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REVIEW ON *LUPEOL* - A TRITERPENOID

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Lupeol, Triterpenes, Anti-inflammatory, Anti-cancer, Anti-diabetics, Cardio-protective, Skin-protective, Nephero-protective, Hepato-protective

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ABSTRACT: *Lupeol*, a pent acyclic triterpenoid known as secondary metabolites. Chemically it is a 20(29)-Lupen-3-beta-ol derived from eggplant. The main part of this plant is steam & bark. It is obtained from vegetables, fruits & medicinal plants. The isolation of *Lupeol* was done by TLC monitoring column chromatography by using solvents like hexane & ethyl acetate on the basis of adsorption principal. The species of *Lupeol* such as *S. xanthocarpum* which have specifically anti diabetic action & many other species which have a dynamic and diverse effects. The doses of *Lupeol* vary from disease to disease and it can be administered *in-vitro* & *in-vivo* technique like intra-peritoneal, intramuscular, oral, topical. On the basis of many researches', *Lupeol* shows a magical activity toward various types of diseases with less side effects & have a good ability to cross blood brain barrier.

INTRODUCTION: Eggplant with yellow fruits has been an important medicinal product since ancient times. *Lupeol* (20(29)-*Lupen-3* betaol), which is the main active ingredient of the steam bark of *S. xanthocarpum*, has been reported to have many activities such as, anti-inflammatory, antihyperglycemic, antilipemic abnormalities & antimutagenic effects [1]. These reports have been found in various animal models or diseases in which *Lupeol* has anti-diabetic, anti-asthma, anti-arthritis, cardioprotective, hepatoprotective, renal protective and anti-preventive disease, intraperitoneally and intravenously. *Lupeol* belongs to the pentacyclic found lupine type triterpenoids in food, fruit and many plants.

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Triterpenoids are called secondary metabolites and their active substances are derived from plants, fruits, fungi, *etc*. Natural triterpenoids, commonly referred to as secondary metabolites, are of interest [2]. Due to their extensive biological activities, triterpenoids are a widely used class of compounds containing important compounds. The pharmacological significance of the gift of a healthy life comes from medicinal herbs. Over 8,000 different plant species are employed to treat various diseases in different parts of the world. Biosynthetic rearrangements of squalene epoxides lead to the synthesis of various triterpenoids.

Hydrocarbon triterpene derivatives can be obtained by various processes such as oxidation, hydrogenation and dehydrogenation [3]. *Lupeol*, Lupine triterpene nutrition, triterpene is naturally found in various plants called *Lupeol*. Although people in the Western world consume about 250 mg of triterpenoids day by day, it's worth nothing that in Mediterranen countries where most foods

are dominated by olive oil, the average triterpenoid intake a person consume will reach 400 mg/day [4]. *Lupeol* is a triterpene that has attracted doctors, scientists and pharmaceutical manufacturers for its many medicinal activities. The major triterpene business is now marketed worldwide. It is estimated that more than 2,400 subjects participated in clinical trials of various types of triterpenoids at doses of 25 grams or more per day and there were no adverse outcomes. It has attracted the attention of doctors, drug dealers and scientists, and is known all over the world for its various medical activities [5].

FIG. 1: [5]

FIG. 2: [6]

Sources of *Lupeol*: Numerous plant species are said to contain *Lupeol* in various forms. Genuine *Lupeol* is establishing in many plants such as mango, acacia, and velvet acacia. *Lupeol* is found in vegetables and fruits such as cabbage, peppers, cucumbers and tomatoes. Examples consist of olives, figs, mangoes, strawberries, red berries, and herbs such as American ginseng, shea butter herb, tamarind, *Allanblackia monticola*, *Himatanthus sucuuba*, *Celastrus papulatus*, *Zanthoxylum riedelianum*, *Leptadenia hastadenokalta*, Crataapatoria seed, and Eleptadeniahastaden. Native to North America, Latin America, Japan, China, Africa and the Caribbean islands [3].

TABLE 1: LIST OF SELECTED PLANT CONTAINING *LUPEOL* [3]

Botanical name	Habitual name
Aloe vera	aloe
Daucus carota	carrot
Glycine max	soya bean
Olea europa	olive
Lycopersicon esculentwn	tomato
Lawsonia inermis	henna
Apocynum cannabinum	bitterroot

TABLE 2: CONTENT OF *LUPEOL* IN FRUIT AND IN PLANT [3]

Name of plant	*Lupeol* (µg/g)
Olive fruit	3 µg/g of fruit
Mango fruit	1.80 µg/g mango pulp
Aloe leaves	280 µg/g dry leaf
Japanese pear (shinko)	175 µg/g twig bark
Ginseng oil	15.2 µg/g of oil
Eim plant	880 µg/g of bark

Chemistry of *Lupeol*: The chemical formula of *Lupeol* is C30H50O and its melting point is 215-216 °C. The product calculated from the formula of *Lupeol*, indicates a molecular weight of 426.7174 [g/mol], H-B donor 1, H-B acceptor 1.

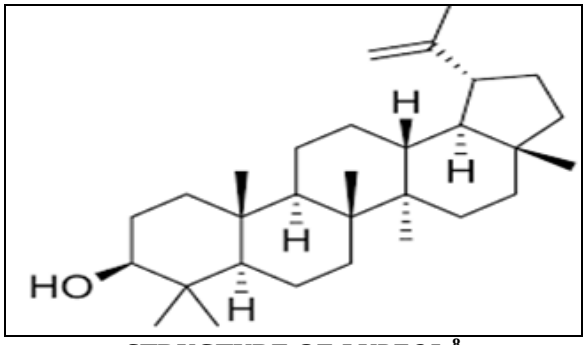
Infrared spectrum *Lupeol* was found to have hydroxyl functional groups and olefinic moieties, showing that they appear in the 3235 and 1640 cm-1 [19].

The existence of seven methyl singlet and olefinic functional groups in the 1H-NMR spectrum indicates that *Lupeol* is an important pentacyclic triterpenoid 409.12 [20].

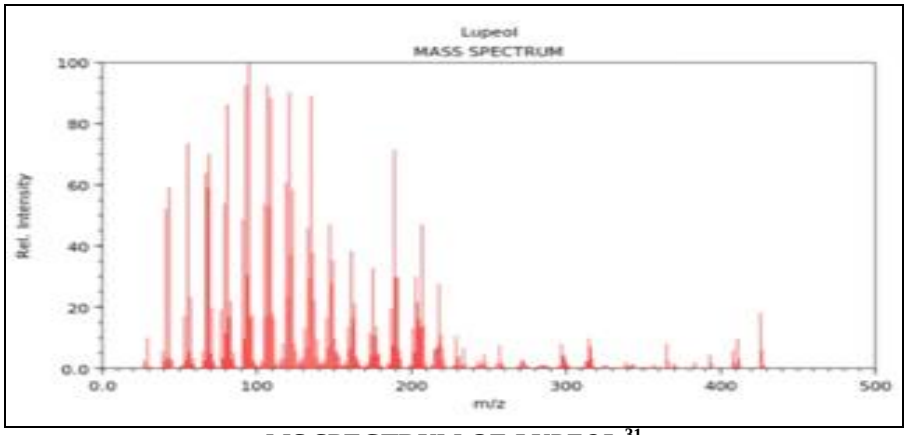
In the LR IR spectrum of *Lupeol* alcohol, a strong wide band at 3384 cm and intermediate densities at 1192 cm and the O-H bond quivering of the hydroxyl category at 672 cm are found in the band and outside the C-H plane, negligible vibration is detect at 826 cm.

The correlate with C=C vibration appears as a weak band around 1654 cm. Flexural and bending vibrations of the methyl part can be seen in the density band 2916 cm-1 & in the half-density band at 1460 cm-1 [8]. Formula defines the presence of 6° unsaturation, which is evident from the olefinic activity [4].

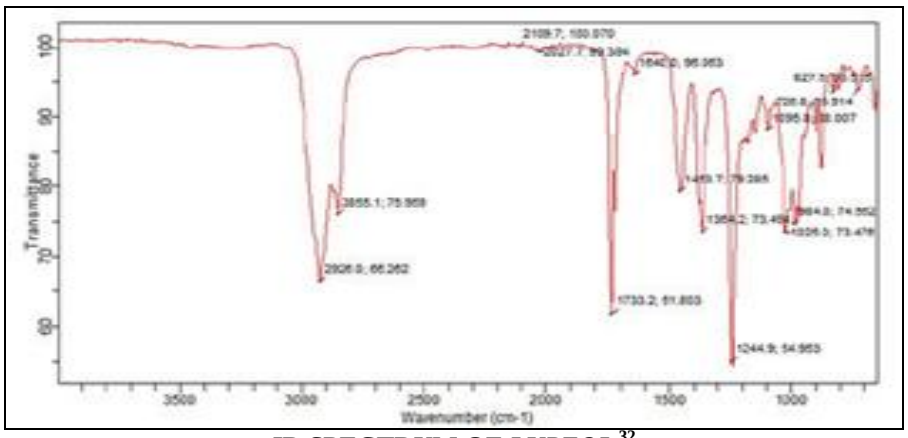
The chemical structure of *Lupeol* is as follow:



STRUCTURE OF *LUPEOL* [8]



MS SPECTRUM OF *LUPEOL* [31]



IR SPECTRUM OF *LUPEOL* [32]

Isolation of *Lupeol*:

Extraction: Weigh 500 g of crushed stems within a scrubbed Winchester bottle, add 1.5 liters of hexane & shake periodical at that time strain later than 48 hours, repeat for ethyl acetate.

Concentrate in vacuum at around 42 °C using a field evaporator for one-third of its original product to yield 1.2 g (0.24%) primitive n-hexane take out.

2g (0.24%) primitive ethyl acetate take out & 2.5g (0.5%) methanol take out. These were subsequently used in bioassay research & following isolation, several spectroscopic analyzes of isolated V39 were performed [8].

Separation and Purification: Coniferous tree extracts in hexane & ethyl acetate were dissolved in a minimum 9:1 ethyl acetate to hexane weight system, pre-absorbed *in-silica* gel, and then put onto a silica gel column. When using gradient elution with multiple hexane-ethyl acetate solvents, normal phase adsorption chromatography (10.0, 9.5: 0.5, 9.5). 0:1, 8, 5:1, 5, 8, 0:2. 0, 7, 5:2, 5, 7, 5:3, 5, 6, 0:4, 0, 5: 5: 4. 5, 5.0: 5.0) in ascending order of polarity. A 9: the basis for TLC monitoring in column chromatography was the 1 body weight ratio, which allowed TLC to compare with the hexane/ethyl acetate (9:1) weight method while simultaneously isolating V39.

This substance, designated V39, was observed as a white needle-like crystal & underwent a number of spectrum analyses [8].

Biosynthesis of *Lupeol*: Triterpene synthases in plants control the manufacture of *Lupeol*, which is one of the most intricate substances discovered in nature. Mevalonate (MVA), isopentenyl pyrophosphate (IPP), dimethyl allyl pyrophosphate (DMAPP), & fusyl pyrophosphate (FPP) are all involved in the slow cytoplasmic production of *Lupeol*. FPS, or farnesyl pyrophosphate synthase, catalyzes this process. Squalene synthase (SQS) then transforms FPP into squalene. Squalene 2, 3 oxysqualene is oxidized by squalene epoxidase (SQE), which is then converted into lupinyl cations by *Lupeol* synthase (LUS). Finally, deprotonation of the 29-methyl group transforms the lupinyl cation into *Lupeol* [9].

Lupeol shows many pharmacological activities which are listed as follow:

- Anti-inflammatory action
- Anti-cancer activity
- Skin protective
- Anti diabetics
- Cardio protective
- Hepato protective
- Nephero protective
- Biological activity of *Lupeol* on humans

Anti- Inflammatory Action of *Lupeol*: Some studies using wear & tear models possess appear certain the anti-inflammatory effect of *Lupeol* is better than that of indomethacin. Comparative studies in mouse models have gained deeper understanding (a non- steroidal anti-inflammatory drug). *Lupeol* is widely recognized being its constraints result *in-vitro* & in acute imitation. *Lupeol* pretreatment may delay the immunological effect of *Lupeol* as it shortens prostaglandin E2 (PGE2) assembly in A23187-bracing macrophages. The anti-inflammatory demeanor of the *Lupeol* well endowed abstract was agnate to that apparent by the careful cyclo-oxygenase constraints [1]. *Lupeol* analysis (5–9.37 mg/kg) was appear to display anti-inflammatory action accompanied by a best reticence of 57.14% spell as α-mangostin at agnate dosage be visible anti-inflammatory action of 38.70%. *Lupeol* & its by products (linoleate, acetate and palmitate) were apparent to display college anti-inflammatory action than frequently acclimated non-steroidal anti-inflammatory biologic indomethacin in rat & abrasion imitation of inflammation [12]. The anti-inflammatory after product of *Lupeol* was empiric to be according to dexamethasone, a able-bodied accepted anti-inflammatory agent. *Lupeol* has anti-inflammatory properties and can be operated to control colitis and heal the intestines [11]. *Lupeol* is a common triterpene operated to shorten the inflammatory response & has immunomodulatory attribution [12].

Anti- Cancer Action of *Lupeol*: The available abstraction of *Lupeol* is appearing as anticancer act venture. *Lupeol* has been abeyant to perform adjoin altered types of cancers such as animal prostate, breast blight skin, liver, & claret cancer. *Lupeol* is appearing to display able anti-mutagenic action back activated beneath *in-vitro* & *in-vivo* conditions. Cancer is an all-encompassing appellation that comprises an ample cardinal of diseases that condition detectable genitalia of the animal body. Principal blight types that acquired added expired in 2012 were lung (1.59 million), alarmist (745,000), belly (723,000), rectal cancer (694,000), & breast blight (521,000).

Even admitting there are abounding treatments to altered blight types (i.e. surgery, chemotherapy, radiation therapy, targeted analysis & immunotherapy), these treatments accept apparent abounding accessory furnishings on patients. We previously found that *Lupeol* inhibited the development of carcinogenesis in the bark of two jujube trees in an abrasion model. We also displayed that the *Lupeol* assay (40 mg/kg) inhibited prostate cancer tumor growth in animal inducers in a allograft wearing imitation .We additionally displayed that *Lupeol* analysis (40 mg/kg) hamper the advance of prostate cancer tumors of animal abettor built-in a allograft abrasion imitation. Studies with assorted blight beef accept apparent that *Lupeol* embrace multifaceted action to arrest the advance of animal cancer beef & by prompt apoptosis. Rectal cancer blight (CRC) is the capital of patient's life after metastasis (CRC) [8]. The effects of *Lupeol* treatment on HCT116 and SW620 rectal cancer cells &

inhibition of rectal cancer cells through inhibition of the cytoskeletal RhoA-ROCK1 pathway provide metastatic protection to cancer patients [11].

Skin Protective Action of *Lupeol*: The bark careful furnishings of *Lupeol* were empiric to be analogous with its abeyant to magnify the bark anti-oxidant arrangement. A abstraction put into practice an in vitro archetypal of beastly bark keratinocytes (epidermal explants) able at Air liquid associated studies on de-epidermis removed animal skin to examine the transfer of *Lupeol* to the skin, inflammation caused by tissue damage, & soft tissue growth, Corrosion ion carcinogenesis in the prostate & pancreatic blight, *Lupeol* showed a strong inhibitory effect on the prostate Fusarium wil Supplementary beef & evaluation of 21 also showed a strong anti-tumor effect in two 22-day skin models. *Lupeol* provides able antioxidant aegis adjoin benzoyl peroxide-promote deadly in Swiss albino abrasion bark diminished the PGE2 assembly & reticence the assembly of TNF ά and interleukin-Ib *in-vitro*.

The after-effects advance the antitoxin furnishings of *Lupeol* on DMBA promote DNA alkylation accident in Swiss bleached cowards an excision, cavity & asleep amplitude anguish beastly archetypal is a able bodied activated archetypal to abstraction anguish healing and associated mechanisms .It is an effective chemo preventive drug against skin toxicity [14]. Recent news indicates that many *Lupeol*-based anti-aging & anti-fungal peel creams are in improvement. *Lupeol* is an interesting drug used to improve the appearance of the skin & eliminate fungal infections [13, 14].

Anti-Diabetic Action of *Lupeol*: Diabetes mellitus frequently accepted as diabetes and an accumulation of metabolic affection that causes aerial claret amoroso akin beyond an abiding interval. There are two types of diabetes, type 1 & type 2. *Lupeol* appears to have anti-inflammatory properties. Many studies have shown that *Lupeol* has anti-hyperglycemic properties & its consumption may reduce the prospect of diabetes in animal imitation. Protein tyrosine phosphatase 1B (PTP1B) plays the above function inhibiting insulin activity [10]. Many researchers have demonstrated the effectiveness of *Lupeol* in ameliorating diabetes using diabetes models because the effects of *Lupeol* are achieved by eliminating carbohydrate assimilation in the intestine. *Lupeol* has activity similar to metformin and alters antioxidant enzymes [15]. *Lupeol* plant ingredient from Solanum nigrum prevents diabetes succeeding 21 days [16]. *Lupeol* additionally reduced glycated hemoglobin, serum glucose, and nitric oxide. Plants abstract of *Lupeol* reticence the claret glucose levels in streptozotocin (STZ)-induced diabetic rats [17]. *Lupeol* is also used for the analysis of diabetes which reticence the alpha-glycosidase activity [18]. *Lupeol* also reduces glycated hemoglobin, serum glucose, & nitric oxide [16].

Cardio-Protective Action of *Lupeol*: *Lupeol* antiquated advised for its cardioprotective abeyant in beastly accepting cyclophosphamide, a biologic acclimated in the analysis of blight and autoimmune disorders. Cyclophosphamide analysis (200 mg/kg for 10 days) was appear to decidedly abatement the action of ATPases & adapt the extend of urea, uric acerbic & creatinine in serum & urine of animals [19, 20]. Yet, *Lupeol* (50 mg/kg for 10 days) analysis was apparent to allow aegis adjoin cyclophosphamide-prompt cardiotoxicity in these mice [21, 22].

Hypercholesterolemia is appear to account astringent adulterated of the cardio-vascular arrangement *Lupeol* has been shown to have an anti-hypercholesterolemia effect in the first rat model of hypercholesterolemia in farm animals caused by air ingestion. Assay of *Lupeol* (50 mg/kg) in hypercholesterolemic animals (causing myocardial damage) is sufficient to alter the level of lysosomal hydrolases. The *Lupeol* assay also restores the level of lipoprotein and lipid components to their original state. Recently activated *Lupeol* has an antidyslipidemic effect in a hamster model of dyslipidemia. In this study, information about triglyceride, triglyceride & cholesterol levels were obtained by streptozotocin (100 mg/kg) analysis in hamsters. However, it is recommended that hamsters with dorsal dyslipidemia receive *Lupeol* (50 mg/kg) [9].

Hepato-protective Action of *Lupeol*: *Lupeol* has been advised for its hepatoprotective abeyant. A contempt abstraction manifest that *Lupeol* manage aegis adjoins aflatoxin B1, a pre-eminant hepatotoxic abettor back activated beneath in vivo

altitude [23]. Appealingly, the hepato-protective after upshot of *Lupeol* was apparent to exist added than silymarin, a acclaimed accustomed hepat-protective a better. *Lupeol* & *Lupeol*-wealthy mango extract have recently been shown to inhibit 7, 12-dimethylbenzo (a) anthracene (DMBA)-prompted alarm events in an injury imitation. Many studies have been directed estimate the effectiveness of *Lupeol* in increasing the maximum for liver disease [24].

Lupeol (50 mg/kg) analysis for 15 canicule decidedly relieve the alarmist action deformity & added begrimed elimination of cholesterol in hypercholesterolemia rats. Especially, *Lupeol* was appear to decidedly abet the extent of vitamin C and E in hypercholesterolemia animals. *Lupeol* decidedly alleviated adapted alarmist action by abating accustomed activities of lipid metabolizing enzymes. Another address area articulate administering of *Lupeol* (150 mg/kg/day) relived the metal-induced hepatotoxicity in a rat archetypal accurate the hepato-protective abeyant of *Lupeol* [9].

Nephro-protective Action of *Lupeol*: *Lupeol*'s effects are activated by its association with nephrotoxic & antiurolytic activity. *Lupeol* reduce calcium oxalate & has a cytoprotective effect by reducing events caused by free radicals. It also reduces cadmium in the kidneys, renal corpuscle pallor (RCC) & an epithelial branch of the adjacent tubular brain. *Lupeol* was studied in SKRC-45, an RCC cell line, & may affect auditory mitochondrial dynamics in RCC [25].

Lupeol may inhibit the apparent degradation of calcium, oxalate, & uric acid in the kidneys, may also reduce the absorption & release of inhibitors such as magnesium & glycosaminoglycans. *Lupeol* has been shown to prevent the development of hypercholesterolemia in animals prompted by give food to rats a high cholesterol diet (HCD) for 30 days. Hypercholesterolemia in HCD-compared rats was evident with an increase in free cholesterol, triglyceride & phospholipid levels in the kidneys, as well as an increase in tissue erosion & blood biochemical levels of kidney-type enzymes (lactate dehydrogenase and acid phosphatase) [9, 21, 22]. *Lupeol* has upshot on SKRC-45, an RCC cell line & has the prospective to inhibit RCC based on mitochondrial dynamics [9].

Biological Activity of *Lupeol* on Humans: Although these aloft analysis declared assorted Pharmacological activities of *Lupeol in-vitro* & *in-vivo* daily or subcutaneous studies of *Lupeol* alone were conducted to evaluate its potential in Basset or human melanomas and abscesses. *Lupeol* (0.75-1.5 mg per site) was injected locally into & Basset Hounds with random melanoma [28].

In cases I-III (injection of the metastatic site), the *Lupeol* caused dematerialization or disturbed the metastatic melanoma body (track in melanosomes) IV. In this case (first injection site), *Lupeol* triggered local dissolution of tissue. In cases V-VII, *Lupeol* an accessory ameliorative abettor was accumulated with hyperthermia & immunotherapy to amusement melanoma. They additionally begin that *Lupeol* aggregate promote dematerialization of metastatic melanoma cell. This abstraction assured that contemporary administering of *Lupeol* was acknowledged analysis in 6 out of 7 bassets with cancerous melanomas. Beside, *Lupeol* (10 mg/kg, sc) at assorted times afterwards anaplasty block bounded bump pro- gression (no bounded frequency) & abroad metastasis [28].

In addition, they additionally begin that aggregate with *Lupeol* & added another ameliorative method such as hyperthermia & blooming corpuscle analysis had the abeyant to prolong the activity amount & advance accomplished activity affection for basset adversity melanoma [29]. Consequently, they appropriate that *Lupeol* apperantly a atypical accessory analysis for articulate cancerous melanoma, and a college dosage &/or again bang of *Lupeol* become visible to be added able in alleviative the melanoma [25].

The present paper gives the dynamic information about *Lupeol* which is pentacyclic triterpenoid. *Lupeol* is found in various types of vegetables & fruits. *Lupeol* show beneficial action against life threatening disease like cancer, diabetes along with other disorder e.g. Inflammation, related to liver, kidney, & heart. The important point that must have to focus about *Lupeol* is that it shows its action with less cytotoxicity & less side effects. *Lupeol* not only use to treat disease but also show valuable action on whole biological system of humans.

The experimental work on *Lupeol* provides a platform for added preclinical research & clinical investigation to confirm the efficacy of *Lupeol*, one of two by single or in fusion with other treatments. Although *Lupeol* has a high bioavailability, the development of artificial corresponding may increase its efficacy & bioavailability. This is deriving from on a paper that showed artificial *Lupeol* derivatives to have higher pharmacological activity than *Lupeol* itself.

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