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Recent updates on Phytoceuticals used in Pancreatitis

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ABSTRACT

Pancreatitis is a disease in which the pancreas becomes inflamed. Pancreatic damage happens when the digestive enzymes are activated before they are released into the small intestine and begin attacking the pancreas. There are two forms of pancreatitis: acute and chronic. Of the many causes of pancreatitis, the most common are alcohol consumption and gallstones. Medicinal plants have essential role in Pancreatitis. This review focuses the various medicinal plants and their phyo-active constituent effect against pancreatitis.

Keywords: Pancreatitis, Medicinal plants, Phytoceuticals & Traditional uses.

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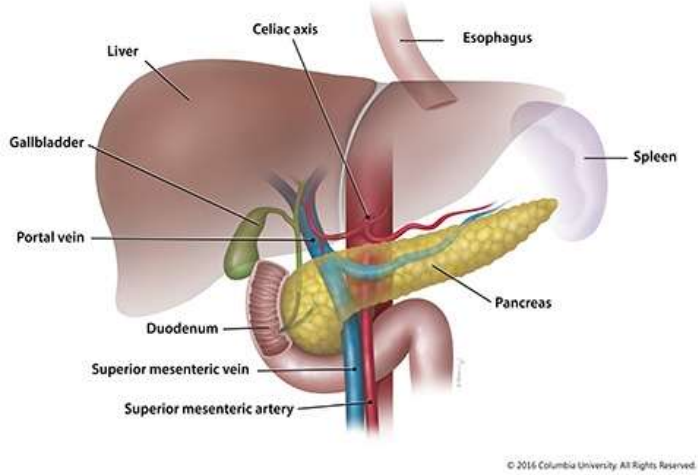
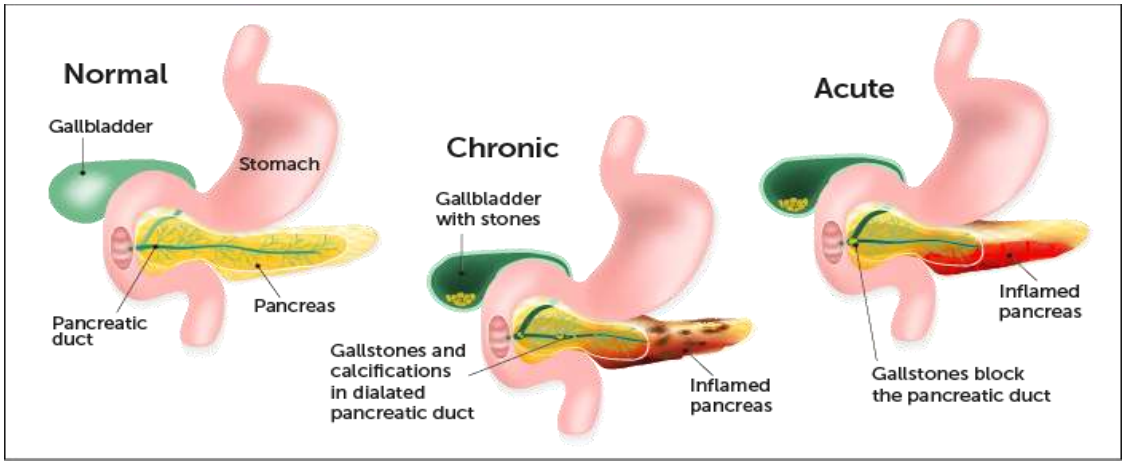
INTRODUCTION

The pancreas is about 6 inches long and sits across the back of the abdomen, behind the stomach. The head of the pancreas is on the right side of the abdomen and is connected to the duodenum (the first section of the small intestine) through a small tube called the pancreatic duct. The narrow end of the pancreas, called the tail, extends to the left side of the body[1]. The pancreas is a large gland behind the stomach and next to the small intestine. The pancreas does two main functions. It releases powerful digestive enzymes into the small intestine to aid the digestion of food. It releases the hormones insulin and glucagon into the bloodstream. These hormones help the body control how it uses food for energy.



Pancreatitis is a disease in which the pancreas becomes inflamed. Pancreatic damage happens when the digestive enzymes are activated before they are released into the small intestine and begin attacking the pancreas. There are two forms of pancreatitis: acute and chronic. Acute pancreatitis is an acute inflammatory disorder of the pancreas caused by an intracellular activation of pancreatic digestive enzymes. The destruction of pancreatic parenchyma induces a systemic activation of coagulation, kinin, complement and fibrinolytic cascades with liberation of cytokines and reactive oxygen metabolites which, if severe and overwhelming, can lead to shock, acute renal failure and the acute respiratory distress syndrome. In approximately 45% of cases the disorder is associated with cholelithiasis, with ethanol abuse accounting for a further 35% of patients. In 10% of patients no cause may be found. In severe cases, acute pancreatitis can result in bleeding into the gland, serious tissue damage, infection, and cyst formation. Severe pancreatitis can also harm other vital organs such as the heart, lungs, and kidneys[2-3].



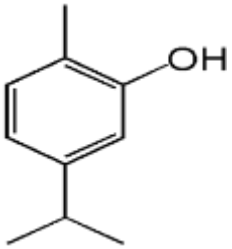
Pancreatitis

Symptoms of Pancreatitis	
Acute pancreatitis	**Chronic pancreatitis**
Upper abdominal pain, Abdominal pain that radiates to your back, Abdominal pain that feels worse after eating, Fever, Rapid pulse, Nausea, Vomiting, Tenderness when touching the abdomen	Upper abdominal pain, Losing weight without trying & Oily, smelly stools (steatorrhea).

Pharmacological activity of medicinal plants is often known as a result of millennia of trial and error but they have to be carefully investigated if we wish to develop new drug that meet the criteria of modern treatment. Since time immemorial man has used various parts of plants in the treatment and prevention of many ailments. Historically all medicinal preparations were derived from plants, whether in the simple form of plant parts or in the more complex form of crude extracts, mixtures, etc. Today a substantial number of drugs are developed from plants which are active against a number of diseases. The majority of these involve the isolation of the active ingredient (chemical compound) found in a particular medicinal plant and its subsequent modification. In the developed countries 25 percent of the medical drugs are based on plants and their derivatives and the use of medicinal plants is well known among the indigenous people in rural areas of many developing countries[4].

Various medicinal plants and their Phytoceuticals used against Pancreatitis

Carvacrol (5-isopropyl-2-methylphenol) is a biologically active monoterpene phenol abundantly present in the essential oils of many Lamiaceae aromatic/ethnomedicinal plants.



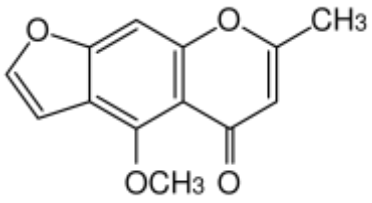
The toxic and beneficial (in a dose of 10 mg/kg) properties of carvacrol were assessed by measuring serum α-amylase and lipase activities, tissue malondialdehyde (MDA) content, and pathohistological changes in pancreatic tissue[5].

Euphorbia kansui is a well-known traditional Chinese medicine.

Euphorbia kansui is a Traditional Chinese Medicine widely used for the treatment of oedema, ascites and asthma. However, its serious hepatotoxicity hinders its safe clinical application[6]. Effects of euphorbia kansui on serum levels of inflammatory factors in patients with severe acute pancreatitis were investigated, and the mechanisms underlying the role of Euphorbia kansui in the treatment of severe acute pancreatitis. According to the experimental results, euphorbia kansui effectively reduced the expression of inflammation related cytokines, such as NF-κB, TNF-α, sTNFR, IL-6, and IL-8, in the serum of patients with severe acute pancreatitis. It was also proposed that euphorbia kansui slowed down the release of inflammatory factors and treated SAP by inhibiting the activation of the NF-κB signaling pathway[7].

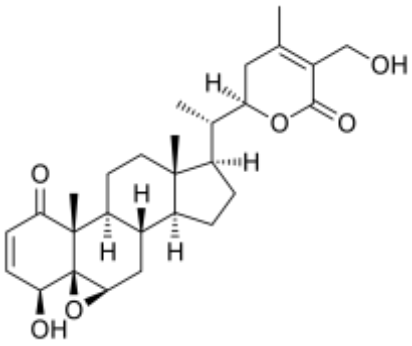
Ammi visnaga belongs to the family Apiaceae and it is a herbaceous medicinal plant. Many times, *A. visnaga* is weed as well as used in many countries as herbal medicine for different purposes. Ancient records reveal various medicinal properties of A. visnaga as a popular source to cure variety of different ailments. The plant is used directly as a herb or as a component for production of a number of herbal medicines used in the cure of renal colic, ureteric stones, angina pectoris, the coronary vessels, cardiovascular disorders and asthma. Also it is used as a folk medicine for vitiligo and psoriasis[8].

Visnagin is an organic chemical compound with the molecular formula $C_{13}H_{10}O_4$ It is a furanochromone, a compound derivative of chromone (1,4-benzopyrone) and furan.



The studied was carried on vasnagin against acute pancreatitis(AP). Visnagin mid dose (30 mg/kg), visnagin high dose (60 mg/kg) and visnagin control (60 mg/kg). AP was induced by six injections of cerulein (50 μg/kg, i.p.) on the 7th day and the animals were sacrificed after 6 h of last cerulein dose. Visnagin was found to be effective in reducing plasma amylase and lipase levels, reduced cerulein induced oxidative stress. Visnagin dose dependently decreased the expression of IL-1β, IL-6, TNF-α and IL-17. Above findings indicate that visnagin has substantial potential to prevent cerulein induced AP[9].

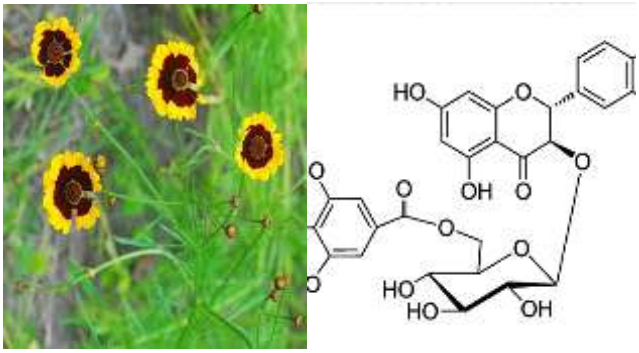
Withaferin A (WA) isolated from *Withania somnifera* (Ashwagandha) has recently become an attractive phytochemical under investigation in various preclinical studies for treatment of different cancer types[10].



Withaferin A

This study was carried out Withaferin A (WFA) against Cerulein-induced acute pancreatitis in mice. Increased levels of MDA, NO, and expression of myeloperoxidase and nitrotyrosine in the parameters estimated add evidence to the role of oxidative stress and inflammation in acute pancreatitis. WFA evidently altered these conditions upon pretreatment. The result revealed that this novel steroidal compound has potent anti-inflammatory property. Natural compounds can therefore be good remedies against many diseases if incorporated in routine diet as dietary supplement[11].

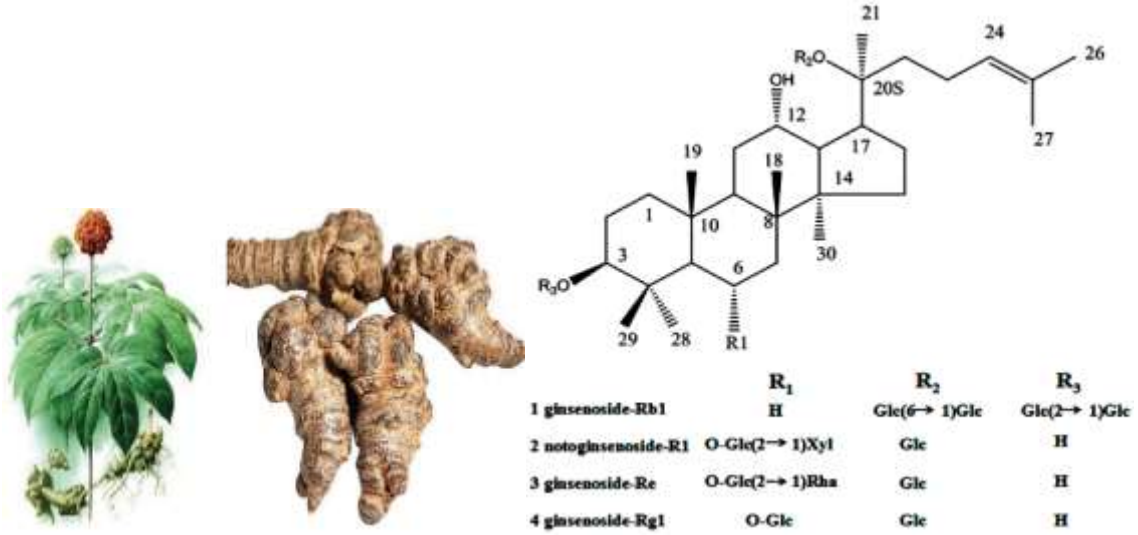
Coreopsis tinctoria (Asteraceae) occurs only in North America and certain provinces of China Flowers of this plant are widely used in folk medicine for diabetes, hypertonia, hyperlipidemia , coronary disease , and as an agent for insomnia, an anti-inflammatory, and a natural antioxidant[12.]



(2 R,3 R)-taxifolin7-O-β-D-glucopyranoside

The effects of flavonoids isolated from *C. tinctoria* on experimental AP and explore the potential mechanism was carried out. A flavonoid was intraperitoneally administered at 0, 4, and 8 h after the first caerulein injection or post-operation. Disease severity, oxidative stress and antioxidant markers were determined. The result reveal that the total flavonoids extract and flavonoids 1-6 (C1-C6) exhibited different capacities in reducing necrotic cell death pathway activation with 0.5 mM C1, (2 R,3 R)-taxifolin 7-O-β-D-glucopyranoside, having the best effect. C1 also significantly reduced NaT-induced ROS production and ATP depletion. C1 at 12.5 mg/kg and 8.7 mg/kg (equivalent to 12.5 mg/kg for mice) significantly reduced histopathological, biochemical and immunological parameters in the caerulein-, TLCS- and NaT-induced AP models, respectively. C1 administration increased pancreatic nuclear factor erythroid 2-related factor 2 (Nrf2) and Nrf2-medicated haeme oxygenase-1 expression and elevated pancreatic antioxidant enzymes superoxide dismutase and glutathione peroxidase levels[13].

Panax notoginseng (Burk) F. H. Chen, as traditional Chinese medicine, has a long history of high clinical value, such as anti-inflammatory, anti-oxidation, inhibition of platelet aggregation, regulation of blood glucose and blood pressure, inhibition of neuronal apoptosis, and neuronal protection, and its main ingredients are Panax notoginseng saponins (PNS). Currently, Panax notoginseng (Burk) F. H. Chen may improve mental function, have anti-insomnia and anti-depression effects, alleviate anxiety, and decrease neural network excitation[14].

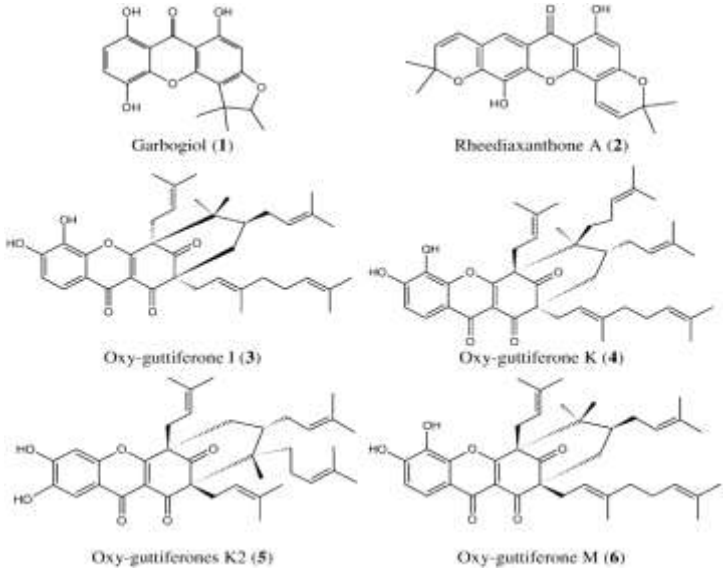


	R_1	R_2	R_3
1 ginsenoside-Rb1	H	Glc(6→1)Glc	Glc(2→1)Glc
2 notoginsenoside-R1	O-Glc(2→1)Xyl	Glc	H
3 ginsenoside-Re	O-Glc(2→1)Rha	Glc	H
4 ginsenoside-Rg1	O-Glc	Glc	H

Panax notoginseng saponins

The study was carried out to assess the protection effects of Panax notoginseng saponins in the taurocholate-induced rat model of acute pancreatitis (AP) and explore underlying mechanisms. The outcome of study showed that Panax notoginseng saponins significantly reduced taurocholate-induced pancreas injury and autophagy and increased apoptosis. The significant protection effects of Panax notoginseng saponins suggested its potential in treating taurocholate induced-acute pancreatitis[15].

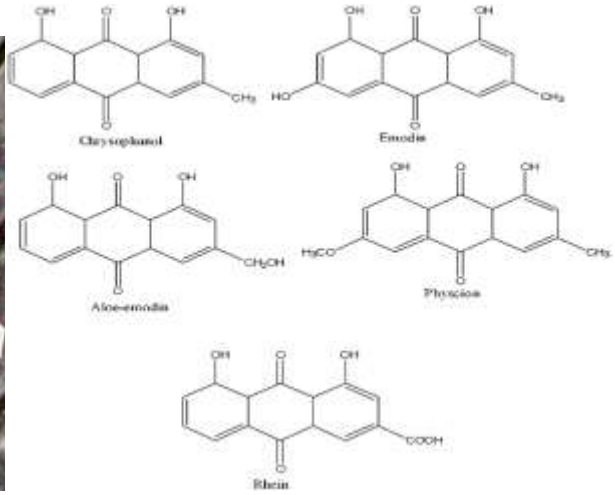
Garcinia cambogia The parts of the plant Garcinia cambogia commonly known as Malabar tamarind, have been used by many Asian countries in traditional medicine for treating intestinal parasites, constipation, cancer, piles, bowel complaints, rheumatism, edema, delayed menstruation, demulcent, bilious affections and other diseases. The root contains the xanthone called garbogiol. The bark of the stem contains benzophenones such as garcinol and isogarcinol. Malabar tamarind is shown to possess antioxidant, antihelmintic, anticattarhal, anti-cancer and antimicrobial activities. The rind of the fruit is the most extensively studied part of the plant. Hydroxycitric acid, the most abundant constituent of the fruit rind apart from the other constituents, has reported to be the active principle for many of its useful properties[16].



The study was carried out by Bystrak *etal* on Garcinia Cambogia against Diabetic Ketoacidosis, and Pancreatitis. The bioactive present in plant showed significant effect on AP[17].

Rhubarb

Rheum emodi or Himalayan rhubarb is a perennial herb belongs to family Polygonaceae. It has been used in various traditional systems as laxative, tonic, diuretic and to treat fever, cough, indigestion, menstrual disorder since ancient times. Rheum emodi possess a number of phytoconstituents and these are: anthraquinones, anthrones, stilbenes, oxanthrone ethers and esters, flavonoids, lignans, phenols, carbohydrate and oxalic acid . The most common constituents of Rheum emodi are anthraquinone and stilbene[18].



The therapeutic effect of rhubarb extract on acute pancreatitis was investigated. The serum AMY and TNF-α levels increased in acute pancreatitis. The rhubarb reduced the serum AMY and TNF-α level in rats with acute pancreatitis and reduced the pathological changes of pancreas and other tissues[19].

Spatholobus suberectus belonging to the Leguminosae family (Fabaceae), is a widely used traditional medicine for the treatment of anemia, menoxenia, and rheumatism. Component analysis of S. suberectus showed that the herb contains various types of Phenolic compounds, including flavones, isoflavonoids, flavanones, flavanonols, and chalcones . The herb has been shown to have diverse benefits including anti-inflammatory, antioxidant, and antirheumatic effects[20].

The effect of *Spatholobus suberectus* stem extract (SS) in the management of pancreatitis alone and in combination with heparin was studied. Consequences of this study reveals that treatment with SS alone and in combination with heparin significantly increase in prothrombin time and pancreatic blood flow than negative control group. There was significant decrease in concentration of IL-Iβ and D-dimer and activity of amylase and lipase in SS and heparin treated group than negative control group. Pancreatic DNA synthesis was also found to be reduced in SS and heparin alone and in combination treated group. Histopathology study also reveals that treatment with SS and heparin alone and in combination reduces edema, hemorrhages, leukocyte infiltration in the TS of pancreatic tissues[21].

Other medicinal plants effective against pancreatitis are tabulated.

S. No.	Medicinal Plant	Reference
1.	Phenolic compounds isolated from *Dioscorea zingiberensis*	22
2.	*Acanthopanax*	23
3.	*Brassica oleraceae* The pancreato-protective effect of may be attributed to well-known anti-inflammatory flavonoids, luteolin, quercetin and myricetin.	24
4.	Ethanol extract (95%) of *Calendula officinalis* flowers	25
5.	*Mimosa pudica*(Sensitive plant), also called humble plant, plant in the pea family (Fabaceae).	26

CONCLUSION

Acute pancreatitis is frequently encountered on the emergency surgical take. Once the diagnosis is made, clinical efforts should concurrently concentrate on investigating for the underlying etiology and managing the condition by anticipating its complications, which can be aided by using any of the severity scoring systems described. Management of acute pancreatitis is largely supportive. For diagnosis of acute pancreatitis, serum amylase is commonly used for early diagnosis of acute pancreatitis while lipase is used to confirm acute pancreatitis in a patient with elevated amylase level. Medicinal plants are of great significance to the health of individuals and communities. Due to their great importance, demand of medicinal plants has increased numerous folds. The present review focuses important medicinal plants which is effective against pancreatitis. The present literature gives pathway for further study and processing of Phytoceuticals of various medicinal plants which used as supplement to cure pancreatitis.

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