IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
June 2019 Vol.:15, Issue:3

Evaluation of Anti Arthritic Activity of the Ethanolic Extract of *Pyrus communis* Fruit (EEPC) Incomplete Freund's Adjuvant Induced Rheumatoid Arthritis in Wistar Rats

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ISSN 2349-7203
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Submission: 26 May 2019
Accepted: 31 May 2019
Published: 30 June 2019

HUMAN JOURNALS
www.ijppr.humanjournals.com

Keywords: Rheumatoid arthritis, cytokines, *Pyrus communis*, Complete Freund's adjuvant.

ABSTRACT

Rheumatoid arthritis (RA) is a chronic inflammatory and systemic autoimmune disease affecting people predominantly between the ages of 20-50 years with an unpredictable course. About 1 % of the world's population is afflicted by rheumatoid arthritis and is two to three times more common in women than men. There are different types of arthritis. Rheumatoid arthritis is due to the presence of pro-inflammatory markers, cytokines, and leukotrienes The primary inflammatory markers are IL-1, TNF-α, IL-6, IL-15, IL-16, IL-17, IL-18, and granulocyte macrophage-colony stimulating factor, chemokines such as IL-8, macrophage inflammatory protein-1, and monocyte chemoattractant protein-1. TNF-α blockade, IL-1 blockade, B cells therapy, IL-6 blockade, and angiogenesis blockade are a therapeutic target for treatment. The complete Freund's adjuvant-induced rheumatoid arthritic Wistar rats are involved to evaluate the anti-arthritic activity of *Pyrus communis*. The *Pyrus communis* is commonly known as Pear fruit having numerous pharmacological properties. Therefore the ethanolic extract of *Pyrus communis* has greater potential to produce a beneficial effect in complete Freund's adjuvant-induced rheumatoid arthritic rats.

INTRODUCTION

Rheumatoid arthritis (RA) is a long-term autoimmune disorder of unknown etiology[1] that primarily affects joints. It typically results in warm, swollen, and painful joints. Pain and stiffness often worsen the health condition of the patients with rheumatoid arthritis identified and characterized by articular[2] inflammation, the formation of inflammatory and invasive tissue, rheumatoid pannus which leads to the destruction of joints. Analgesic[3] (pain killers) and Anti-inflammatory drugs, including steroids, are used to suppress the symptoms, while disease-modifying Anti-rheumatic drugs (DMARDs)[4], newer therapies such as anti-tumor necrosis factor (TNF)-α[5] therapy are often required to inhibit the immune process. However, all of these agents are associated with numerous side effects. In recent days, researchers are directed towards the traditional system of medicine for the discovery of drugs that are long-acting anti-inflammatory with minimum side effects. This rheumatoid arthritis affects 20% of the population of the world in female and male[6]. It is caused by a number of pro-inflammatory molecules released by macrophages and eicosanoids[7] such as prostaglandins[8], leukotrienes and cytokines[9].

The joints most commonly affected by arthritis are weight-bearing joints, such as feet, knees, hips, spine and other joints, such as finger and thumb joints. Symptoms of arthritis[10] can include reduced ability to move the joint, stiffness, especially in the morning, difficulty performing daily activities, disability, long term (chronic) pain, etc.

MATERIALS AND METHODS

Female Wistar rats of body weight 120-200 g were used for the study. The rats were maintained under standard environmental conditions and were fed with standard pellet diet and water ad libitum. All the Experimental procedures were carried out in accordance with Committee for the purpose of Control and Supervision of Experiments on Animal (CPCSEA) guidelines and all the experimental procedures were approved by 15/321/PO/Re/S/01/CPCSEA/dated 12/10/18.

The protocol was approved by the Animal Ethics Committee constituted for the purpose as per CPCSEA Guideline.

Preparation of extract: The powdered fruit of *Pyrus communis* **(EEPC)** were taken. The process of extraction is done by using a Soxhlet[11] apparatus, which is a Hot extraction method.

Nature of phytoconstituent: The nature of phytoconstituent present in EEPC is carbohydrates, alkaloids, tannins and phenolics, flavonoids and glycosides. The nature of phytoconstituent absent in EEPC are proteins and amino acids, triterpenoids, saponins, fixed oils, steroids, gums, and mucilage.

Preparation and administration of dose: The rats (six) in each group (four) were induced with 0.2 ml of Complete Freund's Adjuvant which is dissolved in Liquid Paraffin. The disease (arthritis) is induced delicately into the Sub-plantar region of the hind paw. In Group I, the animals was treated with distilled water for 21 days daily throughout the study. In Group II, a single injection of 0.2 ml of complete Freund's adjuvant was dissolved in liquid paraffin and injected into the sub-plantar region of the left hind paw on day 1. In Group III, CFA induced animals were administrated with 0.75mg/kg of methotrexate orally for 21 days throughout the study. In Group IV and Group V, CFA induced animals was administrated with 200mg/kg and 400mg/kg of EEPC orally for 21 days throughout the study. The following parameters like paw edema volume, body weight, locomotor activity was measured on day 1, 5, 10, 15, 20 and recorded. The blood was collected on the 21st day after the last dose of methotrexate and EEPC 200 and 400 mg/kg for Group III, IV and V respectively.

Acute oral toxicity: The acute oral toxicity class method is a stepwise procedure with 3 animals of single-sex to assess the short term toxicity of test substance. An average of 2-4 steps may be involved to decide the acute toxicity of the plant material which depends on the mortality and morbidity status of the animals. The procedure is reproducible where usage of animals is minimal (Test Guidelines 423).

Paw edema volume: The paw edema volume in each rat was measured on the day (1, 5, 10, 15, 20) by using plethysmometer.

Body weight: The body weight was recorded at different time intervals on the day (1, 5, 10, 15, 20) by using calibrated measuring balance and the mark was kept at zero. Each animal was placed in the balance and the weight was recorded.

Locomotor activity: The locomotor activity was recorded in each animal on the day (1, 5, 10, 15, 20) respectively by using actophotometer. In a digital Actophotometer, a continuous beam of light falls on photoelectric cells.

Histopathology analysis: The animals were sacrificed on day 21, the ankle joints were removed and preserved in 10% buffered formalin for 24 hours. It was followed by decalcification in 5% formic acid, processed for paraffin embedding sectioned at 50 µm thickness. The sections were stained with hematoxylin and eosin H & E and evaluated under a light microscope for the presence of hyperplasia of synovium, pannus formation, and destruction of joint space.

X-ray radiography: Rats were anesthetized on day 21. Radiographs were taken with X-ray apparatus for lateral and mediolateral projection.

Statistical analysis: Data were analyzed using one-way ANOVA followed by Dunnett's test and expressed as Mean± Standard Error of Mean (SEM). Statistical analyses were performed using Graph Pad Prism version 7.01, for windows. Differences between mean values of different groups were considered statistically significant at ($P<0.001$)***, ($P<0.01$)**, ($P<0.05$)*, ns- nonsignificant.

RESULTS

ACUTE ORAL TOXICITY:

No toxic symptoms were observed after administration of different dose levels of extract up to a maximum of 2000mg/kg p.o. according to OECD guideline 423; and in addition, the higher dose of 2000mg/kg dose was administered to a group of animals. No symptoms or adverse events were identified. Hence, the safe tolerable dose was used as a therapeutic dose for further pharmacological study. From this experiment, the minimum and maximum therapeutic dose level of EEPC extracts were studied as 200mg/kg and 400mg/kg.

INVIVO ANTI-ARTHRITIC STUDY RESULTS:

Group, I is compared with Group II, III, IV, and V are considered as a.

Group II is compared with Group III, IV, V is considered as b.

Paw edema volume (Table no. 1)**:**

Effect of EEPC on CFA induced rheumatoid arthritis rats showing changes in paw edema volume

1st DAY

When compared to Group I, there was a non significant increase in paw edema volume in Group II (ns), decrease in paw edema volume in Group III and Group V(P<0.01), Group IV(P<0.05). When compared to Group II, there was a significant decrease in paw edema volume in Group III, Group IV and Group V (P<0.001).

5th DAY

When compared to Group I, there was a significant increase in paw edema volume in Group II (P<0.05), decrease in paw edema volume in Group III and Group IV (P<0.05), Group V (P<0.01). When compared to Group II, there was a significant decrease in paw edema volume in Group III, Group IV and Group V (P<0.01).

10th DAY

When compared to Group I, there was a significant increase in paw edema volume in Group II (P<0.01), decrease in paw edema volume in Group III and Group IV (P<0.05), Group V (P<0.01). When compared to Group II, there was a significant decrease in paw edema volume in Group III, Group IV and Group V (P<0.01).

15th DAY

When compared to Group I, there was a significant increase in paw edema volume in Group II (P<0.01), decrease in paw edema volume in Group III, Group IV and Group V (P<0.05). When compared to Group II, there was a significant decrease in paw edema volume in Group III, Group IV and Group V (P<0.01).

20th DAY

When compared to Group I, there was a significant increase in paw edema volume in Group II (P<0.001), nonsignificant decrease in paw edema volume in Group III, Group IV and

Group V (ns). When compared to Group II, there was a significant decrease in paw edema volume in Group III, Group IV and Group V (P<0.05).

Body weight (Table no. 2)**:**

Effect of EEPC on CFA induced rheumatoid arthritis rats showing changes in body weight

1st DAY

When compared to Group I, there was a significant decrease in body weight in Group II and Group III (P<0.01), Group IV (P<0.05), increase in body weight in Group V (P<0.01). When compared to Group II, there was a significant increase in body weight in Group III, Group IV and Group V (P<0.001).

5th DAY

When compared to Group I, there was a significant decrease in body weight in Group II, Group III and Group IV (P<0.05), Group V (P<0.01). When compared to Group II, there was a significant increase in body weight in Group III, Group IV and Group V (P<0.01).

10th DAY

When compared to Group I, there was a nonsignificant decrease in Group II (ns), Group III, Group IV and Group V (P<0.05). When compared to Group II, there was significant decrease (P<0.01) in body weight in Group III (P<0.01), increase in body weight in Group IV and Group V (P<0.01).

15th DAY

When compared to Group I, there was a significant decrease in body weight in Group II (P<0.01), Group III, Group IV and Group V (P<0.05). When compared to Group II, there was a significant decrease in body weight in Group III and Group IV (P<0.01), increase in body weight in Group V (P<0.01).

20th DAY

When compared to Group I, there was a significant decrease in body weight in Group II (P<0.001), increase in body weight in Group III (P<0.01), Group V (P<0.001), nonsignificant

decrease in body weight in Group IV (ns). When compared to Group II, there was a significant increase in body weight in Group III and Group IV (P<0.05), increase in body weight in Group V (P<0.01).

Locomotor activity (Table no. 3)**:**

Effect of EEPC on CFA induced rheumatoid arthritis rats showing changes in locomotor activity

1st DAY

When compared to Group I, there was a significant decrease in locomotor activity in Group II, Group III, Group IV and Group V (P<0.01). When compared to Group II, there was a significant increase in locomotor activity in Group III, Group IV and Group V (P<0.001).

5th DAY

When compared to Group I, there was a significant decrease in locomotor activity in Group II (P<0.01), Group IV and Group V (P<0.01), nonsignificant decrease in locomotor activity in Group III (ns). When compared to Group II, there was a significant increase in locomotor activity in Group III and Group IV (P<0.001), Group V (P<0.01).

10th DAY

When compared to Group I, there was a significant decrease in locomotor activity in Group II, Group III, Group IV and Group V (P<0.01). When compared to Group II, there was a significant increase in locomotor activity in Group III and Group V (P<0.001), a decrease in locomotor activity in Group V (P<0.001).

15th DAY

When compared to Group I, there was a significant decrease in locomotor activity in Group II (P<0.05), Group III, Group IV and Group V (P<0.01). When compared to Group II, there was a significant increase in locomotor activity in Group III and Group V (P<0.001), a decrease in locomotor activity in Group IV (P<0.001).

20th DAY

When compared to Group I, there was a significant decrease in locomotor activity in Group II, Group III, Group IV and Group V (P<0.01). When compared to Group II, there was a significant increase in locomotor activity in Group III, Group IV and Group V (P<0.001).

***IN VITRO* ANTI-ARTHRITIC STUDY RESULTS:**

Effect of EEPC on protein estimation in CFA induced rheumatoid arthritis rats (Table no. 4)**:**

When compared to Group I, there was a significant increase in protein level in Group II, Group III and Group V (P<0.01), Group IV (P<0.05). When compared to Group II, there was a significant decrease in protein level in Group III and Group V (P<0.01), nonsignificant decrease in protein level in Group IV (ns).

Effect of EEPC on protease inhibition in CFA induced rheumatoid arthritis rats (Table no. 4)**:**

When compared to Group I, there was a significant decrease in protease inhibition in Group II (P<0.001), nonsignificant decrease in protease inhibition in Group III (ns), increase in protease inhibition in Group IV (P<0.05), Group V (P<0.001). When compared to Group II, there was a significant increase in protease inhibition in Group III (P<0.01), Group V (P<0.01), nonsignificant increase in protease inhibition in Group IV (ns).

Effect of EEPC on protein denaturation in CFA induced rheumatoid arthritis rats

(Table no.4)**:**

When compared to Group I, there was a significant decrease in protein denaturation in Group II (P<0.05), increase in protein denaturation in Group III (P<0.001), Group V (P<0.01), nonsignificant increase in protein denaturation in Group IV (ns). When compared to Group II, there was a nonsignificant increase in protein denaturation in Group III (ns), increase in protein denaturation in Group IV (P<0.01), Group V (P<0.001).

HISTOPATHOLOGY ANALYSIS OF ANKLE JOINTS:

Group I

No pannus formation and no inflammatory cells infiltration noticed.

Group II

Severe pannus formation (chronic arthritis) surrounding the joints.

Group III

Moderate pannus formation in which proliferation of fibrovascular tissue or granulation tissue.

Group IV

The bone structure appeared normal, no erosion noticed.

Group V

Bone and cartilage surrounding the joints appeared normal.

X-RAY RADIOGRAPHY OF JOINTS:

Group I

Control group with no degenerative joint changes.

Group II

Excess soft tissue volume, joint space and degenerative joint changes.

Group III

Moderate soft tissue volume, joint space and degenerative joint changes.

Group IV

Pronounced soft tissue volume, joint space, and degenerative joint changes.

Group V

Low to moderate soft tissue volume, joint space, and degenerative joint changes.

Table.no.1: Effect of EEPC on CFA induced rheumatoid arthritis rats showing changes in Paw Edema Volume

GROUPS	1st DAY	5th DAY	10th DAY	15th DAY	20th DAY
GROUP I	0.54 ±0.01	0.56 ±0.01	0.54 ±0.01	0.56 ±0.01	0.56 ±0.02
GROUP II	0.55 ±0.02 a^{ns}	0.64 ±0.01 a*	0.70 ±0.01 a**	0.75 ±0.02 a**	0.81 ±0.02 a***
GROUP III	0.49 ±0.01 a**b***	0.38 ±0.01 a*b**	0.33 ±0.02 a*b**	0.30 ±0.01 a*b**	0.28 ±0.01 a^{ns} b*
GROUP IV	0.52 ±0.02 a*b***	0.41 ±0.01 a*b**	0.32 ±0.02 a*b**	0.30 ±0.01 a*b**	0.28 ±0.01 a^{ns} b*
GROUP V	0.48 ±0.02 a**b***	0.32 ±0.01 a**b**	0.26 ±0.01 a**b**	0.22 ±0.01 a*b**	0.17 ±0.01 a^{nd} b*

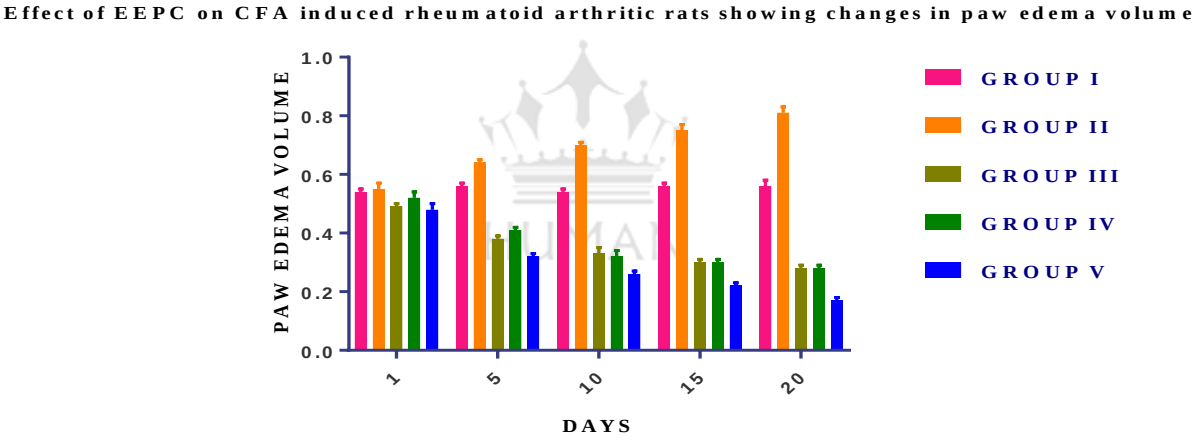


Table no. 2: Effect of EEPC on CFA induced rheumatoid arthritic rats showing changes in Body Weight

GROUPS	1st DAY	5th DAY	10th DAY	15th DAY	20th DAY
GROUP I	160±0.02	155±0.01	150±0.01	153±0.02	154±0.01
GROUP II	140±0.01 a**	130±0.01 a*	120±0.02 a^{ns}	120±0.02 a**	92±0.02 a***
GROUP III	150±0.01 a**b***	140±0.02 a*b**	110±0.01 a*b**	100±0.01 a*b**	155±0.01 a** b*
GROUP IV	150±0.02 a*b***	140±0.02 a*b**	130±0.01 a*b**	120±0.01 a*b**	100±0.01 a^{nd} b*
GROUP V	165±0.02 a**b***	150±0.02 a**b**	140±0.02 a*b**	145±0.01 a*b**	170±0.01 a*** b**

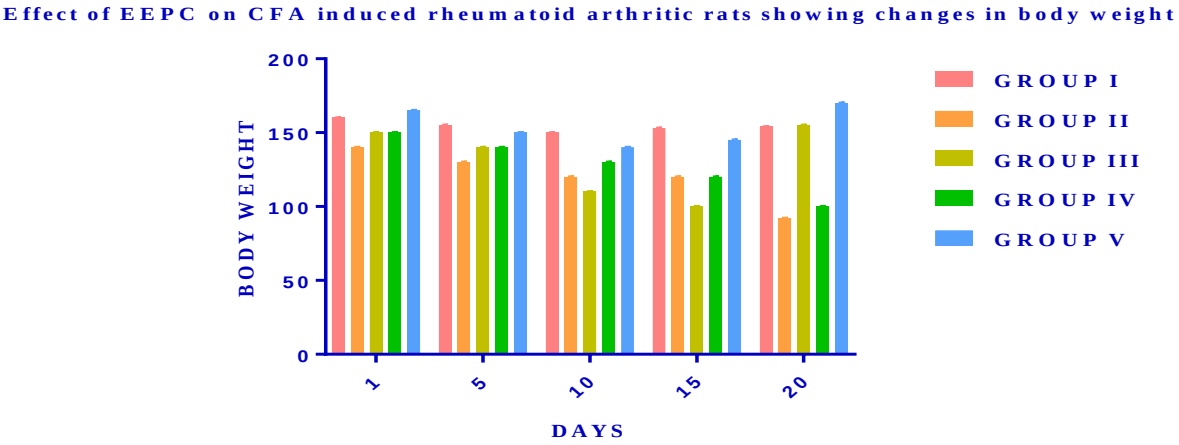


Table no. 3: Effect of EEPC on CFA induced rheumatoid arthritic rats showing changes in Locomotor Activity

GROUPS	1st DAY	5th DAY	10th DAY	15th DAY	20th DAY
GROUP I	132.5±0.02	126.25±0.46	125.5±0.24	121.66±0.43	120±0.42
GROUP II	122.0±0.15 a**	118.5±0.45 a**	112±0.29 a**	110±0.15 a*	100±0.15 a**
GROUP III	128±0.19 a**b***	120±0.13 a^{ns}b***	115.25±0.25 a**b***	113.6±0.23 a**b***	110±0.22 a**b***
GROUP IV	125.5±0.13 a**b***	121±0.18 a**b***	110.75±0.10 a**b***	100±0.56 a**b***	100±0.45 a**b***
GROUP V	124.4±0.73 a**b***	120.7±0.47 a**b**	116±0.12 a**b***	115.66±0.38 a**b***	112±0.35 a**b***

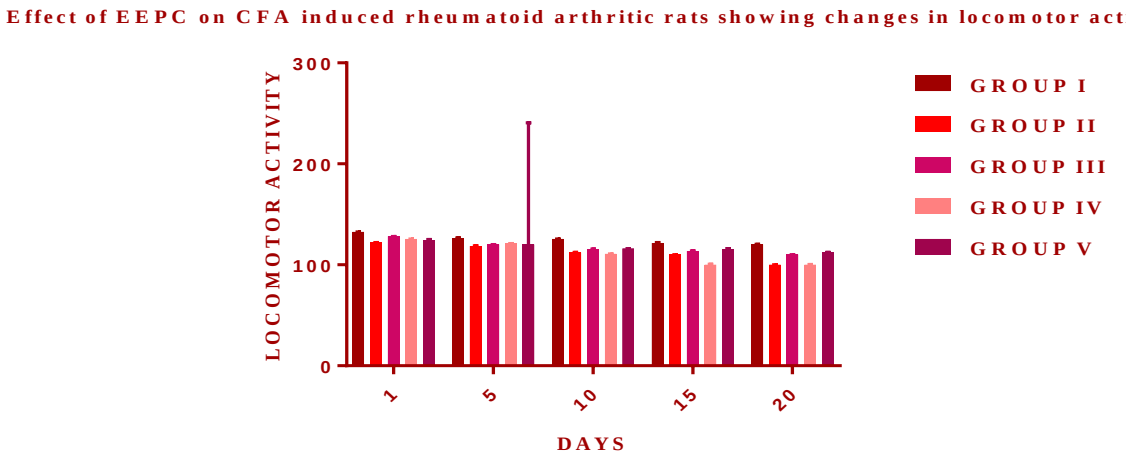
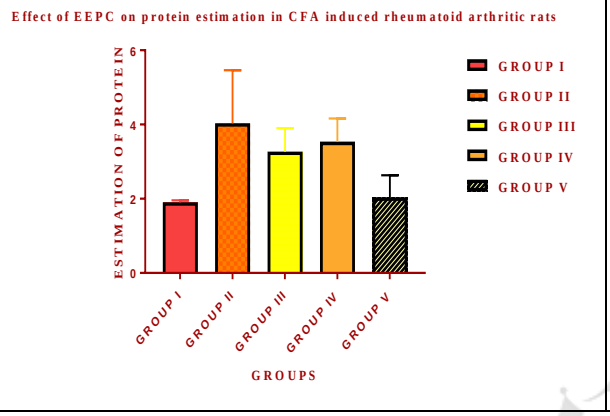
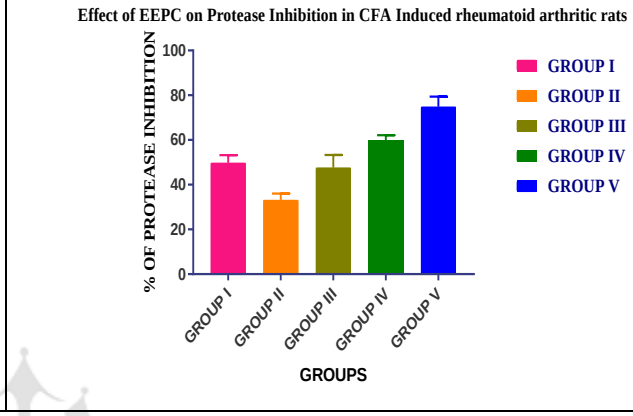
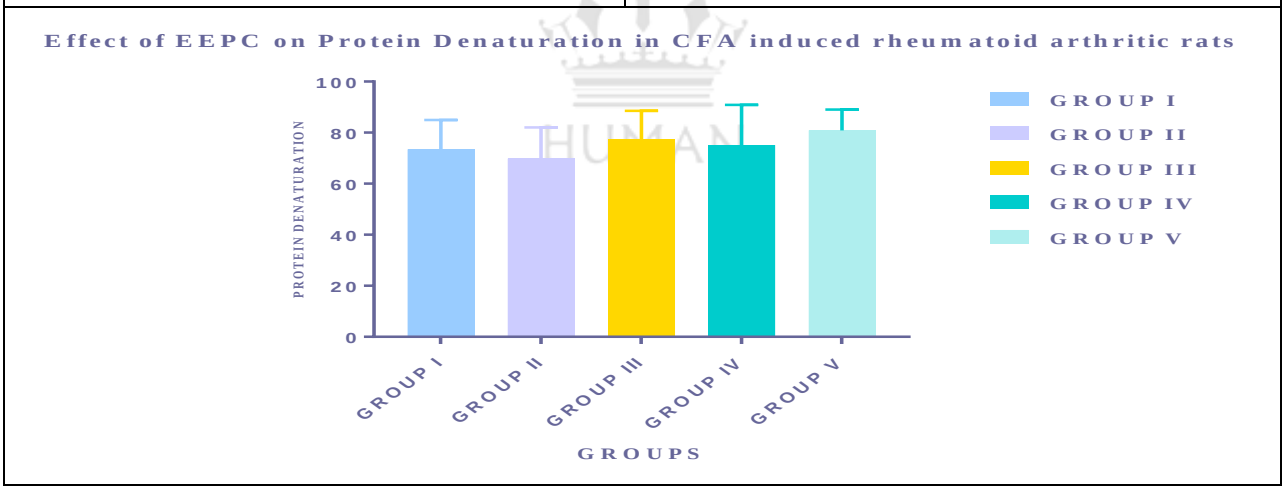


Table no. 4: Effect of EEPC on Protein Estimation, Protease inhibition and Protein denaturation in CFA induced rheumatoid arthritic rats.

GROUPS	ESTIMATION OF PROTEIN	%INHIBITION OF PROTEASE (Trypsin)	% OF PROTEIN DENATURATION
GROUP I	1.9±0.05	49.75±3.42	73.45±5.15
GROUP II	4.033±1.43a**	33.23±2.84a***	69.78±5.47a*
GROUP III	3.267±0.636a**b**	47.59±5.67a^{ns}b**	77.42±4.96a***b^{ns}
GROUP IV	3.533±0.63a*b^{ns}	59.74±2.35a*b^{ns}	75.15±7.04a^{ns}b**
GROUP V	2.033±0.60a**b**	74.88±4.51a***b**	80.91±3.62a**b***







DISCUSSION

Rheumatoid arthritis (RA) is a chronic autoimmune disease. It causes joints to swell and can result in pain, stiffness and progressive loss of function. In addition to joint pain and stiffness, people with RA may also have symptoms such as weight loss, low-grade fever, and fatigue. RA often affects pairs of joints in the wrists and hands. Over time, other joints can be affected such as shoulders, elbows, knees, feet, and ankles [(12)]. This rheumatoid arthritis affects 20% of the population of the world in female and male. Indian sub-continent is a rich source of plant and animal wealth which is due to its varied geographical climate regions. It

is a well-known fact that traditional system of medicines always played an important role in meeting the global health care needs. The herbal medicines provide essential compounds with active principles having no or minimum side effects [13] and useful for arthritis control. There are many medicinal plants which exert anti-arthritic activity at a particular dose. The isolation of lead compound is responsible for improving the better treatment of rheumatoid arthritis. Pear has Anti-microbial activity[14], Anti-oxidant activity[15], Cholesterol-lowering activity[16], Anti-cancer activity[17,18,19], Anti-diabetic activity[16], Skin-whitening effect[20], Wound healing effect[21], Immune booster[20], Action on urinary system[22] and Weight loss effect[23]. Methotrexate is used as a standard drug. It shows marginal effects on humoral or cellular immune responses. The mechanism of action of methotrexate in RA is more anti-inflammatory than immunosuppressive. The inhibition of interleukin-1 (IL-1) activity or other inflammatory cytokines by methotrexate play an important role in the anti-inflammatory effect of methotrexate. Methotrexate has crucial effects, initiated by some cytokines (IL-1, IL-6, tumor necrosis factor), which plays a major role in RA and other inflammatory diseases[24]. Complete Freund's adjuvant is composed of inactivated and dried Mycobacterium tuberculosis. Complete Freund's adjuvant is a water in oil adjuvant. Freund had suggested three categories of the mechanism of action [25] Prolongation of a presence of antigens at the site of injection. More effective "transport of the antigens to the lymphatic system and to the lungs, where the adjuvant promotes the accumulation of cells concerned with the immune response". Other mechanism remains unidentified because their classification requires knowledge about "how antibodies are formed and how sensitization develops". The synovitis, swelling and joint damage that characterize RA are the end results of complex autoimmune and inflammatory processes that involve components of both the innate and adaptive immune systems[26]. The membrane produces sac surrounding the joint. Collagen is gradually destroyed, narrowing the joint space and finally damaging bone. Thus EEPC decreases the paw edema volume. The decrease in body weight in the arthritic rats compared to the normal control rats in the current study is in concordance with the fact that rheumatoid arthritis (RA) is associated with loss of lean tissues, which contain most of the body's protein. The reduction in body weight gain may also be attributed to muscle wasting in experimental arthritis, occurring due to enhanced protein breakdown by the ubiquitin-proteasome proteolytic pathway [27]. Thus EEPC increases the body weight of the animals. Inflammatory synovitis and dysfunction of the muscle-tendon [28] junctions are postulated mechanisms leading to instability of the joints and loss of hind paw function which results in a decrease in locomotor activity. Thus EEPC increases the locomotor activity of the animals.

Fibroblast-like synoviocytes which are specialized cell type present in the synovium of joints. These cells play a crucial role in the pathogenesis of chronic inflammatory diseases, such as rheumatoid arthritis. Total protein consists of albumin, globulins, and fibrinogen in plasma. Proteins function to control oncotic pressure, transport substances (hemoglobin, lipids, calcium) and promote inflammation. The decrease in total protein levels is due to a decrease in albumin concentration. Thus EEPC decreases the protein level such as albumin and globulin.

Protease such as trypsin is essential enzymes that mediate the hydrolytic breakdown of peptide bonds in proteins. The protease inhibitor acts as an irreversible and competitive substrate. It competes with proteins to bind to trypsin. Therefore, protease inhibitor such as trypsin is considered as an anti-nutritional factor. Thus EEPC increases the protease inhibition. Rheumatoid arthritis showed a significant rise in alpha-antitrypsin [(29)], alpha-antichymotrypsin and inter-alpha-trypsin inhibitor in serum as well as in a synovial fluid. In synovial fluid, the inhibitors were present in their native form. Antiproteases are probably involved in the protection of tissues against proteolytic enzymes which are released from leucocytes and other cells in various pathological states by limiting the proteolytic activity. It is widely held that proteolytic enzymes in rheumatoid arthritis are responsible for much of the tissue damage in affected joints.

Production of auto-antigens in certain rheumatic diseases may be due to in vivo denaturation of proteins. Mechanism of denaturation probably involves alteration in electrostatic[(30)], hydrogen, hydrophobic and disulfide bonding. When a protein is denatured, secondary and tertiary structures are altered but the peptide bonds of the primary structure between the amino acids are left intact. Thus EEPC inhibits the protein denaturation. Protein denaturation is a process in which protein lose their tertiary structure and secondary structure by application of external stress or compound such as strong acid or base concentration. Denaturation [(30)] of protein is a well-documented cause of inflammation. Several anti-inflammatory drugs have shown dose-dependent ability to inhibit protein denaturation. Histopathology provides a noticeable morphological distinctiveness as a practical and unambiguous pathognomonic sign of Rheumatoid arthritis. The histopathological analysis identified the ability of the bones to re-form upon treatment with EEPC. Bone structures re-calcified upon treatment with the EEPC dose-dependently. The EEPC exhibited good therapeutic potential from the study results and is therefore consistent with earlier findings

that the ability of a drug to suppress inflammation, synovitis and protect a joint is desired in rheumatoid arthritis therapy. Radiographic changes in Rheumatoid arthritis conditions are useful diagnostic measures which indicate the severity of the disease. Soft tissue swelling is the earlier radiographic sign, whereas prominent radiographic changes like bony erosions and narrowing of joint spaces can be observed only in the developed stages (final stages) of arthritis. In the negative control, soft tissue swelling along with narrowing of the joint spaces was severe which implies the bony destruction in arthritic condition. Standard (Methotrexate) have prevented this bony destruction and also there is moderate swelling of the joint. Similarly, according to histopathological studies, EEPC has shown significant prevention against bony destruction by showing less soft tissue swelling and narrowing of joint spaces in the 21 days of treatment when compared with the negative control.

CONCLUSION:

The anti-arthritic in-vivo activity of fruits of *Pyrus communis* showed a decrease in paw edema volume and body weight but increase in locomotor activity in complete Freund's adjuvant-induced rheumatoid arthritis rats.

Further, the anti-arthritic activity is evidenced by a reduction in total protein, inhibition of protease and percentage of protein denaturation.

Further, the anti-arthritic activity of fruit of *Pyrus communis* is evidenced by histopathology analysis of ankle joints incomplete Freund's adjuvant-induced rheumatoid arthritic rats.

Further, the anti-arthritic activity of fruit of *Pyrus communis* is evidenced by X-ray radiography analysis of ankle joints incomplete Freund's adjuvant-induced rheumatoid arthritic rats.

Thus, it may be concluded that fruits of *Pyrus communis* produced significant anti-arthritic activity in complete Freund's adjuvant-induced rheumatoid arthritic rats.

Further work is necessary to elucidate the mechanism of action involved in the anti-arthritic activity of fruits of *Pyrus communis* with special reference to phytochemicals.

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