INTRODUCTION

Inflammation is a defensive response mechanism of the body against the injurious stimuli, which helps to remove the harmful stimuli and initiate the process of healing of tissue. Inflammatory process involves a series of events that can be elicited by numerous stimuli such as infectious agents, ischemia, antigen-antibody interaction, and thermal, or other physical injury. At a macroscopic level, the response to injurious stimuli usually is accompanied by clinical signs of erythema, edema, tenderness, and pain.

Inflammatory responses occur in three distinct phases, namely (1) an acute transient phase, characterized by local vasodilation and increased capillary permeability; (2) a delayed, sub-acute phase, most prominently represented by infiltration of leukocytes and phagocytic cells, and (3) a chronic proliferative phase, in which tissue degeneration and fibrosis occur. All the above mentioned processes of inflammation are mediated by the inflammatory mediators such as prostaglandins leukotrienes, histamine, and serotonin.

When a tissue is injured, from any cause prostaglandin synthesis in that tissue increases. Prostaglandins have two major actions: They are mediators of inflammation and they also sensitize pain receptors at the nerve endings, lowering their threshold of response to stimuli and allowing other mediators of inflammation, e.g., histamine, serotonin, and bradykinin to intensify the activation of the sensory nerve endings. Naturally, a drug that inhibits the
synthesis of prostaglandins and leukotrienes can be of use in treating inflammation. Moreover, one way of inhibiting their synthesis is by inhibiting the enzymes cycloxygenase and lipoxygenase.

Chemically, benzofurans are heterocyclic compounds containing fused benzene and furan rings. Benzofuran moiety constitute core of several interesting pharmacologically active products. They possess antibacterial, antifungal, anti-inflammatory, and antidepressant activity. Benzofurans have been known to inhibit the enzymes cycloxygenase and lipoxygenase, which are for the reasons mentioned above could be of use in treating inflammation. So, we undertook this study to screen the anti-inflammatory activity of the synthetic benzofuran compound, 3,4-dihydro-4-oxo-benzofuro-(3,2-d) pyrimidine-2-propionic acid.

**MATERIALS AND METHODS**

Benzofuran compound 3,4-Dihydro-4-oxo-benzofuro-(3,2-d) pyrimidine-2-propionic acid was the test drug under study, it is a white solid, insoluble water with following formula,

\[
\text{C}_9\text{H}_7\text{NO}_3
\]

The benzofuran compound which was originally synthesized in the chemistry laboratory of Gulbarga University by Dr. Y. Agasimundin, reader in Chemistry, Gulbarga University, Gulbarga was used for the study.

Phenyl butazone that is a 3,5-dioxo-1,2-diphenyl-4-n-butyl pyrazolidine, a pyrazolone derivative, a well-known anti-inflammatory drug was used as standard drug was obtained from Pacific Pharmaceuticals Pvt. Ltd., Bangalore. All the aforementioned drugs were administered by mouth as a suspension with 2% gum acacia, in the dose of 100 mg/kg body weight with help of polythene tube. The control animals received an equal volume of plain 2% gum acacia suspension.

Animals used in the present study were Wistar albino rats of either sex of average weight 120 to 200 g, which were in bred in the central animal house, were used for experiment. The study was done after getting the clearance of Institutional Animal Ethical Committee.

All the animals were allowed food and water ad libitum both being withdrawn just before the experiment. The animals were housed in a polypropylene cage under standard conditions in dim light and noise free room.

The above animals were divided into two main groups, one for the carrageenin-induced inflammation and the other for turpentine-induced peritonitis.

Carrageenin-induced rat paw edema model; In this model the first group of rats were sub divided into three groups of six rats each, one group of rats acted as control which was treated with 2% gum acacia orally, another group received standard drug phenyl butazone in the dose of 100 mg/kg body weight orally, the remaining group was treated with the test compound the benzofuran in the dose of 100 mg/kg body weight orally.

All the drugs were given 1 h prior to the subplantar injection of inflammation inducing agent carrageenin in 0.05 ml in the right hind paw.

The right hind paw volume was measured by using mercury plethysmograph, immediately after the subplantar injection of carrageenin, (0 h volume), and also at the end of 4 h. The difference between the 0 h paw edema volume and volume after 4 h indicated the actual edema.

So the mean paw edema volume in animals treated with drugs groupwise was compared with that in the control group, and the anti-inflammatory activity of drugs was measured by the formula.

\[
\text{Percent of inhibition of edema, i.e., anti-inflammatory activity} = 100 \left[1 - \frac{V_t}{V_c}\right]
\]

where \(V_t\) is the mean volume of paw edema in drug-treated group, and \(V_c\) is the mean volume of paw edema in the control group.

Turpentine-induced peritonitis model; in this model also rats were divided into three groups of six each. Here, again 2% gum acacia acted as control and 100 mg/kg of phenylbutazone as standard drug and benzofuran in the dose of 100 mg/kg as test drug. Peritonitis was induced by intraperitoneal injection of 0.5 ml of turpentine. All the drugs were given orally with gum acacia as a suspending agent, 1 h prior to intraperitoneal injection of 0.5 ml of turpentine. After the end of 4 h, the animals were sacrificed and the exudates were collected and measured immediately by cutting open the abdomen. The same formula was used as in the carrageenin method in order to calculate the percent of anti-inflammatory activity.

**Statistical Analysis**

All the data obtained were tabled as mean and standard error of mean, the data were analysed using Student’s t-test.

**RESULTS**

There was significant reduction in the amount of rat paw volume in carrageenin model, i.e., the percent of inhibition...
of edema formation was significantly higher as compared to control group. Moreover, the amount of reduction in exudates formation in turpentine-induced peritonitis model was also significant in both the models the percent of anti-inflammatory activity of test drug was statistically significant with $P < 0.05$ in both the models.

The Table 1 illustrates that the test compound benzofuran has got significant anti-inflammatory activity as compared to control in the carrageenin-induced rat paw model.

All the drugs are administered orally in the dose of 100 mg/kg body weight.

In Table 2 also it is seen that the test drug benzofuran has got significant anti-inflammatory activity as compared to control.

All the drugs are administered orally in the dose of 100 mg/kg body weight.

The Figure 1 clearly shows that the percent of inhibition of edema formation is significantly higher with test drug under study.

The Figure 2 illustrates that the amount of exudates formation is significantly lower in the benzofuran group, i.e., the percent of inhibition of exudates formation is significantly higher than the control group.

**DISCUSSION**

Inflammation can be defined as “the local reaction of vascularized tissue to injury.” Acute inflammation is a stereotypical response to all forms of injury, whatever the causative agent, it is of relatively short duration, lasting for few minutes to several hours or 1-2 days, and its main characteristics are exudation of fluid and plasma protein and emigration of leukocytes. All these effects of acute inflammation are mainly mediated by prostaglandins, leukotrienes and histamine.

Arthritis, arthralgia of major and minor joints is the burning problem of the age old populations affecting both the population equally well. The remedies for the same of the curative efforts are still a mirage however the present study throws a light on the usage of Benzofuran compounds, because of their anti-fungal, anti-microbials properties and exploratory, anti-inflammatory activity of the said compound requires further evaluation as to consider for human trials for their aforesaid properties, however

<table>
<thead>
<tr>
<th>Groups</th>
<th>Mean paw edema volume (cm)$\pm$SEM</th>
<th>Percent inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.58±0.036</td>
<td>0.27±0.024</td>
</tr>
<tr>
<td>Phenylbutazone (standard)</td>
<td>0.36±0.03</td>
<td>53.44*</td>
</tr>
<tr>
<td>Benzofuran (test drug)</td>
<td></td>
<td>37.93*</td>
</tr>
</tbody>
</table>

*Indicates highly significant: $P<0.001$, SEM: Standard error for mean

<table>
<thead>
<tr>
<th>Groups</th>
<th>Mean peritoneal exudates volume (ml)$\pm$SEM</th>
<th>Percent inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>3.33±0.15</td>
<td>-</td>
</tr>
<tr>
<td>Phenylbutazone (standard)</td>
<td>1.87±0.12</td>
<td>43.84**</td>
</tr>
<tr>
<td>Benzofuran (test drug)</td>
<td>2.77±0.11</td>
<td>16.82*</td>
</tr>
</tbody>
</table>

**Indicates highly significant: $P<0.001$, *indicates significant: $P<0.05$, SEM: Standard error for mean
the toxic effects and therapeutic benefits with minimal adverse effects are those criteria’s, which still needs to be fathomed out.

In our study, we observed that the test drug benzofuran showed significant anti-inflammatory activity in both the models. These observations can be explained on the basis that benzofurans are potent inhibitors of cyclooxygenase and lipooxygenase enzymes which are responsible for the synthesis of mediators of inflammation like prostaglandins and leukotrienes. From structure activity relationship, presence of certain functions like – COOH in benzofuran derivatives also contributes to the increase in potency of the test drug. Recently, metallopeptinases have been implicated as mediators of inflammation, and fusion of pyrimidine group to benzofurans also potentiates their anti-inflammatory activity by inhibition of metallopeptinases.

CONCLUSION

With all the above-mentioned considerations we conclude that the test drug benzofuran has got significant anti-inflammatory activity and further detailed work with this benzofuran compound, in different dosage profiles might be worth undertaking.

REFERENCES


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