

The results showed that indomethacin at 10 mg/kg and *T. procumbens* at 250 mg/kg and 500 mg/kg ameliorate the weight loss that occurs during arthritis [Table 1].

The latency of the arthritic secondary response ended after a few days and was characterized by joint swelling and nodule events on the 7th day. Administration of *T. procumbens* (250 mg/kg) significantly ($P < 0.01$) protected against joint swelling in paws in rats with induced arthritis compared with the arthritis control group. But a significant reduction was observed from day 11 to day 13 in the *T. procumbens*-treated (250 mg/kg) group. However, the effects of *T. procumbens* treatment at 500 mg/kg were found to be significant ($P < 0.001$) from the initial stage of

the secondary response and were maintained throughout the experiment. They were significant ($P < 0.01$) 15-19 days after FCA injection compared with the group treated with the reference standard, indomethacin at 10 mg/kg [Table 2].

As shown in Table 3, elevated SGOT and SGPT levels and reduced RBC, ESR and Hb levels were observed in the arthritic controls compared with the normal controls. Administration of the ethanolic extract of *T. procumbens* to arthritic rats (Group-3, Group-4, Group-5) enhanced the Hb and RBC levels compared with the arthritic control group.

Clinical analysis of rheumatoid arthritis allows therapeutic monitoring, which remains the standard method for evaluating the progress of the disease. The loss of articular cartilage leads to diminished joint spaces, which may be brought about through a variety of pathological mechanisms. The normal knee bone structure of normal control animals may be seen in Figure 1. In contrast, the arthritis control animals exhibit a loss of articular cartilage, severe soft tissue swelling and reduced joint spaces. The degree of bone resorption, diminution of joint spaces and swelling of tissue were markedly reduced in *T. procumbens* at 500 mg/kg. The lower dose of *T. procumbens* (250 mg/kg) produced similar results. The standard drug, indomethacin, also produced fractional tibial epiphysis, and the appearance of the femoral

Table 1: Effect of ethanolic extract of *T. procumbens* on rodent growth

Group (n=5 in each group)	Body weight (g)		Increase in body weight (%)
	Initial	Final	
Normal control	179±1.62	190.23±2.89	6.27
Arthritis control	183.30±1.66	190.23±2.49	3.78
<i>T. procumbens</i> , 250 mg/kg	171.80±1.05	181.33±0.35	5.54
<i>T. procumbens</i> , 500 mg/kg	179±1.52	188.46±7.39	5.28
Indomethacin	160.13±0.18	172.16±1.30	7.51

Table 2: Anti-arthritic activity of ethanolic extract of *T. procumbens* compared with indomethacin in injected paw (swelling volume [ml]±SEM)

Treatment	Post-insult time of assay (days)										
	1	3	5	7	9	11	13	15	17	19	21
Normal control	0.12±0.00	0.10±0.00	0.10±0.00	0.10±0.00	0.10±0.00	0.10±0.00	0.10±0.00	0.10±0.00	0.10±0.00	0.11±0.00	0.10±0.00
Arthritic control	0.74±0.00	0.85±0.00	1.05±0.00 ^{###}	1.19±0.00 ^{###}	0.93±0.00 ^{###}	0.85±0.01 ^{###}	0.85±0.01 ^{###}	0.86±0.01 ^{###}	0.86±0.01 ^{###}	0.88±0.01 ^{###}	0.91±0.01 ^{###}
<i>T. procumbens</i> , 250 mg/kg	0.72±0.01	0.74±0.00	0.91±0.01 ^{###}	0.88±0.01 ^{###}	0.89±0.00*	0.70±0.00 ^{###}	0.66±0.01 ^{###}	0.69±0.01 ^{###}	0.73±0.01 ^{###}	0.67±0.00 ^{###}	0.75±0.01 ^{###}
<i>T. procumbens</i> , 500 mg/kg	0.71±0.01	0.79±0.00	0.93±0.01 ^{###}	0.86±0.01 ^{###}	0.83±0.00 ^{###}	0.80±0.00 ^{###}	0.68±0.00 ^{###}	0.74±0.01 ^{###}	0.53±0.01 ^{###}	0.51±0.01 ^{###}	0.70±0.01 ^{###}
Indomethacin, 10 mg/kg	0.64±0.00	0.74±0.00	0.85±0.00 ^{###}	0.79±0.00 ^{###}	0.79±0.00 ^{###}	0.67±0.00 ^{###}	0.73±0.00 ^{###}	0.74±0.00 ^{###}	0.63±0.00 ^{###}	0.62±0.01 ^{###}	0.57±0.01 ^{###}

Values are expressed as mean±SEM; n=5 rats in each group; ^{*} $P < 0.001$ compared with arthritic control; ^{###} $P < 0.001$ compared with normal control (Repeated measures ANOVA followed by Bonferroni test.)

Table 3: Effect of the ethanolic extract of *T. procumbens* on biochemical and hematological parameters

Group	Biochemical parameter		Haematological parameter			
	SGOT (U/L)	SGPbT (U/L)	WBC (cells/cu.mm)	RBC (millions/cu.mm)	ESR (mm/hr)	Hb (gm/dl)
Normal control	105.26±0.13	55.68±0.72	7.31±0.06	4.90±0.05	3.27±0.20	13.05±0.24
Arthritic control	232.68±1.98	158.72±1.72	7.67±0.10 ^{##}	3.65±0.23 ^{###}	7.18±0.16 ^{###}	8.87±0.203 ^{###}
<i>T. procumbens</i> , 250 mg/kg	181.86±2.13 ^{###}	127.86±3.39 ^{###}	7.25±0.03	4.81±0.22	5.31±0.15 ^{###}	9.57±0.115 ^{###}
<i>T. procumbens</i> , 500 mg/kg	149.91±2.67 ^{###}	112.64±1.19 ^{###}	7.29±0.01	4.57±0.14	4.79±0.13 ^{###}	10.38±0.31 ^{###}
Indomethacin, 10 mg/kg	126.25±0.77 ^{###}	93.02±1.62 ^{###}	7.36±0.01	4.58±0.04	4.15±0.12 ^{**}	12.14±0.23

Values are expressed as mean±SEM, n = 5 rats in each group, ^{###} $P < 0.001$, ^{**} $P < 0.01$ compared with arthritic control, ^{###} $P < 0.001$, ^{##} $P < 0.01$ compared with normal control (Repeated measures ANOVA followed by Bonferroni test); WBC=White Blood Cell; RBC=The Red Blood Cell; HB=Hemoglobin; ESR=Erythrocyte Sedimentation Rate

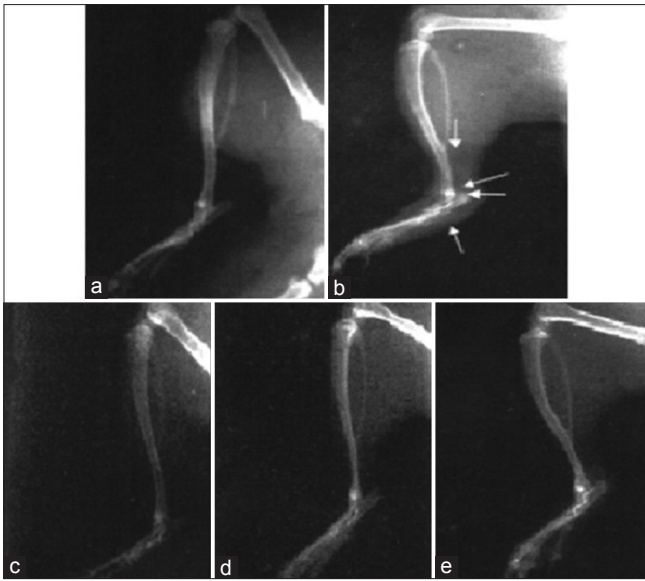


Figure 1: Effect of ethanolic extract of *T. procumbens* (TP) on arthritis (a) normal control animal showing the normal knee bone structure (b) animal with FCA-induced arthritis (c) animal with FCA-induced arthritis treated with *T. procumbens*, 250 mg/kg (d) animal with FCA-induced arthritis treated with *T. procumbens*, 500 mg/kg, showing reduced joint spaces and decreased paw oedema (e) animal with FCA-induced arthritis treated with indomethacin, 10 mg/kg, showing fractional tibial epiphysis

condyle was normal, with no soft tissue swelling [Figure 1]. The animals treated with *T. procumbens* (500 mg/kg) and indomethacin showed a significant decrease in paw oedema volume and increased joint spaces compared with the arthritic control group.

DISCUSSION

T. procumbens at 250 and 500 mg/kg displayed significant anti-arthritis activity, and the activity was comparable with that of indomethacin. *T. procumbens* significantly increased the body weight of animals compared with the arthritic controls. The anti-arthritis activity of *T. procumbens* is comparable with that of the standard drug indomethacin.

There is increasing evidence that lysosomal enzymes play an important role in the development of acute and chronic inflammations.^[18] Most of the anti-inflammatory drugs exert their beneficial effects by inhibiting the release of these enzymes, which is one of the inflammatory processes, or by stabilizing the lysosomal membrane. So we can assume that our drug extract acts by inhibiting the lysosomal enzymes or stabilizing the membrane.

The arthritic control animals showed marked increases in the levels of the liver markers, whereas *T. procumbens* inhibited the increase in liver markers induced by FCA.

Previous studies found that FCA also alters the biochemical and oxidative parameters.^[19] FCA-induced arthritis is used to study the pathogenesis of rheumatoid arthritis for testing therapeutics.^[20] One of the reasons for the wide utilization of this model is a strong correlation between the efficacy of therapeutic agents in this model and in rheumatoid arthritis in humans, and this model is characterized by a very rapid erosive disease. Bacterial peptidoglycan and muramyl dipeptide are responsible for the induction of adjuvant arthritis.^[9,10]

Changes in body weight have also been used to assess the course of the disease and the response to therapy using anti-inflammatory drugs. Adjuvant arthritis is characterized by reduced body weight, and the weight loss is associated with an increased production of pro-inflammatory cytokines such as TNF- α and interleukin- α .

In the present study, the arthritic rats exhibited a reduced RBC count, reduced Hb level and increased ESR level.^[21] All these symptoms indicate an anaemic condition, which is a common diagnostic feature in patients with chronic arthritis. The ESR is an estimate of the suspension stability of RBCs in plasma.^[15] It is related to the number and size of the red blood cells and to the relative concentration of plasma proteins, especially fibrinogen and β globulins. An increase in the ESR is an indication of active but obscure disease processes. The acute phase proteins in ESR produce inflammation similar to that produced by an injection, injury, surgery or tissue necrosis.^[20] The treatment with *T. procumbens* extract improved the RBC count, Hb level and ESR to a near-normal level, indicating significant recovery from the anaemic condition and arthritic progress, thus establishing that the extract has a significant role in arthritic conditions.

WBCs are a major component of the body's immune system. Indications for a WBC count include infections and inflammatory disease.^[6,22] In arthritic conditions there is a mild to moderate rise in the WBC count due to a release of IL-1B. IL-1B increases the production of both granulocyte colony stimulating factor and macrophage colony stimulating factor.^[9,23] The WBC count was increased in the arthritic group. Migration of leukocytes produces a significant decrease in the WBC count. Apart from prostaglandin, other cyclooxygenase products and various cells involved in inflammatory changes and free radical activities have all been implicated in the development of rat adjuvant arthritis.^[10]

The radiographic analysis of the knee joint in the arthritic and drug-treated animals further supported and confirmed the potent dose-dependent anti-arthritis effect of the ethanolic extract of *T. procumbens* ethanolic extract, which suppresses

pathological changes, such as pannus formation and bone destruction.^[24] The anti-arthritis effect of *T. procumbens* is comparable with that of indomethacin, and this action may be due to inhibition of the enzyme cyclooxygenase. However, further studies are required to confirm the effect of *T. procumbens* on cyclooxygenase inhibition.

Our phytochemical investigation revealed the presence of flavonoids. Sterols are known to inhibit articular swelling, reduce the arthritis index and down regulate the content of IL-1B and TNF- α in inflamed tissues of arthritic rats.^[25,26]

CONCLUSION

The ethanolic whole plant extract of *T. procumbens* exerts an anti-arthritis activity by significantly altering the pathogenesis during FCA-induced arthritis in female SD rats without exerting any side effects.

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