

Evaluation of Anti-inflammatory Effects of *Ficus hispida* L. leaves extract against Carrageenan induced Paw Edema in Rats

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Abstract:

Inflammation is a part of the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells or irritants. It is characterized by redness, swollen joints, joint pain, its stiffness and loss of joint function. The developments of potent anti-inflammatory drugs from the natural products are now under considerations due to the various side-effects produced by the use of conventional drugs. The plant *Ficus hispida* L., an ethanomedicinally important plant, well distributed species of tropical fig tree. All parts of this plant are found to be acrid, astringent, bitter, coolant and have activity against dysentery, ulcers, biliousness, psoriasis, anemia, piles and jaundice. In present investigation, Hexane leaf extract of *Ficus hispida* L. was studied for its anti-inflammatory potential for 30 mins., 60mins. and 90 mins. against Carrageenan induced rat paw edema. Significant anti-inflammatory activity was observed in doses-150 mg/kg and 300 mg/kg of *Ficus hispida* leaf extract within 90mins when compared with standards Prednisolone (Steroidal control) and Dichlofenac (Non-steroidal control). This activity may be due to presence of phytosterols in extract.

Keywords: Inflammation, *Ficus hispida* L. Anti-inflammatory activity, Phytosterols

INTRODUCTION:

Inflammation is a normal, protective response to tissue injury caused by physical trauma, noxious chemicals or microbiological agents. There are mainly two types of inflammation which are: (1) Acute inflammation, is associated with increased vascular permeability, capillary infiltration and emigration of leukocytes. (2) Chronic inflammation, is associated with infiltration of mononuclear immune cells, macrophages, monocytes, neutrophils, fibroblast activation, proliferation (angiogenesis) and fibrosis. Inflammation is a common clinical condition and rheumatoid arthritis (RA) is a chronic debilitating autoimmune disorder [1], that affects about 1% of the population in developed countries [2]. The classic signs of inflammation are local redness, swelling, pain, heat and loss of function [3]. Inflammation is currently treated by NSAIDs (Non-Steroidal Anti-Inflammatory Drugs). The conventional drug available in the market to treat inflammation produces various side-effects. Due to these side-effects, there is need for the search of newer drugs with less or no side-effects. A natural product from medicinal plants plays a major role to cure many diseases associated with inflammation. Natural products are rich source for discovery of new drugs because of their chemical diversity [4].

An ethanomedicinally important plant, *Ficus hispida* L., is a shrub or medium sized tree, History of the use of *Ficus hispida* dates back to the time of Charaka when he advised the juice obtained from the fig to be taken with jaggery as a sramsana (mild purgative) in the treatment of switra (vitiligo) [5]. Preliminary phytochemical investigations of *Ficus hispida* have shown the presence of alkaloids, carbohydrates, proteins and amino acids, sterols, phenols, flavonoids, gums and mucilage, glycosides, saponins, and terpenes. Some reports show that *Ficus hispida* bark contains lupeol acetate, β -amyrine acetate, β -sitosterol [6]. In Malay Medicine the decoction of the leaves is given to aid childbirth [7]. 50% ethanolic extract of leaves of *Ficus*

hispida was found to be nontoxic upto a dose of 2000 mg/kg [8].

β -sitosterol and stigmasterol have found to be significant anti-inflammatory activity viz., 65% and 67%; respectively with standard diclofenac exhibiting 68% inhibition. Derivatives betasitosteryl acetate and stigmasteryl acetate showed 61% and 62% inhibition; respectively. Thus, phytosterols and derivatives of *Tridax procumbens* leaves can be used as leads to make future drug candidates to treat inflammatory conditions [9].

The main objective of this work is to evaluate the effect of phytosterols present in *Ficus hispida* L. leaves extract on anti-inflammatory activity in rats.

MATERIALS AND METHODS:

Chemicals and Materials Used:

Carrageenan (Himedia), Dichlofenac, Prednisolone, DMSO, Saline water, *Sprague dawley* (SD) Rats, Plethysmometer.

“Carrageenan-induced Paw Edema in Rats” [10]:

Experiment was done at the animal house located at Priyadarshani J.L. College of Pharmacy, Nagpur. Experiments were carried out on healthy SD rats (either sex) weighing 150-300 grams. The animal experimental protocol was approved by the Institutional Animal Ethics Committee (CPCSEA). Animals were housed in polypropylene cages with stainless still grill top at $25 \pm 2^\circ\text{C}$. They were fed a standard diet of pellets and tapped water.

The rats were divided into 7 groups (Number of rats, $n = 3$ per group). All the groups were treated as follows:

First group (negative control) (GI) = vehicle only (DMSO-40% + Saline),

Second group (positive control-1) (GII) = Prednisolone (10 mg/kg) (Steroidal control)

Third group (positive control-2) (GIII) = Dichlofenac (10 mg/kg) (Non-steroidal control)

Forth group (GIV) = Plant Extract (FHE) (150 mg/kg)

Fifth group (GV) = Plant Extract (FHE) (300 mg/kg)
 Dichlofenac Drug was injected to Second group animals through the intraperitoneal region. Drugs were administered orally to all other groups' animals. After thirty mins of drug administration, edema was induced by the injection of 0.1 ml 1% Carrageenan in normal saline into the plantar aponeurosis of the left hand paw. Hind paw volume (an index of swelling) was measured using a plethysmograph on Plethysmometer before injection and after 30mins, 60 mins and 90 mins after Carrageenan

injection. The difference between the initial and subsequent paw volume reading gave the actual oedema volume.

The percent inhibition of inflammation was calculated using the formula,

$$\% \text{ Inhibition} = \frac{1-V_t}{V_c} \times 100$$

Where,

V_c = Oedema Volume in control

V_t = Oedema Volume in the group treated with drug

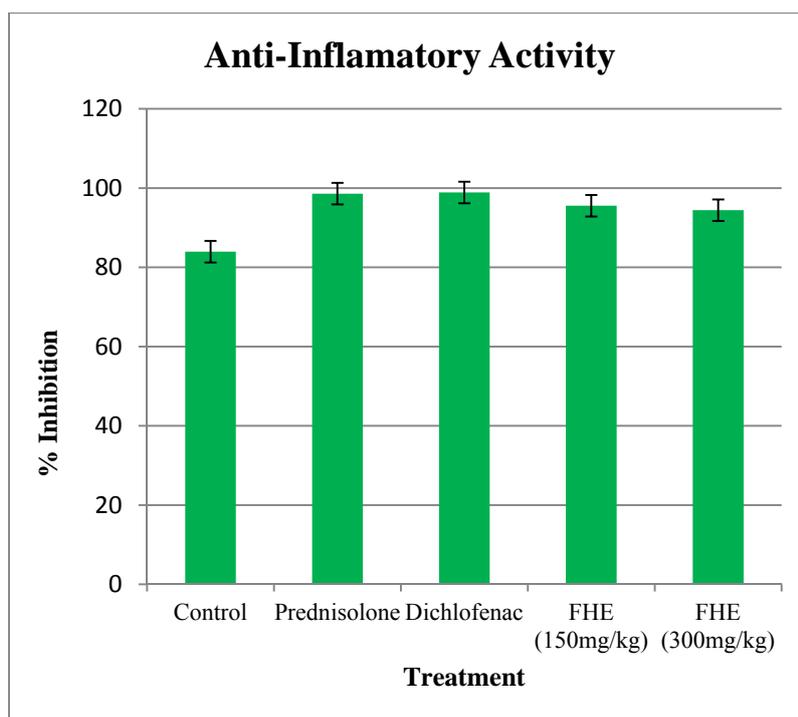
Table 1. Observation for paw edema

Group No.	Sample	Dose mg/kg	Rats (R)	Dispalcement of water for Normal Rats (ml)	Dispalcement of water for Carragennan induced Rats (ml)			
					0min	30min	60min	90min
GI	Control	-	R1	0.57	2.11	1.45	0.87	0.82
			R2	0.67	2.12	1.23	0.96	0.91
			R3	0.65	2.15	1.06	0.91	0.88
GII	Prednisolone	10	R1	0.60	2.18	0.73	0.60	0.61
			R2	0.65	2.12	0.69	0.67	0.67
			R3	0.52	1.89	0.71	0.55	0.55
GIII	Dichlofenac	10	R1	0.52	2.13	0.53	0.53	0.52
			R2	0.57	2.09	0.71	0.69	0.59
			R3	0.65	2.11	1.69	0.95	0.67
GIV	FHE (Dose1)	150	R1	0.57	2.05	0.65	0.64	0.62
			R2	0.58	2.08	0.71	0.68	0.65
			R3	0.60	1.73	0.75	0.70	0.66
GV	FHE (Dose2)	300	R1	0.53	2.03	0.78	0.61	0.59
			R2	0.54	2.09	0.71	0.69	0.65
			R3	0.76	1.65	0.99	0.81	0.81

Table 2. % Inhibition

Group No.	Sample	Dose mg/kg	% Inhibition			Mean ± SEM
			R1	R2	R3	
GI	Control	-	83.766	83.448	84.667	83.960 ± 0.365
GII	Prednisolone	10	99.367	98.639	97.810	98.605 ± 0.450
GIII	Dichlofenac	10	99.382	98.684	98.630	98.899 ± 0.242
GIV	FHE (Dose1)	150	96.621	95.33	94.690	95.547 ± 0.568*
GV	FHE (Dose2)	300	96	92.903	94.382	94.428 ± 0.894**

Values are Mean ± SEM (n = 3), Statistical analysis followed by One Way ANOVA-Dunnett's test, where, * represents significant at p<0.05, ** represents very significant at p<0.01, when compared to standards Dichlofenac (GIII) and Prednisolone (GII) individually.



Graph 1: Anti-inflammatory Activity

RESULTS AND DISCUSSION:

Inflammation is a localized reaction that produces redness, warmth, swelling, and pain as a result of infection, irritation, or injury. Inflammation can be external or internal. Hima Bindu, *et al.* (2014) reported in their study that when the treatment of Carrageenan induced paw edema in rats, there was highly significant decreased paw volume was seen after treated with Diclofenac and high dose of *Musa paradisiaca* leaves extract and that activity was proved to be due to presence of flavonoids, phytosterols and tannins in extract.

Administration of 10mg/kg of a methanolic extract of the aerial parts of *Fraxinus micrantha* produced significant anti-inflammatory effects against carrageenan-induced acute inflammation in mice that was comparable to one of the standard drug (Phenylbutazone) used in the treatment [11]. In the present research, the inflammation was highest after 90mins in control (only induction of Carrageenan) than the edema in rats fed with standards, Prednisolone (Steroidal Standard), Dichlofenac (Non-Steroidal Standard) and in plant *Ficus hispida* (FHE) with doses 150mg/kg and 300 mg/kg. This proved that standards, Prednisolone (Steroidal Standard), Dichlofenac (Non-Steroidal Standard) and plant extract FHE has shown a noteworthy effect on inflammation which decreases the edema within 90mins. However %inhibition of standards Dichlofenac (Non-Steroidal Standard) and Prednisolone (Steroidal Standard) was observed to be much similar.

% inhibition was found to be more in dose 150mg/kg than the dose 300 mg/kg which were **95.547%**. This proves that dose 150mg/kg of FHE is more effective on inflammation (Table 2, Graph 1).

STATISTICAL ANALYSIS:

The mean paw volume was expressed in terms of mean \pm SEM and statistical analysis was done to check the significance by using ANOVA technique and employing Dunnett's test thereafter, with the readings showing statistical significance at $P < 0.01$, $p < 0.05$.

Thus the plant extract of *Ficus hispida* (FHE) with doses-150mg/kg and 300 mg/kg has shown a significant reduction in the paw edema of rats.

CONCLUSION:

The present study was carried out to find out the evaluation of anti-inflammatory activity of extract of *Ficus hispida* L. leaves in rats. From the results we concluded that the *Ficus hispida* leaves extract at doses-150mg/kg and 300 mg/kg produces significant decreased in carrageenan induced paw edema in rats when compared with the activity of standards Dichlofenac (Non-Steroidal Standard) and Prednisolone (Steroidal Standard). This activity may be due to presence phytosterols in extract.

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