A COMPARATIVE STUDY ON THE ANTI-INFLAMMATORY EFFECTS OF TRIVIDHA PAKA OF KSHEERABALA TAILA

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ABSTRACT

Non-steroidal anti-inflammatory drugs (NSAID) owing to its exceedingly speckled side effects and adversities are in the verge of a moribund reliance. Ksheerabala Taila, a sage old Ayurveda remedy remarkably emphasised in the treatment of Vata Vyadhi and Vatarakta is well used since ages as an anti-inflammatory medicine. Developing researches have demonstrated its efficacy to counter neuro toxicity and subsequently validated its neuro protective effect. Though, the much acclaimed traditional wisdom regarding its anti-inflammatory action is neither scientifically appraised nor compared with any standards. The aim of the study was to scientifically establish the anti-inflammatory effect of Ksheerabala Taila by comparing it with the standard anti-inflammatory drug Diclofenac and to assess the specific Paka (stage) that exhibits it more. The study confirmed oral anti-inflammatory effect of Ksheerabala Taila which significantly (P < 0.01) inhibited the (6 h) late onset carrageenan-induced rat paw oedema in Wistar strain Albino rats. This activity was found to be more in Mrdu and Madhya Paka of Ksheerabala Taila. The study could also conclude that the anti-inflammatory effect exhibited by Ksheerabala Taila was comparable to that of Diclofenac and Ksheerabala Taila could be an appropriate alternative to the potentially harmful NSAID’s.

Key Words: NSAID, Ksheerabala Taila, Anti-inflammatory activity, carrageenan, Mrdu Paka and Madhya Paka.

INTRODUCTION

Sneha kalpana (Oleagenous preparation) is a secondary formulation in which Taila (Sesame oil) or Ghrta (ghee) are used as the media into which the active principles of the drugs are extracted. It is a pharmaceutical process to prepare oleaginous medicaments in which the kalka, kwatha and drava dravya 1 taken in specific proportions, are subjected to unique heating pattern and duration. It is mainly aimed at the mass transfer of the aqueous and lipid-soluble active principles. The Trividha Paka (Three stages) i.e. Mrdu, Madhya and Khara are the imperative stages 2 of a sneha Kalpana which possesses specific therapeutic utility 3 and administration routes. This specificity is due to the difference in the concentration of drugs in different Pakas.

Ksheerabala is one among the sneha kalpana prepared by using Go Ksheera (Cow’s milk), Balamoola Kalka (paste of Sida rhombifolia root), Balamoola kashaya (decocotion of Sida rhombifolia root) and Tila Taila (Sesame oil). It has a Rasayana (rejuvenation) property and is used in therapeutics both topically and systemically. It is indicated in all Vata Vyadhis, mainly in Vatarakta 4; an inflammatory condition.

Inflammation is defined as the reaction of vascularised living tissue to injury. It is closely intertwined with the process of repair. 5 Inflammation can be classified as either acute or chronic. The increased movement of plasma and leukocytes (especially granulocytes) from the blood into the injured tissues as an initial response of the body against the harmful stimuli results in Acute Inflammation.

The present study was intended to experimentally evaluate and establish the anti-inflammatory activity of Ksheerabala Taila by comparing it with Diclofenac, a standard anti-inflammatory drug in acute inflammation models of experimental rats. The study was also projected to identify the specific Paka of Ksheerabala taila that serves the purpose more effectually.

MATERIALS AND METHODS

Animals

Wistar strain albino rats of either sex weighing between 180-280 g were obtained from the animal house of S.D.M centre for research in Ayurveda and allied sciences. The animals were fed with rat pellet feed (Amrut brand) and tap water was given ad libitum. Animals were maintained under normal ambient conditions. The protocol was approved by the Institutional Animal Ethics Committee with Approval number SDM - CAU- 13-14-16.

Investigational Drug and Dosage Preparation

The preparation of Ksheerabala Taila was carried out as per the reference of Sahasra yoga 6 and Ayurvedic Formulary of India. The Taila Paka was assessed in par with the pharmaceutical parameters explained in Sharangdhar Samhitā. The drug source of Bala was identified as Sida rhombifolia by the Dravya Guna Department of S.D.M. Ayurveda College Udupi. The test drugs viz. Mrdu, Madhya and Khara Paka of Ksheerabala Taila were prepared in the Department of Rasa Shatra and Bhaishajya...
Anti-Oedema Assay introduced by Winter et al. method of carrageenan induced inflammation as the rat by the injection of a phlogistic agent (irritant). Drugs to inhibit the oedema produced in the hind paw of the rat was taken as standard and administered with the standard dose for each animal. The test drugs were administered once daily for five consecutive days. On 5th day prior to Carrageenan injection the initial paw volume of left hind paw was measured using a Plethysmometer and this was considered as initial paw volume.

An hour after drug administration; 0.1 ml of freshly prepared 1% Carrageenan in sterile saline solution was injected to the sub-planter Apo neurosis of the left hind limb to produce the paw oedema. The rats were administered with the tap water in the dose of 2 ml/100g body weight to ensure uniform hydration. This is supposed to minimize the variation in oedema formation. The intensity of oedema formation was recorded after 2nd, 3rd, 6th hour and 24th hour after Carrageenan injection.

Results were expressed as percentage increase in paw volume in comparison to the initial values. Percentage increase in paw volumes were calculated by subtracting the initial paw volumes from the paw volumes obtained after the injection of the phlogistic agent (irritant). The method of carrageenan induced inflammation as introduced by Winter et al. (1962) was adopted in this study owing to its benefits like high specificity, lack of drawbacks, easy availability of albino rats and carrageenan and easy measurability of paw volume of rats.

**Procedure**

The test drug was administered once daily for five consecutive days. An hour after drug administration; 0.1 ml of freshly prepared 1% Carrageenan in sterile saline solution was injected to the sub-planter Apo neurosis of the left hind limb to produce the paw oedema. The rats were administered with the tap water in the dose of 2 ml/100g body weight to ensure uniform hydration. This is supposed to minimize the variation in oedema formation. The intensity of oedema formation was recorded after 2nd, 3rd, 6th hour and 24th hour after Carrageenan injection.

The data obtained were statistically analysed using one way ANOVA followed by Dunnet’s multiple ‘t’ test as Post hoc test with ‘p’ value <0.05 considered as statistically significant.

**OBSERVATIONS & RESULTS**

### Table 1: Effect of Trividha Paka of KBT in % Change in Paw Volume in First Hour

| Group       | % increase in paw volume | % Change |SEM
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Control</td>
<td>35.58±6.72</td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td>29.57±6.21</td>
<td>16.89*</td>
</tr>
<tr>
<td>Mrdu paka</td>
<td>26.73±4.50</td>
<td>24.87*</td>
</tr>
<tr>
<td>Madhya paka</td>
<td>21.71±6.50</td>
<td>38.98*</td>
</tr>
<tr>
<td>Khara paka</td>
<td>52.70±8.95</td>
<td>48.11**</td>
</tr>
</tbody>
</table>

Data: Mean±SEM

### Table 2: Effect of Trividha Paka of KBT in % Change in Paw Volume in Third Hour

| Group       | % increase in paw volume | % Change |SEM
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Control</td>
<td>81.80±7.02</td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td>42.96±10.55</td>
<td>47.48*</td>
</tr>
<tr>
<td>Mrdu paka</td>
<td>35.80±5.66</td>
<td>56.23*</td>
</tr>
<tr>
<td>Madhya paka</td>
<td>48.47±13.49</td>
<td>40.70*</td>
</tr>
<tr>
<td>Khara paka</td>
<td>83.70±15.88</td>
<td>2.32*</td>
</tr>
</tbody>
</table>

Data: Mean±SEM

### Table 3: Effect of Trividha Paka of KBT in % Change in Paw Volume in Sixth Hour

| Group       | % increase in paw volume | % Change |SEM
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Control</td>
<td>93.38±8.47</td>
<td>-</td>
</tr>
<tr>
<td>Standard</td>
<td>32.85±7.48**</td>
<td>64.82*</td>
</tr>
<tr>
<td>Mrdu paka</td>
<td>42.24±4.81**</td>
<td>54.76*</td>
</tr>
<tr>
<td>Madhya paka</td>
<td>35.20±6.63**</td>
<td>73.01*</td>
</tr>
<tr>
<td>Khara paka</td>
<td>60.89±9.20**</td>
<td>34.79*</td>
</tr>
</tbody>
</table>

Data: Mean±SEM ** P<0.01

### Table 4: Effect of Trividhapa KBT in % Change in Paw Volume in 24th Hour

| Group       | % increase in paw volume | % Change |SEM
<table>
<thead>
<tr>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>16.41±1.76</td>
<td>-</td>
</tr>
<tr>
<td>Standard</td>
<td>22.01±8.75</td>
<td>34.12*</td>
</tr>
<tr>
<td>Mrdu paka</td>
<td>4.19±2.35</td>
<td>74.46*</td>
</tr>
<tr>
<td>Madhya paka</td>
<td>9.25±1.63</td>
<td>43.63*</td>
</tr>
<tr>
<td>Khara paka</td>
<td>21.29±5.99</td>
<td>29.73*</td>
</tr>
</tbody>
</table>

Data: Mean±SEM
The effect of Trividha paka of Ksheerabala Taila on paw volume during 1ST, 3rd, 6th and 24th hour has been depicted in Tables 1, 2, 3 and 4 respectively. During 1ST hour and 3rd hour Mrdu and Madhya paka of Ksheerabala taila along with standard group, though non-significant showed a decrease in % increase in paw volume while Khara paka caused an increase of the same. While in the 6th hour all the four groups produced a statistically significant decrease in % increase in paw volume. Again in the 24th hour Mrdu and Madhya paka resulted in a decrease while khara paka and standard group caused an increase in % increase in paw volume.

DISCUSSION

Carrageenan induced paw oedema test is commonly used as a primary test for acute inflammation and to screen the ability of the test drug to reduce local oedema induced by carrageenan. The particular inflammation created by carrageenan was found to be biphasic. The early phase lasting for 1 to 2 hours after carrageenan injection is mainly mediated by histamine serotonin, and increased synthesis of prostaglandins in the damaged tissue surroundings. The late phase is sustained by prostaglandins released and mediated by bradykinins, leukotrienes secreted by polymorphonuclear cells and tissue macrophages.
The anti-inflammatory activity was expressed as percentage increase in paw volume by Ksheerabala Taila prepared in three different Pakas Viz. Mrdu, Madhya and Khara. The present study reported potent anti-inflammatory activity by Mrdu and Madhya Paka of Ksheerabala Taila during 3rd and 6th hour after carrageenan injection in the plantar region of rats paw. The Mrdu and Madhya Paka of Ksheerabala Taila exhibited significant anti-inflammatory activity (**p<0.01, *p<0.05) by reducing the paw volume.

Thus the test drug has a potential to inhibit the release of inflammatory mediators such as prostaglandins, leukotrienes and bradykinins from polymorphonuclear cells and tissue macrophages. In conclusion the present study supports the therapeutic use of Ksheerabala Taila and its potential role in the inflammatory disease conditions. It would be interesting to study and elucidate the mechanism of action involved in the anti-inflammatory activity reported above.

To focus on the influence of Paka on the expression of anti-inflammatory activity has shown that Mrdu and Madhya Paka samples produce moderate activity by 3rd hour (Table 2) and significant activity was reached at the 6th hour (Table 3). This is indicative of its influence over the second phase of carrageenan oedema formation. In contrast to this; in Khara Paka sample there was a pro-inflammatory moderate response at first hour (Table 1) indicating early phase changes, nil effect at third hour and weak to moderate activity at 6th hour was observed. This shows that Khara Paka has a marked influence over the expression of the desired pharmacological activity. The reason why reduced activity was observed required to be probed.

Further in Mrdu Paka and Madhya Paka models, though non-significant, anti-inflammatory activity persisted even at 24th hour (Table 4) where as in Khara Paka sample a mild pro-inflammatory effect was observed. Inter group analysis of the test sample response indicated significantly better effect in Madhya Paka sample at 3rd and 6th hour in comparison to the Khara Paka sample. This clearly shows the influence of correct preparatory procedures on the quality of the product with respect to expression of pharmacological effect.

It is important to note that; the degree of reduction in acute inflammation achieved by Mrdu and Madhya Paka of Ksheerabala Taila was comparatively greater than that of the standard drug Diclofenac; however, this difference was statistically insignificant. Interestingly, in the 24th hour, Mrudu and Madhya Paka of Ksheerabala Taila continued the anti-inflammatory action, while the standard drug, Diclofenac showed mild pro inflammatory influence. This difference though statistically non-significant, ascertains the fact that Mrdu and Madhya Paka of Ksheerabala Taila is equally effective to Diclofenac in reducing inflammation.

CONCLUSION

This study was designed and carried out to assess the anti-inflammatory activity of Trividha Paka of Ksheerabala Taila against acute inflammation represented by carrageenan oedema. In addition to this effect of these preparations were also compared to the standard anti-inflammatory drug; Diclofenac. Significant anti-inflammatory activity with late onset was observed in the Mrdu and Madhya Paka of Ksheerabala taila. The effect was good and significant. However, In Khara Paka of Ksheerabala taila, only moderate anti-inflammatory activity at 6th hour was observed. This clearly indicates that Khara Paka reduces the therapeutic efficacy of Ksheerabala taila. In addition, Mrdu and Madhya Paka of Ksheerabala Taila were found to be effective anti-inflammatory agents which can be comparable to Diclofenac. Further clinical and experimental studies are required to explore and establish the effectiveness of Ksheerabala Taila as a safe and effective alternative for harmful NSAID’s.

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