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Research Article

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Anti-inflammatory activity of quercetin in acute, sub-acute and chronic phases of inflammtion in animal models

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ABSTRACT

Quercetin was studied on different model of inflammation like acute, sub-acute and chronic models. Studies were performed using different agent induced-paw edema viz., Dextran-induced paw edema, Formalin-induced paw edema and Cotton Wool Granuloma model. The dose 20 mg/kg of Quercetin were tested orally and Indomethacin at the dose of 10 mg/kg was used as standard. Thus it is revealed from the screening model that the quercetin possesses anti-inflammatory activity.

Key Words Quercetin , Dextran,Formalin,and Chronic inflammation.

INTRODUCTION

Inflammation is the protective phenomena and a response that occurs if an injury takes place due to some internal and external factors [1].The main bases of inflammation is based on two function of limiting demage and promoting repairment of tissues. Although inflammation is banificial in providing defense against infection inveders, it may become unchecked in case of pathogenesis of chronic inflammatory disease[2]. The main mechanism of inflammation is that the cell related with inflammation etc on cell membrane to cause the release of lysosomal enzyme arachidonic acid and various eicosanoids are produced [3].

Inflammation may be acute sub-acute and chronic occurs in three different phases. The first phase consist of increase in vascular permeability resulting in secretion of fluid from the blood into the interstitial space, the second phase comprises of leukocytes infiltration from the blood into the tissue and the third phase formation of granuloma and tissue repairment take place.

EXPERIMENTAL SCECTION

Drugs and chemicals

Quercetin was purchased from Yarrow Chem Products Mumbai. Dextran Sodium was a gift sample from a pharmaceutical company. Formalin (Formaldehyde 37-41%) was purchased from Sd Fine-Chem Limited Mumbai. And Indomethacin was purchased from Balaji Drugs.

Animals

Both sex wistar rats of age 150-250g were obtained from Indian veterinary research institute, Izzat Nagar, Bareilly U.P. All animals were housed in polypropylene cages in a temperature-controlled room at 24 ± 1^{o}c. The animals were

fed with pelleted and free access to water throughout the experiment. This study got approved from Institutional Animal Ethical Committee (IAEC).

Determination of Anti-inflammatory Activity

The Quercetin was investigated for anti-inflammatory activity in rat's animals. Three following models were used in this study:-

1. For acute inflammation

Dextran induced Paw edema

2. For sub-acute inflammation

Formalin induced paw edema

3. For chronic inflammation

Cotton wool granuloma

Dextran-induced Paw Edema Model

The rats of this experiment were divided into three groups, each groups contain six rats. Acute anti-inflammatory effect was evaluated by dextran-induced paw edema induced according to edema assay [4,5]. 0.1 ml of Freshly prepared 1.0% w/v dextran sodium in normal saline (0.9% w/v NaCl) was injected to the sub plantar region of right hind paw of rats (6,7).The Quercetin were suspended in normal saline & administered orally to rats 1 hour before dextran injection. Indomethacin (10 mg/kg b.w) was given to standard group. And paw thickness will be measured using vernier calipers at 0, 1, 2, 3, 4, and 5h (8). And after its percentage inhibition was calculate by this formula.

Calculating % Inhibition:

$$= \frac{\textbf{Control-Test}\times 100}{\textbf{Control}}$$

Formalin-induced paw edema

The rats of this experiment were divided into three groups, each groups contain six rats. Drug was administred by oral route and after 30 min. of drug administration [9,10], 1st and 3rd day Formalin was injected (0.1ml of 2%) in to right hind paw of rats by sub plantar route [11]. Drug was administered once a day for 7 days. And on 7th day after 1hr. of experimental period paw thickness was measured by Vernier calipers [11]. And after its percentage inhibition was calculates by this formula.

Calculating % Inhibition:

$$= \frac{\textbf{Control-Test}\times 100}{\textbf{Control}}$$

Cotton Pellet Granuloma Model

In cotton pellet granuloma model the animals were divided into three groups, each group contains six rats. Rats were anaesthetized with diethylether. The back skin was shaved with scyssor and disinfected with70% ethanol [11]. Sterile preweighed cotton pellets (10 mg) were implanted in the dorsal region of each rat through a single needle incision [12,13,14]. Drug, Indomethacin and control vehicle were administered daily for 10 days (0 to 10 days). On the 11th day the pellets were dissected out, dried at 60° C, for 24 hrs,[15] then wet and the dry weight was determined [16]. The weight of the cotton pellet before implantation is subtracted from the weight of the dried, granuloma pellets. The results were expressed as mean ± SEM. The differences were compared using one-way ANOVA followed by t test.

Statistical Analysis

The results were expressed as mean + SEM, Statistical significance was determined by one way

ANOVA (Analysis of Variance) followed by t test by using the Graphpad Instant version and compared with control.

Table 1: Anti-inflammatory activity of Quercetin on Dextran induced paw edema in rats

Groups / Treatment	Dose (mg/kg, p.o)	Edema Size Means (mm)± SEM (%Inhibition) 1hr.	2hr.	3hr.	4hr.	5hr.
Group 1/ Control	….	2.7±0.28	3.0±0.18	3.1±0.006	3.2±0.024	3.7±0.28
Group 2/ Quercetin	20	2.0±0.013* (25.92%)	2.1±0.012*** (29.03%)	2.1±0.018*** (32.25%)	2.0±0.013*** (37.5%)	2.0±0.018*** (45.95%)
Group 3/Indomethacin	10	2.1±0.050 (22.22%)	2.2±0.013*** (26.66%)	2.2±0.012*** (29.03%)	2.2±0.006*** (31.25%)	2.1±0.013** (43.24%)

*Results are mean ±S.E.M. (n=6) *P<0.05, **p<0.01 & ***P<0.001 compared to control*

Table 2: Anti-inflammatory activity of Quercetin on Formalin -induced paw edema in rats

Groups / Treatment	Dose (mg/kg, p.o)	Mean increase in paw thickness after 6 days (mm)	%Inhibition
Group 1/ Control	…..	3.8±0.29	
Group 2/ Quercetin	20	2.1±0.012***	44.75%
Group 3/Indomethacin	10	2.2±0.018**	42.105%

*Results are mean ±S.E.M. (n=6) *P<0.05, **p<0.01 & ***P<0.001 compared to control*

Table 3: Anti-inflammatory activity of Quercetin on Cotton Wool Granuloma in rats

Groups / Treatment	Dose (mg/kg, p.o)	Wet weight (mg) (% Inhibition)	Dry Weight (mg) (% Inhibition)
Group 1/ Control	.....	170±9.3	65±2.9
Group 2/ Quercetin	20	77±6.7 (54.70%) *	48±4.4 (26.15%)*
Group 3/Indomethacin	10	110±6.7 (35.29%)	50±2.9 (23.07%)

*Results are mean ±S.E.M. (n=6) *P<0.05 & **p<0.01 compared to control*

RESULTS AND DISCUSSION

The drug was tested for the anti-inflammatory activity using Dextran-induced paw edema , formalin-induced paw edema and cotton wool granuloma models, the result are tabulated in table-1,2,and 3.

Among them only quercetin (20mg/kg) in the test group shows maximum activity (45.95%) compared with the control group in reducing the edema by using dextran-induced edema model. The maximum percentage inhibition of test drug quercetin is 44.75% when using formalin-induced paw edema and the maximum percentage inhibition of test drug quercetin is 26.15 % when using cotton wool granuloma model. Therefore quercetin was screened using formalin-induced paw edema and cotton wool granuloma models to find out conclusive result in anti-inflammatory activity.

After injection in mice and rats extremities, Dextran that induces anaphylactic reaction which is characterized by extravasation and edema formation, as a consequence of liberation of histamine and serotonin from mast cells[16,17].

Formalin induced paw edema which is a sub-acute inflammation results from cell damage, which provokes the production of endogeneous mediators. Histamine, serotonin, prostaglandins, and bradykinin are example of some endogeneous mediators inhibition of edema induced by formalin in rats is one of the most suitable test procedures to screen antiarthritic and anti-inflammatory agents as it closely resembles human arthritis [17] .
The cotton pellet granuloma is use as proliferate phase of inflammation. During the inflammatory process migration of WBC takes place which is the biological marker. Enlargement of spleen occur as spleen has the phagocyte nature [18].

CONCLUSION

It may can be concluded that quercetin has shown anti-inflammatory activity against formalin-induced paw edema and cotton wool granuloma model, therefore quercetin (20mg/kg) shows the moderate activity in dextran-induced paw edema model. Quercetin showed better activity profile compared to the others models of anti-inflammatory activity. This study demonstrates the efficacy of quercetin as an anti-inflammatory agent.

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