Review Article

Lupeol: Bioactive triterpenoid act as anti-inflammatory agent

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Abstract

Since the earliest times, herbs have been used for the treatment of human diseases. One of the chief bioactive compounds is lupeol, a phytosterol, and triterpene. It is widely found in fruit sources and vegetables. Many types of research have been done, and the researchers have reported numerous important pharmacological activities of lupeol. The preclinical studies of lupeol using a variety of in-vitro studies found that lupeol is a very potent bioactive compound. It can be used as an anti-inflammatory, anti-microbial, anti-protozoal, an antiproliferative, anti-invasive, anti-angiogenic cholesterol-lowering agent, and antioxidant. It is also using for wound healing, diabetes, cardiovascular disease, kidney disease, and arthritis treatment. This review especially covers all research work regarding anti-inflammatory action and summarized all the mechanism action regarding the anti-inflammatory action of lupeol. The inflammatory preventive prospects of lupeol and represented its potential anti-inflammatory drug targets. Some more research work needs to do and develop specific derivatives that would be the valuable drug anti-inflammatory. The potential derivatives of lupeol reduced the side effects of the marketed drug.

Keywords: Bioactive compounds, lupeol, phytosterol, triterpene, anti-inflammatory

Introduction

Since the earliest times, herbs have been used for the treatment of human diseases. One of the chief bioactive compounds is lupeol, a phytosterol, and triterpene. It is widely found in fruit sources and vegetables. A number of researches have been done, and the researchers have been reported several important pharmacological activities of lupeol such as an anti-inflammatory, anti-microbial, anti-protozoal, antiproliferative, anti-invasive, anti-angiogenic cholesterol-lowering agent, and antioxidant. It is also using for wound healing, diabetes, cardiovascular disease, kidney disease, and arthritis treatment. The lupeol is found mainly from the surface of plant barks, stems, leaves, and fruit waxes. The research explored oak leaves of a number of species like Quercus robur, Q. [illegible], Q. ilex and Q. [illegible] as a potential herbal source of lupeol. It was extracted and isolated from Quercus leaves using maceration with $CHCl_3$ at room temperature, after isolated by using silica column (normal phase), and were using as mobile phase hexane (100%), hexane: ethyl acetate (90:10) and hexane: ethyl acetate (80:20) respectively. Lupeol in oak leaves was identified by 13C NMR and quantified by GC-MS. Quercus [illegible] leaves were an abundant source of lupeol. The Pimenta racemosa var. ozua (Myrtaceae) is a tropical herbal plant. It is traditionally used in different inflammatory processes in Caribbean region. The methanol extract of the leaves, were found a terpenic compound that is identified as lupeol. It has been isolated for the first time using these species. The anti-cyclooxygenase activity has been used for determining the bioactivity of lupeol in this research (Garcia et al., 2013).

Herbal sources of lupeol

The *Angelonia angustifolia* Benth. is a small herbaceous herbal plant. This plant is traditionally used as an anti-

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inflammatory remedy by indigenous cultures in Latin America area. It is also used as a ornamental plant. The researchers have been found a major chemical constituent of this plant is lupeol that is present in large quantities in the aerial structures of the plant. The lupeol modulates the expression or activity of several molecules such as cytokines IL-2, IL-4, IL-5, IL-β, proteases, α-glucosidase, cFLIP, Bcl-2, and NFκB. lupeol and its mechanisms of action (Siddique et al., 2011; Bonner et al., 2009).

Reported research works:

They were investigated anti-inflammatory, antinociceptive, antipyretic and ulcerogenic properties, and compare with non-steroidal anti-inflammatory drug such indomethacin. They were found that Lupeol, lupeol linoleate, and indomethacin showed a reduction in paw swelling significantly than indomethacin drugs. They revealed that lupeol was not shown off any antinociceptive, antipyretic, and ulcerogenic actions. They concluded that the mechanism of action of triterpenes is different from the non-steroidal anti-inflammatory indomethacin drug (Geetha et al., 2001).

The methanol leaves extract of Pimenta racemosa var. ozua having lupeol. It is effective against acute inflammation actions by oral route, and when topically applied. The anti-inflammatory property of the plant extract was found to similar to that exhibited by the selective cyclo-oxygenase inhibitor, compare than indomethacin. On the other hand, the decline of myeloperoxidase (MPO) activity shows that the action mechanism. It is related to the neutrophil migration (Fernandez 2001). The amount of lupeol in the roots of A. angustifolia herbal plant significantly. It is a significant reduction of inflammation of the skin. The presence of topically therapeutic levels of lupeol in A. angustifolia is due to the presence of bioactive molecule lupeol. (Devyap et al., 2014).

Inflammatory bowel disease (IBD)

The most common chronic disease of the bowel is inflammatory bowel disease (IBD). It is including ulcerative colitis and Crohn's disease and is a chronic inflammatory disease found in the lower gastrointestinal tract. They reported that the predominance of the classically activated (M1) macrophages versus the alternatively activated (M2) macrophages. It plays a role in the development of inflammatory bowel disease (IBD). The pentacyclic triterpene lupeol is a potent anti-inflammatory natural product, against bowel disease without side effects. The lupeol has been shown to potentially inhibit pro-inflammatory cytokine production. Researchers suggested lupeol can modulate macrophage polarization, thereby beneficial to IBD (Zhu et al., 2016). Lupeol bioactive compounds also inhibited LPS-induced IκBα phosphorylation degradation and the DNA binding activity of NF-κB. The oral administration of lupeol drastically decreased the colitis activity and histologic scores in both acute and chronic murine colitis models. The lupeol blocks the NF-κB signaling in DCs and murine macrophages, and attenuate experimental murine colitis. These all results of data represented that lupeol is a potential therapeutic agent for inflammatory bowel disease (Lee et al., 2016). A series of heterocyclic derivatives of lupeol have been developed that are including oxlates, pyrazines along with amines and esters. They were evaluated for anti-inflammatory activity. Lupeol inhibits lipopolysaccharide (LPS) induced nitric oxide (NO) production using RAW 264.7 and J774A.1 cells. These findings suggest that the derivatives of lupeol could be a lead to potent inhibitors of NO (Shinde et al., 2014).

The lupeol is having low water solubility property. Many researchers have been developed an alternative formulation to increase the water solubility of lupeol using nanotechnology. Several methods for the development of nanosized particles such as emulsification-solvent-evaporation, and size distribution, etc (Ramirez et al., 2013). The bioactive molecule lupeol is also used as a nutraceutical without damaging wild populations. (Devyap et al., 2014).

Two pentacyclic triterpenes, namely lupeol and lupeol linoleate, were investigated for their anti-inflammatory, antinociceptive, antipyretic, and ulcerogenic properties (Geetha et al., 2001). The good source of lupeol is A. annamita over other herbal sources. It is due to its wild variety and ability to grow throughout the year. The A. annamita can be used cheaply and easily available as a source for the lupeol (Langhorst et al., 2013). These results indicated that lupenone, lupeol, and ethanolic extracts of Adenophora triphylla var. japonica. It regulates the production and gene expression of mucin, by directly acting on airway epithelial cells. They confirm that the Adenophora triphylla var. japonica is a traditional remedy for diverse inflammatory pulmonary diseases (Yoon et al., 2015).

Antiulcer activity and anti-inflammatory activity

Many researchers reported that the esters derivatives of lupeol possess better antiulcer activity as compared to the lupeol bioactive compound. They were recommended that lupeol skeleton having potential activity need further investigation for the development of more potent and without toxic new antiulcer agents for beneficial use (Lakshmi et al., 2014). Lupeol bioactive compounds have been reported for the better management of viper venom-induced long-term tissue destruction (Katkar et al., 2015).

The lupeol has novel anti-proliferative and apoptotic potential that may help design strategies to fight skin cancer (Nigam et al., 2009).

Significantly, lupeol at its efficient therapeutic doses shows no toxicity to usual cells and tissues. The utility of Lupeol is as a therapeutic and chemopreventive agent for the treatment and management of inflammation (Saleem et al., 2009). They were found that lupeol linoleate appeared to be even more effective than lupeol. The triterpene lupeol and its linoleate ester in ameliorating (Sudhahar et al., 2007). The lupeol, a triterpene bioactive compound was showing beneficial effects as a therapeutic and preventive agent for various disorders. Many studies have been confirmed that lupeol possesses strong activities such as antioxidative, anti-inflammatory, antiarthritic, antimutagenic, and antimalarial, both in vitro and in vivo, and at its effective therapeutic doses exhibit no toxicity to normal cells and tissues (Wu et al., 2013). The derivatives of lupeol regulate the production and gene expression of mucin, by directly acting on airway epithelial cells. In addition, the results of experiments represented the mechanism of Adenophora triphylla var. japonica. It is traditionally used for the treatment of inflammatory pulmonary diseases (Yong Pil Yoon, 2011).

Mechanism of action of lupeol

1. Anti-cyclooxygenase activity has been used for determining bioactivity of lupeol in this research.

2. The reduction of MPO activity.

3. It is potentially able to modulate macrophage polarization, thereby beneficial to IBD due to inhibiting (Microphages) M1 and promoting (Microphages)M2 macrophages.

4. Cytokine production in IECs and murine macrophages. It also inhibited LPS-induced IκBα phosphorylation degradation and the DNA binding activity of NF- κB. The oral administration of lupeol significantly reduced this cellular activity.

5. Inhibition of lipopolysaccharide (LPS) induced nitric oxide (NO) production.

Conclusion

The lupeol is a triterpene phytosterol, which is usually found in edible fruits, and vegetable sources. The various studies concluded that lupeol has a potential bioactive compound, and it acts as an anti-inflammatory, anti-microbial, anti-protozoal, antiproliferative, anti-invasive, anti-angiogenic, and cholesterol-lowering agent. Anti-cyclooxygenase activity has been used for determining the bioactivity of lupeol in this research. The basic mechanism behind anti-inflammatory action is the reduction of MPO activity, potentially able to modulate macrophage polarization, inhibiting (Microphages)M1 and promoting (Microphages)M2 macrophages, inhibited LPS-induced IκBα phosphorylation degradation and the DNA binding activity of NF- κB and Inhibition of lipopolysaccharide (LPS) induced nitric oxide (NO) production. This mini-review discusses in detail the preclinical studies conducted with lupeol and provides an insight into its mechanisms of action on anti-inflammatory action. It could be used for many other diseases.

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