

## ANTI-INFLAMMATORY ACTIVITY OF TRAUMEEL (A HOMEOPATHIC PREPARATION) IN EXPERIMENTAL ANIMALS-RATS

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### ABSTRACT

**Objective:** To evaluate the anti-inflammatory effect of traumeel on acute and chronic inflammatory experimental animal models (rats).

**Methods:** The traumeel, a homeo medicinal preparation was tested for its efficacy in acute and chronic inflammatory rats. In acute models: Rat paw edema method was used. In this model, rats were divided into four groups, six rats each. Group-I (NC), received 2% GA 2 ml, Group-II (PC) received aspirin (200 mg/kg), Group-III, intravenous received low dose (6CH) and high dose (300CH) of traumeel, preparation orally. Edema was developed in injected paw. Immediately the foot edema volume was measured at 0 hr and at the end of 3<sup>rd</sup> hr with a plethysmograph. The percentage of inhibition of edema by drugs was measured and compared between the test, control and standard groups. In chronic models: Granuloma method was used, and test drugs were given for 7 days. The animals were divided and treated same as in the acute model. After 7 days treatment, on 8<sup>th</sup> day animals were sacrificed each implanted pellet was extracted with adherent granulation tissue. These pellets were dried and weighed. The known weight was deducted from granulation tissue weight. The mean weight of granulation tissue and difference in weight of granulation tissue for each group was calculated, and the percentage of inhibition of inflammation was calculated.

**Results:** The percentage of inhibition of edema in the acute model with 6CH, 300CH after 3 hrs is 51%, 76% respectively and with aspirin is 79%. In chronic models, the percentage of inhibition of granulation tissue with 6CH, 300CH after 7 days is 19.5%, 32.85%, respectively and with aspirin is 41.95%. The reduction of inflammation was statistically significant in each group is ( $p < 0.001$ ).

**Conclusion:** Traumeel, a homeo preparation is a best alternative drug for the treatment of acute inflammatory conditions with no side effects.

**Keywords:** Inflammation, Traumeel preparation, Carrageenan, Aspirin.

### INTRODUCTION

Inflammation is a local response of living mammalian tissues to the injury. It is a body defense reaction in order to eliminate or limit the spread of injurious agents. These are various components to an inflammatory reaction that can contribute to the associated symptoms and tissue injury. Edema formation, leukocyte infiltration, and granuloma formation represent such components of inflammation [1]. Edema formation in the paw is the result of a synergism between various inflammatory mediators that increase vascular permeability or that increase blood flow [2]. Several experimental models of paw edema have been described. Carrageenan induced paw edema is widely used for determining the acute phase of inflammation. Histamine, 5HT, bradykinin are the first detectable mediators in the early phase of carrageenan induced inflammation [3], whereas prostaglandins are detectable in the late phase of inflammation [4]. Drugs that are in use presently for the management of pain and inflammatory condition are either narcotics e.g. opioids or non-narcotics e.g. salicylates and corticosteroids e.g. hydrocortisone. All of these drugs possess well known side and toxic effects. Moreover synthetic drugs are very expensive to develop and whose cost of development ranges from 0.5 to 5 million dollars. On the contrary, many medicines of plant origin had been used since a long time without any adverse effects. Exploring the healing power of plants is an ancient concept. For centuries, people have been trying to alleviate and treat disease with different plant extracts and formulations [5]. It is, therefore, essential that efforts should be made to introduce new medicinal plants to develop cheaper drugs. Plants represent still a large untapped source of structurally novel compounds that might serve as lead for the development of novel drugs [6]. Screening of the plants for their biological activity is done on the basis of either their chemotaxonomic investigation or ethnobotanical knowledge for a particular disease. Identification of a particular compound against a

specific disease is a challenging long process. Importance of the plant lies in their biologically active principles. There are two types of plant chemicals, primary metabolites such as sugars, proteins, amino acids, chlorophylls, etc. The other category of chemicals is called secondary metabolites that include alkaloids, terpenoids, saponins and phenolic compounds. These chemicals exert a significant physiological effect on the mammalian system. According to the literature available, traumeel is used for the treatment of various acute and chronic inflammatory conditions by homeopathic physicians. In the present study, traumeel was selected to screening of its anti-inflammatory property in experimental animal models.

### METHODS

Institutional Animal Ethics Committee permission was taken before starting the study. The study was conducted strictly in accordance with the protocol.

In the present study, the homeopathic drug traumeel was screened, for its anti-inflammatory activity and compared with that of the standard drug aspirin in acute and chronic inflammatory animal models.

### Traumeel preparation

Traumeel is available in two potencies (6CH, 300CH), was taken from homeo stores after approval of homeo physician Dr. Shankara Shastri, Hyderabad, Andhra Pradesh. The drug is supplied by Dr. William Schwabe India Private Limited, in collaboration with DHU-Arzneimittel Germany, A-36, Sector-60, Phase III Noida-201301.

Traumeel being the one of the more extensively proven and widely used remedies in the Materia Medica presents a formidable array of symptoms for the beginner to study.

Traumeel is a fixed combination of diluted plant and mineral extracts. It has been available over the counter in Germany for over 60 years and in Austria for over 40 years, and is currently available in approximately 50 countries, including the USA. The combination is currently used to treat acute musculoskeletal injuries, such as sprains and traumatic injuries, and as supportive therapy in pain and inflammation of the musculoskeletal system. It can be used in the form of tablets, drops, injection solution, ointment, and gel.

Components of traumeel (e.g., ointment, tablets, and ampoules).

The ingredients of traumeel have been used for many years for therapeutic purposes, such as for pain (*Atropa belladonna*), inflammation (*Echinacea*), bruising (*Arnica montana*), wound healing (*Matricaria recutita*, *Calendula officinalis*), bleeding (*Achillea millefolium*), edema (*Mercurius solubilis*), and infections (*Hepar sulfuris*). Based on such observations, traumeel was developed by the German physician, Dr. Hans-Heinrich Reckeweg in the 1930s; he combined botanical and mineral substances to produce this natural medicine to treat musculoskeletal injuries and inflammation.

A pilot study was carried out with the drug, traumeel effect on the hind paw edema in rat, suggested anti-inflammatory effect. The observation made during the pilot study carried beyond 4 hrs did not reveal any significant difference from that of 3 to 4 hrs of observation. Hence in the present study, the final observations were made at the end of 3 hrs.

#### Chemicals

All the drugs (1% carrageenan, aspirin, gum acacia, ether, 5% povidone iodine) used in the study were of pharmaceutical grade. Carrageenan was supplied by Sigma Chemical Company, Hyderabad, aspirin was supplied by Dr. Reddy's Laboratory, Hyderabad, India.

#### Experimental animals

Wister albino rats (150-200 g) of either sex were used in this study. The animals were supplied from Sainath Agencies, Hyderabad, Andhra Pradesh, India. They were randomly distributed into groups and housed in cages (six/cage) and maintained under standard conditions at 26±2°C and relative humidity 44-56% and 10 hrs light: 14 hrs dark cycles each day for 1 week before and during the experiments. All animals were fed a standard rodent pellet diet and water. So this study was cleared by Institutional Animal Ethical Committee.

#### Anti-inflammatory activity

The animals were divided into four groups (n=6). Group-I served as control, received the vehicle only (4% gum acacia 1 ml/100 g bw p.o). Group-II served as a standard, received aspirin (200 mg/kg p.o). Group-III and Group-IV served as a test, received traumeel preparations low dose 6CH (1 ml/100 g bw), high dose 300CH (1 ml/100 g bw) respectively.

#### Carrageenan induced paw edema

The test was used to determine the anti-inflammatory activity of the traumeel by the method of Winter *et al.* (1962) [7]. The animals pretreated with traumeel or aspirin 1 hr before were injected with 0.1 ml of 1% carrageenan solution into the sub-plantar region of the right hind paw. Paw volume was measured by dislocation of the mercury column in a plethysmometer immediately after carrageenan application at 0 hr and at the end of 3 hrs after the stimulus. Reduction in the paw volume compared to the control group animals was considered as anti-inflammatory response.

#### Rexin pellet induced granuloma

The test was performed on the rats using rexin pellet induced granuloma method. The rats were anesthetized under light ether anesthesia and an incision was made on the lumbar region by blunted forceps, a subcutaneous tunnel was made and a sterilized rexin pellet (100±1 mg) was inserted in the groin area. All the animals received either traumeel or aspirin or vehicle (4% gum acacia) orally depending

upon their respective grouping animals for 7 days from the day of rexin pellet insertion (Winter *et al.* 1962) [7]. On the 8<sup>th</sup> day, animals were sacrificed, and rexin pellets were removed and dried to constant mass. The weight of the test and standard animal's pellets were compared with control animal pellets.

#### Statistical analysis

The results were expressed as mean±standard error mean the difference between experimental groups was compared by one-way analysis of variance (ANOVA) followed by Dennett's test. The results were considered statistically significant when the p<0.0001.

#### RESULTS

Traumeel a homeopathic preparation is used extensively for pain and inflammatory conditions in homeo practice. So drug was selected to evaluate for anti-inflammatory activity in acute and chronic experimental animal models, and the results are summarized in Tables 1 and 2.

The traumeel preparation on carrageenan induced paw edema in rats is shown in Table 1. The results obtained indicates that the drug found to have significant (p<0.001) anti-inflammatory activity in rats. The traumeel at the test doses 300CH, 6CH 1 ml/100 g bw. Reduced the edema induced by carrageenan by 76, 51% respectively at the end of 3<sup>rd</sup> hr, whereas standard drug showed 79% of inhibition as compared to the control group (no inhibition).

The traumeel preparation was screened for rexin pellet-induced granuloma in rats, and the results are shown in Table 2. The drug inhibited 32.85 and 19.5% inhibition of granuloma formation at the doses 300CH, 6CH 1 ml/100 g bw, respectively. Whereas standard drug aspirin showed 41.65% when compared with the control group (no inhibition).

#### DISCUSSION

In spite of tremendous development in the field of synthetic drugs during recent era, they are found to have some or other side effects, whereas plant products or homeo drugs still hold their own unique place, by the way of having no side effects. Therefore, a systemic approach should be made to find out the efficacy of homeo preparation against inflammation so as to exploit them as herbal anti-inflammatory agents. The enzyme, phospholipase A2, is known to be responsible for the formation of mediators of inflammation such as prostaglandins and leukotrienes which by attracting polymorphonuclear leukocytes to the site of inflammation would lead to tissue damage probably by the release of free radicals. Phospholipase A2 converts phospholipids in the cell membrane into arachidonic acid, which is highly reactive and is rapidly metabolized by cyclooxygenase to prostaglandins, which are major components that induce pain and inflammation [8].

It is well known that carrageenan induced paw edema is characterized by biphasic event with involvement of different inflammatory mediators. In the first phase (during the first 2 hrs after carrageenan injection), chemical mediators such as histamine and serotonin play role, while in second phase (3-4 hrs after carrageenan injection), kinin and prostaglandins are involved [9]. Our results revealed that administration of traumeel preparation inhibits the edema starting from the 1<sup>st</sup> hr and all phases of inflammation, which is probably inhibition of different aspects and chemical mediators of inflammation.

The rexin pellet granuloma is widely used to evaluate the transudative and proliferative components of the chronic inflammation. The moist weight of the pellets correlates with transudes, the dry weight of the pellet correlate with the amount of granulomatous tissues [10]. Chronic inflammation occurs by means of the development of proliferate cells. These cells can be either spread or in granuloma form. Non-steroidal anti-inflammatory drugs decrease the size of

**Table 1: Effect of traumeel on carrageenan induced rat paw edema at 0 hr and at the end of 3 hrs**

Groups	Dose (mg/kg)	Paw volume (ml)		% Inhibition
		0 hr	3 hrs	
Control	4% gum acacia	1.012±0.001	0.762±0.089	0
Standard	2% aspirin (200 mg/kg)	0.740±0.005*	0.159±0.013***	79
Test-1	300CH traumeel	1.138±0.059	0.181±0.013***	76
Test-2	6CH traumeel	1.156±0.032	0.329±0.026***	51

Standard: Aspirin (200 mg/kg bw), Test drug: Traumeel: 300CH, 6CH potencies (1 ml/100 g bw). Each value is the mean±SEM for six rats \*p<0.05, \*\*p<0.01, \*\*\*p<0.0001 compared with control. SEM: Standard error of mean

**Table 2: Effect of traumeel on rexin pellet granuloma in rats on 8<sup>th</sup> day**

Groups	Dose (mg/kg)	Granuloma dry weight (mg)	% Inhibition
Control	4% gum acacia	86.64±3.074	0
Standard	2% aspirin (200 mg/kg)	61.36±3.610*	41.65
Test-1	300CH traumeel	63.72±2.149*	32.85
Test-2	6CH traumeel	75.69±2.251*	19.5

Standard: Aspirin (200 mg/kg bw), Traumeel: 300CH, 6CH potencies (1 ml/100 g bw). Each value is the mean±SEM for six rats \*p<0.05, \*\*p<0.01, \*\*\*p<0.0001 compared with control. SEM: Standard error mean

granuloma that results from cellular reaction by inhibiting granulocyte infiltration, preventing the generation of collagen fibers and suppressing mucopolysaccharides [11]. The traumeel preparation showed less anti-inflammatory activity in rexin pellet induced granuloma when compared with acute study and found to be less effective in chronic inflammatory conditions, which reflected its efficacy in inhibiting the increasing in the number of fibroblasts and synthesis of collagen and mucopolysaccharides during the granuloma tissue formation.

There is increasing evidence that lysosomal enzymes play an important role in the development of acute and chronic inflammation [12]. Most of the anti-inflammatory drugs exert their beneficial effects by inhibiting either release of these enzymes or by stabilizing lysosomal membrane, which is one of the major events responsible for the inflammatory process [13]. So we can assume that our drug, traumeel might be acting by either inhibiting the lysosomal enzymes or stabilizing the membrane.

From above studies, it is quite apparent that the traumeel preparation possesses significant anti-inflammatory activity in acute inflammation and less effective in chronic inflammation. The study justifies its use in acute inflammation as suggested in the folklore medicines.

## CONCLUSION

Traumeel preparation a homeopathic drug possess anti-inflammatory activity more effectively in acute inflammatory conditions than chronic inflammation with low toxicity and

better therapeutic index and compared with standard drug aspirin.

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