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Research Article

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### Anti-Arthritic Activity of Ethanolic Extract of Root of *Momordica charantia* against FCA Induced Arthritis

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#### ABSTRACT

The present investigation is aimed to evaluate anti-arthritic activity of the ethanol extract of root of *Momordica charantia* (EEMR) by using Freund's complete adjuvant (FCA) induced arthritis model which is a extensively used model for *in-vivo* study of anti-arthritic activity. Arthritis assessment was carried out on basis of parameters *i.e.* arthritis score, joint diameter and paw volume. The standard drug was diclofenac sodium. The findings of present study showed that EEMR in dose of 400 mg/kg produced more significant reduction in arthritis score, joint diameter and paw volume as compare to 200 mg/kg. On the basis of results, it can be concluded that EEMR showed significant anti-arthritic activity. It may be due to presence of phytochemicals such as flavonoids, alkaloids, tannins etc.

**Keywords:** *Momordica charantia*, Anti-arthritic activity, Freund's complete adjuvant, Rheumatoid arthritis.

#### INTRODUCTION

India has a rich assortment of medicinal plants distributed in different geographical and ecological conditions widespread in the country. Plants have been used since prehistoric times for treatment of various Health

Organization (WHO) as many as 80% of the world's population depend on the traditional medicine for their primary healthcare needs. [1]

Rheumatoid arthritis (RA) is a chronic inflammatory condition of the connective tissues throughout the body, especially around the joints. It is most common

inflammatory arthritis and affects about one percent of the population. It affects three times more women than men. [2] RA is an autoimmune disease triggered by exposure of a genetically susceptible host to an unknown arthritogenic antigen. It is the continuing autoimmune reaction, with activation of CD4+ helper T cells and other lymphocytes, and the local release of inflammatory mediators and cytokines that ultimately destroys the joints. [3]

*charantia* is commonly known as bitter gourd or bitter melon in English and karela in Hindi. [4] It is a climber, widely cultivated as food in Asia, Africa and South America. It is also found all over India and cultivated up to an altitude of 1500 m. The word *Momordica* is derived from the Latin word *Mordeo* which means to bite and the species name is derived from Greek word and it means beautiful flower. [5] *M. charantia* is very useful as antidiabetic, anti-inflammatory, antioxidant, antitumor, antiulcer, hypoglycemic, immunostimulant etc. [6] The root of *M. charantia* is useful in arthritis. [7] Our research

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group has already reported the anti-arthritic potential of EEMR by using *in-vitro* models. [8] The present investigation was undertaken to evaluate the anti-arthritic activity of EEMR by using *in-vivo* models for further confirmation of the results of the *in-vitro* study.

## MATERIALS AND METHODS

### Plant Materials

*Momordica charantia* roots were collected from Sanjay Nursery, Mohara, Sagar (M.P.). The root was identified and authenticated by Dr. Archana Verma, Head, Department of Botany, Govt. Girl's Degree College, Sagar (M.P.).

### Preparation of Extract

The roots of *M. charantia* were powdered mechanically through mesh sieve. The powdered plant parts were extracted with solvent ethanol by continuous hot percolation method using soxhlet apparatus. The filtrate of the extracts was concentrated to dryness. Percentage yield was found to be 94.2%

### Photochemical screening

Preliminary photochemical screening of EEMR was carried out by previous established procedures. [9]

### Chemical

FCA (Sigma Aldrich, USA), Diclofenac (Synd Pharmaceuical Pvt. Ltd., Hyderabad). All other chemicals and reagents used for study were of analytical grade.

### Animals

Healthy adult male Sprague Dawley rats were used (150-200 g). The animals were fed with commercially available feed and were maintained under standard conditions of the temperature ( $25 \pm 5^\circ\text{C}$ ) and 12/12 h light /dark cycle. The experimental protocols were approved by the Institutional Animal Ethics Committee (IAEC).

### Acute toxicity studies

Evaluation of acute toxicity of the EEMR was carried out according to OECD (Organization for Economic Co-operation Development) guidelines.

### FCA model (Freund's complete adjuvant induced arthritis)

Adjuvant-induced chronic arthritis

The animals were divided into five groups (n=6), as follows:

(A) Non-arthritic animals

**Group I:** Normal animals

(B) Arthritic animals:

**Group II:** Vehicle control animals

**Group III:** Drug treated animals: received EEMR 200 mg/kg

**Group IV:** Drug treated animals: received EEMR 400 mg/kg

**Group V:** Drug treated animals: received standard drug diclofenac sodium 4 mg/kg.

Arthritis was induced to all the groups of animals except vehicle control group by a single injection of 0.1 mL FCA into sub-plantar region of left hind paw. The dosing of the entire group started from day 12 once

daily orally. Anti-arthritic activity of EEMR was evaluated on joint diameter, paw volume, arthritis score on day 4<sup>th</sup>, 7<sup>th</sup>, 14<sup>th</sup>, 21<sup>st</sup>.

### Behavioral Assessment

#### Arthritic score

The morphological features of the arthritis like redness, swelling and erythema were monitored by set visual criteria as follows: normal paw = 0, mild swelling and erythema of digits = 1, swelling and erythema of the digits = 2, severe swelling and erythema = 3, gross deformity and inability to use the limb = 4 on respective days. Thus, the maximum possible score for both hind paws. [10]

#### Paw volume

The paw volume of both hind paws was measured just before FCA injection on day 0 and on 4<sup>th</sup>, 7<sup>th</sup>, 14<sup>th</sup>, 21<sup>st</sup> days using a plethysmometer. [11]

#### Joint diameter

Before injection joint diameter were measured using a vernier caliper after which FCA was administered. The joint diameter was measured again on day 1<sup>st</sup>, 4<sup>th</sup>, 7<sup>th</sup>, 14<sup>th</sup>, and 21<sup>st</sup>. [12]

#### Statistical analysis

The results were expressed as mean  $\pm$  SEM. Statistical comparison was made between the drug-treated group and arthritic-control group. Statistical difference between two means was determined by one-way ANOVA followed by Dunnett's test. All statistical analyses were performed using Graph Pad Prism software (San Diego, CA). Data was considered statistical significant at  $P < 0.05$ .

## RESULTS

### Acute toxicity studies

EEMR showed no signs and symptoms such as diarrhea, convulsion, and coma up to 2000 mg/kg dose.

### Phytochemical screening

The EEMR showed the presence of various phytochemicals *i.e.* amino acid, alkaloid, flavonoids and tannin.

### FCA induced arthritis

Sub plantar administration of FCA in rat paw resulted in significant production of inflammation primarily which was progressively maintained for 21 days. After the 12<sup>th</sup> days of FCA injection immune response was occurred this induced secondary arthritis.

### Effect of EEMR arthritis score

All the groups of rats administered with FCA started showing signs of clinical inflammation in one or more hind paws. The arthritic score was significantly increased from day 7<sup>th</sup> to 12<sup>th</sup> in control rats which remained significantly increased till the end of the study *i.e.* up to 21<sup>st</sup> day. On comparison from disease control group, standard drug group showed significant and dose dependant decreased in arthritic score from day 14<sup>th</sup> ( $P < 0.05$ ) and 21<sup>th</sup> ( $P < 0.001$ ). Treatment with EEMR (200 mg/kg) showed significant decreased in arthritic score on 21<sup>th</sup> ( $P < 0.001$ ) as compared to control

rats. Treatment with EEMR (400 mg/kg) showed significant decreased in arthritic score from day 14<sup>th</sup> ( $P<0.05$ ) and 21<sup>st</sup> ( $P<0.01$ ) (Table 1).

#### Effect of EEMR on paw volume

The paw volume was significantly increased from day 7<sup>th</sup> to 12<sup>th</sup> in control rats which remained significantly increased till the end of the study *i.e.* up to 21<sup>st</sup> day. On comparison from disease control group, standard drug group showed significant and dose dependant decreased in paw volume from day 14<sup>th</sup> ( $P<0.05$ ) and 21<sup>st</sup> ( $P<0.01$ ). Treatment with EEMR (200 mg/kg) showed significant decreased in paw volume on 21<sup>st</sup> ( $P<0.05$ ) as compared to control rats. Treatment with EEMR (400 mg/kg) showed significant decreased in paw volume from day 14<sup>th</sup> ( $P<0.01$ ) and 21<sup>st</sup> ( $P<0.001$ ) (Table 2).

#### Effect of EEMR on joint diameter

There was a significant increase in the joint diameter in all the FCA induced arthritis groups when compared to the normal and control groups. The joint diameter was significantly increased from day 7<sup>th</sup> to 12<sup>th</sup> in control rats which remained significantly increased till the end of the study *i.e.* up to 21<sup>st</sup> day. On comparison from disease control group, standard drug group showed significant and dose dependant decreased in joint diameter from day 14<sup>th</sup> ( $P<0.01$ ) and 21<sup>st</sup> ( $P<0.001$ ). Treatment with EEMR (200 mg/kg) showed significant decreased in joint diameter on 21<sup>st</sup> ( $P<0.05$ ) as compared to control rats. Treatment with EEMR (400

mg/kg) showed significant decreased in joint diameter from day 14<sup>th</sup> ( $P<0.01$ ) and 21<sup>st</sup> ( $P<0.001$ ) (Table 3).

#### DISCUSSION

FCA induced arthritis is one of the most widely used models for evaluating the agents with potential anti-arthritic activity, as it has been shown to share number of clinical and immunological features with human arthritis. FCA induced arthritis is a primary and secondary chronic arthritis. Primary is inflammatory phase where generation of prostaglandin occurs and secondary immunological state in which auto antibodies is generated. The model of adjuvant-induced arthritis in rats has been extensively used in the study of inflammatory processes and validated as a model of chronic pain and rheumatoid arthritis. [13]

Arthritis score is index of the joint inflammation after immunization. In the present investigation, a significant reduction in the arthritis score distinguishes the immunosuppressive effects of EEMR from its anti-inflammatory effects. [10]

The acute stage of arthritis is characterized by signs of hyperalgesia, lack of mobility and pause in body weight gain; during the acute period, hind paw and fore paw joint diameters increase. [14] Change in joint diameter is important determinants during RA. Treatment with EEMR (200 and 400 mg/kg) significantly decreased the joint diameter as compared to the arthritic control animals.

**Table: 1 Effect of EEMR on arthritis score**

| Group & treatment | Days    |                 |                 |                  |                  |
|-------------------|---------|-----------------|-----------------|------------------|------------------|
|                   | 0       | 4 <sup>th</sup> | 7 <sup>th</sup> | 14 <sup>th</sup> | 21 <sup>st</sup> |
| Normal            | 0 ± 0.0 | 0 ± 0.0         | 0 ± 0.0         | 0 ± 0.0          | 0 ± 0.0          |
| Disease control   | 0 ± 0.0 | 2 ± 0.0         | 1.83 ± 0.15     | 1.88 ± 0.18      | 2.34 ± 0.33      |
| Standard drug     | 0 ± 0.0 | 1.66 ± 0.33     | 1.65 ± 0.34     | 1.2 ± 0.0*       | 0.533 ± 0.66***  |
| EEMR 200 mg/kg    | 0 ± 0.0 | 2.60 ± 0.33     | 2.66 ± 0.33     | 1.55 ± 0.33*     | 0.78 ± 0.03*     |
| EEMR 400 mg/kg    | 0 ± 0.0 | 2 ± 0.57        | 2.33 ± 0.33     | 1.00 ± 0.0**     | 0.553 ± 0.22**   |

Value expressed as Mean ± SEM \* $P<0.05$  significant \*\* $P<0.01$  moderately significant and \*\*\* $P<0.001$  highly significant as compared to control group.

**Table: 2 Effect of EEMR on paw volume**

| Group & treatment | Days         |                 |                 |                  |                  |
|-------------------|--------------|-----------------|-----------------|------------------|------------------|
|                   | 0            | 4 <sup>th</sup> | 7 <sup>th</sup> | 14 <sup>th</sup> | 21 <sup>st</sup> |
| Normal            | 0.73 ± 0.88  | 0.72 ± 0.62     | 0.74 ± 0.19     | 0.75 ± 0.78      | 0.71 ± 0.81      |
| Disease control   | 0.76 ± 0.088 | 1.20 ± 0.11     | 1.43 ± 0.14     | 1.76 ± 0.13      | 1.93 ± 0.03      |
| Standard drug     | 0.76 ± 0.08  | 1.167 ± 0.88    | 1.40 ± 0.05     | 1.30 ± 0.0574*   | 1.63 ± 0.033**   |
| Test 200mg/kg     | 0.80 ± 0.10  | 1.23 ± 0.12     | 1.30 ± 0.10     | 1.20 ± 0.054*    | 1.36 ± 0.067*    |
| Test 400mg/kg     | 0.76 ± 0.03  | 1.20 ± 0.11     | 1.39 ± 0.15     | 1.13 ± 0.033**   | 1.33 ± 0.034***  |

Value expressed as Mean ± SEM \* $P<0.05$  significant \*\* $P<0.01$  moderately significant and \*\*\* $P<0.001$  highly significant as compared to control group.

**Table: 3 Effect of EEMR on joint diameter (mm)**

| Group & treatment | Days    |                 |                 |                  |                  |
|-------------------|---------|-----------------|-----------------|------------------|------------------|
|                   | 0       | 4 <sup>th</sup> | 7 <sup>th</sup> | 14 <sup>th</sup> | 21 <sup>st</sup> |
| Normal            | 0.3 ± 0 | 0.08 ± 0.07     | 0.05 ± 0.07     | 0.02 ± 0.01      | 0.01 ± 0.01      |
| Disease control   | 0.2 ± 0 | 2.21 ± 0.33     | 2.44 ± 0.051    | 2.83 ± 0.021     | 2.95 ± 0.03      |
| Standard drug     | 0.3 ± 0 | 1.19 ± 0.15     | 2.11 ± 0.033    | 1.31 ± 0.01**    | 0.42 ± 0.19***   |
| EEMR 200mg/kg     | 0.4 ± 0 | 2.32 ± 0.26     | 2.09 ± 0.43     | 1.22 ± 0.08*     | 0.88 ± 0.49*     |
| EEMR 400mg/kg     | 0.2 ± 0 | 1.61 ± 0.33     | 1.96 ± 0.66     | 1.15 ± 0.25**    | 0.58 ± 0.029***  |

Value expressed as Mean ± SEM \* $P<0.05$  significant \*\* $P<0.01$  moderately significant and \*\*\* $P<0.001$  highly significant as compared to control group

The findings of present study showed that EEMR in dose of 400 mg/kg produced more significant reduction in arthritis score, joint diameter and paw volume as compare to 200 mg/kg.

Literature revealed that *Momordica charantia* contains a range of biologically active phytochemicals including triterpens, proteins, steroids, alkaloids, saponins, flavonoids etc. Phytochemical investigation of EEMR also showed presence of flavonoids, alkaloids, carbohydrates, protein and tannin. This is well known that flavonoids, alkaloids, tannins are responsible for significant anti-arthritis and anti-inflammatory activity. The presence of these phytochemicals in extract may be responsible for anti-arthritis activity of EEMR.

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