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Full Length Research Paper

Evaluation of red and white seed extracts of *Abrus precatorius* Linn. against freund's complete adjuvant induced arthritis in rats.

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Abrus precatorius **(Fam: Leguminosae) is a folklore medicinal plant traditionally indicated to treat cancer, ulcer and fever. The purpose of the present study was aimed to evaluate the comparative therapeutic potential of both *A. precatorius* white (APW) and *A. precatorius* Red (APR) seed extracts on Freund's complete adjuvant induced arthritis in rats. The investigated result showed that the APW (250 mg/kg) significantly ($p<0.001$) inhibited the FCA induced arthritis and increased paw withdrawal latency indicating a protective effect against arthritis induced nociceptive behavior during rheumatoid arthritis in a dose-dependent manner. Moreover APR (250 mg/kg) also tends to suppress the inflammation at $p<0.05$ level significance but at the later phase. Therefore APW treatment found to possess potent anti-arthritic activity with least toxicity (no ulcerogenic) and the treatment significantly inhibited the development phase of arthritis, which is further supported by its radiographic analysis and its anti-inflammatory effect was comparable to that of indomethacin (10 mg/kg). Both the extracts exhibited significant ($p<0.001$) anti pyretic activity in brewer's yeast induced pyrexia.**

Key words: *Abrus precatorius* (Leguminosae), Freund's adjuvant induced arthritis, antinociceptive, antipyretic effects.

INTRODUCTION

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 proto-type of such groups of illness with chronic systemic disorders to be considered an autoimmune disease with destructive inflammatory polyarticular joint potentially resulting in progressive destructtion of articular and periarticular structure. Persistent inflammation produces swollen joints with severe synovitis, decreased nociceptive threshold, and massive subsynovial 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 (Feldmann et al., 1996; Koch et al., 1998). This result in a high degree of morbidity resulting in disturbed daily life of the patient.

Corticosteroids have not been able to fully control the incidence because of the limitations and risk of side effects. Many patients and practitioners are seeking alternative approaches to provide an effective cure in the treatment of disease and to overcome the serious drawbacks such as gastro intestinal bleeding and bone loss (Sarziputtini et al., 2000). Hence there is an urgent need to find safer compound for the management of rheumatoid arthritis.

The plant *Abrus precatorius* Linn popularly known as Rosary pea, jequirity bean belong to the family leguminosae (Fabaceae) is found through out India in hedges and bushes in exposed areas. The seeds are deadly poisonous but it has been reported that the toxic form of abrin gets converted to mitogenic form upon long refrigerated storage. Usually seeds are of two types one is scarlet with black spot and the other variety is pure white and traditionally used against leucoderma, wounds, alopecia, asthma, tubercular glands, leprosy, fever, ulcer and tumor (Khare, 2004; Vaidyarathnam, 1995). Several researchers have reported early the antitumor efficacy of the red seed variety of *A. precatorius* (Ramnath et al., 2002;

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Ohba et al., 1997). Anam et al. (2001) have reported the anti-inflammatory activity from the real parts of the plant. This plant is mainly focused traditionally and scientifically for its anti tumor potential. Tumor promoters usually recruit inflammatory cells to application site and the development of cancer may also act by aggravating inflammation in the tissue and vice versa. Inflammatory cells are also capable of inducing genotoxic effects. Hence it is likely the anti cancer agents may possess anti-inflammatory activity (Rosin et al., 1994)

In view of the importance of this herbal plant the present study aims to evaluate the comparative therapeutic effects of red and white seed variety of *A. precatorius* against Freund's complete adjuvant induced arthritis in rat model which is the best and most widely used experimental model for arthritis with clinical and laboratory features which closely mimic the clinical features of human rheumatoid disease (Pearson and Wood, 1963; Taurog et al*.,* 1988; Billingham et al., 1990) This model is sensitive to anti inflammatory and immune inhibiting medicines and considers to be relevant for the study of phathophysiological and pharmacological control of inflammation process as well as for the evaluation of anti nociceptive potential of drugs (Butler et al., 1992: Besson and Guiilbaud, 1988).

MATERIALS AND METHODS

Red and White seed variety of *A. precatorius* were collected from Kollimallai hills, Salem district in Tamil Nadu during the month of April – May. Dr. V. Nandhagopalan, Plant taxonomist, National College, Tamil Nadu, India, authenticated the plants with a voucher specimen no: R.H.T: 12751. A voucher specimen has been stored in the Department of Pharmaceutical Technology, Jadavpur University.

Preparation of extracts

The dried, coarse powder of both seed varieties of *A. precatorius* were extracted with soxhlet extraction apparatus using ethanol. The resultant extract was concentrated using rotary vacuum evaporator. The extract of *A. precatorius* red seed and white seeds (APR and APW) were then freeze dried and stored in vacuum desiccators. The yield of APR and APW was found to be 23 and 16% respectively.

Animals

Wistar rats (150 – 200 g) and Swiss albino mice (18 – 22 g) of either sex were used in this study. They were maintained under controlled temperature (23 ± 2^{o}C) and relative humidity (40 – 60%) with standard environmental conditions of 12/12 light/dark cycle in the Departmental animal house. They were housed in polypro-pylene cages with free access of food and water *ad libitum*. The cages were cleaned daily by changing the sawdust bedding.

The experimental protocol was approved by Institute's animal ethical committee; care and use of laboratory animals were confirmed to national guidelines. All the doses of the test extract were fixed from the acute toxicity studies.

Pharmacological experiment

All the experiments were conducted in the pharmacological research laboratory between 9.00 am - 9.00 pm at a standard environmental condition (24 ± 2^{o}C). The drug solutions for the experiments were prepared freshly.

Acute toxicity studies

Swiss albino mice of either sex weighing 18 – 22 g were randomly distributed to 8 different groups with 10 animals in each group. The animals were fasted overnight and the drug was administered orally at dose levels of 50, 100, 200, 400, 800, 1600, 3200, and 6400 mg/kg of body weight. The animals were closely observed for the first 12 h for any toxic symptoms and for 72 h for mortality rate (Ecobichon, 1997).

Freund's adjuvant induced arthritis

Freund's complete adjuvant (FCA)

5 mg of heat killed mycobacterium tuberculosis cell (being killed at 60^{o}C in 15 – 20 min in the autoclave) was finely ground using a mortar and pestle. Sufficient liquid paraffin was added and thoroughly triturated to make a 5 mg/ml suspension.

Incomplete Freund's adjuvant

The liquid paraffin is referred in the study as incomplete Freund's adjuvant.

Induction of arthritis

Wistar rats were randomly divided into seven groups of six animals each where, Group I – Vehicle control (0.5 ml normal saline). Group II – Arthritis control (0.5ml normal saline). Group III and IV - APW (125 and 250 mg/kg/day, p.o.). Group V and VI - APR (125 and 250 mg/kg/day, p.o.). Group VII - Indomethacin (10 mg/kg/day, p.o.)

The method described by Newbould in 1963 was employed with some modifications. Adjuvant arthritis was induced by subcutaneous injection of FCA (0.1ml) into sub plantar tissue of the right hind paw of each rat. The test groups consisted of FCA- injected rats challenged with the respective doses of the test drugs administered orally 24 h before FCA injection while, the vehicle control rats were injected with 0.1 ml of liquid paraffin (Incomplete Freund's Adjuvant) only. The drug treatments were continued daily on the same time after the challenge for 19 more days. The swelling in the injected and contralateral hind paws of the rats were monitored daily using liquid displacement plethysmometer (Ugo Basile, Italy). Increase in the extent of erythema and edema of the tissues shows the severity of the inflammation. The difference in severity of arthritis between the experimental groups and arthritis control group were statistically analyzed.

Anti – nociceptive activity

Hot plate method was used to assess the hyperalgesia of FCA induced arthritis rats by determining the latency of withdrawal to noxious thermal stimuli. The time of reaction to painful stimuli of the arthritis rats placed on the plate heated at 55 $\pm$ 0.5^{o}C was recorded on every alternate day after the induction of arthritis with the maximum cutoff period of 15 s. The increase in reaction time against the arthritis control group was analyzed statistically.

Radiographic analysis

Animals were anesthetized with sodium pentobarbitone (45 mg/kg, i.p.) and placed in X-ray machine for the radiographic analysis of

Table 1. Effect of APR and APW against Freund's complete adjuvant induced paw edema on injected paw (primary response)

Post insult time in days	Swelling volume (ml)±SEM on injected paw					
	Arthritis Control	APR (125 mg/kg)	APR (250 mg/kg)	APW (250 mg/kg)	APW (125 mg/kg)	Indomethacin (10 mg/kg)
01	0.68±0.02	0.66±0.02	0.59±0.02	0.56±0.03 [a]	0.62±0.05	0.53±0.02 [a]
02	0.82±0.03	0.82±0.02	0.79±0.01	0.68±0.03 [ab]	0.71±0.02[a]	0.64±0.04 [ab]
05	1.00±0.05	0.90±0.02	0.85±0.02 [a]	0.76±0.04 [ab]	0.80±0.02 [ab]	0.70±0.02 [ab]
07	1.13±0.07	0.95±0.02	0.82±0.01 [ab]	0.72±0.03 [ab]	0.88±0.02[ab]	0.68±0.03 [ab]
09	0.87±0.01	0.81±0.02	0.74±0.03 [a]	0.69±0.02 [ab]	0.75±0.03 [a]	0.63±0.02 [ab]
13	0.79±0.01	0.74±0.04	0.68±0.03 [a]	0.60±0.03 [ab]	0.64±0.03 [a]	0.53±0.03 [ab]
15	0.80±0.01	0.66±0.03 [a]	0.64±0.03 [a]	0.55±0.03 [ab]	0.61±0.05 [ab]	0.57±0.03 [ab]
17	0.82±0.03	0.74±0.04	0.70±0.04 [a]	0.52±0.03 [ab]	0.65±0.04 [ab]	0.48±0.04 [ab]
19	0.86±0.02	0.71±0.02 [a]	0.74±0.02 [a]	0.49±0.02 [ab]	0.67±0.03 [ab]	0.44±0.05 [ab]

All the values are expressed as mean ± SEM (n = 6). Statistical significance was calculated by ANOVA followed by post hoc Dunnett's test ([a] $p<0.05$; [b]$p<0.001$)

the tibiotarsal joint. X-ray was taken at the joints of the contralateral hind paw for the confirmation and evaluation of the severity of arthritis in FCA induced rats.

Ulcerogenic activity

The stomach of the different groups of the animals was excised and cut along the greater curvature for examining the signs of ulcers such as lesions or bleeding if any during chronic treatment.

Antipyretic activity

Hyperpyrexia was produced in different groups of rats by injecting subcutaneously (1ml/kg) aqueous suspension of 12% Brewer's yeast in normal saline (w/v) Rats developing 1°C or more rise in rectal temperature 18 h after the injection of yeast were selected for the test and treated with 0.5 ml normal saline p.o, which served as control. Group 2 –5 received the test extracts (APW and APR, 125 and 250 mg/kg respectively). Group 6 were treated with 25 mg/kg, p.o, acetylsalicylic acid and served as reference standard. The rectal temperature was recorded at time interval of 1, 2, 3, 4 h by electro thermometer (DCT 1002) (Loux et al., 1972).

RESULTS

Acute toxicity studies

In acute toxicity study no lethality was observed up to the dose 6400 mg/kg during the 72 h period for APW. Where as the LD_{50} value for APR was found to be 2500 mg/kg. Hence $1/10^{th}$ of LD_{50} dose (250 mg/kg) of APR was selected as a maximum therapeutic dose and 125 mg/kg was selected as lower dose for both the extracts for performing the comparative pharmacological activity.

Effect of APR and APW on primary response of FCA induced Arthritis rat

The paw volume of the right paw was measured and taken into consideration for evaluating the possible anti-inflammatory effect of APW and APR extracts on rheumatoid arthritis. After the onset of inflammation the peak incidence in swelling reached during 5^{th}-7^{th} day with the increase in paw volume at the maximum of 1.13 ml for the arthritis control. The edema on the animals treated with APW (250 mg/kg) and Indomethacin (10 mg/kg) group began to subside gradually ($p<0.001$) when compared with arthritic control. The effect of APW 250 mg/kg on this primary reaction was found to be high at the earlier of 2^{nd} day after FCA injection and was maintained until the termination of the experiment. The decrease in swelling was not significant for APR (125 mg/kg), whereas there was significant decrease ($p< 0.05$) in swelling for APR 250 mg/kg but the reduction was comparably prominent only from day 5 after FCA injection. Therefore APW (250 mg/kg) observed for its significant effect in preventing the primary systemic response and it is capable of inhibiting the development phase of arthritis and APW (250 mg/kg) alone was more effective than the other treated group and the inhibitory effects was in pair with the standard Indomethacin (10 mg/kg) (Table 1 and Figure 1).

Effect of APW and APR on secondary response on FCA induced arthritis rat

The latent secondary response that occurs after few days and characterized by joint swelling and nodule formation in the contralateral paw was first evident on the 7^{th} day. The administration of APW (125 mg/kg) and APR (250 mg/kg) extract significantly ($P<0.05$) protected against joint swelling in arthritis-induced paw when compared with Arthritis control group. But the significant reduction first found only from day 11 - 13. No significant reduction in joint swelling was observed on APR (125 mg/kg). However the effect of APW (250 mg/kg) treatment was found to be significant ($p<0.001$) from the initial stage of secondary response and maintained through out the experiment

Table 2. Effect of APR and APW against Freund's complete adjuvant induced paw edema on contralateral paw (secondary systemic response)

Post insult time in days	Swelling volume (ml) ± SEM on non - injected paw					
	Arthritis Control	APW (125 mg/kg)	APW (250 mg/kg)	APR (125 mg/kg)	APR (250 mg/kg)	Indomethacin (10 mg/kg)
07	0.28±0.02	0.23±0.04	0.16±0.04 [a]	0.26±0.03	0.20±0.03	0.18±0.02
09	0.37±0.02	0.30±0.03	0.20±0.04 [a]	0.34±0.04	0.33±0.04	0.18±0.02 [a]
11	0.45±0.03	0.41±0.04	0.29±0.02 [a]	0.42±0.03	0.37±0.03 [a]	0.24±0.02 [a]
13	0.69±0.03	0.55±0.05 [a]	0.48±0.04 [a]	0.69±0.04	0.51±0.02 [a]	0.36±0.03 [ab]
15	0.86±0.05	0.67±0.04 [a]	0.52±0.05 [ab]	0.82±0.02	0.60±0.04 [a]	0.41±0.03 [ab]
17	0.91±0.04	0.74±0.04 [a]	0.56±0.04 [ab]	0.88±0.03	0.71±0.02 [a]	0.50±0.04 [ab]
19	1.1±0.06	0.78±0.04 [a]	0.63±0.03 [ab]	0.95±0.07	0.76±0.02 [a]	0.58±0.04 [ab]

All the values are expressed as mean ± SEM (n = 6). Statistical significance was calculated by ANOVA followed by post hoc Dunnett's test ([a] $p<0.05$; [b] $p<0.001$).

Table 3. Antinociceptive effect of APR and APW on Freud's complete adjuvant induced arthritis rats.

Treatment	Dose (mg/kg)	Reaction time (sec) during treatment					
		Day 2	Day 6	Day 8	Day 12	Day 14	Day 19
Vehicle control	N.S (0.5ml)	6.16±0.47	5.12±0.21	4.78±0.49	5.34±0.25	5.58±0.60	4.84±0.56
Arthritis control	N.S (0.5ml)	4.20±0.36	3.16±0.44	3.72±0.42	3.33±0.33	4.26±0.51	3.50±0.47
APR	125	6.00±0.36 [a]	4.16±0.74	3.66±0.33	5.00±0.36 [a]	6.20±0.29 [a]	5.70±0.42 [a]
APR	250	8.00±0.51 [ab]	7.50±0.42 [ab]	6.33±0.42 [ab]	7.83±0.30 [ab]	8.12±0.49 [ab]	7.62±0.51 [ab]
APW	250	9.16±0.30 [ab]	8.80±0.42 [ab]	8.50±0.45 [ab]	8.83±0.47 [ab]	10.14±0.63 [ab]	10.56±0.52 [ab]
APW	125	7.50±0.22 [ab]	7.00±0.36 [ab]	6.66±0.49 [ab]	6.83±0.33 [ab]	7.21±0.44 [ab]	7.62±0.32 [ab]
Indomethacin	10	8.86±0.30 [ab]	8.66±0.21 [ab]	8.33±0.33 [ab]	8.76±0.33 [ab]	8.62±0.54 [ab]	9.12±0.56 [ab]

All the values are expressed as mean±SEM (n=6). Statistical significance was calculated by ANOVA followed by post hoc Dunnett's test ([a] $p<0.05$; [b] $p<0.001$). N.S- Normal saline

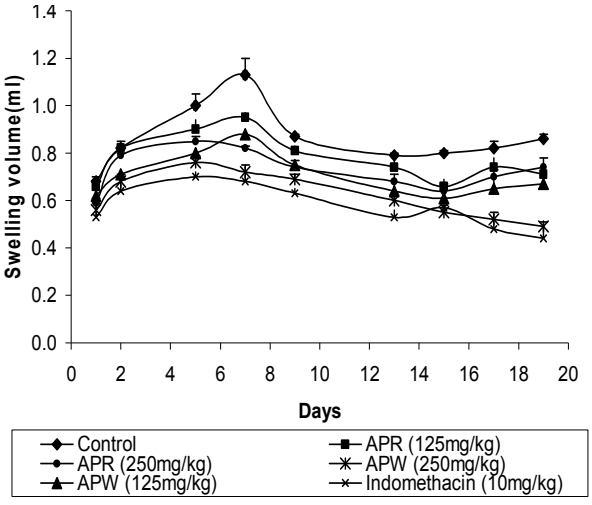

Figure 1. Effect of APR and APW against Freund's complete Adjuvant induced paw edema on injected paw (primary response).

and shows $p<0.001$ level significance during 15 – 19 days after FCA injection as that of the group treated with the reference standard Indomethacin (10 mg/kg) (Table 2 and Figure 2).

Anti nociceptive response on arthritis rats

The result in Table 3 shows the withdrawal latency of arthritic animals to thermal stimuli. The groups treated

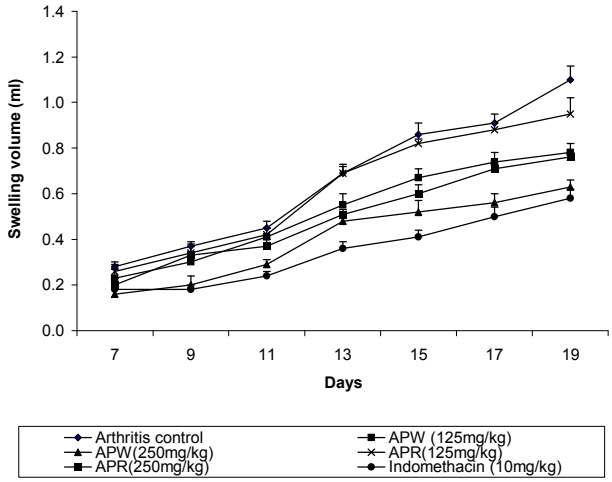

Figure 2. Effect of APR and APW against Freund's complete Adjuvant induced paw edema on contralateral paw (secondary systemic response).

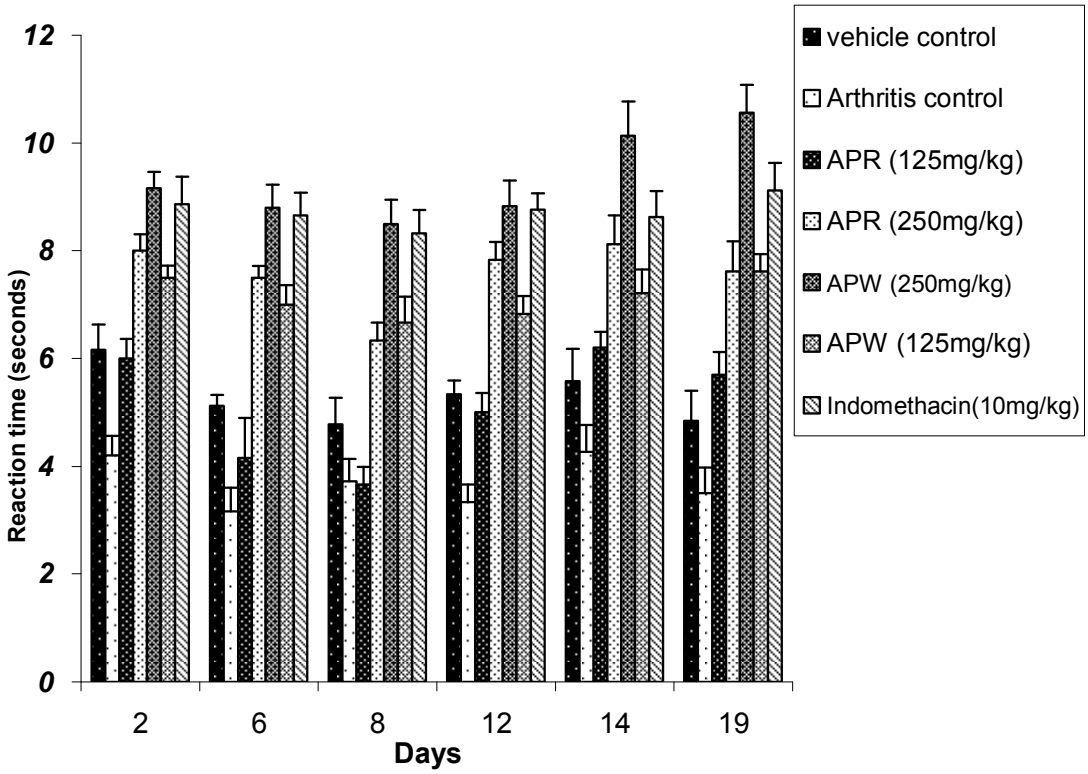

Figure 3. Antinociceptive effect of APR and APW on Freund's complete adjuvant induced arthritis rats.

Table 4. Effect of APR and APW on body weight against Freund's complete induced arthritis rats.

Treatment	Dose (mg/kg)	Body weight (g)		% increase in body weight
		Initial	Final	
Vehicle control	N.S (0.5 ml)	190.5 ± 7.11	245.83 ± 9.26 [a]	29.04
Arthritis control	N.S (0.5 ml)	187.83 ± 7.45	193.00 ± 10.32	2.75
APR	250	194.17 ± 8.07	210.50 ± 10.68	11.5
APW	125	189.33 ± 9.25	234.26 ± 11.40 [a]	23.73
Indomethacin	10	192.00 ± 7.74	230.30 ± 12.46 [a]	20.15

All the values are expressed as mean ± SEM (n = 6). Statistical significance was calculated by ANOVA followed by post hoc Dunnett's test ([a] $p<0.05$; [b] $p<0.001$). N.S- Normal saline.

with APW and APR (250 mg/kg) showed augmented paw withdrawal latency compared to arthritis control group from the day 2 till day19 after FCA injection. The result showed significant difference between APR (125 mg/kg) treated groups and arthritis control groups at $p<0.05$ level only found from the day 12 after FCA injection. Whereas the arthritis control animals showed no increase in withdrawal latency to thermal stimuli at any point after FCA injection during the course of 19 days study (Figure 3).

Effect on body weight

The arthritis control animals exhibited a significant decrease in body weight when compared with vehicle control group. The result showed the APW (250 mg/kg) and Indomethacin could ameliorate the weight loss occurred during arthritis. But APR do not show much difference when compare to arthritis control (Table 4).

Radiographic analysis of the tibiotarsal joint

The clinical analysis of RA allows therapeutic monitoring which remains the standard method for evaluating the disease progress. The loss of articular cartilage leads to diminished joint space, which may be brought about a variety of pathological mechanism. The degree of bone resorption, diminished joint space and tissue swelling was markedly reduced in APR (250 mg/kg) and the lower

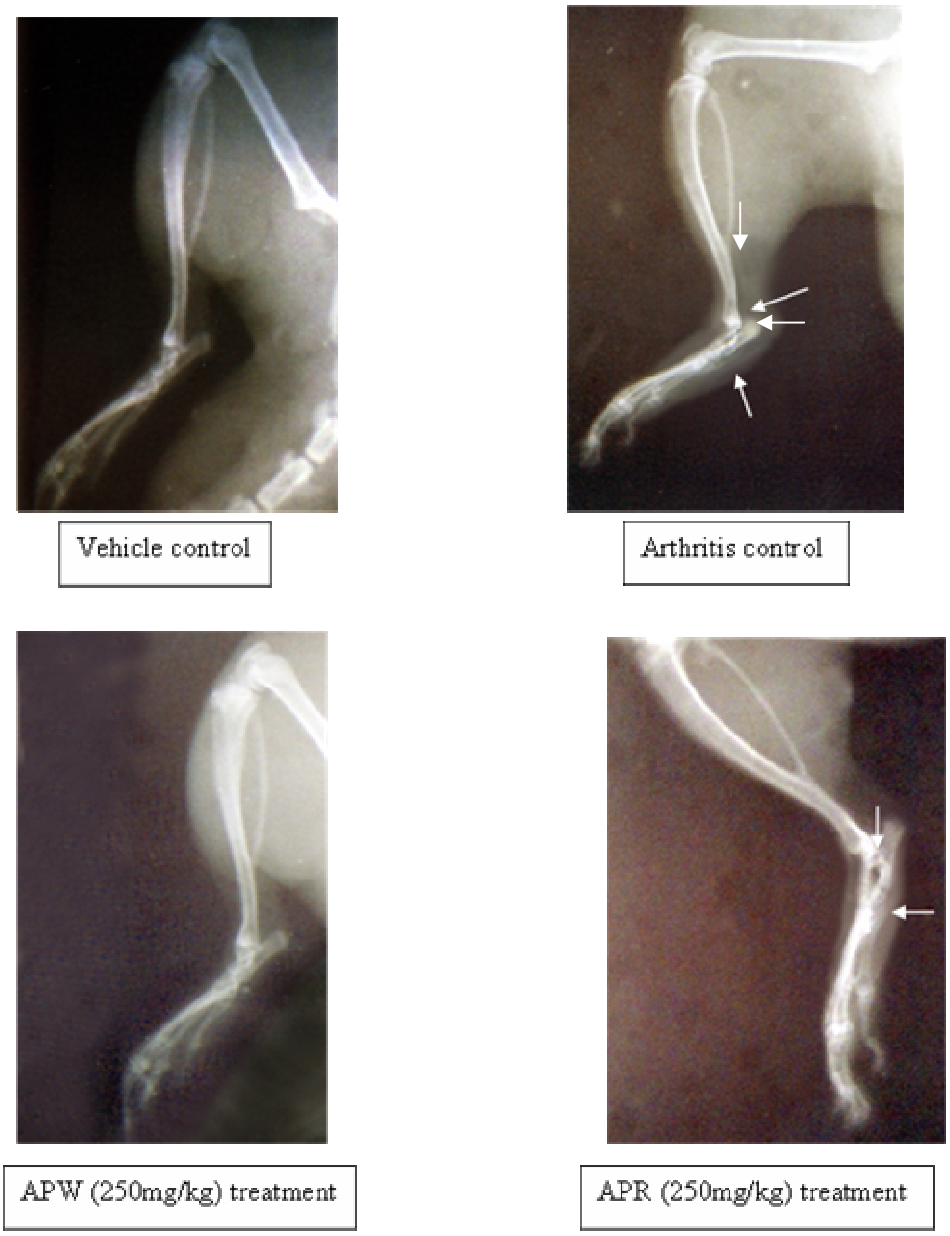

Figure 4. Adiographic changes in joints of control and FCA induced rats. No evidence of pathological changes was observed in vehicle control animals. Arthritis control showing severe inflammation with diffused joint space and bone erosion (indicated by arrows). APW (250 mg/kg) treatment shows clear joint space with no evidence of bone erosion and inflammation. APR (250 mg/kg) treatment shows mild inflammation with diffusion in joint space.

dose of APW also shows the similar result. Where as no abnormal pathology was revealed in the radiographic analysis of APW (250 mg/kg) treated rats (Figure 4).

Antipyretic activity

Table 5 shows the antipyretic activity of both the extracts in rat model. Considerable elevation in the rectal temperature was found in control group of animals. The rise in the rectal temperature was found to show graded responses according to the concentration of the doses. Both the extracts APW and APR (250 mg/kg) showed significant ($P<0.001$) decrease in rectal temperature, where as APW and APR (125 mg/kg) showed significance at $p<0.05$ level.

DISCUSSION

In this present study, the result demonstrated the effect of APW and APR seed extracts on FCA induced arthritis

Table 5. Effect of *Abrus precatorius* on brewer's yeast induced pyrexia in rats.

Treatment & Dose (mg/kg)	Basal Rectal temp.^{0}C	Temp. 18 h after yeast induction	Temperature(^{0}C) after treatment (in hours)			
			1	2	3	4
Control (N.S.0.5ml)	37.20±0.11	38.12±0.21	39.20±0.25	39.66±0.19	39.32±0.21	38.83±0.16
APW (125)	36.86±0.24	38.65±0.28	38.53±0.13	37.69±0.21 [a]	37.57±0.21 [a]	37.34±0.42[a]
APW (250)	37.56±0.35	38.46±0.21	37.60±0.31 [a]	36.53±0.40 [ab]	36.24 ±0.33 [ab]	36.48±0.30 [ab]
APR (125)	37.73±0.14	38.25±0.25	38.78±0.45	37.83±0.37 [a]	37.62±0.16 [a]	37.78±0.37 [a]
APR (250)	36.63±0.12	38.62±0.35	37.72±0.30 [a]	37.42±0.41[a]	36.34±0.27[ab]	36.57±0.33 [ab]
Acetyl salicylic acid (25)	37.46±0.42	38.42±0.28	37.56±0.32 [a]	36.15±0.44 [ab]	36.12±0.14 [ab]	36.35±0.24[ab]

All the values are expressed as mean ± SEM (n = 6). Statistical significance was calculated by ANOVA followed by post hoc Dunnett's test ([a] p<0.05; [b]p<0.001). N.S- Normal saline.

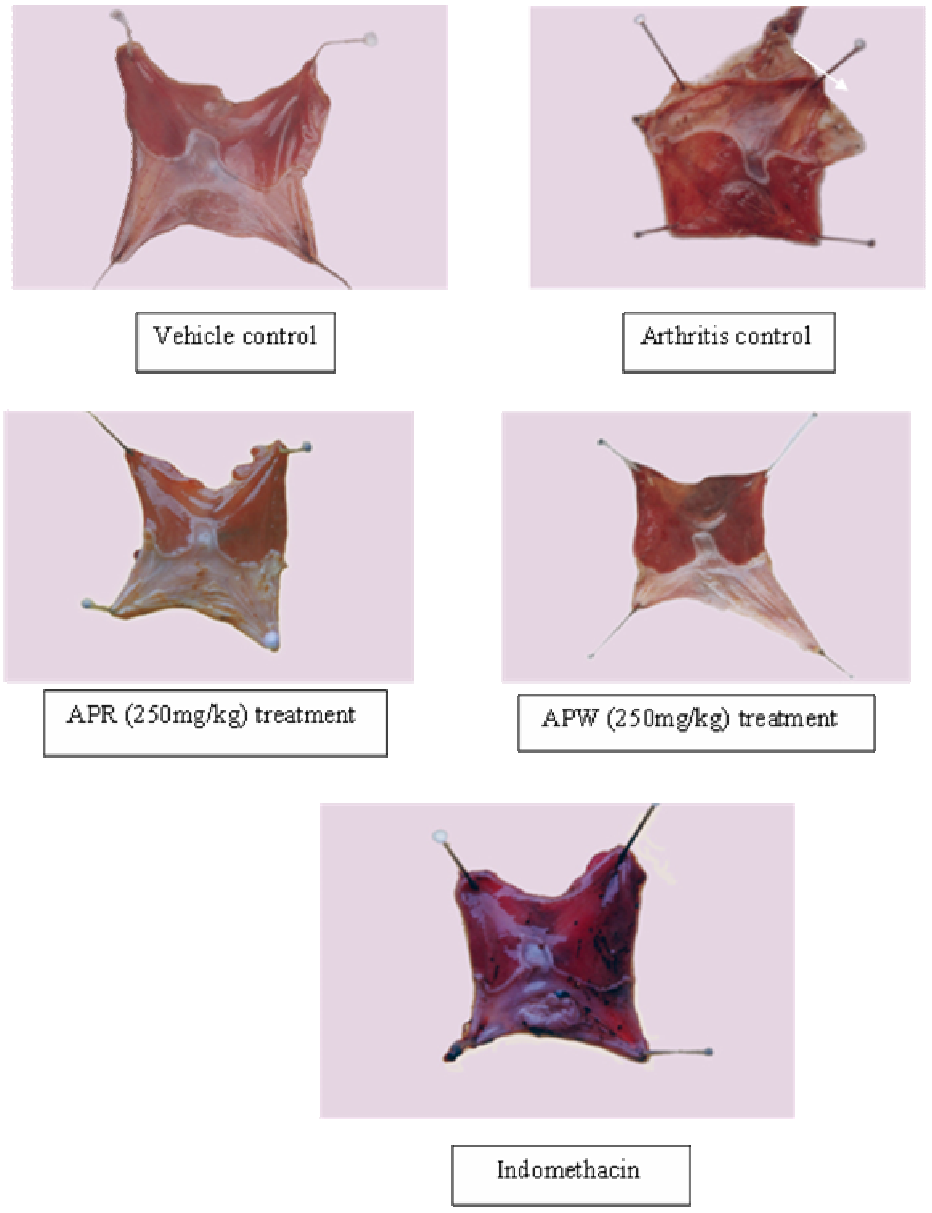

Figure 5. Macroscopic examination of the stomach of vehicle control and FCA induced rats. No evidence of bleeding or ulcers was observed in the stomach of vehicle control, APW and APR (250 mg/kg) treated animals. Indomethacin (10 mg/kg) treatment shows severe gastro intestinal bleeding and ulcers. Arthritis control shows mild ulcers.

model in rats, selected to evaluate their efficacy against the proliferateive phase of inflammation. Freund's adjuvant – induced arthritis is widely used chronic model for inflammation. One of the reasons for the wide utilization of this model is due to the strong correlation between the efficacy of therapeutic agents in this model and in rheumatoid arthritis in humans and it is characterized by very rapid erosive disease (Hunneyball et al., 1986).

After FCA injection on the rat hind paw, a pronounced swelling and hyperalgesia appeared with no involvement of the contralateral paw. This response is usually considered as a primary reaction. There is also a delayed hypersensitive response (Chedid, 1976) which is considered as latent secondary systemic response known to induce arthritis occurs after few days on the contra lateral paw and characterized by tibiotarsal joint swelling and nodule formation in the tail. Hyperalgesia is one of the major phenomenon of arthritis and it is more evident during the acute phase of arthritis (Calvino et al., 1987). Reduced nociceptive threshold in arthritis rats is characterized by spontaneous behavior such as protection of the affected paw by curving or elevation of the paw and avoiding the support of the body on the paw (Clatworthy et al., 1995). This reduced pain threshold in FCA animals thus reveals in the arthritis control group. FCA induced arthritis rat model also served as a model in several studies for the evaluation of chronic pain in different ways using thermal or mechanical stimuli. Evaluation of pain threshold in arthritis animals by nociceptive thermal stimuli such as hot plate, which serves as a model for quantitative estimation of hyperalgesia related behaviors (Hargreaves et al., 1988).

According to our result and investigation more pronounced and reliable anti-inflammatory activity was observed in APW (250 mg/kg), which significantly ($p<0.001$) inhibitted the development phase of chronic joint swelling induced by FCA on both the paws. The anti nociceptive effect of both extracts on arthritis rats were also evaluated by hot plate method in which the result shows delayed withdrawal latency for APW (250 mg/kg) at $p<0.001$level significance from thermal nociceptive threshold and proved its potency as an anti inflammatory and analgesic agent in FCA induced chronic model in dose dependent manner than the APR extract. Adjuvant arthritis is characterized by reduced weight loss (Campo et al., 2003) and the body weight loss is associated with increased production of pro-inflammatory cytokines such as TNF-α and interleukin –1 (Roubenoff et al., 1997). Treatment with APW extract shows significant ($p<0.05$) increase in body weight as that of vehicle control group.

The radiographic analysis of the tibiotarsal joint in arthritis and drug treated animals further supported and confirms the potent antiarthritic effect of APW in a dose dependent manner which suppress the pathological changes, such as pannus formation and bone destruction. In case of APR treatment, reveals only a mild antiarthritic effect when compared with APW.

NSAIDs, glococorticoids or so called disease–modifying drugs such as gold or methotrexate are prescribed for the treatment of rheumatoid arthritis. The limitations of these therapies are their well-known toxicity and variation in clinical efficacy (Anseth et al., 1998). Conventional NSAIDs that exhibit their activity by inhibiting cyclooxygenase (COX), which catalyzes the prostaglandin biosynthesis, may induce gastric ulceration and kidney failure (Awouetrs et al., 1978) due to COX-1 inhibition. COX-1 is necessary for the maintenance of stomach lining, interfering with its activity causes gastrointestinal disturbances such as bleeding ulcers. Where as inhibition of COX-2 shown to have a lower rate of gastro intestinal bleeding (Silverstein et al., 2000) hence COX-2 is responsible to exert normal cell physiology including regulation of vascular homeostasis, renal blood flow (Brater et al., 2001) and inflammatory process (Masferrer et al., 1994). Macroscopic examination of the gastric mucosa of the APW and APR treated rats did not reveal any treatment related tissue damage. The mechanism of anti-inflammatory effect of both the seed extracts of *A. precatorius* without any gastric lesions led us to believe that they did not interfere with prostanoid production. They might also act by selective inhibition of either COX-2 or LOX pathway, which produces leukotrienes from arachidonic acid. When only COX-2 is blocked, the LOX pathway still produces the potent mediator of inflammation. Hence in the development of new drugs for anti inflammation dual inhibition of LOX/COX has been suggested to be a desirable approach (Florucci et al., 2001)

Both the extract exerts similar significance ($p<0.001$) in reducing the hyperpyrexia induced by Brewer's Yeast. The lower dose of APW and APR 250 mg/kg more or less shows similar significance ($p<0.05$).

It is interesting to note that APW treatment was found to be more effective and exhibited significant ($p<0.001$) anti arthritic activity against adjuvant-induced arthritis experimentally with less toxicity (no ulcerogenic), compared to APR treatment. From these investigated results strongly suggest that APW alone have strong anti-inflammatory property and alleviated the extent of inflammatory reaction, which proved itself to be more effective, and an active drug of choice for the long treatment of chronic inflammatory conditions like RA with gastric ulcer, which is common. Although the underlying suppressive mechanism of both the extracts are still not clear, we are continuing the further investigation which are necessary to elucidate the exact mechanism of both the extracts.

Conclusion

The result presently discussed concluded the APW alone exerts potent anti arthritic activity by significantly ($p < 0.001$) altering the pathogenesis during arthritis without exerting any side effect during the chronic treatment and proved itself to be the best for the treatment of arthritis than APR extract. Radiographic analysis further confirms

the above findings. The present data do not clearly indicate the mechanism of action; hence it is necessary to elucidate the clear mechanism in our future studies.

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