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This issue carries an article ranked 1 and was published in 1980, and received 149 citations.

Preliminary study on antirheumatic activity of curcumin (diferuloyl methane)

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A short term, double blind, cross-over study was carried out in 18 patients with 'definite' rheumatoid arthritis to compare the antirheumatic activity of curcumin (diferuloyl methane) 1200 mg/day with phenylbutazone 300 mg/day. Subjective and objective assessment in patients who were not taking corticosteroids just prior to the study showed significant ($P<0.05$) improvement in morning stiffness, walking time and joint swelling, following two weeks of curcumin or phenylbutazone therapy. Grip strength, articular index and ESR did not change following administration of either of the compounds. Although a significant improvement was noted in both the groups by the observer, patients assessed significant improvement only with phenylbutazone.

There is considerable hope of finding active antirheumatic compounds from indigenous plants. The rhizome of turmeric i.e. Curcuma longa Linn (Hindi: Haldi), is widely used in indigenous medicine\(^1\). Curcumin (diferuloyl methane) is an important constituent of the rhizome and is commonly used as a spice in cooking and also as a dyeing agent. Recently, significant anti-inflammatory activity of curcumin has been demonstrated\(^2,3\) in acute and chronic models of experimental inflammation in rats and mice. We have been assessing antirheumatic activity of indigenous herbal drugs and report here the initial encouraging results of a clinical trial of curcumin in rheumatoid arthritis patients attending the Rheumatology Clinic of this Institute.

Material and Methods

Eighteen patients (16 females and 2 males), suffering from definite rheumatoid arthritis\(^4\) were inducted into the study after an informed consent. Their ages ranged between 22 and 48 years (mean: 36.3 years) and the duration of articular symptoms ranged from 9 to 96 months (means: 38.6 months). All had significant reducible disease-activity, as judged by the physician. Patients less than 20 years or more than 55 years of age and those on second line drugs or with hepatic/renal function impairment or peptic ulcer disease were excluded. Four days before the study was initiated all anti-inflammatory drugs were stopped and the patients were allocated to a random
sequence of phenylbutazone and curcumin. Each drug was prepared in identical opaque capsules to mask the yellow colour of curcumin. Total daily dose of phenylbutazone was 300 mg and that of curcumin 1200 mg and both were administered in three divided doses.

Rheumatic activity was assessed by the same observer at the beginning of the study (baseline) and at the end of each treatment period. Duration of morning stiffness was recorded in minutes. Fatigue time was recorded as the period in hours between waking up and when the patient felt tired. Time required to walk 25 feet was recorded as walking time. Objective parameters measured for the disease activity were articular index of joint tenderness and grip strength of both the hands. Overall general improvement was recorded on the patient's and observer's assessment of progress (5 = poor, 4 = slight improvement, 3 = moderate improvement, 2 = much better, and 1 = very much better).

Pre-trial and fortnightly blood counts, erythrocyte sedimentation rate (ESR), hepatic and renal function tests and faecal blood loss were also undertaken. Side effects were recorded.

Results

All the 18 patients completed the study on none of the patients in either of the groups had any side effects during the trial period. There was no significant change in the blood pressure, pulse, haemoglobin, hepatic or renal function during the study.

The details of observations on response to treatment with subjective and objective assessments are given in the Table.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Phenylbutazone</th>
<th>Curcumin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning stiffness (minutes)</td>
<td>132.5 ± 17.0</td>
<td>97.2 ± 17.0*</td>
<td>124.2 ± 17.0*</td>
</tr>
<tr>
<td>Walking time (sec./25 ft)</td>
<td>15.4 ± 1.2</td>
<td>12.4 ± 1.0*</td>
<td>13.8 ± 1.5*</td>
</tr>
<tr>
<td>Fatigue time (h)</td>
<td>3.8 ± 0.6</td>
<td>5.4 ± 0.7*</td>
<td>3.9 ± 0.5</td>
</tr>
<tr>
<td>Grip strength (mm of Hg)</td>
<td>67.7 ± 6.9</td>
<td>70.3 ± 6.4</td>
<td>66.4 ± 6.4</td>
</tr>
<tr>
<td>Articular index</td>
<td>79.6 ± 9.8</td>
<td>72.7 ± 10.5</td>
<td>75.9 ± 11.1</td>
</tr>
<tr>
<td>ESR (mm first h)</td>
<td>40.4 ± 4.0</td>
<td>39.5 ± 4.6</td>
<td>45.6 ± 3.4</td>
</tr>
<tr>
<td>Swelling</td>
<td>168 ± 3.3</td>
<td>112 ± 2.6**</td>
<td>125 ± 2.4**</td>
</tr>
<tr>
<td>Overall assessment :</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observer</td>
<td>3.8 ± 0.2</td>
<td>3.1 ± 0.2†</td>
<td>3.4 ± 0.1*</td>
</tr>
<tr>
<td>Patient</td>
<td>4.2 ± 0.2</td>
<td>3.3 ± 0.2*</td>
<td>3.9 ± 0.3</td>
</tr>
</tbody>
</table>

*P < 0.05; **P < 0.02; †P < 0.001

Values of phenylbutazone and curcumin were compared with baseline values.
Antirheumatic activity of curcumin

Both curcumin and phenylbutazone showed antirheumatic activity. A significant improvement in morning stiffness, walking time, and joint swelling occurred with both the drugs. Neither of them improved the grip strength, articular index or ESR. Fatigue time improved with phenylbutazone only. Both patient and the observer assessed improvement at the end of phenylbutazone period. However, such an improvement was noted by the observer alone at the end of curcumin period.

Discussion

There are no published clinical studies on antirheumatic activity of curcumin. The results of our short term preliminary clinical study show, for the first time, convincing evidence of the antirheumatic activity of curcumin in patients with rheumatoid arthritis. The antirheumatic activity of 1200 mg of curcumin was comparable to that of 300 mg phenylbutazone. Neither of the drugs improved grip strength, articular index for pain or ESR and this may possibly be due to the short period of study, long duration of articular manifestations with destructive changes or less than optimal dosage. Absence of significant analgesic activity in curcumin may partly explain the lack of improvement in the articular index.

The complete absence of any side effects during the study period is very encouraging and merits a thorough study on curcumin's potential as a safe antirheumatic drug. Further studies are in progress in this direction.

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References


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