Original Research Article

A Brief Review On Anti-Inflammatory And Anti-Urolithic Effect Of Citrus Medica

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Abstract:
Citrus medica, commonly known as lemon or Buddha's hand, is a fruit plant with a long history in medicine and cultivation. This review will give an overview of the various activities associated with Citrus medica and highlights its medicinal and cultural importance. Plants exhibit many biological activities including antioxidant, antibacterial, anti-inflammatory properties. This review will provide brief summary about its chemical constituents and their pharmacological action. Citrus medica have about 16 chemical constituents like phenolics, vitamin C, flavonoids, linalool, decanal, nonanal, and pectin, responsible for various pharmacological actions includes anti-inflammatory and urolithiasis.[1][2]

INTRODUCTION:

Here we take the 2 disease anti-inflammatory and urolithiasis. Anti-inflammatory is the activity that used in the treatment of inflammation.

Inflammatory The Greek word for inflammation, phlogosis, was derived from the Latin flamma, which means fire, and was used to describe the most complicated human expressions of the phenomena as a defense mechanism against harm or aggression1. Galen (3rd century AD) and John Hunter (1794), an English physician of the 18th century, both identified this occurrence as the body's response to injury.[3]

This disease is a general term for many medical conditions caused by inflammation, the body's response to injury, infection, or lack of stimuli. Inflammation is a complex biological process that involves the activation of the immune system and the release of numerous signaling molecules. Inflammation is an important and important part of the body's defense mechanisms, but chronic pain or excessive inflammation can lead to many diseases.[4]

Urolithiasis, commonly known as kidney stones, is the formation of stones and salts in the urine. These stones can appear anywhere in the urinary tract, including the kidneys, ureters, bladder, and

urethra. The third most common condition of the urinary system, affecting 2-3% of the general population, is urolithiasis. If left untreated, urinary calculi can have catastrophic health effects such severe blockage, hydronephrosis, infection, and urinary tract bleeding.Common methods for removing calculi include surgery, lithotripsy, and local calculus disruption with a high-power laser. However, there is a chance that these operations will cause an acute renal damage, which will reduce renal function. Additionally, a rise in stone recurrence is seen. A viable alternative therapy must be developed because the recurrence rate without preventative treatment is roughly 10% after the first year, 33% after the fifth year, and 50% after the tenth year.

Stones can vary in size and composition and can cause severe pain and discomfort when passing through urine.The most common type of stone is the calcium stone, which is made up of calcium oxalate or calcium phosphate. Other types include uric acid stones, formed by excess uric acid in the urine, and struvite stones, which can appear in response to an infection of the urinary system. Cystine stones are rare and are caused by a genetic condition in which the amino acid cystine builds up in the urine. Symptoms of urolithiasis range from mild to severe and can include:

Pain: The most common symptom is severe pain, often called renal colic, which occurs when the stone moves and blocks urine. The pain usually starts in the back or side and can spread to the abdomen and groin. Hematuria: Blood in the urine is a common symptom of urinary tract irritation caused by stones.

Frequency of urination: Some people may experience increased urination, as well as pain or discomfort when urinating.

Nausea and vomiting: Pain accompanied by kidney stones can cause nausea and vomiting.

Urinary tract infections: Stones can cause urinary tract infections by creating a favorable environment for bacteria to grow. Diagnosis of urolithiasis is usually made by a combination of history, physical examination, and imaging such as ultrasound, CT scan, or x-rays. The choice of treatment depends on the size and location of the stone as well as the severity of the symptoms. Smaller stones may go away quickly with increased fluids and pain management, but larger stones may require medical attention.[5]

Citrus medica, commonly known as lemon, is a large, aromatic citrus fruit from the Rutaceae family. It is one of the earliest types of citrus fruit from which many other citrus fruits have been derived by hybridization and cultivation. This fruit is believed to have originated in Southeast Asia and is now cultivated in many parts of the world for culinary and medicinal purposes.

Citrus medica

Keyfeatures of Citrus Medica include:
Symptoms: Lemon fruit is large and irregular, usually lumpy or thick and rough. The color of the skin varies from green to yellow depending on the degree of maturity.

Medicinal Uses: Lemon is used in traditional medicine for its health benefits. It is sometimes used for its digestion and the prevention of nausea. However, scientific research on these benefits is limited. Religious and Cultural Significance: Yuzu has religious and cultural significance in many cultures. For example, it is one of the four bells used during the Jewish holiday of Sukkot and is important in Hinduism and Buddhism. Scent: The essential oil extracted from the scent of citron is used in perfumery for its pleasant and refreshing scent.

Important History: Yuzu has a long history and is considered one of the oldest citrus fruits. It has been cultivated and traded for centuries, contributing to the development of other citrus cultivars.

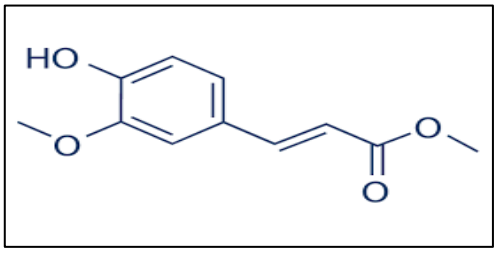
Scientific classification:-[6]

Domain:	Eukaryote
Kingdom:	Citrus
Class:	Dicotyledons
Order:	Sapindales
Family:	Rutaceae
Genus:	Citrus L.
Species:	C. medica
Biological source:	Part of citron fruit

Citrus medica is made up of 16 chemical constituents like :-
1.Methyl ferulic acid
2.Dihydro-N-caffeoyltyramine
3.Acacetin
4. β-ecdysterone
5. (-)-balanophonin
6. p-methoxy cinnamic acid
7. umbelliferone
8. ferulic acid
9. procatechualdehyde
10.Diosmetin
11. 4-methoxy salicylic acid
12. β-amyrin acetate
13. epigallocatechin
14. betulinic acid
15. lupeol
16. nicotinamide [7]

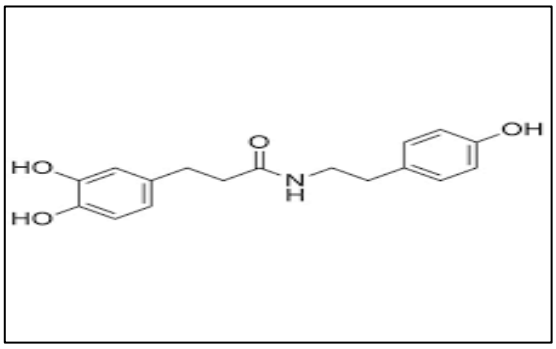
Chemicals and Activity:-

1.Methyl ferulic acid:-



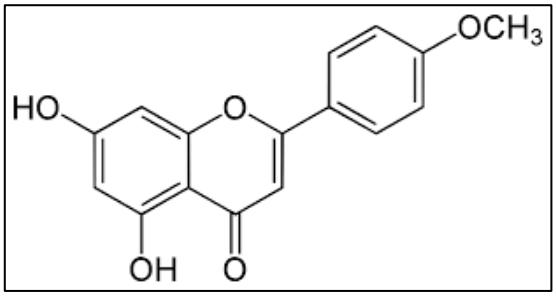
Due to its antioxidant properties, ferulic acid has an anti-urolithiatic action by decreasing the oxidative stress caused by ethylene glycol, which in turn prevents the development of renal calculi.
According to research, antioxidants from plants have the potential to be used as anti-urolithiatic drugs to treat kidney stone development and recurrence after surgery . This study examined the ability of ferulic acid to prevent the formation of renal calculi in rats after exposure to ethylene glycol. Renal calculi made of calcium oxalate crystals develop in a rat model of ethylene glycol-induced urolithiasis.
The effects of plant-derived antioxidants on urolithiasis models' urine and serum levels of calcium, magnesium, oxalate, pH, uric acid, urea, and creatinine have been previously described. The findings that ferulic acid was able to prevent the development of renal calculi by changing these broad factors are consistent with this. Inflammation of the kidney brought on by the harmful effects of toxicants is another cause of urolithiasis . Due to its anti-inflammatory effects, ferulic acid stopped the inflammatory process, decreasing the likelihood of renal calculi development. [8]

2. Dihydro-N-caffeoyltyramine:-



A new phenolic amide called dihydro-N-caffeoyltyramine (DHCT) was discovered in the root bark of Lycium chinense Miller. In the current work, we looked at how DHCT affected macrophages' expression of the pro-inflammatory enzyme cyclooxygenase (COX-2) that is produced by the hormone phorbol 12-myristate 13-acetate (PMA). Treatment with DHCT prevented COX-2 mRNA and protein from being induced by PMA.[9]

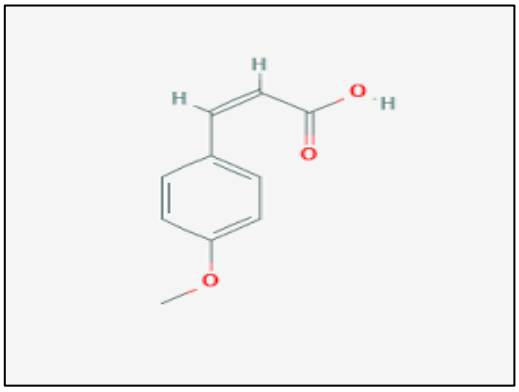
3.Acacetin:-



Systemic administration of acacetin decreased visceral and inflammatory nociception and prevented the formalin-induced oedema. In the mechanism of the acacetin antinociceptive effect, 5-HT1A, GABA/BDZs and opioid receptors but not the NO-cGMP-K+ channel pathway seem to be involved. The data presented prove acacetin to be potentially useful in the therapy of pain-related diseases.[10]

Acacetin's anti-inflammatory action, which could increase the expression of specific critical AOEs and inactivate the NF-B signaling pathway in our in vivo model, was the main mediator of its protective impact against sepsis-induced ALI.[11]

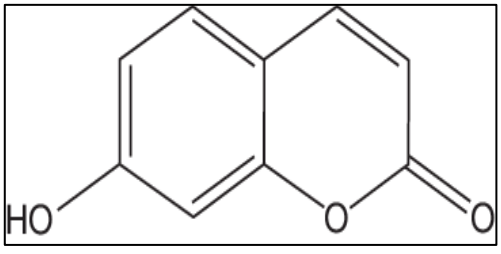
4. p-methoxy cinnamic acid:-



Malonic acid and various benzaldehyde derivatives were combined in a Knoevenagel condensation process with pyridine and hydrochloric acid to create various cinnamic acid derivatives. Raney nickel and 10% KOH, respectively, produced para methoxy-cinnamic acid. By using petroleum spirit/ethyl acetate to elute, column chromatography (CC) was used to purify the final products.

Para-methoxy-cinnamic acid at the second hour with 2 mg/kg dose level produced 54.0% inhibition of inflammation.[12]

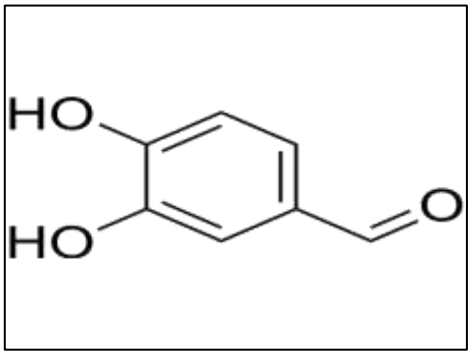
5. Umbelliferone:-



Umbelliferone, a key anti-inflammatory component of A. decursiva, exerts its anti-inflammatory effects by blocking the NF-B activation pathway, which in turn prevents the synthesis of inflammatory mediators.[13]

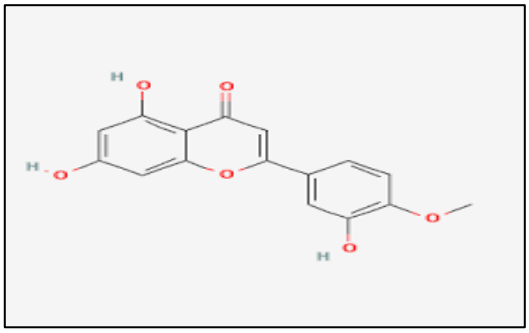
An inflammatory response is characterized by the expressing of a number of pro-inflammatory mediator genes. Therefore, Anti-inflammatory activity of umbelliferone was monitored by evaluating the gene level of inflammatory related enzyme like iNOS and COX-2, Cytokines.[14]

6.Protoctechualdehyde:-



Protocatechualdehyde is a phenolic aldehyde.[15] Chronic kidney disease progresses due to the aggravation of tubulointerstitial fibrosis (TIF) caused by accumulation of fibrosis products and persistent chronic inflammation. The objective of this research was to examine the impact of protocatechualdehyde (PCA), a naturally occurring phenolic acid compound that was extracted from Citrus medica, on the fibrosis and inflammation caused by unilateral ureteral obstruction (UUO) and to clarify the underlying mechanism in primary renal tubular epithelial cells (TECs).[16]

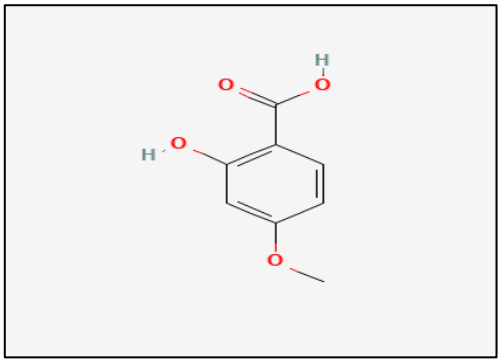
7.Diosmetin:-



Citrus fruits naturally contain diosmetin (3', 5, 7-trihydroxy-4'-methoxyflavone), the aglycone portion of flavonoid glycosides diosmin.[17] Diosmetin's anti-inflammatory properties in atopic dermatitis. In DNCB-induced atopic dermatitis, diosmetin reduces the quantity of mast cells, macrophage infiltration, and cytokine activation. Diosmetin suppresses NO generation and iNOS expression in activated macrophagy induced by IL-4 and LPS. It also inhibits the activation of the JAK/STAT and MAP kinase pathway.[18]

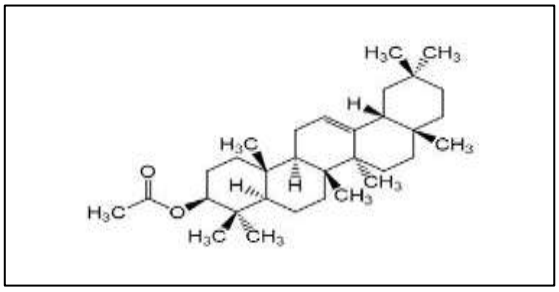
Diosmetin has a protective mechanisam against kidney stone. Examined diosmin's effects (at 2.5–160 nM) on the several stages of kidney stone formation processes, such as COM crystallization, growth, aggregation, adhesion between crystals and cells, internalization into renal tubular cells, and extracellular matrix (ECM) invasion.[19]

8.4-Methoxy salicylic acid:-



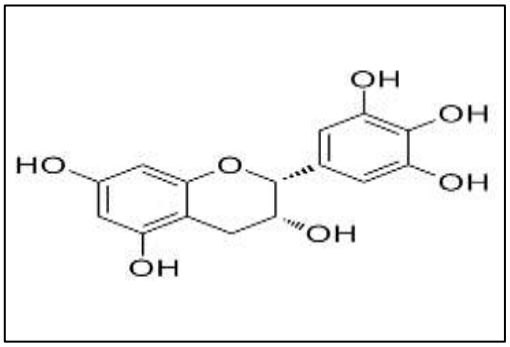
Salicylic acid is the compound that gives aspirin its anti-inflammatory properties. Their therapeutic effects are believed to be mediated via a variety of pathways, such as direct activation of AMPK, regulation of NF-κB activity, and inhibition of cyclo-oxygenases.[20]

9.β-amyrin acetate:-



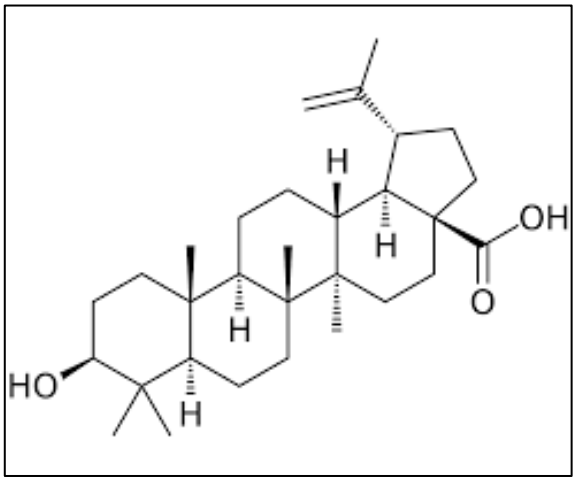
The treatment of β-amyrin resulted in a significant decrease in edema in a dose-dependent manner. In rats, paw edema caused by carrageenan exhibited 97% reduction when 100 µg of β-amyrin was administered.[21]β-amyrin might act as an ideal anti-inflammatory agent to halt the progression of liver fibrosis to chronicity.[22]

10. epigallocatechin:-



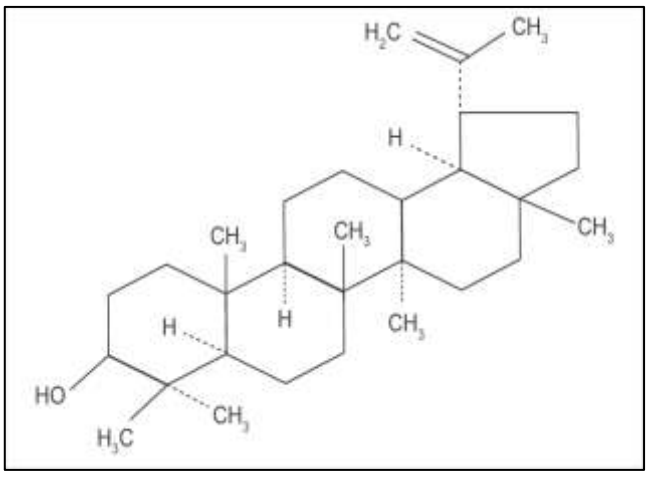
Additionally, epigallocatechin reduces the stimulus's cytotoxic effect and downregulates a significant amount of common pro-inflammatory cytokines, both of which are essential for the continuation of ID.[23] After replacing the microscale particle-loaded medium with fresh medium, the expression levels of TNF-α, IL-1β, and IL-6 were measured at 24 hours and 8 hours to evaluate the anti-inflammatory effects of EGCG-loaded microparticles on LPS-treated fibroblasts.[24]
When quercetin was combined with EGCG, the reversal was more powerful. Further research is required to determine the precise mechanism of action and additional tissue expression that could be useful in the future for creating this as a possible kidney stone treatment plan.[25]

11.Betulinic acid:-



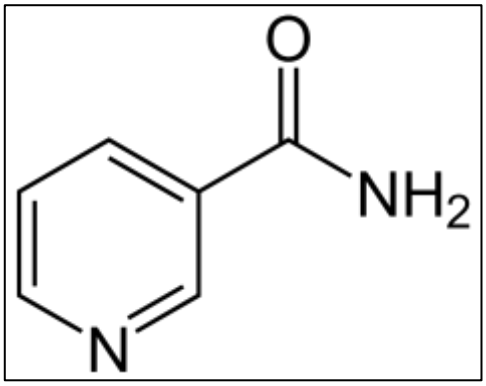
In vitro and in vivo studies using various disease models demonstrated the versatility of betulinic acid in modulating several important mediators in the inflammatory process, such as COX-2, ICAM-1, IL-1β, IL-6, IL-12, MCP-1, PGE2, and TNF. Betulinic acid is a pentacyclic triterpene of the lupane type that may be the starting point for the creation of novel anti-inflammatory drugs.[26]
Betulinic acid used in combination with quercetin for anti urolithic activity in cunjuction with io enhancer.[27] Giving pentacyclic triterpenes to rats with hyperoxaluria, such as lupeol and its structural counterpart betulin, minimized tubular damage and decreased kidney crystal deposition indicators.[28]

12.Lupeol:-



The anti-inflammatory properties of lupeol were probably due to its capacity to inhibit the synthesis of certain pro-inflammatory mediators.[29] Lupeol can reduce inflammation by preventing cytokine release and related pathway regulation, preventing ROS production, controlling the redox balance, and controlling related.[30]
Lupeol's antiurolithiatic activity was evaluated in rats using weight measurement of the stone, urine and serum biochemical analysis, and renal and bladder histology. Lupeol decreased the size of the prepared stones in addition to preventing the development of vesical calculi.[31]

13.Nicotinamide:-



Nicotinamide has the ability to significantly suppress the proinflammatory cytokine response of IL-1β, IL-6, IL-8, and TNFα after endotoxin stimulation of human whole blood, suggesting that it may have therapeutic value as a modulator of cytokine effects in inflammatory disease.[32] RSV and nicotinamide's synergistic effect on PARP1 activation could offer a possible treatment approach for inflammatory illnesses.[33]

CONCLUSION:-

As *citrus medica* have so many medicinal values and considers as one of the most important herbs for treatment of kidney stone along with ease in pain and inflammation in urinary tract. So this article had summarise the chemical constituents which are responsible for this dual property and effectiveness of herb as anti-inflammatory and anti-urolithic. So this can provide the guideline for preparation of effective medicine which can treat the problem in effective manner and will not have any toxic side effects like allopathy medicines as it is believed that this can treat it from the root.

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