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EVALUATION OF ANTI INFLAMMATORY ACTIVITY OF WITHANIA SOMNIFERA: ROLE IN ARTHRITIS

Pharmacology

Dr. Pankaj Kumar Modi MBBS, MD (Pharmacology) Assistant Professor, Ananta institute of medical sciences & research center, Rajsamand (Rajasthan)

Dr. Vipin Kumar* MBBS, MD (Pharmacology) Assistant Professor, SN Medical College, Agra (UP) *Corresponding Author

ABSTRACT

Objectives of present study was to evaluate the anti-inflammatory activity of Withania Somnifera in experimentally induced inflammation in albino rats. Inflammation was induced by non-immunological and Immunological methods and measured by standard methods. For each set of experiment, animals were divided in five groups of six animals each. 1stgroup was given normal saline, 2nd group standard anti-inflammatory drug and 3rd, 4&5th groups were given *Withania Somnifera* in doses of 400, 800 & 1600mg/kg respectively. In present study it is found that Withania Somnifera show significant anti-inflammatory activity. So *Withania Somnifera* exhibited significant and promising anti-inflammatory activity in all the experimental models.

KEYWORDS

Arthritis, Anti-inflammatory, Withania Somnifera.

Introduction - Arthritis, a joint disorder showing all the cardinal signs of inflammation like joint stiffness, swelling, redness, and warmth. Anti-inflammatory drugs are one of the mainstays in the treatment of arthritis. An ideal anti-inflammatory drug for arthritis is one which limits complications of arthritis as well as has fewer side effects. Steroidal drugs are good Anti-inflammatory agents but show various serious side effects (1). So many non-steroidal anti-inflammatory drugs (NSAIDs) have come to light but due to gastrointestinal toxicity prolong use of these drugs are also not recommended (2). Some new selective COX-2 inhibitors NSAIDs spare from GI side effects but there use is also restricted due to cardiac toxicity (3). It is, therefore, essential that efforts should be made to introduce new drugs which are much safer as well as effective.

Some herbal formulation have shown potential for anti-inflammatory activity and at the same time they are also claimed to be free from side effects which limit the usage of the above mentioned conventional synthetic allopathic drugs.

Withania somnifera has been claimed by vaids (ayurvedic physicians) to be effective in the treatment of arthritis. However; scientific studies are not available to ratify their claims. Therefore, the present study is envisaged to evaluate the above claimed activity of Withania somnifera.

Material and Methods - The study was conducted on healthy albino rats. The study protocol was approved by the Institutional Animal Ethics Committee (IAEC) and was executed according to the guidelines of the committee for the purpose of control and supervision of the experiments on animals (CPCSEA), India (4).

Inflammation was induced by both non immunological and immunological methods. In each experiment animals were divided in 5 groups. 1st group was control normal saline group, 2nd was standard anti-inflammatory drug group and 3rd, 4 and 5th group were given Withenia somnifera in doses of 400, 800 &1600 mg/kg respectively. Standard agent used in non immunological method was indomethacin and for immunological method, dexamethasone.

(1) Carrageenan induced acute Non-immunological inflammation method - Acute inflammation is produced with help of Carrageenan injected subcutaneously into the sub planter tissue of the right hind paw of albino rates. The paw volume was measured by plethysmometric method before giving standard and test drugs.(5,6) After 1hr of administration of drugs all these animals were challenged with carrageenan 0.1 ml of 1% solution in distilled water to induce paw edema. 3 hrs after the carrageenan administration, paw volume was again measured. The results in the drug treated rats were compared with that of control group.

(2) Complete Freund's adjuvant induced immunological inflammation method - Immunological inflammation was produced with 0.25 ml of Complete Freund's Adjuvant (1mg killed mycobacterium per ml) subcutaneously into the planter surface of the left hind paw on day 1. On day 14 respective groups of animals were treated with standard and test drugs orally once and followed by 0.1 ml of 10 TU was injected intradermally into the flanks which were previously depilated. After 24 and 48 hr diameter of tuberculin reaction was measured (7).

Statistics - Results were expressed as mean ± SD. Statistical differences between the groups were tested by ANOVA.

Results -

Carrageenan induced acute Non-immunological inflammation method - Both Indomethacin (5mg/kg) and *Withania Somnifera* in the doses of 400, 800, 1600 mg/kg significantly decreased the paw edema volume induced by carrageenan as compared with control group. At 400mg/kg dose *of Withania Somnifera* results were significant (P<0.05). As the dose increased inhibition was highly significant (P<0.001) like indomethacin. (Table 1)

Table 1- Effect of W. somnifera and indomethacin on carrageenan induced hind paw volume in albino rats

Drug	Dose (mg/ kg,oral)	Paw Volume (ml) ± SD		% inhibition in Paw Volume
		Initial	3hrs	
Saline	5 ml	0.61±0.01	0.96±0.02	
Indomethacin	5	0.61±0.02	0.79±0.01**	48.57
W. somnifera	400	0.59±0.01	0.86±0.02*	23.01
W. somnifera	800	0.57±0.01	0.82±0.02**	28.57
W. somnifera	1600	0.59±0.01	0.81±0.01**	37.14

**P<0.001 (as compared to saline treated group)
*P<0.05 (as compared to saline treated group)

Complete Freund's adjuvant induced immunological inflammation method - *Withania Somnifera* in the dose of 400mg/kg showed no significant suppression of tuberculin reaction while at the dose of 800mg/kg *Withania Somnifera* showed significant suppression (p<0.05) at 24 hours, while at 48 hr suppression is highly significant(p<0.001). (Table 2)

Table 2 - Effect of W. somnifera and dexamethasone on tuberculin sensitivity test in albino rats

Drug	Dose (mg/kg, oral)	24 hrs		48 hrs	
		Diameter of wheal (mm) ±SD	% inhibition	Diameter of wheal (mm) ±SD	% inhibition
Normal Saline	5 ml	11.33±0.57		11.33±0.57	
Dexamethasone	0.5	3.66±0.66**	67.70	3.34±0.56**	70.53

W. somnifera	400	10.33±0.56	8.83	9.67±0.55	14.66
W. somnifera	800	8.60±0.57*	24.10	8.32±0.55**	26.57
W. somnifera	1600	6.30±0.57**	44.40	5.66±0.60**	51.05

**P<0.001 (as compared to saline treated group)
*P<0.05 (as compared to saline treated group)

Discussion - Although non steroidal anti-inflammatory drugs and disease modifying anti rheumatic drugs (DMARD's) are rapidly emerging for treatment of rheumatoid arthritis, ideal and safe drugs are yet to be found.

Herbal plant, *Withania somnifera* has been claimed by ayurvedic physicians to be effective in the treatment of various types of arthritides. However there is lack of scientific studies to ratify their claim. Therefore a preclinical study was undertaken to explore its anti-inflammatory activity.

Inhibition of edema observed in carrageenan model may be due to the ability of the *Withania somnifera* to inhibit mediators of inflammation. Anti inflammatory activity of indomethacin is due to inhibition of cyclo-oxygenase enzyme (8). Similarly *Withania somnifera* may inhibit cyclo-oxygenase enzyme like indomethacin.

Immunological mechanism (Delayed hypersensitivity) is responsible for some inflammatory diseases (9). It is easily elicited in sensitized rats in the form of tuberculin reaction. At the dose of 400 mg/kg *Withania somnifera* showed insignificant activity but was found to be significantly effective in the doses of 800mg/kg and 1600mg/kg. The protective activity of *Withania somnifera* at these doses is comparable to that of dexamethasone. Steroidal constituent of Withania somnifera may be responsible for this as steroid suppress T cell activity which is responsible for delayed hypersensitivity (10).

All anti-inflammatory drugs are not equally effective in suppressing all components of the inflammatory response but *Withania somnifera* in the present investigation exhibited significant and promising anti-inflammatory activity in both experimental models (immunological and non immunological) which cover the different phases of inflammatory response.

Although the results of the present pharmacological study establish the anti-inflammatory activity of Withania somnifera, the exact mechanism of action of *Withania somnifera* needs further exploration. So that it could be used more rationally for treatment of different inflammatory disorders.

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