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Original Article

Ethanolic Extract of *Equisetum arvense*: A Potential Agent against Rheumatoid Arthritis in Wistar Rats with Freund's Complete Adjuvant-Induced Arthritis

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ABSTRACT

Background: Rheumatoid arthritis, a global autoimmune affliction affecting 0.3-1% of the population, is characterized by chronic inflammation and systemic symptoms. Dissatisfaction with conventional treatments leads individuals with chronic pain in rheumatoid arthritis to explore alternative medicine. Herbal remedies, including *Equisetum arvense* extract, are studied for their anti-inflammatory potential. **Aim:** This research focuses on evaluating the impact of *E. arvense* extract on experimentally induced rheumatoid arthritis in rats, presenting a promising alternative for complementary approaches. **Materials and Methods:** In the study, rats received oral doses of *Equisetum arvense* ethanolic extract at 50 mg/kg and 100 mg/kg, followed by induction with Complete Freund's Adjuvant in the hind paw on day 0. Physical parameters like body weight and paw volume were assessed on days 0, 8, 16 and 22. Hematological parameters, including RBC count, Hb levels, ESR, total WBC count, and platelet count, were measured. Histopathological studies were conducted for a comprehensive assessment. **Results:** They showed both doses of *Equisetum arvense* extract significantly reduced paw volume compared to the CFA-induced group. Extract administration elevated RBC and Hb levels, approaching normalcy. Increases in WBC count and ESR were notably mitigated. Rats treated with the extract demonstrated protection against bone deterioration and reduced soft tissue swelling. Hispathology of tibiotarsal joints *E. arvense* treated rats exhibited joint protection, reducing cartilage destruction and decreased vascularity. **Conclusion:** The *Equisetum arvense* showed diminished cartilage destruction and decreased vascularity compared to arthritic rats. The *Equisetum arvense* exhibits potent anti-rheumatoid activity, emphasizing its potential as an alternative therapeutic approach for rheumatoid arthritis.

Keywords: *Equisetum arvense*, Complete Freund's adjuvant, Hemoglobin, Inflammation, Joints.

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INTRODUCTION

Rheumatoid Arthritis (RA) is characterized by enduring, symmetrical, inflammatory, and systemic manifestations, representing an autoimmune disorder. It affects around 0.3 to 1% of the worldwide population and commonly manifests between the ages of 50 and 60. Notably, rheumatoid arthritis tends to have a higher prevalence in women compared to men.[1] People with RA frequently encounter joint deformities, coupled with a progressive decline in functionality and harm to cartilage and bone. In terms of its features, rheumatoid arthritis unfolds through identifiable pathological phases. Early indications involve warmth, swelling, pain, and diminished joint function, while advanced stages exhibit different degrees of joint rigidity and deformities, frequently accompanied by bone deterioration and an elevated likelihood of disability.[2] As rheumatoid arthritis advances, it prominently affects the small joints in the feet and hands, resulting in a slow and painful swelling. This is accompanied by an anomalous and heightened growth of the synovium, the development of pannus, and changes in the morphology of the joint.[3]

Rheumatoid arthritis can appear in individuals of various age groups, impacting children, adolescents, and the elderly. When the condition manifests in individuals below 16 years of age, it resembles, though not precisely, the adult form and is labeled as juvenile idiopathic arthritis, formerly recognized as rheumatoid arthritis.

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Freund's adjuvants are crucial elements in the initiation protocols of many experimental animal models for autoimmune diseases. Generally, it is understood that both Incomplete Freund's Adjuvant (IFA) and Complete Freund's Adjuvant (CFA) prolong the presence of the injected auto-antigen. This is accomplished by aiding the effective delivery of the auto-antigen to the immune system and providing a diverse set of signals to the innate component of the immune system. Consequently, this result in altered leukocyte proliferation and differentiation.[4] Complete Freund's Adjuvant (CFA) plays a vital role in eliciting cell-mediated responses such as Delayed-Type Hypersensitivity (DTH) and specific experimental autoimmune diseases.[5]

The key goals in addressing rheumatoid arthritis revolve around controlling inflammation, easing pain, and reducing disability linked to the disorder. Typically, the treatment approach involves a blend of medications, occupational or physical therapy, and consistent exercise. Surgical procedures may be essential for individuals experiencing joint damage. Contemporary treatments have shown the ability to impede or stop joint deterioration. Although over-the-counter NSAIDs like ibuprofen are an option, many individuals with RA often necessitate prescription NSAIDs owing to their higher potency, prolonged effectiveness, and the requirement for fewer daily doses.[6]

Disease-Modifying Anti-Rheumatic Drugs (DMARDs) have emerged as the cornerstone of rheumatoid arthritis treatment. Methotrexate stands out as the primary anchor in DMARD therapy and is generally well-tolerated, with most gastrointestinal side effects being manageable. Another DMARD, Leflunomide, operates by targeting lymphocytes, specifically inhibiting pyrimidine synthesis.[7]

Hence, this current study employs *Equisetum arvense*, a plant, to investigate its potential utility in the context of rheumatoid arthritis. Furthermore, various other plants may also be examined for their effectiveness in treating rheumatoid arthritis.[8] *Equisetum arvense*, commonly known as Horsetail, is a perennial herb known for its abundant growth, originally indigenous to the northern hemisphere. This Equisetum species is prevalent in regions including Canada, the USA, the Himalayas, and the northeastern part of India.[9] Horsetail boasts a distinctive appearance with a creeping, string-like rootstock and roots emerging at the nodes, giving rise to numerous hollow stems. These stems consist of one set of whorled, slender, and upright branches each. Some stems can reach heights ranging from 2 to 24 inches, with as many as 20 segments. Fertile stems, appearing in early spring, are typically unbranched, thick, succulent, and showcase colors ranging from brownish to whitish, measuring 10 to 30 cm in height. *Equisetum arvense*, a longstanding element of traditional medicine, has been employed to address diverse conditions such as tuberculosis, kidney and bladder catarrh, profuse menstruation, nasal and pulmonary hemorrhages, brittle nails, and hair loss, rheumatic conditions, gout, slow wound healing, swelling, fractures, and frostbite.[9]

The literature underscores that the anti-rheumatoid arthritic activity is attributed to alkaloids, phytosterols, tannin, triterpenoids, and various phenolic compounds. These include flavonoids, styrylpyrones, phenolic acid, and kynumeric acid.[5] Nevertheless, conclusive information regarding the anti-rheumatoid arthritic properties of the investigated plant is lacking, and the pharmacological profile of the plant remains incomplete. Given these circumstances, the current study has been specifically crafted to address these gaps.

MATERIALS AND METHODS

Accumulation and extraction of plant product

The *Equisetum arvense* plant was collected from Kohima, Nagaland, India, was taxonomically verified by expert at the Dr Kuntal Das, Department of Pharmacognosy, Krupanidhi College of Pharmacy, Bengaluru and subsequently air-dried at room temperature (25°C) for a period of five days. Subsequently, it was ground into a consistent powder. The entire plant material was minced, and extraction was carried out using a 50% ethanol-water solution. The mixture underwent stirring and maceration at room temperature (21±3°C) for duration of 15 days. Afterward, the ethanol was evaporated, and the resultant extract was stored at -20°C with a concentration of 5% until required. Before use, the extract was suspended in a 0.9% NaCl solution to achieve the desired concentration. This process resulted in the production of the ethanolic extract of *Equisetum arvense*. Plant extraction yield and Qualitative tests were conducted to identify the chemical constituents present in the extract.[10]

Preliminary phytochemical studies

Preliminary phytochemical analysis such as alkaloids, carbohydrates, flavonoids, saponins, tannins and protein was undertaken as per definitive methods for the comparative assimilations of phytoconstituent.[10,11]

Experimental Animals

The experiments were conducted using female Wistar albino rats weighing between 200-250 g, sourced from the Central Animal House at Krupanidhi College of Pharmacy. The rats were accommodated in polypropylene cages with three rats per cage, lined with husk and renewed every 24 hr. They were kept in a controlled environment with a 12 hr light/dark cycle, maintained at approximately 24°C with 50% humidity. The rats had *ad libitum* access to tap water and a standard pellet diet (Purina Chow). The study protocol received approval from the Institutional Animal Ethic Committee (2021/PCOL/51/KCP/IAEC) and adhered to the guidelines set by the Committee for the Purpose of Control and Supervision on Experimental Animals (CPCSEA). The

animals were housed in accordance with standard conditions in an animal facility.

Experimental Model

The Wistar Albino Rats were weighed and divided into following groups consisting of 6 animals in each groups.

Group 1: Control group: Normal control rats (Rats will be feed on normal diet).

Group 2: Positive group: Complete Freund's adjuvant (CFA) induced arthritic rats.

Group 3: Low dose group: CFA+Low dose of *Equisetum arvense* plant extract (50 mg/kg)

Group 4: High dose group: CFA+High dose of *Equisetum arvense* plant extract (100 mg/kg).

Group 5: Standard Drug group: CFA+Ibuprofen (15 mg/kg)[12] Experiment was continued for 22 days.

Following oral administration of the test and standard drug, animals were subjected to treatment with Complete Freund's adjuvant (0.1 mL) on the sub-plantar surface of the hind paw region after a 30-minute interval. This specific day was designated as day 0. The administration of drug treatment was sustained for duration of 22 days.

Physical Parameters

Physical parameters of the rats, including alterations in body weight, paw volume, and motor coordination, were assessed on the 0^{th}, 7^{th}, 13^{th}, 17^{th} and 22^{nd} days of treatment period using a weighing balance, plethysmometer, and rotarod, respectively.

Hematological Parameters

Estimation of RBC and WBC using Neubauer's chamber, hemoglobin was estimated by hemoglobinometer and ESR was determined by Wintrobe Method.

Histopathological Examination

Upon completion of the study, all rats were humanely euthanized using excess anesthesia, and tibiotarsal joints were obtained from each experimental group. Subsequently, these collected joints underwent processing for histopathological examination.

Statistical Analysis

Statistical analysis was performed using GraphPad Prism 10.0.2 software, employing one-way ANOVA followed by Dunnett's test. The results are presented as mean±SEM, with significance indicated by $p < 0.05$.

RESULTS

Plant Extraction Yield

The yields of *Equisetum arvense* dry weights were calculated as,

$$\text{Yield \%} = \frac{\text{Weight of extract (g)} \times 100}{\text{Weight of dry sample (g)}}$$

Equisetum arvense yield of extract with 35.2% of the original dry weight. The extract of *Equisetum arvense* dark green colour and semi hard viscous texture.

Preliminary phytochemical investigation

Results obtained after phytochemical investigation (Table 1).

Effect of *Equisetum arvense* extract, Ibuprofen on body weight

Complete Freund's Adjuvant (CFA) caused significant decrease in body weight when compared to control rats. Treatment with *Equisetum arvense* extract and Ibuprofen showed a change in body weight to near normal levels.

CFA control rats exhibited lower body weight gain compared to normal rats, potentially attributed to the elicitation of an immune response. In contrast, rats treated with a high dose and those treated with Ibuprofen demonstrated a notable and significant increase in body weight compared to the CFA-treated rats. Effect of *Equisetum arvense* extract, Ibuprofen on Complete Freund's Adjuvant (CFA) induced changes in body weight (Table 2).

Effect of *Equisetum arvense* extract, Ibuprofen on paw volume

Complete Freund's Adjuvant (CFA) induced a significant elevation in paw volume compared to the control group in rats. Treatment with *Equisetum arvense* extract and Ibuprofen resulted in a substantial reduction in paw volume, bringing it close to normal levels. Immunization through sub plantar administration of FCA led to an initial increase in paw volume compared to the vehicle-treated group. The peak paw volume was observed on day 7, followed by a slight decrease, which persisted until the end of the study. Administration of *Equisetum arvense* extract at doses of 50 mg/kg and 100 mg/kg demonstrated a significant ($p<0.05$) and dose-dependent decrease in paw volume during the study period (Table 3).

Effect of *Equisetum arvense* extract, Ibuprofen in fall of time

The administration of Complete Freund's Adjuvant (CFA) resulted in a significant decrease in the latency to fall during the rotarod test compared to the control group of rats. However, treatment with *Equisetum arvense* extract at doses of 50 mg/kg and 100 mg/kg, as well as Ibuprofen at a dose of 15 mg/kg, led to a notable increase in the latency to fall. This increase was found to be statistically significant ($p<0.05$) when compared to the CFA

Table 1: Result of Phytochemical Analysis.

Sl. No.	Name of the test	Observation	Inference
1	Alkaloids		
	Dragendroff's test	Orange-red precipitate	+
	Mayer's test	Cream colored precipitate	+
	Hager's test	Yellow colored precipitate	+
2	Carbohydrates		
	Benedict's test	No change in color	-
	Fehling's test	No change in color	-
3	Flavonoids		
	Lead acetate test	Bluish green precipitate	+
4.	Proteins/ Aminoacids		
	Biuret test	Formation of Violet color precipitate	+
	Xanthoproteic acid	Formation of Yellow color precipitate	+
	Millons test	Formation of White color precipitate	+
	Ninhydrin test	Formation of White color precipitate	+
5.	Saponins	Formation of honey comb like froth	+
6.	Shinoda test	Red color precipitate	+
7.	Tannins		
	Lead acetate solution	Yellow color precipitate	+

(Positive sign (+) shows presence and Negative sign (-) shows absence).

Table 2: Effect of *Equisetum arvense*, Ibuprofen on CFA induced changes in body on Weight 1st, 7th, 13th, 17th, 22nd day.

Body weight (g)	1st day	7th day	13th day	17th day	22nd day
Control	211.6±7.52	205±5.47	208.3±2.5	215±3.16	221.6±2.5
Positive (CFA Induced)	210±6.32	180±6.32***	170±6.32***	163.3±5.16***	155±5.47***
Low Dose (50 mg/kg)	213.3±5.16	185±5.4*	180±6.3*	185±5.4*	180±6.3*
High Dose (100 mg/kg)	216.6±5.16	200 ±5.4##	190±6.32##	190.8±3.7##	210±5.4##
Standard (15 mg/kg)	218.3±4.08	190±5.477**	195±4.08**	200±5.4**	220±3.16**

*** indicates $p<0.001$ when compared to normal group.## $p<0.01$, * $p<0.05$ when compared to positive group.

control group, suggesting an improvement in motor coordination in rats treated with *Equisetum arvense* extract and Ibuprofen (Table 4).

Effect of *Equisetum arvense* extract, Ibuprofen on Complete Freund's adjuvant (CFA) induced changes in RBC, WBC, HB, and ESR

The administration of Complete Freund's Adjuvant (CFA) resulted in a notable reduction in Hemoglobin (Hb) and Red Blood Cell (RBC) levels compared to healthy rats. However, when *Equisetum arvense* extract and Ibuprofen were administered to the diseased rats, there was a significant improvement in the levels of RBC and Hb, restoring them to normal levels. Furthermore, the increased White Blood Cell (WBC) count and Erythrocyte Sedimentation Rate (ESR) observed in the CFA-treated groups were effectively alleviated in the groups treated with the extract (Table 5).

Table 3: Effect of *Equisetum arvense* extract, Ibuprofen on Complete Freund's Adjuvant (CFA) Induced changes in paw volume.

Paw Volume	1st day	7th day	13th day	17th day	22nd day
Control	0.5±0.08	0.53±0.08	0.56±0.08	0.55±0.14	0.56±0.08
Positive (CFA Induced)	1.8±0.089****	2.13±0.08****	2.6±0.08****	2.0±1.98****	2.1±0.08****
Low Dose (50 mg/kg)	1.6±0.08**	1.6±0.10**	1.35±0.10**	1.28±0.07**	1.05±0.05**
High Dose (100 mg/kg)	1.56±0.29**	1.45±0.05**	1.28±0.12**	1.1 ±0.08**	0.98±0.07**
Standard (15 mg/kg)	1.28±0.07***	1.33±0.08***	1.18±0.04***	1.03±0.08****	0.95±0.12***

Where, ****indicates $p<0.0001$ when compared to normal group.***$p<0.001$, *$p<0.01$ when compared to positive group.

Table 4: Effect of *Equisetum arvense*, Ibuprofen on CFA induced change in fall of time on 1st, 7th, 13th, 17th, 22nd day.

Fall of time (sec)	1st day	7th day	13th day	17th day	22nd day
Control	80±4.03	78±0.75	75±0.89	70±4.47	72.5±2.73
Positive (CFA Induced)	55.8±2.04***	27.5±2.73***	18.3±2.58***	11.6±2.58***	15.8±2.04***
Low Dose (50 mg/kg)	45±5.4*	48±4.19*	46±4.91*	40±1.09*	45±0.89*
High Dose (100 mg/kg)	55±0.89**	58±1.09**	55±1.26**	55±1.26**	58±0.63**
Standard (15 mg/kg)	56±3.16**	58±0.63**	62±0.63**	64±0.63**	65±1.09**

Where, ***indicates $p<0.0001$ when compared to normal group.**$p<0.001$, *$p<0.05$ when compared to positive group.

Table 5: Effect of *Equisetum arvense*, Ibuprofen on CFA induced change in R B C, WBC, Hb, ESR.

Blood paramter s	RBC (10^6xµL)	WBC (10^3xµL)	Hb (gm/dL)	ESR (mm/hr)
Control	7.32±0.22	9.6±0.31	14.18±0.75	1.26±0.16
Positive (CFA Induced)	3.68±0.38****	22.44±1.52****	6.45±0.18****	51.16±6.27****
Low Dose (50 mg/kg)	4.75±0.4***	19.25±0.36****	7.51±0.76****	24.83±2.1****
High Dose (100 mg/kg)	5.25±0.42***	15.25±0.72****	9.28±0.37****	9.98±0.32****
Standard (15 mg/kg)	6.16±0.12****	11.1±0.33****	11.4±0.36****	8.5±0.70****

Where, ****indicate $p<0.0001$ when compared to the normal group.***indicate $p<0.001$ when compared to the positive group.

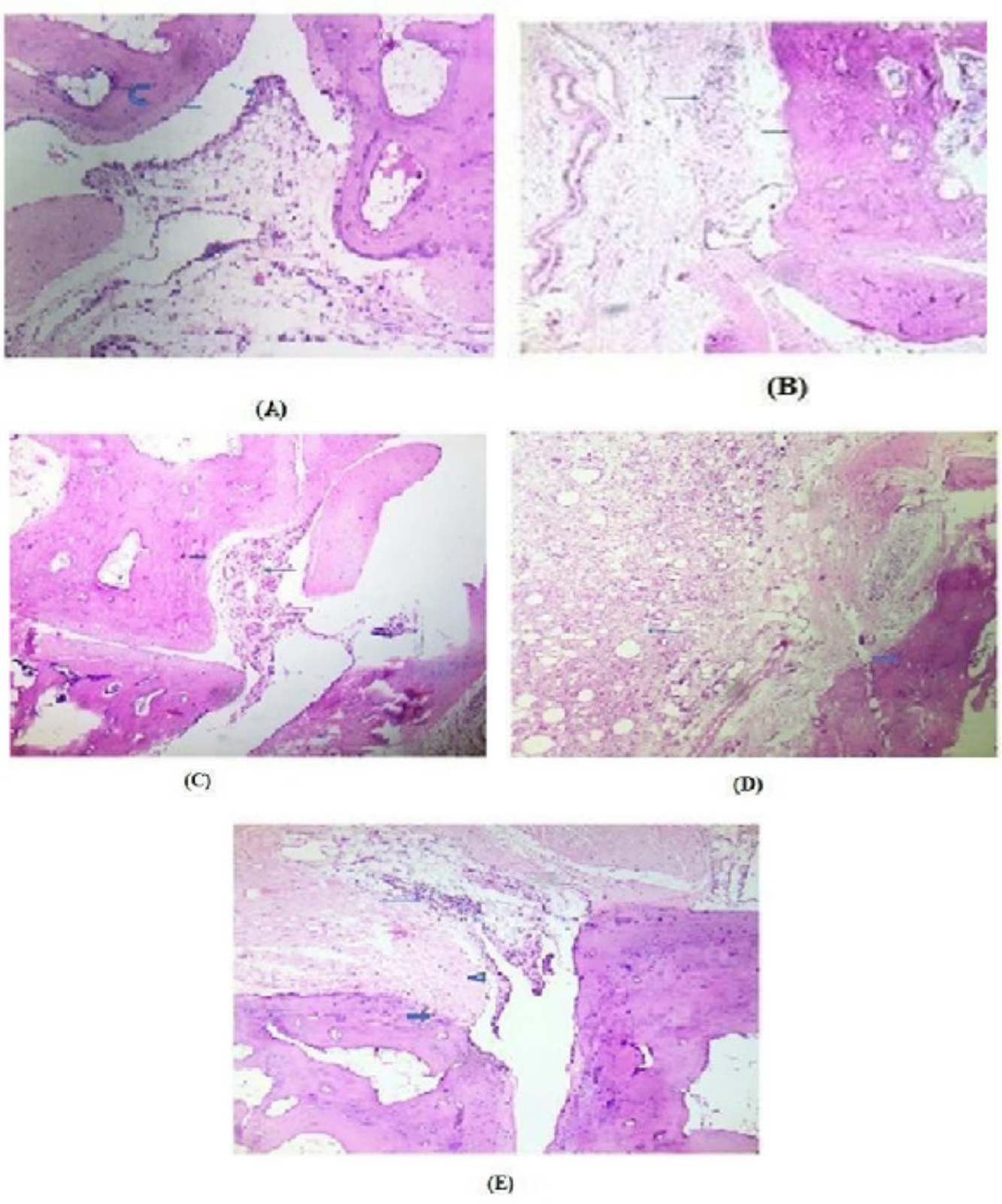

Figure 1: Effect of *Equisetum arvense* plant extract, ibuprofen on tibiotarsal joints. (A) Normal control group, Normal synovial epithelium, cartilaginous tissue is well preserved and normal Subchondral osteoids were observed. (B) Complete Freund's adjuvant Induced group, destruction of cartilage and erosion of osteoid and increased inflammatory and vascularity. (C) Low dose group (50 mg/kg), Less Focal Destruction of cartilage and erosion of osteoid and Mild Inflammatory cells, synovial hyperplasia and vascularity in the adjacent structures were observed. (D) High dose group (100 mg/kg), No destruction of cartilage and erosion of osteoid and No inflammatory cells were observed. (E) Ibuprofen group (15 mg/kg), No destruction of cartilage and erosion of osteoid and No inflammatory cells were observed.

Effect of Equisetum arvense extract, Ibuprofen in Histopathology of joints

Histopathological examinations of the tibiotarsal joints revealed cartilage destruction, osteoid erosion, inflammatory cell infiltration, and increased vascularity in neighboring tissues in animals treated with CFA. The vehicle-treated group exhibited normal synovial epithelium, cartilaginous tissue, and subchondral osteoid in the tibiotarsal joint. In the Ibuprofen-treated group, there was cartilage destruction, osteoid erosion, inflammatory cell infiltration, and synovial hyperplasia. Rats treated with *E. arvense* demonstrated joint protection in comparison to arthritic rats, manifesting reduced cartilage destruction. The group treated with 100 mg/kg exhibited diminished cartilage destruction and reduced vascularity in adjacent structures. However, the 50 mg/kg dose of *E. arvense* resulted in cartilage destruction, osteoid erosion, synovial hyperplasia, and increased vascularity in adjacent structures (Figure 1).

DISCUSSION

Recently, there has been an increasing emphasis on natural products as a substantial area of investigation for developing new therapeutic agents. This is propelled by their improved safety profile and more economical nature.[13] Rheumatoid arthritis, a common autoimmune disorder, is frequently examined using the FCA-induced arthritic model, acknowledged as an exemplary animal model for immunologically simulating rheumatoid arthritis. This arthritis model induced by FCA serves as a representation of chronic polyarthritis in animals, displaying features that closely resemble those observed in rheumatoid arthritis.[14] The arthritic model induced by complete Freund's adjuvant, marked by chronically mediated inflammation of immunological origin, is considered the most efficacious experimental model for emulating rheumatoid arthritis.[15] The FCA model, widely recognized for studying inflammation in rats, employs a formulation comprising inactivated and desiccated mycobacterium. This composition effectively induces cell-mediated immunity, leading to the production of immunoglobulins.[16] Arthritis induced by Freund's Complete Adjuvant (FCA) leads to significant and persistent swelling in the hind paw, referred to as primary arthritis. This swelling persists for a week and is associated with the production of prostaglandins.[10] In the adjuvant-induced arthritis model, rats demonstrate sustained swelling in multiple joints, accompanied by the infiltration of inflammatory cells, along with joint cartilage erosion and bone destruction and remodeling. These features closely mirror those observed in human rheumatoid disease.[17]

The aim of the current study was to explore the potential anti-rheumatoid activity of *Equisetum arvense* plant extract with minimal side effects in a model of rheumatoid arthritis induced by Complete Freund's adjuvant. The evaluation of the anti-rheumatic effects of *Equisetum arvense* extract primarily relied on *in vivo* studies conducted in this research.

The ethanolic extract of *Equisetum arvense* showcased a noteworthy reducing property, primarily attributed to its high content of kynumeric acid. This compound is believed to contribute to the antioxidant activity, given that phenolic compounds are known for their direct antioxidant and anti-inflammatory properties. Notably, kynumeric acid is a component of human synovial fluid, and its levels were observed to be lower in patients with rheumatoid arthritis compared to those with osteoarthritis. *In vitro* studies indicated that KYNA demonstrated inhibitory effects on the proliferation and viability of fibroblasts, and it augmented the anti-proliferative action of anti-rheumatic drugs. Therefore, *Equisetum arvense*, with its kynumeric acid content, has the potential to inhibit the proliferation of synoviocytes.[18] The evolution of disease status and the effectiveness of anti-inflammatory treatment exhibit an indirect correlation with variations in body weight. Rheumatoid arthritis is linked to weight loss and a decline in lean body mass, referred to as rheumatoid cachexia. This condition contributes to diminished physical activity, muscle strength, and compromised daily performance. Researchers have noted metabolic changes in arthritic rats, observing a reduction in the absorption of 14C-glucose and 14C-leucine in the intestines under inflammatory conditions. Treatment with anti-inflammatory drugs was found to enhance the diminished absorption capacity.

In the current study, rats treated with FCA exhibited a lower increase in body weight compared to arthritic rats treated with Ibuprofen and *Equisetum arvense* extract. This suggests that the enhanced body weight gain observed in the latter groups may be attributed to the restoration of intestinal absorption capacity, indicating effective management of rheumatoid cachexia.[10]

The investigation demonstrated that rats treated with Complete Freund's Adjuvant (CFA) displayed an elevation in paw volume, indicative of arthritis. The administration of *Equisetum arvense* extract postponed the onset and mitigated the severity of the disease, as evidenced by a reduction in paw volume. This beneficial effect was attributed to the inhibition of inflammatory mediator release, highlighting the anti-inflammatory potential of the extract. The effectiveness of the extract at a dose of 100 mg/kg was comparable to that of the standard drug, Ibuprofen, a widely used non-steroidal anti-inflammatory drug for arthritis treatment.[13]

Ibuprofen effectively hindered the progression of adjuvant-induced arthritis, aligning with earlier findings. *Equisetum arvense* doses of 50 mg/kg and 100 mg/kg exhibited substantial and dose-dependent suppression of paw swelling in arthritic rats. Treated animals displayed notably milder manifestations of chronic inflammatory reactions, including reduced swelling,

redness, arthralgia, and joint inactivity, compared to rats treated with *Equisetum arvense*.[17]

The reduction in RBC count and hemoglobin level observed in arthritic rats indicated an anemic condition, possibly resulting from abnormal iron storage and bone marrow non-responsiveness. A noteworthy rise in leukocyte count in arthritic rats suggested immune system stimulation. Both *Equisetum arvense* extract and Ibuprofen treatment exhibited immune-modulating effects.

Elevated Erythrocyte Sedimentation Rate (ESR) in arthritis was indicative of inflammation, and the significant reduction in ESR in *Equisetum arvense* extract and Ibuprofen-treated rats underscored their anti-inflammatory potential.[16]

Histopathological examinations of tibiotarsal joints illustrated the effectiveness of *Equisetum arvense* extract in arthritis treatment, surpassing the pathology observed in Ibuprofen-treated arthritic animals. The extract demonstrated joint protection by mitigating cartilage destruction, with the 100 mg/kg dose exhibiting significant efficacy in reducing both cartilage destruction and vascularity. However, the 50 mg/kg dose led to cartilage destruction, erosion of osteoid, synovial hyperplasia, and increased vascularity in adjacent structures, emphasizing potential dose-dependent effects.[15] In summary, *Equisetum arvense* extract exhibited anti-rheumatoid activity, alleviating inflammation, weight loss, and joint damage across various doses.

CONCLUSION

In summary, this study highlighted the significant anti-rheumatoid potential of both *Equisetum arvense* extract and Ibuprofen in addressing Complete Freund's adjuvant-induced rheumatoid arthritis. The extract's rich content of phenolic compounds likely contributed to its antioxidant activity, given the well-established direct antioxidant properties of phenolic compounds. Furthermore, the presence of KYNA in the extract was identified as a factor inhibiting the proliferation and viability of fibroblasts, thereby enhancing its anti-proliferative action. Future investigations exploring the effects of *Equisetum arvense* extract in combination with various drugs used in the treatment of rheumatoid arthritis patients would be valuable, aiming to alleviate morbidity associated with the condition.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

CFA: Complete Freund's adjuvant; **DTH:** Delayed Type Hypersensitivity**; DMARD'S:** Disease Modifying Anti-Rheumatic Drugs; **ESR:** Erythrocyte Sedimentation Rate; **Hb:** Hemoglobin; **IFA:** Incomplete Freund's adjuvant; **KYNA:** Kynumeric Acid; **NSAID'S:** Non-Steroidal Anti-Inflammatory Drugs; **RA:** Rheumatoid Arthritis; **RBC:** Red Blood Cells; **WBC:** White Blood Cells.

SUMMARY

Equisetum arvense extract exhibited anti-rheumatoid activity, alleviating inflammation, weight loss, and joint damage Equisetum arvense treated rats produced joint protection compared to arthritic rats by reducing destruction of cartilage. Rats treated with 100mg/kg showed reduction in destruction of cartilage and decreased vascularity in the adjacent structures. Dose 50 mg/kg of Equisetum arvense showed destruction of cartilage and erosion of osteiod along with synovial hyperplasia and vascularity in adjacent structures.

This study demonstrates that Equisetum arvense extract exerted anti-rheumatoid effect on CFA induced rheumatoid arthritis in rats. The mechanism might be associated with the enhancement of antioxidant defense system. It could provide experimental evidence to support the rationality of combinatorial use of it in the prevention of the onset and progression of rheumatoid arthritis

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