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EVALUATION OF ANTIINFLAMMATORY ACTIVITY OF MOMORDICA CYMBALARIA AGAINST CARRAGEENAN INDUCED AIR POUCH MODEL IN WISTAR RATS

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Abstract:

Inflammation is a multifaceted biological response shown by living tissues to the injury. It is an inbuilt body defense mechanism evoked by various stimuli such as disease causing organisms, ecological factors, ischemia, immunological reactions, biological factors and free radicals. It eliminates or limits the spread of pathogens. Momordica cymbalaria (Cucurbitaceae) had been used widely for its reported biological activities in traditional system of medicine. The present work is an attempt to investigate anti-inflammatory activity of various fractions of Momordica cymbalaria fruit on Carrageenan induced air pouch model in wistar rats. Butanol fraction of Momordica cymbalaria (BFM) showed dose dependent reduction in exudate volume. The effects of BFM were significant at every test dose as compared to standard. The results of the study recommend that the crude ethanolic extract of Momordica cymbalaria (CEE), chloroform fraction of Momordica cymbalaria (CFM) and BFM in dissimilar doses significantly restrained carrageenan provoked exudate volume, monocyte and neutrophil count in rats and exhibited significant anti-inflammatory action. Further detailed molecular investigation is necessary to delineate the underlying protective mechanism of Momordica cymbalaria against inflammation.

Key words: *Inflammation, Carrageenan, Airpouch, Monocytes, Neutrophils.*

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INTRODUCTION:

Inflammation is a reaction of a living cell or tissues in response to injury, infection or irritation/infiltration. The cardinal signs of inflammation include pain, swelling, redness and fever. Inflammation could be induced by various conditions that bring about the release of inflammatory mediators such as histamine, prostaglandins, nitric oxide, serotonin, cytokines, leukotrienes, platelet activating factor and substance P [1]. When there is loss of homeostatic control of defense, inflammation plays a detrimental role that contributes to the appearance and worsening of diseases [2]. The currently available drugs for the treatment of inflammation include non-steroidal antiinflammatory drugs (NSAIDs). Cyclooxygenase (COX-1 and COX-2) and lipoxygenase (5-LOX) are the major enzymes involved in inflammatory processes in mammalian cells [3]. Despite their efficiency, non-steroidal antiinflammatory drugs such as NSAIDs; e.g. aspirin, ibuprofen and indomethacin and selective COX-2 inhibitors such as celecoxib and rofecoxib possess serious adverse effects including collapse of stomach wall leading to internal bleeding and gastric ulcers in the former case [4], whereas increased incidence of cardiovascular issues in the latter case [5,6]. For these reasons, the use of these agents selectively inhibiting COX-2 and 5-LOX is nowadays suggested as one of the promising approaches in the safer management of inflammatory diseases [7,8]. Thus, discovery and development of novel agents with dual inhibitory properties (COX-2/5-LOX) is of significant interest [9].

Plant products are in use from centuries as a remedy for several health ailments. Herbal remedies used in traditional folk medicine have been the source of many drugs [10]. Various drugs from plant origin exhibit many pharmacological activities and so they can be used as therapeutic agents [11]. Several of the botanical species belonging to the genus *Momordica* are used in folk-lore medicine and among them *Momordica charantia* is used as traditional medicine to cure ailments such as antidiabetic, abortifacient, anthelmintic, contraceptive, dysmenorrhea, eczema, emmenagogue, antimalarial, galactagogue, gout, jaundice, abdominal pain, kidney (stone), laxative, leprosy, leucorrhea, piles, pneumonia, psoriasis, purgative, rheumatism, fever and scabies [12]. Besides, *Momordica charantia* other species of the Momordica genus are being studied to identify their constituents as well as for anti-inflammatory activities. Hence the present work is an attempt to investigate anti-inflammatory activity of *Momordica cymbalaria* fruit on carrageenan induced air-pouch model in wistar rats.

MATERIALS AND METHODS:

Collection, identification and authentication of plants

The plant *Momordica cymbalaria* belongs to family Cucurbitaceae. Fruits of *Momordica cymbalaria* were collected in the month of June from the Alva Pharmacy, Mangalore and authenticated by Dr. MD. Mustafa, Assistant Professor, Department of Botany, Kakatiya University,Warangal. The fruits were dried under shade then fine powder was prepared with the help of mixer grinder.

Preparation of Extracts

To identify the active principle(s) of M. cymbalaria crude ethanolic extract of *Momordica cymbalaria* (CEE) was fractionated successively using different organic solvents into chloroform (CFM) and butanol fractions (BFM). The crude ethanolic extract of *Momordica cymbalaria* (CEE), chloroform fraction of *Momordica cymbalaria* (CFM) and butanol fraction of *Momordica cymbalaria* (BFM) were evaluated for its anti-inflammatory activity by carrageenan induced air-pouch method.

Drugs and Reagents

All chemicals used for the experiments were of analytical grade and were purchased from HiMedia and Qualigens Fine Chemicals; Mumbai (India).

In-vivo pharmacological studies

Experimental Animals

Wistar rats of either sex weighing 100–160 g was used in the study and fed with standard laboratory pellet diet; Provimi limited (India), provided water ad libitum and were maintained at 23–25◦C, 35 to 60% humidity, and 12 h light/dark cycle. The rats were acclimatized to the laboratory conditions for a period of 7 days prior to experiment. The experimental protocol (1468/PO/a/11/CPCSEA, June 8th 2011) was duly approved by institutional animal ethics committee (IAEC). Before the experiment, food was withdrawn overnight but adequate water was given to the rats.

Animal Grouping

The animals were divided into 11 groups of six animals each.

Group –I : Control group received acacia (5% of 10ml/ kg i.e. only vehicle).

Group –II : Received Indomethacin 10mg /kg body weight (Standard group)

Group-III : Received 50mg /kg body weight of CEE.

Group-IV : Received 100 mg /kg body weight of CEE.

Group –V : Received 200mg/ kg body weight of CEE.
Group –VI : Received 50mg /kg body weight of CFM.
Group –VII : Received 100mg /kg body weight of CFM.
Group –VIII : Received 200mg/ kg body weight of CFM.
Group –IX : Received 50mg/ kg body weight of BFM.
Group – X : Received l00mg/kg body weight of BFM.
Group –XI : Received 200mg/kg body weight of BFM.

In-vivo pharmacological studies
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Carrageenan Induced Air-Pouch Model
The rats were divided into eleven groups (n = 6). Air-pouch was produced according to the method described by Salvemini *et al*, 1996, briefly, rats were anesthetized and air cavities were produced by subcutaneous injection of 20 ml of sterile air into the intra scapular area of the back (that is, 0 day). An additional 10 ml of air was injected into the cavity every 3rd day (3rd and 6th day) to keep the space open. On the 7th day, 2 ml of 1% solution of carrageenan dissolved in saline was injected directly into the pouch to induce an inflammatory response. The rats were orally pre-treated with either vehicle or CFE/CFM/BFM or indomethacin 2h prior to the injection of carrageenan. The second dose of treatment was repeated after 24 h of the first treatment. 48 h after carrageenan injection, the rats were anesthetized with ether and the pouch was carefully opened by a small incision. The volume of exudates was collected and measured. An aliquot of the exudate was used for differential cell count (neutrophils and monocytes) using a manual cell counter after staining with Wright's stain. The results were expressed as the total number of neutrophils and monocytes.

STATISTICAL ANALYSIS
Results of antiinflammatory activity were expressed as Mean ± SD. Results were analyzed using one way ANOVA. Differences were considered as statistically significant at $p < 0.05$ are compared to control.

RESULTS:
The data is shown in Table 1 and Figure 2 and 3. The CEE, CFM and BFM have shown dose dependent reduction in exudate volume significant ($p < 0.05$) as compared to control group. 10 mg/kg body weight of indomethacin showed significant ($p < 0.05$) result. The BFM showed good activity at low dose than CEE and CFM as compared to standard group. The activity was represented as follows: Indomethacin > BFM > CFM > CEE.

The results of the study recommend that the CEE, CFM and BFM in dissimilar doses significantly restrained carrageenan provoked exudate volume, monocyte and neutrophil count in rats and exhibited significant anti-inflammatory action.

Table.1: Effect of CEE, BFM and BFM on exudate volume, neutrophil and monocyte count in Carrageenan induced air-pouch inflammation

Treatment	Dose	Exudate volume	Neutrophils (X 10cells)	Monocytes (X 10cells)
Control	Vehicle	3.10±0.02	230.60±6.28	85.20±5.55
Indomethacin	10 mg/kg	0.60±0.05*	68.11±1.25*	37.25±4.66*
Crude ethanolic extract(CEE)	50 mg/kg	2.90±0.08	190.21±4.50	71.35±4.82
	100 mg/kg	2.20±0.06*	160.20±3.80*	59.20±3.98*
	200mg/kg	1.60±0.048#	120.54±3.22*#	55.11±2.78*#
Chloroform fraction(CFM)	50 mg/kg	2.30±0.05*	135.53±2.88*	60.23±3.21*
	100 mg/kg	1.50±0.04*#	122.4±2.22*	54.91±2.26*#
	200 mg/kg	1.40±0.03*	121.2±1.99*#	53.11±2.33*#
Butanol fraction(BFM)	50 mg/kg	1.50±0.02*#	115.53±2.22*#	54.12±2.54*#
	100 mg/kg	1.00±0.03*	98.21±1.98*#	43.50±2.22*#
	100 mg/kg	0.90±0.01*#	95.56±1.55*	42.11±2.35*#

***$p \leq 0.05$- As compared to control**
 # $p \leq 0.05$- As compared to indomethacin treated group.

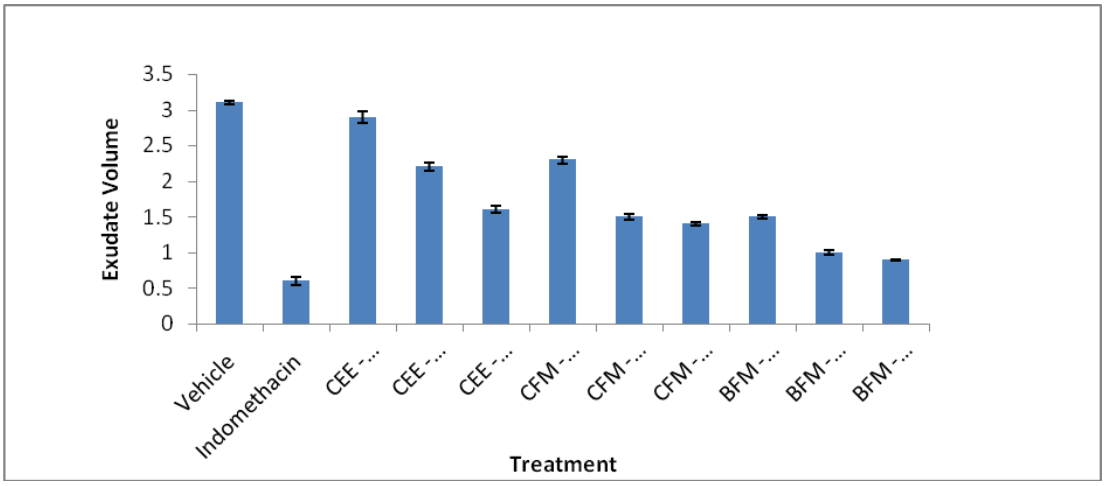


Fig.1: Effect of treatment on exudates volume

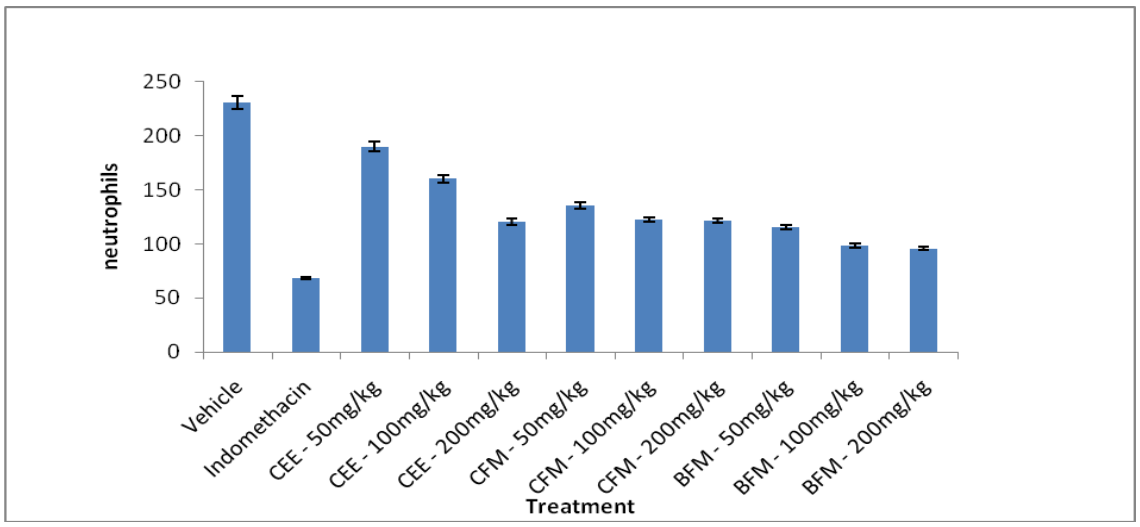


Fig.2: Effect of treatment on neutrophil count

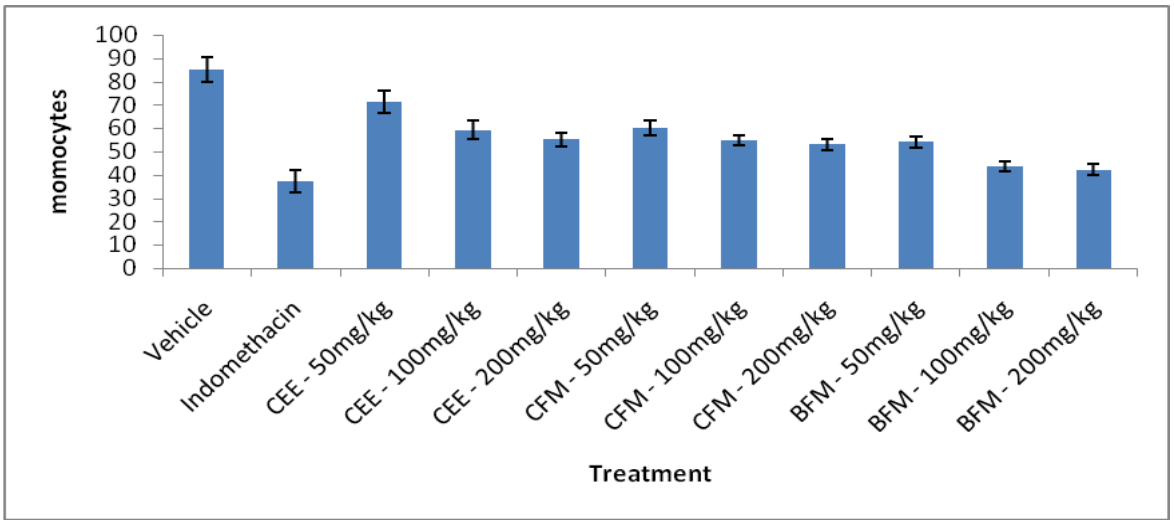


Fig.3: Effect of treatment on monocyte count

DISCUSSION:

In carrageenan-induced air-pouch model degradation of tissues and fibrosis occurs. In the repair process of inflammation, macrophages, neutrophils, fibroblasts proliferation and multiplication of small blood vessels occurs, resulting in formation of a highly vascularised reddish mass known as granulation tissue [13,14]. Thus, in the present investigation the butanol fraction of *Momordica Cymbalaria* (BFM) significantly reduced macrophages, monocytes, neutrophils infiltration. The present findings indicate that the BFM may alter the action of endogenous factors that are involved in the migration of inflammatory mediators to the site of inflammation. There is increasing evidence that lysosomal enzymes play an imperative role in the development of acute and chronic inflammation [15-18]. Most of the anti-inflammatory drugs from plant origin exert their beneficial effects by inhibiting either release of the lysosomal enzymes or by stabilizing lysosomal membrane, which is one of the key events responsible for the inflammatory process (Nair et al., 1988). So, we can imagine that our BFM might be acting by either inhibiting the lysosomal enzymes or by stabilizing the membrane. Here by we conclude that the results obtained in the present investigation revealed the anti-inflammatory activity of *M. cymbalaria in vivo* against carrageenan induced air-pouch model in wistar rats. Out of three fractions butanol fraction of *Momordica cymbalaria* had shown potent anti inflammatory activity. Further detailed molecular investigation is necessary to delineate the underlying protective mechanism of *Momordica cymbalaria* against inflammation.

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CONFLICT OF INTEREST
Authors have no conflicts of interest to declare.

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