Over the past decade, herbal medicine has become a topic of global importance, making an impact on both world health and international trade. Medicinal plants continue to play a central role in the healthcare system of large proportions of the world's population. This is particularly true in developing countries, where herbal medicine has a long and uninterrupted history of use [1]. Pyrexia or fever is caused as a secondary impact of infection, malignancy or other diseases. It is the body's natural defense to create an environment where an infectious agent or damaged tissue cannot survive. Normally the infected or damaged tissue initiates the enhanced formation of pro-inflammatory mediator's which increase the synthesis of prostaglandin E2 (PGE2) near peptic hypothalamus area and thereby by triggering the hypothalamus to elevate the body temperature.

Diospyros is a genus of over 700 species of deciduous and ever-green trees, shrubs, and small bushes. Diospyros virginiana L. is a persimmon species commonly called the American Persimmon from Diospyros virginiana which is used in infusion syrup or vinous administration.

The results showed that the ethanol extracts of leaf of Diospyros virginiana possessed significant antipyretic effect compared to the bark extract.

Conclusion: This study provides evidences for the antipyretic activity of Diospyros virginiana which could partly contribute to its ethno medical use.

Keywords: D. virginiana, Brewer yeast, Rectal temperature, Paracetamol.
The statistical analysis was done by ANOVA [8] followed by Dunner’s test for multiple comparisons. P<0.01 was considered significant in the experiment.

Non-steroid anti-inflammatory drugs are among the most commonly prescribed due to their considerable effectiveness in the treatment of pain, inflammation and rheumatic disorders. Since their drugs have toxic effect to the various organs of the body, search for safe herbal remedies with potent antipyretic activity received momentum recently.

Subcutaneous injection of the pyrogenic dose of yeast produced elevated changes in rectal temperature of the rats as shown in the table. The Diospyros virginiana both extracts caused a dose-dependent decrease in rectal temperature when compared to the control. The ethanolic Diospyros virginiana leaf extracts revealed a significant decrease (P<0.05) in temperature between 2 to 5 h after administration. Diospyros virginiana bark extract showed the significant decrease (P<0.05) in temperature 3 to 5 h respectively. However, paracetamol (10 mg/kg) used as the reference drug caused a greater reduction in the rectal temperature of the rats at the onset-which was significant different (P<0.05), when compared to both control and control treated groups. The antipyretic effect started as from the 1st h after drug and extract administration and was sustained for 4 h while control showed no antipyretic effect in the entire period of experiment.

Antipyretic activity is a characteristic of drugs or compounds which have an inhibitory effect on prostaglandin biosynthesis and an indispensible role of prostaglandins in the febrile response has been demonstrated [9]. In the present pharmacological evaluation, the leaf and bark extract of Diospyros virginiana was extensively investigated for its antipyretic activity against Brewer’s yeast induced pyrexia model in rats. The extracts produced a significant reduction in yeast induced pyrexia in rats dose-dependently and its effect is comparable to that of the standard antipyretic drug (paracetamol) used in this study. The ethanolic extract of the both plant leaf and bark at a dose level of 500 mg/kg exhibited competent, potent and comparable results.

Fever is a result of a finely tuned, complex event that involves both the peripheral immune system and the brain, through which a series of inflammatory and metabolic processes are regulated and it is now commonly accepted that prostaglandin E2 (PGE2) is the final fever mediator in the brain, specifically in the pre optic area of the anterior hypothalamus [10], thus it may be plausible to conclude that the extract inhibits the synthesis of prostaglandins, albeit to a very little extent. Pyrexia is a result of secondary impact of infection, tissue damage, inflammatory graft rejection, malignancy or other diseased states. It is now evident that most of the antipyretic drugs exert their action by inhibiting the enzymatic activity of cyclooxygenase and consequently reducing the levels of PGE2 within the hypothalamic region [11].

A natural antipyretic agent with reduced or no toxicity is therefore, essential. Since antipyretic activity is commonly mentioned as a characteristic of drugs or compounds, which have an inhibitory activity on prostaglandins biosynthesis, the yeast induced hyperpyrexia in rat model was employed to investigate the antipyretic activity of the extract [12], Yeast induced pyrexia is called pathological fever which is due to the production of prostaglandins (PGE2) which set the thermoregulatory center at a higher temperature.

Antipyretics have been shown to suppress fever by inhibiting prostaglandin synthetase, resulting in the blockade of the synthesis of prostaglandin in the brain or suppressing the rise of interleukin-1β production subsequent to interferon production. Flavanoids like baicalin have been shown to exert an antipyretic effect by suppressing TNF-α [13] and its related compounds also exhibit inhibition of arachidonic acid peroxidation, which results in reduction of prostaglandin levels thus reducing the fever and pain. The results of present study indicate that the ethanol leaf extracts of Diospyros virginiana possesses significant antipyretic effect compared to the effect of bark extract on yeast induced hyperthermia in rats. This may be attributed to the presence of flavonoids and saponins in the extracts which may be involved in inhibition of prostaglandin synthesis. Also, there are several mediators or multiprocessors underlining the pathogenesis of fever. Inhibition of any of these mediators may bring about antipyresis.

The present investigation was promoting Diospyros virginiana plant as a promising antipyretic plant species seeking vast multidimensional future research work up to the molecular level to establish new up-to-date scientific data about this plant species and to elucidate its exact mechanism of an antipyretic effect.

### Table 1: Effect of ethanolic extracts of Diospyros virginiana on body temperature in yeast induced pyrexia in experimental animals

<table>
<thead>
<tr>
<th>Groups</th>
<th>Rectal temperature in °C after 18 h of yeast injection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0h</td>
</tr>
<tr>
<td></td>
<td>37.30±0.7</td>
</tr>
<tr>
<td>Group I</td>
<td>40.53±0.11</td>
</tr>
<tr>
<td>Group II</td>
<td>40.43±0.19</td>
</tr>
<tr>
<td>Group III</td>
<td>40.61±0.14</td>
</tr>
<tr>
<td>Group IV</td>
<td>40.58±0.11</td>
</tr>
</tbody>
</table>

Values are expressed as SEM *P<0.01 Vs control, 6 Number of animals were used in each group.

### CONFLICT OF INTERESTS

Declared None.

### REFERENCES