Journal of Pharmaceutical and Scientific Innovation

www.jpsionline.com (ISSN : 2277 -4572)

Research Article

EFFECT OF *OECOPHYLLA SMARAGDINA* ON COMPLETE FREUND'S ADJUVANT INDUCED ARTHRITIS IN ALBINO RAT

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DOI: 10.7897/2277-4572.07495

Received on: 16/06/18 Revised on: 15/07/18 Accepted on: 17/07/18

ABSTRACT

Weaver ant *Oecophylla smaragdina* (OS) belongs to family Formicidae has been used by traditional village people, and also as the indigenous medicine. The present study was planned to induce rheumatoid arthritis in Wistar albino rats by complete Freund's adjuvant in the dose of 100µl. The ethanol extract of *Oecophylla smaragdina* (EEOS) was administered by the oral dose of 200mg/kg, 400mg/kg, for a period of 24 days duration. The Biochemical parameters, haematological parameters, and histopathology of the joint tissue were studied. The *Oecophylla smaragdina* (OS) extract attenuated the rheumatoid arthritis factors induced by complete Freund's adjuvant by the dose-dependent manner. The current study concludes that EEOS extract of both concentrations provides a significant effect of anti-arthritic effects.

Keywords: *Oecophylla smaragdina,* ethanol and Freund's adjuvant

INTRODUCTION

In excess of 80 individual immune system sicknesses have been recognized including Type 1 diabetes, multiple sclerosis, rheumatoid arthritis, inflammatory bowel diseases including Crohn's disease, and ulcerative colitis, haemolytic iron deficiency anaemia, Graves's disease, scleroderma, and Sjogren's syndrome.[1]

The word arthritis implies irritation and inflammation of the joint. Inflammation is a restorative term depicting pain, stiffness, redness and swelling. Arthritis is an ailment that can include any of the joints in the body, regularly happening in the hip, knee, spine or other weight-bearing joints yet can likewise influence the fingers and other non-weight bearing joints. Symptoms of arthritis incorporate joint pain, swelling, solidness and exhaustion. Untreated aggravation can, in the end, prompt joint harm, destruction and inability[2].

The man has "joint inflammation or arthritis " it implies that they have one of these sicknesses/diseases, which include: Osteoarthritis, Rheumatoid arthritis, Gout, pseudo-gout, Septic arthritis, Ankylosing spondylitis, Juvenile idiopathic arthritis and Still's disease. Osteoarthritis affects over 3.8% of individuals while rheumatoid joint inflammation affects around 0.24% of people. Gout affects around 1 to 2% of the Western population at some point or later in their lives. In Australia, around 15% of individuals are affected, while in the United States over 20% have a sort of arthritis[3].

Treatment alternatives fluctuate contingent upon the kind of joint inflammation and incorporate non-intrusive treatment, a way of life changes (counting activity and weight control), orthopedic bracing, and medicines. Joint substitution surgery might be required in disintegrating types of joint inflammation. Medicines can help diminish aggravation in the joint which diminishes damage. In addition, by diminishing inflammation, the joint damage might be moderated. An exercise of the ligament joint is urged to keep up the well-being of the specific joint and the general body of the person. Individual's people with arthritis or joint pain can benefit by both physical and occupational therapy treatment. In joint pain, the joints turn out to be stiff and the scope of movement can be constrained. Non-intrusive treatment has been appeared to altogether enhance work, diminish pain, and postpone requirement for surgical intercession in cutting-edge cases[4].

Exercise endorsed by a physical therapist has been appeared to be more successful than meds in treating osteoarthritis of the knee. Exercise regularly centers on enhancing muscle quality, continuance and flexibility. At times, activities might be intended to prepare to adjust. In some cases, related treatment can furnish help with exercises and additional equipment. There are a few sorts of prescriptions that are utilized for the treatment of joint inflammation. Treatment ordinarily starts with medications that have the least symptoms with assist solutions being included if inadequately effective. Depending upon the sort of joint inflammation or type of arthritis, the medications that are given might be different. [5].

Rheumatoid arthritis (RA) is an immune system in this way, notwithstanding pain medicines, and calming drugs are treated with another class of medication called disease-modifying antirheumatic drugs (DMARDs), which follows up on the immune system to back off the progression of RA. A case of this somewhat medication is Methotrexate. Various rheumatoid surgical medications have been joined in the treatment of arthritis since the 1950s. Arthroscopic surgery for osteoarthritis of the knee gives no extra advantage to enhance physical and medicinal therapy. Further research about is required to decide whether Trans Cutaneous Electrical Nerve Incitement (TENS) for knee osteoarthritis is powerful to control pain. Low-level

laser treatment might be considered for the alleviation of pain, and stiffness related to arthritis. Evidence of advantage is tentative. Pulsed electromagnetic field treatment (PEMF) has a conditional confirmation supporting enhanced working yet no proof of enhanced torment in osteoarthritis. [6]

There are innumerable drugs, procedures, medical aids, and devices directed at coping with the many manifestations of the disease. Yet, there remains an urgent need for finding pharmacological therapies for arthritis which are effective, relatively safe, and least toxic. No single agent could ever be expected to "cure" arthritis in its entirety. In the world, 1.8 million insects are known as species[7]. The weaver ant *Oecophylla smaragdina* as an important biological, and sustainable used resource, insects should be well-developed to assist people dealing with the food crisis. By focusing the benefits the present study includes to evaluate the effect of ethanol extract of *Oecophylla smaragdina* in the management of Rheumatoid Arthritis by using standard pharmacological screening methods in selected animal models.

MATERIALS AND METHODS

Insect-resources utilization

The weaver ant *Oecophylla smaragdina* belongs to family *Formicidae* was authenticated by Dr.K.Vasudevan, Associate Professor, Department of Zoology, Faculty of Science, Annamalai University, Annamalai Nagar, Chidambaram, Tamil Nadu, India.

Extraction method

The ant *Oecophylla smaragdina* (OS) was collected and kept in refrigerator for freeze and dried. The dried ants were extracted under reflux for 2 hrs with 95% ethanol for three times successively[8].

Animal

Wistar albino rats weighing 150-200gm were selected for the present Rheumatoid Arthritis pharmacological screening methods. The rats were maintained in a controlled room temperature (25±2°C) for 12 hr light/dark cycle (lights on 7.00 am) with free access to standard pellet diet and water *ad libitum*. The studies were conducted in accordance with the ethical committee (SBCP/2015-2016/CPCSEA/ IAEC-I/ 1(b).All studies were conducted in accordance with committee for the purpose of control and supervision on experiments on animals (CPCSEA) norms and the national institute of Health guidelines "Guide for the care and use of Laboratory Animals"[9].

Pharmacological Screening Methods

Complete Freund's adjuvant arthritis (CFA)

Arthritis was induced by the injection of 100µl of CFA, (Containing 1mg/ml of heat-killed *Mycobacterium tuberculosis*, 0.85 ml paraffin oil and 0.15 ml of mannide monooleate.) into the sub planter region of right hind paw of rat. The day of CFA injection was considered as day 1. The oral administration of the sample, Indomethacin (10mg/kg, i.p) of all the groups starts from day 14, once daily until day 24. Anti arthritic activity of Ethanolic extract was evaluated the arthritic score on day 0, 4, 7, 10, 12, 14, 16, 19, 21 and day 24. The last day, all the animals were sacrificed under ether anaesthesia the blood was collected by retro-orbital route for haematological parameters. The joints were also cut for histology.

Table 1 Treatment protocol for Complete Freund's adjuvant arthritis

Group	Drug and dose	Number of animals used
Control	Normal saline (5ml/kg, p.o)	6
Negative control	Complete Freund's adjuvant 100µl + Normal saline	6
Standard	Complete Freund's adjuvant 100µl + Indomethacin (10mg/kg, i.p)	6
EEOS 200mg/kg	Complete Freund's adjuvant 100µl + Ethanolic extract (200mg/kg, p.o)	6
EEOS 400mg/kg	Complete Freund's adjuvant 100µl + Ethanolic extract (400mg/kg, p.o)	6

Statistical analysis

Values were expressed as mean ± SEM. The mean difference was analysed using one way ANOVA followed by Dunnett's test. The values were considered significant at $P<0.001$, and $P<0.05$. Analysis was performed using GraphPad prism statistical software (Version 5.03)

RESULT AND DISCUSSION

Colour and Percentage yield of the extracts obtained

350 gm of dried medicinal ant was used for extraction; the extract was distilled and concentrated. Finally, the percentage yield was obtained 7.63%, The colour of extract obtained was brown colour in semisolid consistency.

Identification of chemical constituents

The Ethanolic extract found to contain alkaloids, carbohydrates, steroids, protein, cholesterol, triglycerides and amino acids.

Acute toxicity study

The Ethanolic extract (EEOS) was tested for acute toxicity study in order to fix the dose for the study. Up to 2000mg/kg the extracts were devoid of toxicity. Hence efficacy dose was identified as $1/5^{th}$ and $1/10^{th}$ of maximum tolerated dose and it was fixed as 200 and 400 mg/kg b.w were selected as the dose for testing the activity.

Complete Freund's adjuvant arthritis

Effect on body weight

In normal control group, the body weight was increased normally from 133.3gm on initial day to 145gm on final day (24^{th} day). Negative control group did not show any significant change i.e., 144.16 gm on initial day and 143.33gm on 24^{th} day. Weight of Standard drug on initial day was 126.66 gm, it was increased to 140.83gm on 24^{th} day. EEOS-200 mg/kg and EEOS-400mg/kg treated group showed a marked increase in body weight i.e., 140gm on initial day and 151.66gm on 24^{th} day and 148.33gm on initial day to 165.83gm on 24^{th} day

respectively. So standard drug and EEOS treated groups was also found to increase in body weight when compared with the negative control group. But the negative control group was found to be very less change in body weight. The result of body weight was shown in Table 2.

The mean body weight change from initial day to final day was 11.66 gm for normal animals, 5.83gm for negative control group, 14.16gm for standard treated group, 11.66gm and 17.5 gm for EEOS-200mg/kg and EEOS-400mg/kg treated group respectively. The body weight of standard and EEOS-400mg/kg treated group were increased significantly, when compared to standard the EEOS-400mg shows more increase in body weight. The result of mean change in body weight was shown in Table 2.

Effect on paw volume

The mean difference in paw volume was found to be zero in the normal control group. Paw volume difference was very much higher for the negative control group i.e., 0.27 on 24th day. The group of standard drugs was found to be 0.03 in paw volume. The treated groups EEOS-200 mg/kg, p.o, and EEOS-400 mg/kg, p.o were found to be 0.04, and 0.02 respectively to compare with the negative control group. The paw volume of standard and extract at both concentrations was found to be decreased significantly. Results were shown in Table3.

Effect on serum biochemical parameters

SGOT

In a normal control group, the serum level of SGOT was found to be 59.33U/L. The SGOT level of the negative control group was increased potentially to 119.33U/L. Standard treated group was decreased the elevated level of SGOT to 62.11 U/L when compared to negative control group. The EEOS-200mg/kg p.o, and EEOS-400mg/kg p.o treated groups were decreased the SGOT level to 71.28 U/L, and 65.40U/L respectively when compared to negative control group. The SGOT level of standard, and EEOS-400mg/kg p.o groups were decreased, and it was nearer to normal. The results were shown in Table 4.

SGPT

In a normal control group, the serum level of SGPT was found to be with 21.52 U/L. The SGPT level of the negative control group was increased potentially to 47.53 U/L. Standard treated group was decreased the elevated level of SGPT to 25.11 U/L when compared to negative control group. The EEOS-200mg/kg p.o, and EEOS-400mg/kg p.o treated groups were decreased the SGPT level to 30.33 U/L, and 27.95 U/L respectively when compared to negative control group. The SGPT level of standard, and EEOS-400mg/kg p.o groups were decreased, and it is nearer to normal. The results were shown in Table 4.

Alkaline phosphate

In a normal control group, the serum level of alkaline phosphate was found to be 69.80U/L. The alkaline phosphate level of the negative control group was increased to 147.07U/L when compared to control group. Standard treated group was decreased the elevated level of alkaline phosphate to 75.42 U/L when compared to negative control group. The EEOS-200 mg/kg p.o, and EEOS-400 mg/kg p.o treated groups were decreased to 79.59 U/L, and 76.15U/L respectively when compared to negative control group. The alkaline phosphate level of standard, and EEOS-400mg/kg p.o groups were decreased, and it is nearer to normal. The results were shown in Table4.

Total protein

The normal control group of total protein was found to be 6.40g/dl. The alkaline phosphate level of a negative control group was decreased to 4.5g/dl. Standard treated group increases the decreased level of total protein to 6.55g/dl when compared to negative control group. The EEOS-200mg/kg p.o, and EEOS-400mg/kg p.o treated groups were increased the total protein level to 6.52, and 6.38g/dl respectively when compared to negative control group. The total protein level of standard, and EEOS-400mg/kg p.o groups were increased, and it was nearer to normal. The results were shown in Table 4.

Creatinine

The normal control group of Creatinine was found to be 0.40mg/dl. The Creatinine level of a negative control group was increased potentially to 0.86 mg/dl. Standard treated group was decreased the elevated level of Creatinine to 0.53 mg/dl when compared to negative control group. The EEOS-200mg/kg p.o and EEOS-400mg/kg p.o treated groups were decreased the Creatinine level to 0.60 mg/dl and 0.52 mg/dl respectively when compared to negative control group. The Creatinine level of standard and EEOS-400mg/kg p.o groups was decreased and it is nearer to normal. The results were shown in Table 4. All the Biochemical parameters were done by using Span Diagnostics Ltd, Sachin, Surat, Gujarat

Effect on haematological parameters
RBC

In a normal control group, the RBC level was found to be 8.47× 106/mm3.The RBC level of a negative control group was decreased to 4.76× 106/mm3. The standard treated group was increased the decreased level of RBC to 7.73 × 106/mm3 when compared to negative control group. The EEOS-200mg/kg p.o and EEOS-400mg/kg p.o treated groups were increased the RBC level to 5.74 and 7.53 × 106/mm3 respectively when compared to negative control group. The RBC levels of standard and EEOS-400mg/kg p.o groups were increased and it is nearer to normal. The results were shown in Table 5.

WBC

In normal control group, the WBC level was found to be with $8.25\times 10^3/mm^3$.The WBC level of negative control group was increased potentially to $13.80\times 10^3/mm^3$.Standard treated group was decreased the elevated level of WBC to $8.04 \times 10^3/mm^3$.when compared to negative control group. The EEOS-200mg/kg p.o and EEOS-400mg/kg p.o treated groups were decreased the WBC level to 10.41 and $8.42 \times 10^3/mm^3$ respectively, when compared to negative control group. The WBC level of standard and EEOS-400mg/kg p.o groups was decreased and it is nearer to normal. The results were shown in Table 5.

Haemoglobin

In normal control group, the haemoglobin value was found to be with 13 g%. The haemoglobin level of negative control group was decreased potentially to 8.16 g%. Standard treated group was increased the decreased level of haemoglobin to 12.88 g%, when compared to negative control group. The EEOS-200mg/kg p.o and EEOS-400mg/kg p.o treated groups were increased the

haemoglobin level to 10.68 and 12.56 g% respectively, when compared to negative control group. The haemoglobin levels of standard and EEOS-400mg/kg p.o groups were increased and it is nearer to normal. The results of haemoglobin level were found in Table 5.

ESR

In normal control group of ESR level was found to be 40.88%. The ESR level of negative control group was increased potentially to 76.47%. Standard treated group was decreased the elevated level of ESR to42.93%, when compared to negative control group. The EEOS-200mg/kg p.o and EEOS-400mg/kg p.o treated groups were decreased the ESR level to 46.81% and 41.06% respectively, when compared to negative control group. The ESR level of standard and EEOS-400mg/kg p.o groups was decreased and it is nearer to normal. The result of ESR level was found in Table 5.

Effects on histopathology of the joint tissue

The negative control group shows that the soft tissue bone with mild oedema lymphocytes changes in formaldehyde induced arthritic rat joint. Standard and EEOS 400 mg/kg treated group's shows no specific changes in the paw joints. EEOS 200 mg/kg treated group showed mild inflammation in paw joint and control group shows no specific inflammatory changes. The results were shown in Fig 1.

Table 2. Effect of *Oecophylla smaragdina* on body weight of Complete Freund's adjuvant induced arthritis in albino rats

Group	Drug and dosage form	Initial body weight	Final body weight	Mean difference in body weight
Normal control	Normal saline (5ml/kg, p.o)	128.33±8.4	139.73±6.9	11.40±1.6***
Negative control	CFA (1mg/mL)+ Normal saline	144.16±8.21	143.33±7.49	5.83±1.53
Standard	CFA (1mg/mL)+ Indomethacin (10mg/kg, i.p)	126.66±6.66	140.83±5.54	14.16±2.71***
EEOS	CFA (1mg/mL)+ EEOS (200mg/kg, p.o)	142.37±3.2	153.66±8.72	11.29±3.1***
EEOS	CFA (1mg/mL)+EEOS (400mg/kg, p.o)	148.33±3.1	165.83±3.74	17.5±1.7***

n=6, Data were expressed as Mean± SEM, one-way ANOVA followed by Dunnett's test, All the groups were compared to Negative control, *p<0.05, **p<0.01, ***p< 0.001

Table 3. Effect of *Oecophylla smaragdina* on mean paw volume change in Complete Freund's adjuvant (CFA) induced arthritis in albino rats

Drug and dosage	Mean change in paw volume									
	Day 1	Day 4	Day 7	Day 10	Day 12	Day 14	Day 16	Day 19	Day 21	Day 24
Normal saline (5ml/kg, p.o)	0.00± 0.00***	0.00± 0.00***	0.00± 0.00***	0.00± 0.00***	0.00± 0.00***	0.00± 0.00***	0.00± 0.00***	0.00± 0.00***	0.00± 0.00***	0.00± 0.00***
CFA (1mg/mL) on sub plantar region	0.11± 0.01	0.17± 0.02	0.23± 0.02	0.24± 0.02	0.24± 0.02	0.25± 0.02	0.26± 0.02	0.27± 0.02	0.27± 0.02	0.27± 0.01
CFA (1mg/mL) + Indomethacin (10mg/kg, i.p)	0.12± 0.02***	0.12± 0.02***	0.11± 0.02***	0.11± 0.01***	0.09± 0.02***	0.08± 0.01***	0.06± 0.05***	0.06± 0.08***	0.04± 0.04***	0.03± 0.02***
CFA (1mg/mL) + EEOS (200mg/kg, p.o)	0.16± 0.12***	0.18± 0.02***	0.15± 0.14***	0.14± 0.08***	0.12± 0.05***	0.09± 0.09***	0.06± 0.12***	0.06± 0.08***	0.05± 0.05***	0.04± 0.11***
CFA (1mg/mL) + EEOS (400mg/kg, p.o)	0.16± 0.01***	0.18± 0.05***	0.15± 0.12***	0.11± 0.09***	0.09± 0.11***	0.07± 0.09***	0.06± 0.05***	0.04± 0.05***	0.03± 0.14***	0.02± 0.09***

n=6, Data were expressed as Mean± SEM, one-way ANOVA followed by Dunnett's test, All groups were compared with Negative control, *P<0.05, **P<0.01, ***P<0.001

Table 4 . Effect of *Oecophylla smaragdina* on the biochemical parameters in Complete Freund's adjuvant induced arthritis in albino rats

Group	Drug and dosage	SGOT (U/L)	SGPT (U/L)	ALP(U/L)	Total protein (g/dl)	Creatinine (mg/dl)
Normal control	Normal saline (5ml/kg, p.o)	59.33±1.14***	21.52±0.92***	69.8±0.66***	6.4±0.19***	0.4±0.06***
Negative control	CFA (1mg/mL) + Normal saline	119.33±0.86	47.53±1.07	147.07±0.93	4.5±0.28	0.86±0.02
Standard	CFA (1mg/mL) +Indomethacin (10mg/kg, i.p)	62.11±0.77***	25.11±0.99***	75.42±0.61***	6.55±0.29***	0.53±0.05***
EEOS	CFA (1mg/mL) + EEOS (200mg/kg, p.o)	71.28±1.09***	30.33±0.85***	79.59±1.15***	6.52±0.22***	0.6±0.06***
EEOS	CFA (1mg/mL) + EEOS (400mg/kg, p.o)	65.40±0.82***	27.95±0.82***	76.15±0.88***	6.38±0.22***	0.52±0.05***

n=6, Data expressed as Mean± SEM, one-way ANOVA followed by Dunnett's test, All groups were compared with Negative control, *p<0.05, **p<0.01, ***p< 0.001

Table 5. Effect of *Oecophylla smaragdina* on haematological parameters in Complete Freund's adjuvant induced arthritis in albino rats

Group	Drug and dosage	RBC (x 10^6/mm^3)	WBC (x 10^3/mm^3)	Haemoglobin (g%)	ESR (mm/hr)
Normal control	**Normal saline (5ml/kg, p.o)**	8.47±0.27***	8.25±0.24***	13±0.00***	40.88±.63***
Negative control	**CFA (1mg/mL) + Normal saline**	4.76±0.26	13.8±0.45	8.16±0.16	76.47±1.2
Standard	**CFA (1mg/mL) + Indomethacin (10mg/kg, i.p)**	7.73±0.29***	8.04±0.37***	12.88±0.2***	42.93±0.44***
EEOS	**CFA (1mg/mL) + EEOS (200mg/kg, p.o)**	5.74±0.27**	10.41±0.24***	10.68±0.23**	46.81±0.49***
EEOS	**CFA (1mg/mL) + EEOS (400mg/kg, p.o)**	7.53±0.36***	8.42±0.39***	12.56±0.34***	41.06±0.39***

n=6, Data were expressed as Mean± SEM, One way ANOVA followed by Dunnett's test, All groups were compared with Negative control, *p<0.05, **p<0.01,***p< 0.001

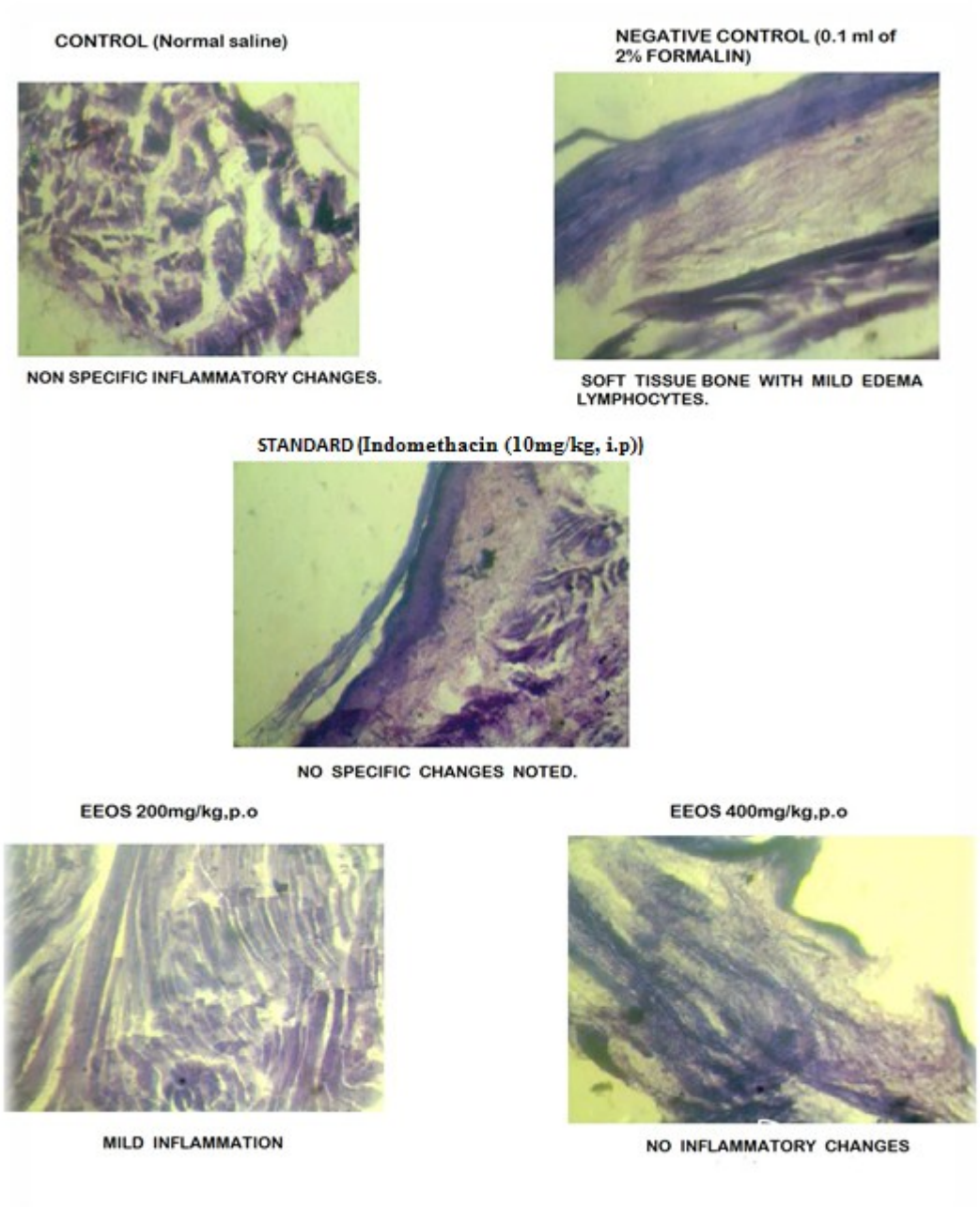

Figure 1 Histopathology of Complete Freund's adjuvant induced arthritic paw joint tissue

DISCUSSION

Anti-arthritic effect of *Oecophylla smaragdina* extract was challenged against Complete Freund's adjuvant induced screening model. In both concentrations of extracts has provided significant activity like standard but EEOS 200 mg/kg p.o extract was less effective when compared to EEOS 400 mg/kg p.o.

Complete Freund's adjuvant induced arthritis is one of most commonly used acute model for assessing anti-arthritic potential of test extract. The development of oedema was development only after administration of Complete Freund's adjuvant 100µl (Containing 1mg/mL) because of release of histamine, serotonin and prostaglandin like substances. The incidence and severity of arthritis were increased, and it was evaluated by bodyweight, blood and serum parameters.

These parameters were important in determining the disease state. Elevated SGOT, SGPT, alkaline phosphate and Creatinine indicated the inflammation state. Decreased total protein level also indicated the same. Anaemia was the most common indication in arthritic patients. In patients with rheumatoid arthritis, RBC and Haemoglobin will be decreased and WBC level and ESR will be elevated. WBC was increased as there was an inflammatory condition. The increased body weight during treatment of standard drug and EEOS at both concentrations may be due to the restoration of absorption capacity of intestine. The extract also shows significant effects on various blood and serum parameters[5].

CONCULSION

It is clear that the EEOS extract at both the concentration (200 and 400 mg/kg, p.o) have anti-arthritic, But EEOS 400mg/kg, p.o was more potent than EEOS 200mg/kg,p.o. From this data we can conclude that effect produced by the extract was dose dependent.

The extract has provided good activity in all the discussed disease this effect due to the chemical constituents present in the extract like alkaloids, carbohydrates, steroids, protein, cholesterol, triglycerides, amino acids. The earlier report suggests that DHA a major component which in found in weaver ant, the DHA was derived from omega 3 fatty acid. It concludes that EEOS extract at both the concentration provide significant effect of *in vivo* models of anti-arthritic study.

There by deep focus should be taken in the analysis part to identify and isolate the active constituent for future studies. So that the active benefit from the weaver ant *Oecophylla smaragdina* will access as a pharmaceutical dosage form to mankind.

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How to cite this article:
Balamurugan K and Natarajan P. Effect of *Oecophylla smaragdina* on complete Freund's adjuvant induced arthritis in albino rat. J Pharm Sci Innov. 2018;7(4): 131-136.
http://dx.doi.org/10.7897/2277-4572.07495

Source of support: Nil, Conflict of interest: None Declared