Antiasthmatic Activity of Alcoholic Extract of *Solanum xanthocarpum*

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Abstract

The present study deals with the phytochemical study and effect of ethanolic extract of roots *Solanum xanthocarpum* by using various in vivo and in vitro animal models. In vitro model like isolated guinea pig ileum preparation was studies to know basic mechanism by which extract shows relaxant activity. The study shows that extract is effective against histamine induced contraction. Animal studies involve use of histamine induced bronchocontraction. These studies showed significant protection at lower doses while further increase in dose level showed reduced activity. The results of these studies indicated usefulness of ethanol extract of *Solanum xanthocarpum* in asthma.

Key words : *Solanum xanthocarpum*, Antiasthmatic, Bronchoconstriction.

Introduction

Herbal medicines are being used by nearly about 80% of the world population for primary health care. Bronchial disease Asthma is very commonly occurring condition that is most difficult to control in chronic stage. In the united state alone asthma affects almost 17 million people & this is a 75% increase in the last 20 yrs. This means that about one out of every 20 adults & close to one out of 13 children today have asthma. An alarming fact is that since 2010, asthma in children under age 5 has risen remarkably. In school age children asthma has risen by 75%. India has alone an estimated 15-20 million asthmatics. Mortality data from developed countries show that the rates varies from 0.1– 0.8 per 10,000 persons aged 5-34. For managing asthma attack symptomatic relief is foremost requirement. In India, in various traditional systems like Ayurveda, Unani & Siddha numerous herbs were mentioned for therapeutic use in asthma[1].

Solanum xanthocarpum Schrad. & Wendl. (Family: Solanaceae) (*S. xanthocarpum*) commonly known as Yellow Berried Nightshade (syn: Kantakari), is a prickly diffuse bright green perennial herb, woody at the base, 2-3 m height found throughout India, mostly in dry places as a weed on road sides and waste lands[2]. The fruits are of 1.3 cm diameter berry, yellow or white with

green veins, surrounded by enlarged calyx. The fruits are known for several traditional medicine uses like anthelmintic, antipyretic, laxative, anti-inflammatory, urinary bladder, enlargement of the liver, antiasthmatic and aphrodisiac activities. The stem, flowers and fruits are prescribed for relief in burning sensation in the feet accompanied by vesicular eruptions. *S. xanthocarpum* has shown antiasthmatic, anti-nociceptive, anti-fungal and molluscicide activities[3]. The fruit paste of it applied externally to the affected area for treating pimples and swellings.

The fruits are reported to contain several steroidal alkaloids like solanacarpine, solanacarpidine, solancarpine, solasonine, solamargine and other constituents like caffeic acid, coumarins like aesculetin and aesculin, steroids carpesterol, diosgenin, campesterol, daucosterol and triterpenes like cycloartanol and cycloartenol were reported from the fruits. *Solanum xanthocarpum*, contain several steroidal alkaloids like solanacarpine and solamargine[4]. Other constituents like caffeic acid coumarins like aesculetin and aesculin, steroids carpesterol, diosgenin, campesterol, daucosterol and triterpenes like cycloartanol and cycloartenol were reported from the fruits. Steroidal glycoalkaloids are: Solasodine, Solanidine, Solasonine, Solanine, Diosgenin (steroidal saponin), Campesterol (sterol). The fruit of *Solanum xanthocarpum* contains alkaloid saponins have a heart stimulating function. It has a high concentration of solasodine alkaloid, a spiroketal alkaloid sapogenin with heterocyclic nitrogen, which is the starting material for the manufacturing of cortisone and sex harmone[5].

MATERIALS AND METHOD

Plant material

The plant of *Solanum xanthocarpum* was collected from the roadside locations of Jaunpur, U.P. region and was authenticated by department of Botany, T.D.P.G. College, Jaunpur. Plant material was preserved in pharmacognosy department of BHU, Varanasi. The fruit of the plant was separated, dried and coarsely powdered.

Preparation of plant extract

The dried powder (1.5 kg) was subjected to hot extraction with EtOH by Soxhlet extractor and after evaporation of the solvent 140 g crude extract was found. Twenty gram of the crude EtOH extract was fractionated into petroleum ether fraction (15 g), chloroform fraction (2 g), ethyl acetate fraction (1 g) and aqueous fraction (2 g). After complete extraction, the solvent was removed by distillation under reduced pressure and extract was concentrated to dryness in vacuum. The percentage of ethanol soluble extractives was calculated with reference to air-dried plant material and the yield was found to be 11.18 ± 0.70 % w/w.

Experimental animals

Guinea pigs of either sex (350-450 g) were selected for present study. Six animals were taken in each group and maintained under standard laboratory conditions. They were allowed free access to standard dry pellet diet and water ad libitum during the experiment. Wister rats weighing 150 -250 and Swiss mice of either sex bread at animal house, Institute of Medical Sciences, BHU, Varanasi were housed at standard condition of temperature (22±1º) and 12/12 h light / dark cycle. They were allowed free access to standard dry pellet diet and water ad libitum during the experiment. All experimental procedures were followed in strict accordance with the guideline prescribed by the Committee for the Purpose of Control and Supervision on Experimental on Animals (CPCSEA).

Phytochemical Study

Alcoholic extract of *Solanum xanthocarpum* processed on column chromatography which identified by TLC and paper chromatography. Each eluents obtained from column chromatography concentrated on water bath and puried by recrystalization. Chemical structure of obtained compound elucidate with the help of elemental analysis, U.V., I.R., ^{1}HNMR and mass spectroscopy[4-6].

Screening of anti-asthmatic activity

In vitro studies on isolated guinea pig ileum Preparation

Overnight fasted guinea pigs were sacrificed using cervical dislocation method. Ileum was quickly dissected out and mounted in an organ bath maintained at 30±0.5°C and containing 20 ml Tyrode's solution under basal tension of 500 mg. The solution was continuously bubbled with air. The responses to drug were recorded on student physiograph using isotonic transducer, which exerted a basal tension equivalent to 500 mg load on tissues. The tissues were allowed to equilibrate for 30 minutes, during which, the bathing solution was changed at every 10 minutes. The contractile responses of ileum to Histamine were recorded in presence and absence of extract of drug[7].

In vivo studies on Acetylcholine and Histamine induced bronchospasm in guinea pigs

Guinea pigs of either sex (350-450 g) were selected and randomly divided into four groups each containing six animals. The animals were kept on fasting overnight before treatment. The ethanolic extract and standard drug were administered orally in 0.5 % CMC. The single dose treatment was given two hour before the study. Later the animals were exposed to an aerosol of 0.25 % histamine and time for preconvulsion state was observed for each animal as described by Sheth *et al*. (1972). After 15 days of washout period, the same animals were treated with the above treatment and time for preconvulsion state was observed for 0.5% acetylcholine bromide aerosol spray[8].

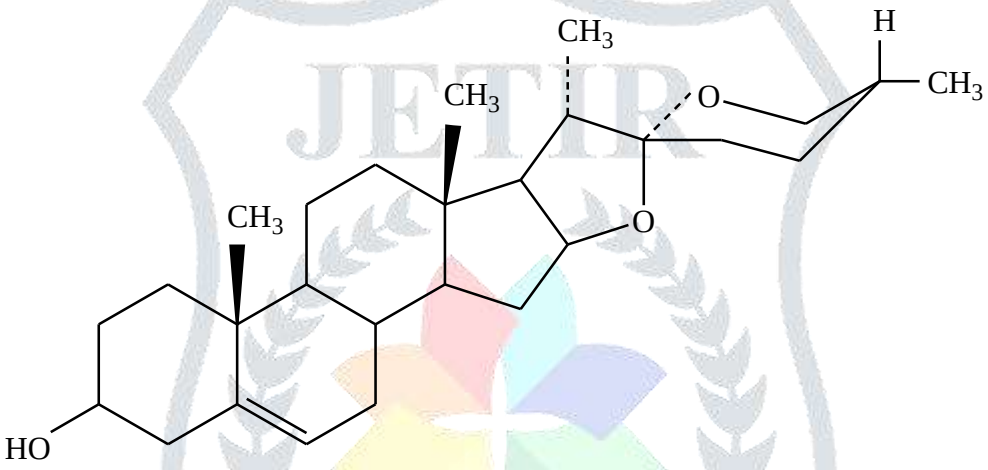
Passive paw anaphylaxis in rats

Wistar rats were given subcutaneously in the doses of 100 mg of egg albumin on day 1, 3 and 5. On day 10 of sensitization, blood was collected and centrifuged to separate serum. Animals were divided into eight groups (n=6). Control group received saline and other groups received single dose of extract 50, 100, 200, 300, 500, 1000 mg/kg p.o. Dexamethasone was used as standard (0.27 mg/kg p.o).Prior to drug treatment animals were sensitized with serum. Next 24

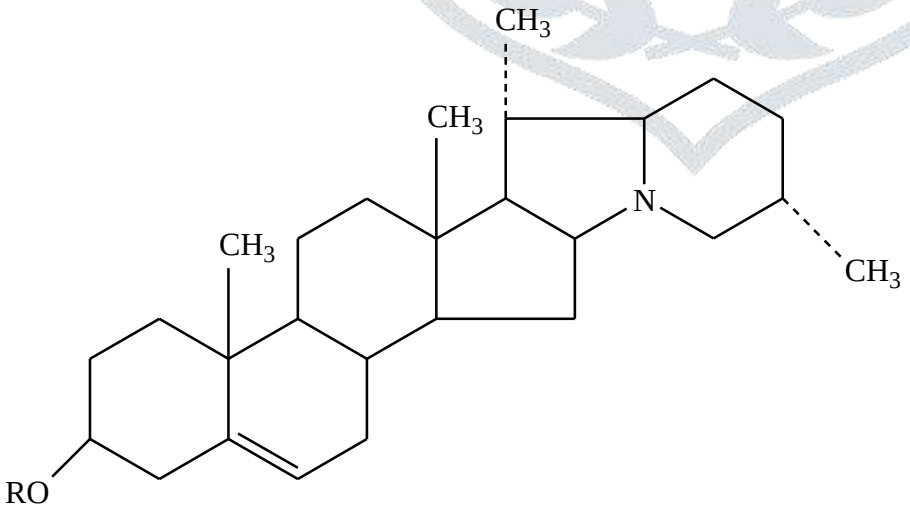
h, after drug treatment animals again challenged with 10 mg egg albumin and edema inhibition was calculated[9].

RESULTS AND DISCUSSION

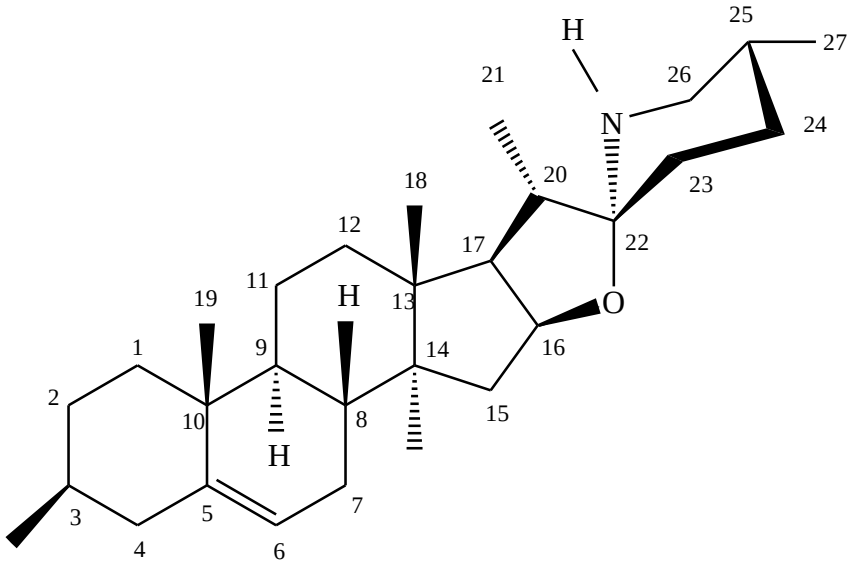
Plants contain alkaloids, sterols, saponins, flavonoids and their glycosides, carbohydrate fatty acid, amino acids etc. Active compound salsodine forms yellow coloured complex with methyl orange extractable in $CHCl_3$. It gives maximum absorbama at 425 nm structure of some isolated compounds which established with the help of spectroscopy are as under:



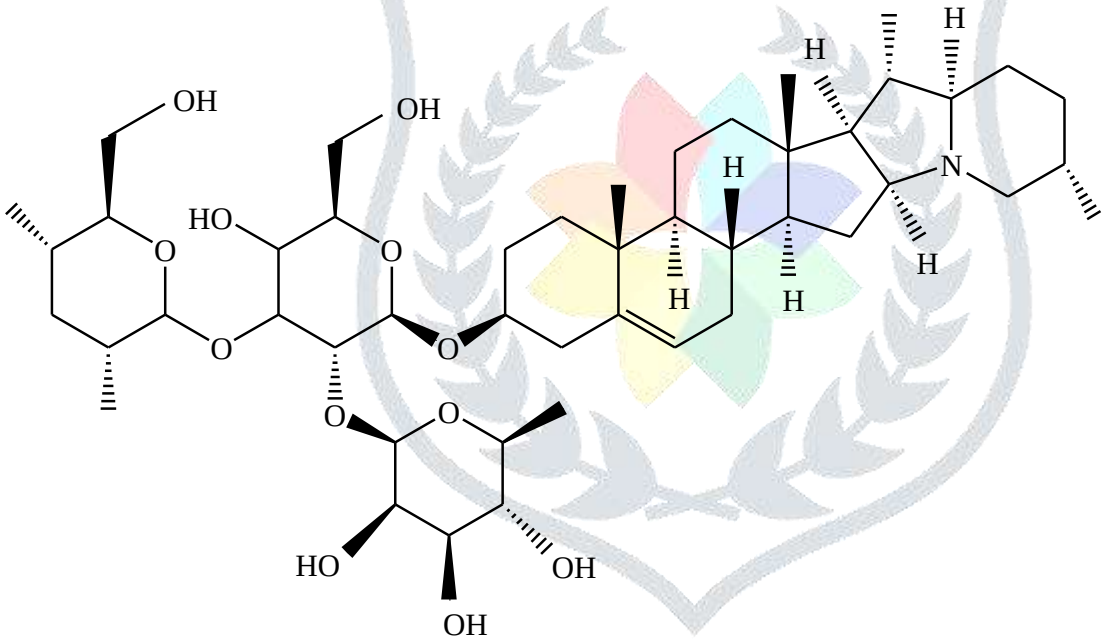
(A) Solasodine



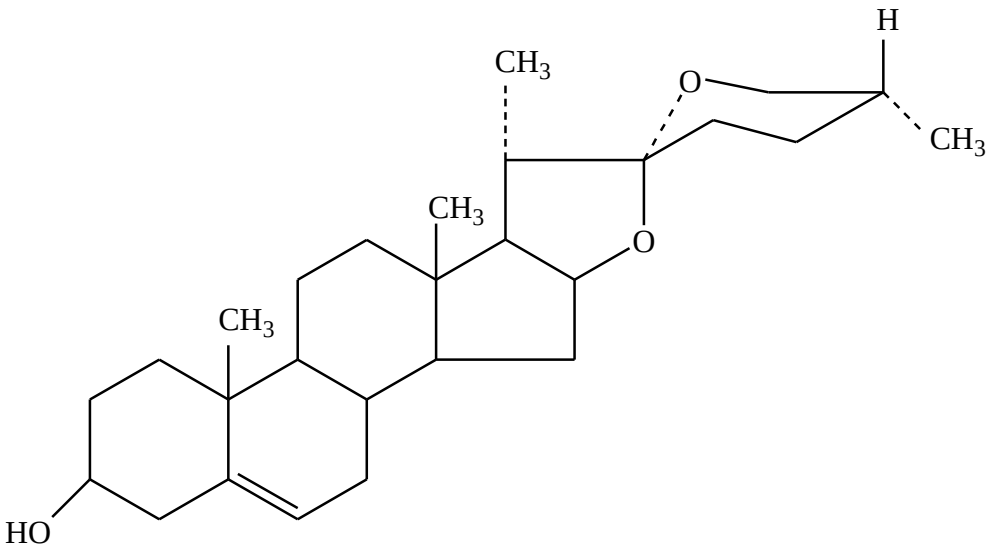
(B) Solanidine



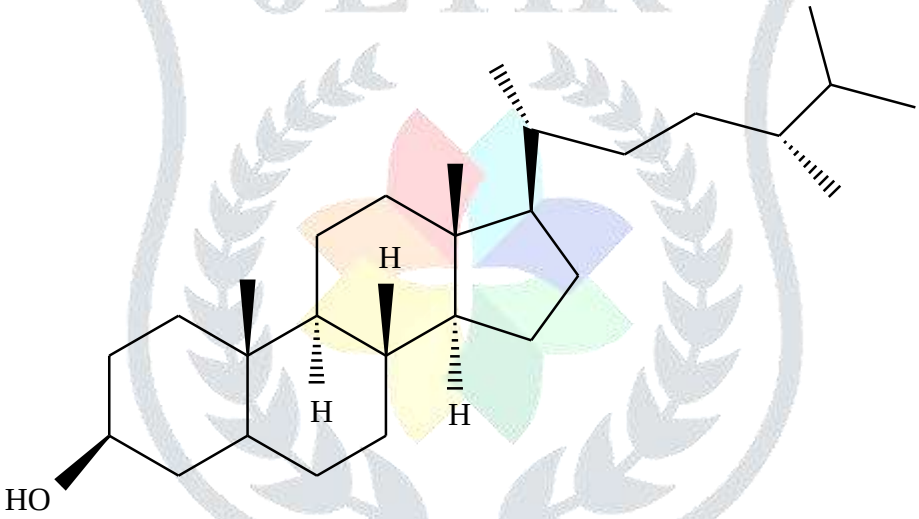
(C) Solasonine



(D) Solanine



(E) Diosgenin (sterodial saponin)



(F) Campesterol (sterol)

The present study dealt with screening of antiasthmatic activity of ethanol extract of *Solanum xanthocarpum*. Bronchial asthma is a chronic inflammatory disease, characterized by both bronchoconstriction and airway inflammation which leads to bronchial hyper responsiveness to various stimuli, in which many cell types play a role, more important being mast cells, eosinophils and T-lymphocytes. Different agonists like acetylcholine, histamine, 5-hydroxyltryptamine and bradykinin are responsible for contractile responses. In isolated guinea pig ileum preparation, there is a right side shift of dose response curve of histamine in the presence

of ethanol extract of *Solanum xanthocarpum* indicating antiasthmatic action [Table-1]. Histamine is one of the major inflammatory mediators in the immediate phase of asthma, causing airway hyper responsiveness and bronchial airway inflammation[10]. The study regarding involvement of H1 and H2 receptors has been done in experimental asthma in guinea pig using respiratory smooth muscle and it was confirmed that there is prominent involvement of H1 receptors as compared to H2 receptors especially in asthma[11].

Table-1: Effect of the ethanol extract of *Solanum xanthocarpum* on histamine-induced contractions

Dose of Histamine (2.5 ug/ml)	**Isolated guinea pig ileum preparation**	
ml	Control group % maximum contraction	Test group % maximum contraction
0.1	14.776±0.925	9.058±1.188
0.2	28.748±0.501	20.534±1.618
0.4	58.488±2.511	38.806±2.163
0.8	83.33±2.988	64.446±1.384
1.6	83.33±2.988	64.446±1.384

Effect of EE of ***Solanum xanthocarpum*** on the histamine induced contraction on the isolated guinea pig preparation was tabulated. All values are expressed as mean SEM of sample size of n=6. All treated groups were compared with controlled group.

The maximum percentage protection i.e. 86.67 % observed at 200mg/kg dose for bronchorelaxant study comparable with that of standard Chlorpheniramine maleate 91.59%. Statistical significance in post treated exposition time and mean exposition time also showed 200 mg/kg as effective dose. Further increase in the dose showed decreased activity[12] [Table-2].

Table-2: Effect of the ethanol extract of *Solanum xanthocarpum* on histamine-induced bronchoconstriction

Groups	**Dose in mg/kg p.o.**	**PCT (before) T1**	**PGT (after) T2**	**Mean exposition time**	**% protection**
1	Control	1.428±0.029	1.505±0.013	0.077±0.034	5.101
2	50	0.923±0.014	1.581±0.074	0.727±0.006	41.44
3	100	1.156±0.015	2.327±0.111	1.166±0.100	50.95
4	200	1.145±0.010	8.595±0.163	7.448±0.076	86.67
5	300	1.287±0.037	4.411±0.138	3.124±0.148	72.24
6	500	1.336±0.032	3.208±0.014	1.873±0.028	58.331
7	1000	1.215±0.065	1.266±0.018	0.074±0.043	7.00
8	CPM (2 mg/kg)	0.907±0.003	10.796±0.103	9.898±0.099	91.59

All values are expressed as mean SEM of sample size of n=6. All treated groups were compared with control group. CPM is Chlopheniramine maleate (2 mg/kg).

Haloperidol induces catalepsy by inhibiting dopamine D2receptors and inhibits dopamine secretion[13]. Dopamine is agonist for adrenaline. Adrenaline is physiological antagonist

of histamine. So as there decrease in dopamine there is imbalance in neurotransmitters means high level of histamine. In this study significant protection against haloperidol-induced catalepsy at dose 300 mg/kg. Further increase in the dose showed decreased activity[14] [Table-3].

Table-3: Effect of the ethanol extract of *Solanum xanthocarpum* on haloperidol-induced catalepsy

Groups	Dose mg/kg	Duration of catalepsy (sec) at mean SEM				
		30 min	60 min	90 min	120 min	150 min
1	Control	216.27±0.36	251.5±2.87	265.57±0.27	280.83±3.92	238.45±28.92
2	100	206.16±0.24	234.06±0.71	215.01±0.67	229.00±0.59	205.45±0.47
3	200	198.82±0.44	228.13±0.37	198.17±0.42	208.67±0.51	190.95±1.45
4	300	102.21±0.37	83.35±1.00	70.73±0.27	52.63±0.37	42.2±0.29
5	500	170.83±0.98	207.55±0.42	195.13±0.84	198.67±0.49	180.33±1.09
6	1000	199.27±0.90	216.45±0.73	184.27±0.76	208.65±0.48	192.65±0.75
7	2000	203.48±0.40	235.5±0.54	219.53±0.39	226.25±0.33	208.33±0.54
8	CPM (10 mg/kg)	89.55±0.54	66.46±0.39	52.53±0.28	32.75±0.35	53.23±0.53

All values are expressed as mean SEM of sample size of n=6. All treated groups were compared with control group. CPM is Chlopheniramine maleate (2 mg/kg).

Allergic asthma is a chronic inflammatory process occurring due to exposure of allergen resulting in the activation of T-lymphocyte with subsequent release of inflammatory mediators. Immuno-modulatingagents are useful in the treatment of asthma by inhibiting the antigen-antibody (AG-AB) reaction and there by inhibiting the release of inflammatory mediators. *Solanum xanthocarpum* has been reported to possess anti-inflammatory activity. Percent inhibition of paw edema volume was calculated and maximum effective dose was observed at 200 mg/kg at different hour intervals[15]. It was found that effect of dose 200 mg/kg was maximum up to 24 h, further percent inhibition goes on decreasing. But still that percent inhibition in paw edema was significantly effective as compare to other doses. Whereas, in statistical analysis of paw edema volume it was observed that 200 mg/kg dose had significant effect comparable that with Dexamethasone. Here also observed that further increase in dose decreased activity [Table-4].

Table-4: Effect of the ethanol extract of *Solanum xanthocarpum* on passive paw anaphylaxis

Groups	Dose mg/kg	Paw edema volume (ml) mean SEM			
		1h	2h	3h	4h
1	Control	0.923±0.02	0.75±0.01	0.626±0.09	0.56±0.05
2	50	0.521±0.06	0.401±0.06	0.343±0.04	0.311±0.01
3	100	0.731±0.03	0.535±0.03	0.433±0.03	0.358±0.02
4	200	0.535±0.03	0.321±0.03	0.331±0.02	0.246±0.02
5	300	0.65±0.03	0.361±0.03	0.431±0.03	0.43±0.03
6	500	0.55±0.02	0.465±0.01	0.486±0.01	0.426±0.01
7	1000	0.587±0.15	0.408±0.11	0.482±0.14	0.401±0.12
8	Dextromethazone	0.426±0.12	0.239±0.06	0.258±0.08	0.245±0.07

	(0.27 mg/kg)				

All values are expressed as mean SEM of sample size of n=6. All treated groups were compared with control group. CPM is Chlopheniramine maleate (2 mg/kg).

Stigmasterol, carpesterol and diosgenin showed antiinflammatory effect. Lupeol present in alcoholic extract of *Solanum xanthocarpum* also acted as multitraget agent with immense anti-inflammatory potential targeting key molecular pathways, which involved nulcear factor Kappa B, CFLIP Fas, Kras, Phosphatidylinosito-3-kinase (13)/AK and Wnt/β catenin in a variety of cell. Lupeol at its effective therapeutic doses exhibited[16].

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