Original Research Article

Evaluation of Anti-inflammatory activity of Qurs-e-Mafasil Jadeed

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ABSTRACT

With an increased incidence of drug toxicity and resistance to allopathic drugs, plant drug formulations could be an interesting alternative. Some plant drugs and phytochemicals are known to be anti-inflammatory properties, and can be of great significance in treatment of inflammatory disorders. These considerations require the scientific evaluation of the most important and commonly used traditional herbal formulations. A study has been done to find anti-inflammatory activity of Qurs-e-Mafasil Jadeed containing Colchicum luteum, Curcuma longa and gum of Acacia Arabica. In this proposed work 2 % aqueous suspension of qurs/tablet powder in gum acacia was used to determine its anti-inflammatory activity by carrageenin induced oedema test and cotton pellet induced granuloma test. Efficacy of this Unani formulation was compared with standard referent drug, Diclofenac sodium. The obtained results using carrageenin oedema test showed decrease in left hind paw volume significantly after 3 hours of carrageenin injection. In cotton pellet induced granuloma test, animals in all the test and standard drug tested groups, shows reduction in granuloma formation significantly. Thus, our results clearly indicate that this test formulation possesses significant anti-inflammatory activity in both acute and sub-acute phase.

Introduction

The Unani System of Medicine, an Indian variant of Greco-Arabic system is being practiced in India for centuries; not only its simple medicaments but also the poly-pharmaceutical preparations have great significance in the treatment of inflammatory conditions. WHO estimates that 4 billion people all over world use herbal medicine. The discovery of vegetable extract of medicinal benefit leads to the isolation of active principle and its subsequent chemical characterization [1]. Despite the potential of the plants to provide us with useful pharmaceutical agents, the field is still poorly studied. Only an estimated 5-10 % of the approximately 3-5 lacs plant species worldwide have been screened for one or more bioactivities [2]. Inflammation is generally considered as an essentially protective response to tissue injury caused by noxious physical, chemical or microbiological stimulus. It is a complex process using various mediators, such as prostaglandins, leukotrienes and platelet activating factor etc. Thus, inhibition of the prostaglandins and other inflammatory mediators could be employed as criteria to evaluate potential anti-inflammatory compounds. The current management of inflammatory diseases is limited to use of anti-inflammatory drugs whose chronic administration is associated with severe adverse effects. Plant derived drugs are slowly emerging as a viable alternative because they are cheap, abundantly available and relatively less toxic [3]. Also, solid form of drug (tablet) has many advantages over conventional powder states owing to its ease of inhalation, taste and more accurate dosage form. Therefore, in the present study, pharmacological characteristic of a Unani compound formulation Qurs-e-Mafasil Jadeed (QMJ) mentioned in “Qarabadeen-e-Majeedi” [4] was investigated. According to the “Qarabadeen-e-Majeedi” the QMJ contains (i) Haldi (Curcuma longa Linn., Dried Rhizome- 25 g), (ii) Colchicum (Colchicum luteum) Baker, Dried Corm- 25 g) and (iii) Samagh-e-Arabi/Gum acacia

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(Acacia arabica Linn., Dried Fine powder- 5 g). Gum acacia powder of (S. d. Fine Chemical Ltd.) was used. Two ingredients Suranjan and Haldi possess anti-inflammatory and anti-arthritic properties: Samagh-e-Arabi/Gum acacia possesses qabiz and demulcent property. Suranjan has purgative (Mushil-e-Balgham) property also and many more actions are attributed to these drugs, described by Unani as well as Modern physicians [5, 7-9].

Materials and Methods

Collection of plant material
The raw materials were purchased from the local market of Aligarh and the sample were authenticated in Pharmacognosy section of the Department of Ilmul Advia, Faculty of Unani Medicine, AMU, Aligarh and found within range of standards as mentioned in the Unani and Ayurvedic Pharmacopoeia of India [6, 10-11].

Animal
The present study was undertaken to evaluate the anti-inflammatory and analgesic activity in healthy albino rats of either sex weighing 150-200g. Animals were housed in groups of 6 animals in cages under hygienic conditions. All experiments were conducted during light phase between 8:00 and 13:00 hrs. All procedures were conducted according to the guidelines of the International association for the study of pain [12]. All the animals were fed, standard animal diet and water, ad-libitum.

Drugs and chemicals
Diclofenac sodium (Voveran, Novartis, India), Carrageenan Type II (Sigma chemical company, USA), Normal Saline (E. Merck Ltd, India), 2% Aqueous Suspension of Qurs/tablets.

Preparation of suspension
The Test formulation (tablets) was coarsely powdered in an iron mortar. The Fresh suspension of powdered drug was prepared in distilled water with 2% gum Acacia powder (S. d. Fine Chemical Ltd.), which was administered orally in the animals with the help of feeding canula after shaking the suspension well. The dose for the animal was calculated by extrapolating the human dose of test drug by conversion factor of 7 for rat [13]. Hence, the three different doses of aq. susp. of test drug taken for the study were 200 mg/kg, 300 mg/kg and 400 mg/kg.

Determination of anti-inflammatory activity

Carrageenin induced oedema test
Oedema represents the acute phase of inflammation in carrageenin-induced paw oedema test. The effect of test drug on carrageenin-induced oedema in rat paw was studied by the method of Winter et al. [14]. It is the simplest and most widely used model for studying the anti-inflammatory activity. Albino rats of either sex, weighing 150-200 gm, were divided in to 5 groups of 6 animals each. The volume of left hind paw was measured plethysmographically before giving the drugs. Animals in Group I served as control and were administered with 20 ml/kg distilled water. The reference drug, Diclofenac Sodium was given to the animals in Group IInd, in a dose of 10 mg/kg, orally. IIIrd, IVth and Vth group were treated with 200 mg/kg, 300 mg/kg and 400 mg/kg of 2 % gum acacia suspension of Test formulation respectively. One hour after the drug/vehicle treatment, 0.1 ml of 1% aqueous solution of Carrageenin in distilled water was injected under the plantar aponeurosis of the left hind paw. The volume of the paw was again measured at 1, 2, 3, 4 and 5 hours after Carrageenin injection. The percentage inhibition of oedema was calculated with reference to negative control by the formula described by Newbould [15].

\[
I = 100 \left(1 - \frac{a - x}{b - y}\right)
\]

Where,

I = Percentage of inhibition
a = Mean left hind Paw volume of Test / Standard animals after Carrageenin injection
b = Mean left hind Paw volume of control animals after Carrageenin injection.
x = Mean left hind Paw volume of Test / Standard animals before Carrageenin injection.
y = Mean left hind Paw volume of control animals before Carrageenin injection

Cotton pellet induced granuloma test
Cotton pellet test was carried out by the method of Winter et al. [16]. The five groups of albino rats of either sex weighing 150-200 g, six in each group was included in this study. After shaving off the fur, the animals were anaesthetized by ether. Sterile pre weighed cotton pellets (20 ± 1mg) were implanted in the ventral region of rats, one near each axilla through a single needle incision. Animals in group I served as control and were administered with 20 ml/kg distilled water. The standard drug was given to the animals in group II, in a dose of 10 mg/kg, orally. Third, fourth and fifth group were treated with 200 mg/kg, 300 mg/kg and 400 mg/kg of aq. suspension of test formulation respectively. Test formulation was administered orally to the respective group of animals for seven consecutive days, from the day of cotton-pellet implantation. On the day one test formulation was administered 30 minutes before cotton pellet implantation. On the eighth day, the animals were anaesthetized again; the cotton pellets were removed surgically and made free from extraneous tissues. The pellets were incubated at 37 °C for 24 h and dried at 60 °C to constant weight. The increase in the dry weight of the pellets was taken as a measure of granuloma formation.
Statistical analysis
The results are expressed as Mean ± SE from n=6 observations. The findings were also analyzed for determining significance of difference by one-way ANOVA test followed by pair-wise comparison of various group by TUKEY. The analysis was carried out by using the online available software [17].

Ethical Permission
The animal experiments which were conducted for the anti-inflammatory activity of the test drug were permitted from the ethical committee of the institution.

Results
The results of carrageenin induced oedema test are presented in Table-1 and the comparison of percentage of inhibition among all the treated groups is shown in Figure-1&2. In the carrageenin oedema test, 10 mg/kg of the standard drug, Diclofenac sodium, higher, medium and lower doses of Aq. suspension of the test formulation were found to decrease the left hind paw volume significantly (p<0.001) 3 hours after carrageenin injection. The percentage inhibition of oedema was found to be 70.38 % with Diclofenac sodium; 48.15 %, 57.41 % and 61.12 % with 200mg/kg, 300mg/kg and 400 mg/kg of Aq. suspension of tablet respectively.

Table 1: Anti-inflammatory effect of the formulation tablet in carrageenin induced oedema test.

<table>
<thead>
<tr>
<th>Group(s)</th>
<th>1 hour after Carrageenin injection</th>
<th>2 hours after Carrageenin injection</th>
<th>3 hours after Carrageenin injection</th>
<th>4 hours after Carrageenin injection</th>
<th>5 hours after Carrageenin injection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Increas e in paw volume in ml (Mean ± SE)</td>
<td>Percenta ge of inhibition (%)</td>
<td>Increas e in paw volume in ml (Mean ± SE)</td>
<td>Percenta ge of inhibition (%)</td>
<td>Increas e in paw volume in ml (Mean ± SE)</td>
</tr>
<tr>
<td>Control</td>
<td>0.39±0.0</td>
<td>-</td>
<td>0.43±0.0</td>
<td>-</td>
<td>0.54±0.0</td>
</tr>
<tr>
<td>Diclofenac sodium (10mg/kg)</td>
<td>0.17±0.0</td>
<td>2</td>
<td>0.14±0.0</td>
<td>2</td>
<td>0.16±0.0</td>
</tr>
<tr>
<td>Aq.Susp. (200mg/K g)</td>
<td>0.31±0.0</td>
<td>3</td>
<td>0.32±0.0</td>
<td>3</td>
<td>0.28±0.0</td>
</tr>
<tr>
<td>Aq.Susp. (300mg/K g)</td>
<td>0.27±0.0</td>
<td>3</td>
<td>0.28±0.0</td>
<td>3</td>
<td>0.23±0.0</td>
</tr>
<tr>
<td>Aq.Susp. (400mg/K g)</td>
<td>0.24±0.0</td>
<td>3</td>
<td>0.25±0.0</td>
<td>3</td>
<td>0.21±0.0</td>
</tr>
</tbody>
</table>

F-Value | 11.99 | 20.97 | 40.07 | 40.74 | 25.69 |

X = Against Control
= Against Aq.Susp. 200 mg/kg
= Against Aq.Susp. 300 mg/kg
= Against Aq.Susp. 400 mg/kg

1 = p < 0.001
Fig. 1: Effect of Qurs-e-Mafasil Jadeed in Carrageenin induced

Fig. 2: Effect of Qurs-e-Mafasil Jadeed in Carrageenin induced
In the cotton pellet induced granuloma test, 10mg/kg of the standard drug Diclofenac sodium, all the three doses of Aq. suspension of the test formulation were found to reduce granuloma formation significantly (p<0.001). The percentage inhibition of granuloma formation was found to be 78.57% with referent drug; while with 200 mg/kg, 300 mg/kg and 400 mg/kg of aq. susp. of tablet, percentage inhibition of granuloma formation was found to be 52.40%, 62.73% and 69.98%, respectively. Results are presented in Table-2 and the comparison of percentage of inhibition among all the treated groups is shown in Figure-3&4.

Table 2: Anti-inflammatory effect of formulation tablet in cotton pellet test

<table>
<thead>
<tr>
<th>Group(s)</th>
<th>Increase in weight of Cotton Pellet in mg (Mean ± SE)</th>
<th>Percent of Inhibition of Granuloma (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>50.17±0.80</td>
<td>—</td>
</tr>
<tr>
<td>Diclofenac sodium (10mg/kg)</td>
<td>10.75±1.18 X(^a) b(^1)</td>
<td>78.57</td>
</tr>
<tr>
<td>Aq.Susp. (200mg/Kg)</td>
<td>23.88±0.93 X(^1)</td>
<td>52.40</td>
</tr>
<tr>
<td>Aq.Susp. (300mg/Kg)</td>
<td>18.70±1.01 X(^1) a(^1)</td>
<td>62.73</td>
</tr>
<tr>
<td>Aq.Susp. (400mg/Kg)</td>
<td>15.06±1.28 X(^1) a(^2)</td>
<td>69.98</td>
</tr>
</tbody>
</table>

\(n=6\)

X = Against Control 1 = p < 0.001
\(a = \) Against aq. Susp. 200mg/Kg
\(b = \) Against aq. Susp. 300mg/Kg
\(c = \) Against aq. Susp. 400mg/Kg
**Effect of the Qurs-e-Mafasil Jadeed in Cotton Pellet Induced Granuloma Test**

![Graph showing inhibition of granuloma formation percentage for different doses of drugs](image)

**Fig. 4: Effect of Qurs-e-Mafasil Jadeed in Cotton pellet induced granuloma test**

**Discussion**

In carrageenin induced oedema test the study shows that all the three doses of the Test Formulation possess anti-inflammatory activity. However, there was no significant difference between the effect of the three doses of aq. susp. of the tablet. The findings of above test indicate that medium and higher doses of aqueous suspension of the tablet possess good protective activity against acute inflammation, near standard drug diclofenac sodium but there is no significant difference of effect between standard drug and medium and higher doses of the test formulation. The carrageenin-induced oedema test has been a popular inflammatory model to investigate anti-inflammatory effect of compounds [18]. This test was carried out in the multi-phasic form, i.e., the inhibition was observed also at 1, 2, 4 and 5 hours after carrageenin injection. This is considered to suggest the mechanism of anti-inflammatory action as different inflammatory mediators predominate in various phases of acute inflammation. Histamine plays the major role at 1 hour, and prostaglandins at 4 and 5 hours, after the inflammatory stimulus [19, 20]. The present study reveals that the test drugs exerted inhibition at all intervals of testing. However, the inhibitory effect was lesser at 1 hours and maximum at 3 hours. The higher dose of aq. susp. of the tablet is active against histamine at 1 hr as equal to the effect of standard drug(not significant difference) and higher and medium dose of the test formulation is active against prostaglandins at 4 hours and 5 hours as equal to standard drug(not significant difference). These findings indicate that medium and higher doses of the tablet oppose the action of most mediators of acute inflammation. The cotton pellet granuloma model is an indicator for the proliferative phase of inflammation [21]. In this test inflammation and granuloma developed during the period of several days. Inflammation involves proliferation of macrophages, neutrophils and fibroblast, which are basic sources of granuloma formation [22]. Hence the decrease in the weight of granuloma indicates that the proliferative phase was effectively suppressed by all the three doses of aqueous suspension of the test drug. The study shows that all the three doses of the Test Formulation possess anti-inflammatory activity. The higher dose of the Test Formulation produces significantly greater effect (p<0.001) than that of lower dose of the test formulation. These findings strongly suggest that the tablet possesses significant effect against sub acute inflammation.

**Conclusion**

The higher dose of aq. susp. of the formulation possesses remarkable anti-inflammatory activity approximately equal to the effect of standard referent agent (Diclofenac sodium). The study offers an improvement in Unani health care by showing the more convenient Tablet form which is more effective than powder and semisolid form of Unani drugs.
Acknowledgment

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Conflict of interest statement

We declare that we have no conflict of interest.

References


