INTRODUCTION

The plant *Tamarindus indica* Linn. popularly known as imli, chincha, belongs to the family Caesalpiniaceae, found throughout India. The plant is used in traditional medicine for the treatment of cold, fever, stomach disorder, diarrhea and jaundice and as skin lesener, antimicrobial agents, (5). Seeds are useful in diarrhoea, dysentery, burning sensation, haematuria, inflammations, hepatic disorders, chronic ulcers. (6).

Adjuvant-induced arthritis (AIA) is an erosive autoimmune polyarthritis involving both humoral and cell mediated immune responses that resemble human rheumatoid arthritis (RA) (4). The immune system is a well-organized and well-regulated system. The deregulation of the immune system may lead to the development of autoimmune diseases. Rheumatoid arthritis (RA) is prototype of such groups of illness with chronic systemic disorders to be considered an autoimmune disease with destructive inflammatory polyarticular joint potentially resulting in progressive destruction of articular and periarticular structure. Persistent inflammation produces swollen joints with severe synovitis, decreased nociceptive threshold, and massive sub synovial infiltration of mononuclear cells, which along with angiogenesis leads to pannus formation. Expansion of the pannus induces bone erosion and cartilage thinning, leading to the loss of joint function (3). Hence there is an urgent need to find safer compound for the management of rheumatoid arthritis.

MATERIALS AND METHODS

The seeds were obtained from the Local area Pune. heated in a hot air oven at 140°C, for 45 min. cooled and cracked to separate their outside brown layer. Only brown-red seed coats were collected and these were then ground into fine powder. Authenticated by Dr. A. M. Mujumdar, Head, Plant Science Division, Agarkar Research Institute, Pune. (Authentication no: 09-06)

Preparation of extracts

The dried, coarse powder of seed coat of *Tamarindus indica* Linn were extracted with soxhlet extraction apparatus using ethanol and distilled water. The resultant extract was concentrated using rotary vacuum evaporator. The yield of ethanolic and aqueous extract was found to be 23 and 30 gm respectively.

**RESULTS**

The alcoholic and aqueous extract of seed coat of *Tamarindus indica* Linn. extract was investigated on rat models of arthritis by Freund's Complete Adjuvant in rats induced acute paw pain and arthritis, evaluated by measuring the squeaking score, paw volume, and weight distribution ratio. The alcoholic and aqueous extract of seed coat of *Tamarindus indica* Linn was administrated orally to rats for 19 days.

**CONCLUSIONS**

These results suggest that *Tamarindus indica* Linn has anti-inflammatory, antinociceptive, and antiarthritic effects in an arthritis animal model. Thus, *Tamarindus indica* Linn should be further studied with regard to use either as a pharmaceutical or as a dietary supplement for the treatment of arthritis.

**Keywords:** *Tamarindus indica* Linn., Adjuvant-induced arthritis, Immunoglobulins, IL-4, Anti-inflammatory, Rat.
Arthritic Rat (FCA) on 21st day

Alcoholic Extract of seed coat of TI on 21st day

Aqueous Extract of seed coat Of TI on 21st day

Diclofenac Control on 21st day

Fig. 3: Effect of different drugs on Rat paw on 21st day of treatment

**Statistical Analysis**

The results were expressed as mean ± SEM. Difference among the data were determined using one way ANOVA followed by Tukey-Kramer multiple comparison test for multiple comparison. Difference between the data were considered significant at P < 0.001

**RESULT**

Preliminary phytochemical studies revealed the presence of Tannins, Alkaloids, Flavanoids. The Aqueous and Ethanolic extract of seed coat of *Tamarindus Indica* Linn. was found to be non-toxic up to 1000 mg/kg. (2)

Table 1: Effect of Various Extracts of *Tamarindus indica* Linn. in Arthritis Induced Rat Paw Edema

<table>
<thead>
<tr>
<th>Groups</th>
<th>Mean Changes in Paw Oedema (Mean ± S.E.M.)</th>
<th>%Inhibition of paw oedema on 21st day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4th day</td>
<td>8th day</td>
</tr>
<tr>
<td>Normal control</td>
<td>0.61±0.13</td>
<td>0.65±0.12</td>
</tr>
<tr>
<td>Arthritic control</td>
<td>4.0±0.08**</td>
<td>4.2±0.08**</td>
</tr>
<tr>
<td>DiclofenacSodium</td>
<td>1.33±0.21*</td>
<td>1.5±0.20**</td>
</tr>
<tr>
<td>AlcoholicExtract</td>
<td>2.36±0.21**</td>
<td>2.53±0.18**</td>
</tr>
<tr>
<td>Aq. Extract</td>
<td>2.0±0.21**</td>
<td>2.23±0.19**</td>
</tr>
</tbody>
</table>

Results are mean ± SEM, n = 6. Significance relative to control (p<0.01)

**=P<0.01** = Very significant;

*=P<0.05* = Less significant.

Aqueous and Alcoholic extract of seed coat of *Tamarindus indica* Linn. significantly inhibited the inflammatory edema, through the expression of IL6 and reduced the production of PGE2 (10). The inhibition was highest in aqueous extracts (Table 1). FCA induced Arthritis in rats is probably the best and most widely used model since it has close similarity to human rheumatoid disease. Shortly after administration of adjuvant into left hind paw of rat, a pronounced swelling appears in injected paw, which persists for several weeks. The determination of swelling appears in injected paw is most objective measurement that can be made to assess the activity (1). The inflammatory mediators are responsible for development of clinical symptoms of inflammation. They cause
vasodilation, increased permeability of blood vessels and migration of leukocytes to the site of inflammation. Cytokines are locally acting protein mediators that are involved in almost all the biological processes including cell growth and activation, inflammation, immunity and differentiation. (7).

Analysis of the expression of cytokines at mRNA levels in patients with arthritis has revealed that many pro-inflammatory cytokines are abundant in synovial tissues and. A preferential activation of type 1 cells in the target tissue suggests that Th1 cytokines are involved in the pathogenesis. The increased expression of inflammatory mediators in arthritic joints is counteracted to some degree by the production of anti-inflammatory Th2 cytokines. Since the balance of Th1/Th2 cytokines is thought to influence the autoimmune diseases like arthritis and that the study allows better understanding of the main mechanisms involved in such diseases.

We tested the ability of aqueous extract and alcoholic extract to control Th1/Th2 cytokine balance in arthritic rats. Aqueous extract and alcoholic extract have been found to show fruitful immunomodulatory activity with respect to arthritis. They induced inhibition of IL-2 production by CD4+ T-cells. IL-2, being a central regulator of immune response, stimulates the synthesis of IFN-γ in T-cells and also induces the secretion of pro-inflammatory cytokines such as TNF-α by activated macrophages (8). The inhibition of IL-2 by aqueous and alcoholic extract of seed coat of *Tamarindus indica* linn is possibly responsible for reduced IFN-γ secretion by CD8+ T cells and TNF-α by macrophages. Since IL-2, IFN-γ and TNF-α are Th1 type (pro-inflammatory) cytokines (9), their inhibition shows a strong correlation with the antiarthritic activity of aqueous extract and alcoholic extract. The findings, therefore, show that aqueous extract and alcoholic extract have potent anti-arthritic activity.

Graph 1: The Mean Changes In Paw Volume against no. of days Indicate Significant Antiarthritic Activity of Aqueous And Alcoholic Extracts of *Tamarindus Indica* Linn.

Graph 2: Shows % Inhibition of Paw Edema On 21 St Day In Which Significant Inhibition Observed In Standard Group. Diclofenac Sodium and Aqueous Extract Of *Tamarindus Indica* Linn Shows Significant Inhibition Of Paw Volume (Graph 2)
DISCUSSION

Anti-inflammatory drugs used for treating chronic inflammatory diseases such as rheumatoid arthritis are typically prescribed long term to properly control the disordered immune system. Thus, there is a strong need to develop safe and effective drugs for the long-term use. Many groups have studied non-steroidal anti-inflammatory small molecules that were derived from natural sources with the aim of developing new treatments for clinical use [11]. For example, curcumin is a polyphenolic compound derived from the dietary spice, turmeric. Recently, curcumin has been shown to possess diverse pharmacological properties, including anti-inflammation, antiproliferation, and antiangiogenesis. [12]

Rheumatoid arthritis is a chronic inflammatory and systemic autoimmune disease characterized by a number of inflammatory and destructive events such as joint pain and swelling, synovial hyperplasia, pannus formation, cartilage and bone destruction, and joint malformation. Many cell populations, various cytokines, and different inflammatory mediators are involved in the generation of the pathological events characteristic of Rheumatoid arthritis. Combination therapy strategies for Rheumatoid arthritis may be more appropriate to target on the complexity and redundancy of the pathological mechanisms of Rheumatoid arthritis.

The plant *Tamarindus indica* Linn popularly known as imli, chincha, belong to the family caesalpinaceae, found throughout India. The plant used in traditional medicine for the treatment of cold, fever, stomach disorder, diarrhea and jaundice and as skin lesiner, antimicrobial agents, (5). Seeds are useful in diarrhoea, dysentery, burning sensation, haematuria, inflammations, hepatic disorders, chronic ulcers. (6).

We found that *Tamarindus indica* Linn significantly inhibited the production of two important pro-inflammatory mediators, IL6 and PGE2, in IL1β-stimulated human FLS. The inhibition of PGE2 production is important due to its central role in triggering pain.

In the present study, we showed that Aqueous and Alcoholic extract of seed coat of *Tamarindus indica* Linn could significantly inhibit the disease progression of AIA and markedly protect the affected joints against cartilage destruction and bone erosion in rats, presumably by suppressing the abundant production of pro-inflammatory cytokines TNF-α, IL-1β, and IL-6 in the blood serum. Therefore, aqueous extract and alcoholic extract of seed coat of *Tamarindus indica* Linn significantly inhibit (P < 0.01) the arthritis and have potent anti-arthritic activity.

CONCLUSION

These results suggest that *Tamarindus indica* Linn has anti-inflammatory, antiinocceptive, and antirheumatic effects in an arthritis animal model. Thus, *Tamarindus indica* Linn should be further studied with regard to use either as a pharmaceutical or as a dietary supplement for the treatment of arthritis.

Abbreviations

AIA :- Adjuvant-induced arthritis , RA : Rheumatoid arthritis ; IL: interleukin; IFN -interferon ; FCA- freunds complete adjuvant ; RA: rheumatoid arthritis; TNF-α: Tumor Necrosis Factor-α ; % Percentage; gp: Group.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

VMM and PB participated in the literature survey, data analysis and the design of the study. PB, VMM & JG performed the experiments. VMM and DMA participated in the preparation of manuscript. All authors read and approved the final manuscript.

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10. Nazir Surtinder Koul, Mushtaq A. Qurishi, Sachin C. Taneja, Sheikh F. Ahmad, SarangBani and Ghulam N. Qazi., *Rheumatoid arthritis; TNF-α-: Tumor Necrosis Factor-α; %*: Percentage; gp: Group. *VMM and PB participated in the literature survey, data analysis and the design of the study. PB, VMM & JG performed the experiments. VMM and DMA participated in the preparation of manuscript. All authors read and approved the final manuscript.*

