube, 1 ml of Folin-Ciocalteu reagent (diluted with distilled water in a 1:2 ratio just before use) and 2 ml of 20% Na_2CO_3 solution were added. The mixture was shaken vigorously, boiled on a water bath for 1 minute, cooled, and then diluted to 25 ml with distilled water. The optical density was measured at 750 nm using a spectrophotometer against a blank.
- **Test for Steroids:** To 0.2 g of each portion, 2 ml of acetic acid was added. The solution was cooled in ice, followed by the careful addition of concentrated H_2SO_4. Development of a color from violet to blue or bluish-green indicates the presence of a steroidal ring (i.e., the aglycone portion of cardiac glycosides).

Figure 2:- Phytochemical Test of Extract

Experimental Animals

Male Wistar rats can be easily bred, low cost, easy to handle. Rats are suitable model for inflammation studies; these show similarity with respect to humans. These animals were suitable for both pharmacokinetic and pharmacodynamic studies. Because of these criteria, rats were selected for the study. In rats it is easy to induce brewer yeast and Tab vaccine. Male Wistar rats with body weight 220- 270gm. They were obtained from animal house of Swami Vivekananda college. All animals were housed under standard control conditions with temperature maintain at 24±2C, humidity: 50% ± 5% and the animals had 12 hrs light: 12 hrs dark cycle. The animals were kept individually in the large spacious hygienic cages during the course of experimental period. The rats were provided free access to food (standard commercial rat chow) and water, and receive human care. All the animals were adapted to laboratory condition for a week before commencement of experiment. The Institutional Animal Ethical Committee of our organization gave its approval to the experimental protocol. (Approval No: IAEC/SVCP/2024/02) and were strictly in accordance with the norms of CCSEA. New Delhi [11].

Acute oral toxicity:

The plant *Duranta erecta* was found to have a safe ethanolic extract when given at doses of 250mg and 500mg per kg of body weight, according to the literature. No mortality was observed at both doses. Therefore, it was reported that the LD50 of the plant extract is 5g/kg of body weight[12].

Experiment Method

A total of 25 healthy adult Wistar rats, all of which were in optimal health and carefully selected for their uniformity, were divided into five distinct experimental groups. Each group consisted of 5 rats, and the division was made to ensure a well-balanced representation of the rats across different conditions. The purpose of this division was to carry out specific research protocols, allowing for a detailed analysis of the results within each group.

Table 5: Animal Group Design-

A Total number of 25 healthy adult Wistar rat were divided into 5 groups each:

S. No.	Groups	No. of Animals
1.	Normal Control	5
2.	Negative Control	5
3.	Low dose of extract (250mg/kg)	5
4.	High dose of extract (500mg/kg)	5
5.	Standard drug : paracetamol (100mg/kg)	5
	Total	25

Figure 3:- Animal Group Design

For assessing antipyretic activity, Brewer's yeast-induced hyperpyrexia and TAB (Typhoid) vaccine-induced pyrexia models were employed, based on the literature survey.

Brewer's Yeast Induced Hyperpyrexia: The animals were fasted overnight before the experiment, but water made available ad libitum. The rats were randomly divided into five groups. Pyrexia was induced by subcutaneous injection of a 20% (w/v) brewer's yeast suspension (10 ml/kg) into the dorsum of the rats. Seventeen hours after the injection, the rectal temperature of each rat was measured using a thermometer. Only rats showing an increase in temperature of at least 0.7°C were used for this study. The rats in two test groups were receive 250 mg/kg and 500 mg/kg of Duranta erecta extract orally. The control group was treated with 2 ml/kg of saline, while the standard group was receive paracetamol (100 mg/kg). The negative control group was administered brewer's yeast. The initial rectal temperature of the rats were recorded, and temperatures were subsequently measured at 60, 90, and 120 minutes post-extract administration. The mean temperature of each group was recorded[13].

Figure 4:- Inducing Brewer's Yeast Suspension

TAB (Typhoid) Vaccine Induced Pyrexia: In this method, the rats were divided into five groups, including two test groups. The control group was receive 2 ml/kg of saline. The normal rectal temperature of a group of rats were recorded using a thermometer at hourly intervals over a period of 4 hours. The TAB vaccine was administered intravenously into the marginal ear vein of the rats at a dose of 0.5 ml/rat. Duranta erecta leaves extract was administered orally at doses of 250 mg/kg and 500 mg/kg, 60 minutes after the TAB vaccine administration, when significant pyrexia is expected. The rectal temperature was recorded every hours up to 3 hours. Paracetamol (100 mg/kg) was used for comparison in the standard group[14].

Figure 5:- Vaccine Used in Experiment

Figure 6:- Inducing TAB Vaccine

Figure 7:- Inducing Standard Drug (Paracetamol) Orally

Parameter to be assessed:

Following parameters were assay:-

- **Body Temperature:**

The body temperature of all rats were measure before and after the experiment by placing thermometer in rectal cavity as pyrexia cause increase in body temperature.

- **Behavioral Studies :**

- **Open Field Test:** The open field test was conducted to measure locomotion, exploration, and anxiety. Each rat was placed in the center of an open field apparatus—a circular wooden box with a diameter of 72 cm and a height of 36 cm, with the floor divided into 16 regions. Rats were assessed individually for 5 minutes, and three parameters were analyzed: (i) **Ambulation**: The number of grid lines crossed by the rat with all four paws; (ii) **Rearing**: The number of times the rat stood on its hind paws[15]

- **WBC Count:**

One milliliter (1 ml) of blood was carefully withdrawn from the tail vein of a rat using a sterile needle and syringe, and the sample was subsequently transported to the laboratory for analysis. The purpose of this procedure was to conduct a white blood cell (WBC) count, which is a vital diagnostic test to assess the immune system's activity and overall health of the animal. The blood sample was handled with utmost care to ensure its integrity, and appropriate steps were taken to preserve the sample during transit for accurate laboratory results.

Figure 8:- Collecting Blood Sample

3. Results:

Extraction:

The ethanolic extract was prepared by soxhlet extraction technique and the % yield was calculated, its physical characteristics were shown in (table no. 6)

Table No. 6: Percentage Extractive Value and Physical Characteristic of Extract

Extract	**%Dry Weight(w/w)**	**Colour**	**Odor**	**Consistency**
Ethanolic extract	60%	Brownish green	Characteristic	Smooth(semi solid)

% yield of extracted compound:

The % of extracted compound was found to be 60 % by using formula shown below & after calculating % yield extract. The extract use to make formulation.

% yield = Practical yield/theoretical yield ×100

% yield = 60/100 × 100

% yield = 60%

Phytochemical screening test:

Table No. 7: Preliminary phytochemical analysis *Duranta erecta* extract:

Phytochemical groups	**Presence/absence**
Alkaloids	++++
Flavonoids	+++
Terpenoids	++++
Saponins	+
Steroids	+
Tannins	++++
Phenolics	++++

- Absent; + Present; ++ Low concentration; +++ Moderate concentration; ++++ High concentration.

Extract was subjected to preliminary phytochemical investigation for detection of Alkaloids, flavonoids, saponins, tannins, Steroids, Phenol and terpenoids. Phytochemical screening was carried out according to protocol.

Evaluation of Anti-pyretic activity:

Table No. 8: Effect of ethanolic extract of *D. erecta* on yeast induced hyperpyrexia in rats

Groups	**Pre-drug temp (℃)**	**Post-drug temp (60min)**	**Post-drug temp (90min)**	**Post-drug temp (120min)**
Normal Control	40.4± 0.3	38.7±0.1	37.3±0.2	37.2±0.3
Negative Control	39.2± 0.4	39.3± 0.3	39.2± 0.3	38.9± 0.3
Low dose of extract	40.5± 0.3	38.8± 0.4	37.6± 0.5	37.0± 0.2*
High dose of extract	40.2± 0.4	38.6± 0.2*	37.1± 0.1**	36.6± 0.3**
Standard drug : paracetamol	39.6± 0.2	38.5± 0.4*	37.1± 0.4*	36.9± 0.4*

Each value is the mean ± S.E.M. of 5 rats. * $P < 0.05$; **$p < 0.01$ compared with control; student's t-test.

In the brewer's yeast induced hyperpyrexia model, artificial hyperthermia was induced by administration of exogenous pyrogens in the form of yeast. General reduction of the rectal temperature was observed 60 minutes, 90 minutes and 120 minutes after oral administration of the highest dose (500 mg / kg) of the extract. The observed antipyretic effect of the extract may be due to the flavonoids and alkaloids contents of the leaves. These flavonoids and alkaloids may act by blockage of the synthesis of prostagladins E2 (– a peripheral fever mediator) through the inhibition of prostaglandins synthetase. Therefore the extract could be mediating it analgesic and antipyretic effects like the non steroidal anti-inflammatory drugs.

Table No. 9: Effect of ethanolic extract of *D. erecta* on vaccine induced hyperpyrexia in rats

Groups	**Pre-drug temp (°C)**	**Post-drug temp (1st hr)**	**Post-drug temp (2nd hr)**	**Post-drug temp (3rd hr)**
Normal Control	40.2±0.3	37.3±0.2	37.6±0.3	37.2±0.3
Negative Control	39.6±0.2	39.3± 0.3	39.2± 0.3	38.9± 0.3
Low dose of extract	39.5±0.6	38.7±0.1	37.6±0.4	36.1±0.2*
High dose of extract	40.3±0.4	37.8±0.3	36.9±0.2*	35.6±0.3**
Standard drug : paracetamol	39.6±0.2	37.5±0.2	36.3±0.3*	35.4±0.3**

Values are expressed as mean ± SEM of five animal per group (n=5). * P < 0.05; **p < 0.01 significant when compared with reference drug paracetamol.

When the extract was administered to rats with established TAB vaccine-induced fever, the fever was significantly reduced and the body temperature was normalized by administration of 250 and 500mg/kg dose intraperitoneally. However, 150mg/kg dose of extract had no effect on the rectal temperature of rats. The response in higher doses was almost comparable to that of paracetamol.

Behavioral Studies:

1) Open field test:

(a) Ambulation frequency

The present results exposed a significant (P<0.001) decrease in ambulation frequency in negative control group as compared with vehicle group. Extract 1, extract 2 and standard drugs group showed significantly increased ambulation frequency as compared to negative control group. Values are expressed as mean ± SEM from both models of 5 animal per group (n=5).

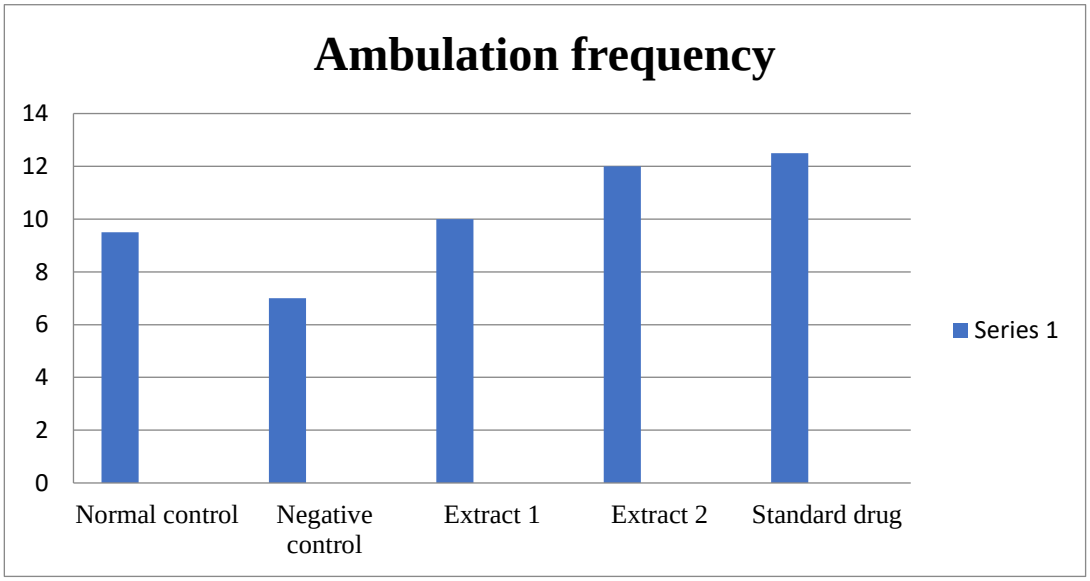

Chart 1:- Ambulation Frequency from Brewer's Yeast Model

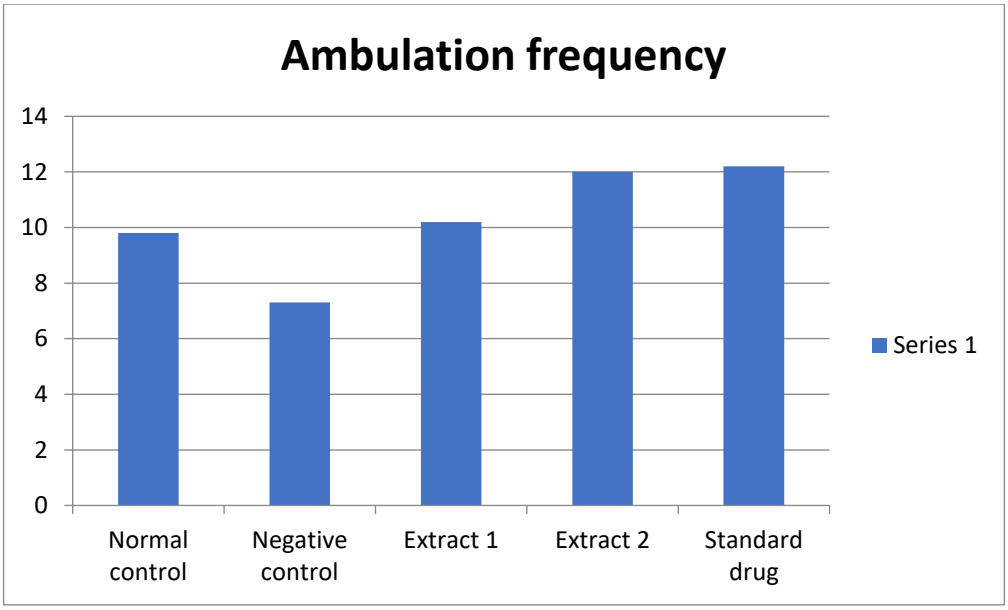

Chart 2:- Ambulation Frequency from TAB Vaccine Model

(b) Rearing frequency

The present results exposed a significant (P<0.001) decrease in rearing frequency in negative control group as compared with vehicle group. Extract 1, extract 2 and standard drugs group showed significantly increased rearing frequency as compared to negative control group. Values are expressed as mean ± SEM from both models of 5 animal per group (n=5).

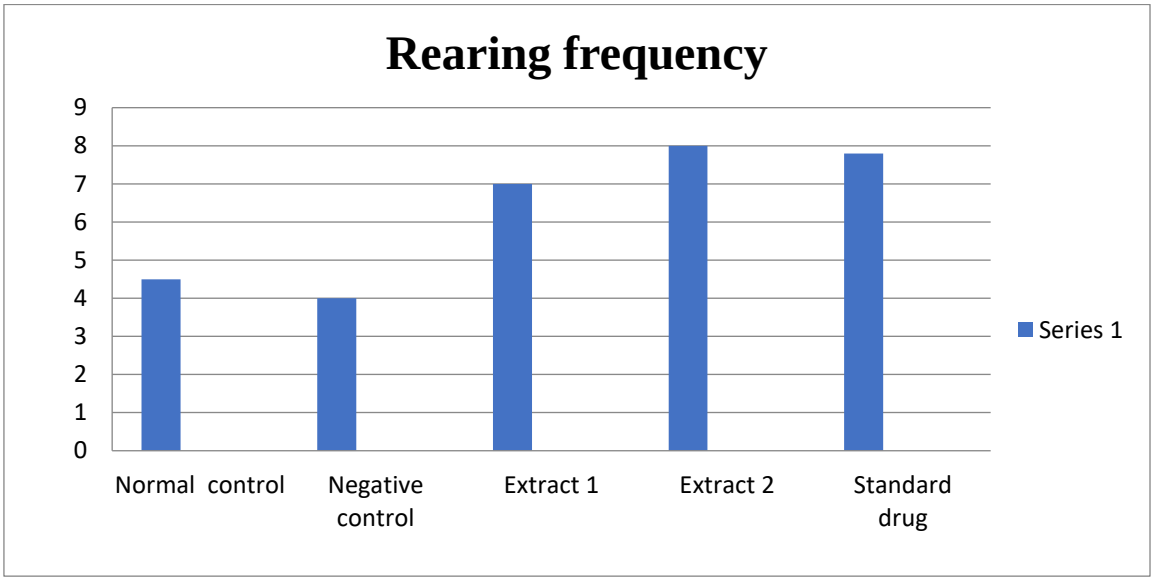

Chart 3:- Rearing Frequency from Brewer's Yeast Model

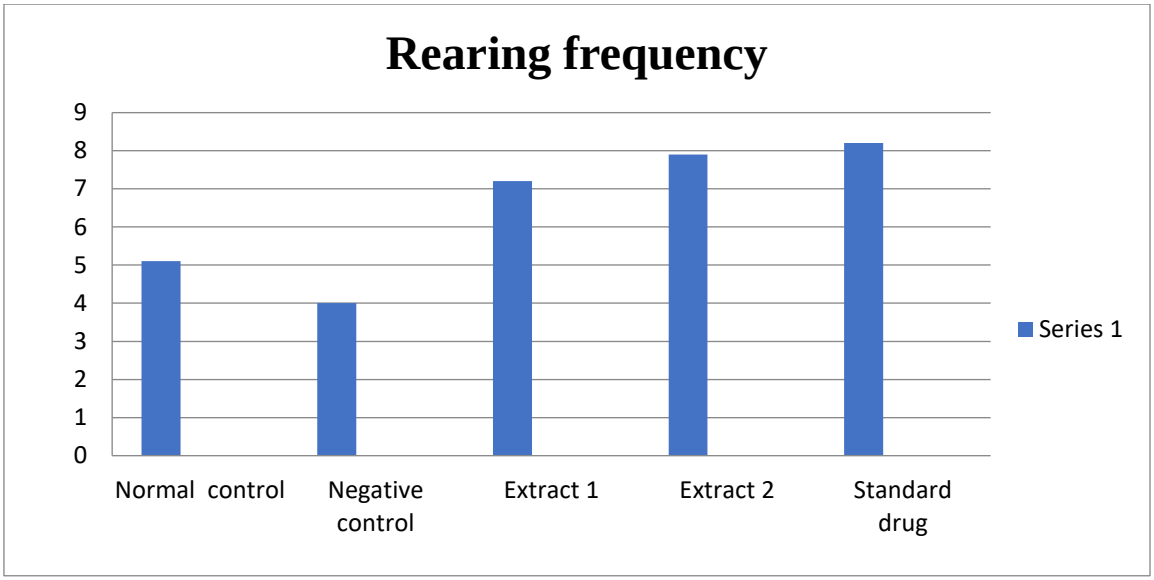

Chart 4:- Rearing Frequency from TAB Vaccine Model

WBC Count:

The present results exposed a significant (P<0.001) increase in WBC count in negative control group as compared with vehicle group. Extract 1, extract 2 and standard drugs group showed significantly decreased WBC count as compared to negative control group. Values are expressed as mean ± SEM from both models of 5 animal per group (n=5).

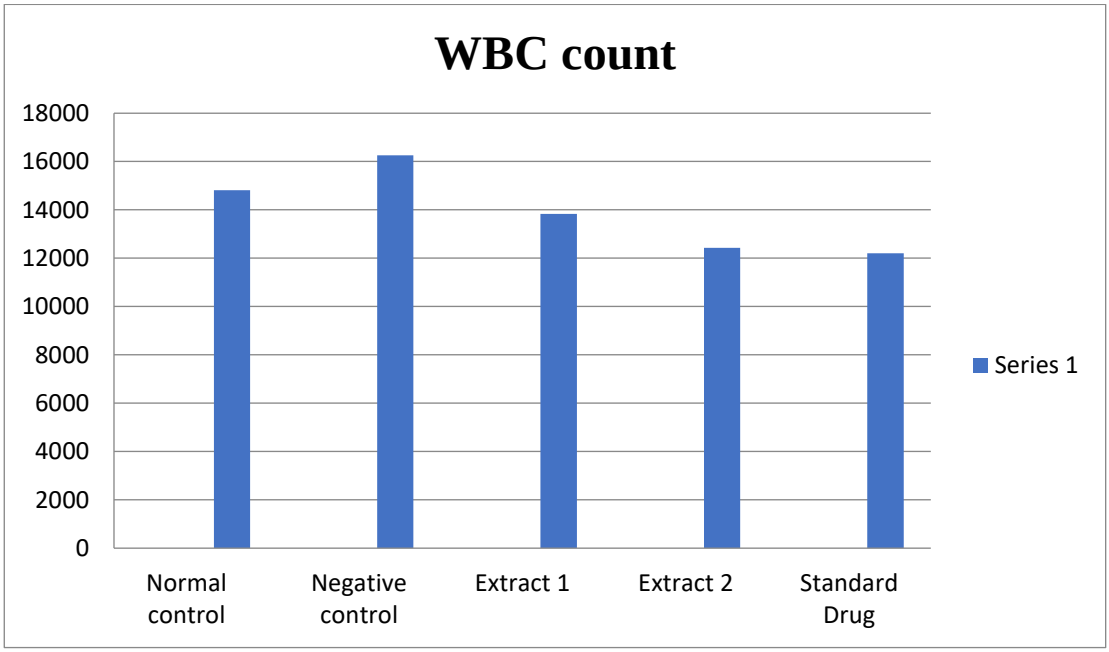

Chart 5:- WBC Counts from Brewer's Yeast Model

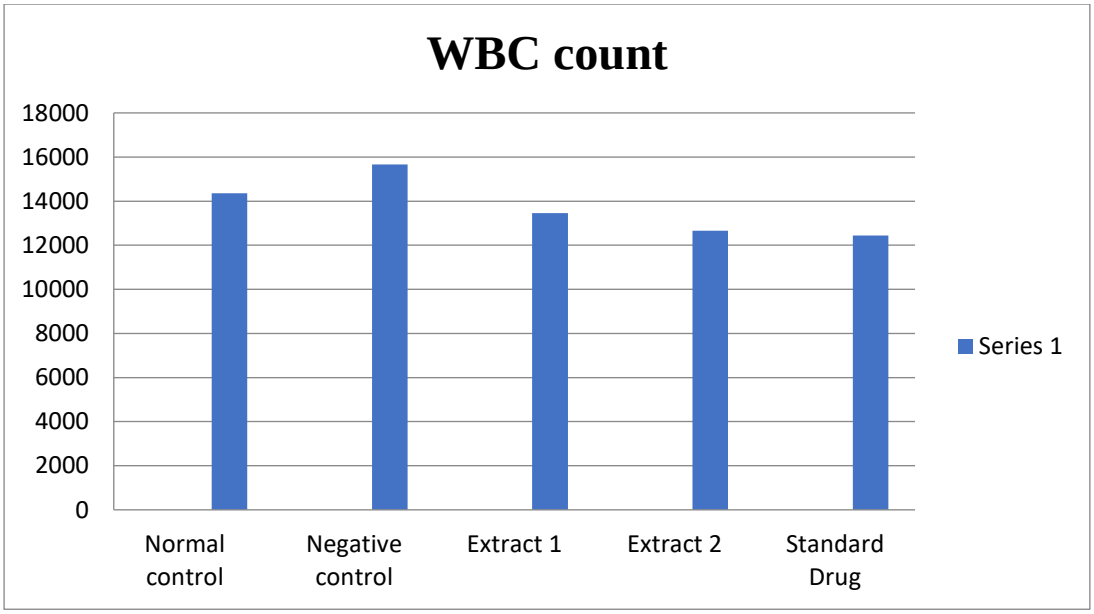

Chart 6:- WBC Counts from TAB Vaccine Model

4. Discussion:

The results of this study suggest that *Duranta erecta* ethanolic extract possesses potent antipyretic properties, as demonstrated by the significant reduction in body temperature in both yeast-induced and vaccine-induced hyperpyrexia models. The presence of bioactive compounds, such as alkaloids and flavonoids, likely contributes to these effects through inhibition of prostaglandin synthesis, which is involved in fever regulation.

The behavioral results, showing increased ambulation and rearing frequencies, suggest that the extract may enhance locomotor and exploratory activity, potentially indicating a mild stimulant effect or improved general well-being of the rats. Additionally, the significant reduction in WBC count suggests that the extract may possess anti-inflammatory effects, further supporting its potential as an anti-inflammatory and antipyretic agent.

These findings are consistent with traditional uses of *Duranta erecta* for treating fever and inflammation. Further studies are needed to fully elucidate the underlying mechanisms and to evaluate the safety and long-term efficacy of this extract.

5. Conclusion:

The ethanolic extract of *Duranta erecta* demonstrated significant antipyretic and behavioral effects in experimental rat models. The phytochemical profile, along with its antipyretic and anti-inflammatory activities, suggests that *Duranta erecta* could be a potential therapeutic agent for managing fever and related inflammatory conditions. Further research is needed to explore its pharmacokinetics and safety profile.

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