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Etiology of Pancreatitis and Rutin Treatment of the Disease

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ABSTRACT
The prevalence and increasing incidence of pancreatic diseases worldwide has brought about difficulties in its clinical management. Despite recent advances in understanding the complex pathogenesis of pancreatitis, disease management remains suboptimal. The purpose of this review is to discuss phytopreparations that have pancreatoprotective potential in acute pancreatitis and whose effectiveness is at least partially based on their ability to modulate cell death. Phytochemicals have a specific protective effect on the body: inhibiting inflammation, for example, rutin, suppressing neutrophil infiltration, and have antioxidant activity.Although many selected phytopreparations offer a promising therapeutic alternative, there is a lack of evidence in humans and additional research is needed to justify their use in the treatment of pancreatitis.

KEYWORDS
Phytopreparations, Rutin, Pancreatitis, Trypsinogen, Phytotherapy,Neutrophil Infiltration, Genetic Pancreatit, Steatorrhoea,Pancreatectomy, L-arginine.

Introduction

Pancreatitis is an acute inflammatory process caused by "self-destruction" of pancreatic tissue under the influence of its own enzymes, and inflammation related to parenchymal cell death.There are 3 main types of pancreatitis: acute pancreatitis, recurrent acute pancreatitis, chronic pancreatitis. In particular, chronic pancreatitis is an irreversible disease that leads to the destruction of healthy pancreatic tissue and the development of fibrous scar tissue.The gradual loss of exocrine and endocrine functions is also accompanied by clinical manifestations such as steatorrhea or steatorrhoea (The definition of steatorrhea is an increase in fat excretion in the stools.), abdominal pain, and diabetes.

The Main Results and Findings

The loss of pancreatic endocrine islet cells subsequently occurs in the course of the disease, since the endocrine cells are dispersed in the pancreatic parenchyma.Patients may develop Type 3 diabetes (pancreatogen), which is complicated by a decrease in glucagon secretion and, therefore, an increase in the risk of hypoglycemia. The disease is

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also caused by a genetic predisposition, mainly caused by mutations in eight genes, *CASR*, *CFTR*, *CLDN2*, *CPA1*, *CTRC*, *PRSS1*, *SBDS* and *SPINK1*, of which the most common gene (11%) was found to be *CFTR*. The discovery of the gene *PRSS1* in 1996 began a new era of genetic discoveries related to the disease. Since then, many genes have been described as pathogens or disease modifiers of pancreatitis. In genetic pancreatitis (GP), cystic fibrosis is associated with mutations in the transmembrane conduction regulator gene (CFTR), the cationic trypsinogen (PRSS1) gene, and the serine protease inhibitor Kasl factor 1 (SPINK1).Genetic testing and early detection of these diseases are currently major challenges in modern medicine. For example, changes in pathogenic CFTRs directly affect the direct management of a new type of bicarbonate-deficient mutation, PRSS1, and disrupt cationic trypsinogen metabolism.

In experiments on mice, it was found that the T7 gene in mice leads to a loss of protein expression by disruption of the locus encoding the cationic trypsinogen, a p.K24R mutation similar to the human PRSS1 mutation p.K23R analog (called T7 K24R mice). However, the severity of acute pancreatitis is partially reduced when exposed to the secretory substance.When a trypsinogen activating gene is mutated, it becomes a pathogen of trypsinogen.It also causes genetic 3c-type diabetes, which is related to pancreatitis in patients with glucose intolerance in such a situation. In acute pancreatitis, the concentration of α-2-macroglobulin in the blood plasma decreases. The main enzyme involved in the activation of pancreatic zymogens is trypsin.Improper activation of trypsinogen to trypsin and inability of the pancreatic tissue to immediately clear active trypsin leads to inflammation of the pancreas.It releases interleukin (IL) -1, IL-6, IL-8, cytokine 2, which contains tumor necrosis factor and platelet-activating factors. This, in turn, leads to the synthesis in the liver of acute-phase reaction proteins such as C-reactive protein (CRP). Physiological Ca^{2+} signals in pancreatic acinar cells control fluid and enzyme secretion, whereas excessive Ca^{2+} signals induced by pathological agents induce destructive processes leading to acute pancreatitis. Ca^{2+} signals in the peri-acinar stellate cells may also play a role in the development of acute pancreatitis Leukocyte migration and activation may be a major determinant of local and systemic complications. Replacement of exocrine parenchyma with fibrous tissue for the treatment of chronic pancreatitis is a key characteristic of chronic pancreatitis.

Understanding the mechanisms of pancreatic fibrogenesis is crucial for the development of prophylactic and therapeutic treatment. Cyclooxygenase-2 (COX-2), a rate-limiting enzyme for prostaglandin synthesis, is expressed in patients with chronic pancreatitis. However, it is unknown whether COX-2 can cause chronic pancreatitis. To study the role of pancreatic acinar COX-2 in fibrogenesis and in the development of chronic pancreatitis, changes in COX-2 externally in pancreatic acinar cells in transgenic mice were observed.And histopathological variation and expression levels of several profibrogenic factors related to chronic pancreatitis were evaluated and there were presented that COX-2 was detected in the pancreas of transgenic mice through Western pancreatic analysis.This suggests that COX-2 expression in pancreatic acinar cells is sufficient to induce chronic pancreatitis.

Determining this method is important in the prevention of chronic pancreatitis.On patients with pancreatitis, endoscopic and surgical procedures were unsuccessful between 1989 and 2012. Currently, improvement in the structure of β cells has been achieved through pancreatectomy and autotransplantation treatment of endocrine islets.Unfortunately, the use of standard medications in acute pancreatitis is still frustrating. Also, available drugs (somatostatin and octreotide) shorten

the half-life of the organ, and the clinical efficacy of the drugs is limited. Consider the effect of several phytopreparations in the treatment of the disease.

Rutin

Rutin - many citrus fruits, grapes, black tea, apple peel, and Amalaki fruits (*Emblica officinalis*) contain large amounts of quercetin ramnoglycoside. Rutin was found to be less absorbed than other quercetin glucosides (rutin was ~ 80% less than other available quercetin glucosides). Herein, it is associated with the conversion of rutin to various compounds (e.g., 3,4-dihydroxyphenylacetic acid, 3,4-dihydroxytoluene) by the intestinal microflora in the colon. In in vitro studies, the 3,4-dihydroxytoluene rutin metabolite showed anti-inflammatory effects in LPS, disabling NF-k B signaling and stimulating RAW 264.7 macrophages[16].Therefore, this metabolite can be used as a potential adjuvant against local and systemic inflammation in pancreatitis. In the acute pancreatitis model under the influence of L-arginine using the anti-necrosis apoptosis method in animal studies, rutin reduced pancreatic injury (decreased necrosis, edema, and infiltration and activity of pancreatic enzymes), as well as enhanced apoptosis. (increase in the number of apoptotic cells in the pancreas). Paradoxically, rutin can antagonize factors involved in other types of cell death, such as pyroptosis. For example, rutin treatment reduces the expression of caspase-1 and pyrine domain (PYD), a spot-like protein (ASC) related to apoptosis.Rutie also plays an important role in oxidative stress processes. In the L-arginine model of acute pancreatitis, in addition to relieving abdominal hyperalgesia (abnormally high sensitivity to pain), rutin reduced oxidative stress (reflected in improved 3-nitrotyrosine levels) and inhibited lipid peroxidation (a decrease in MPO).

Conclusion

It can be concluded from the above, that pancreatitis and diabetes are related diseases. Experimental observations on rats have shown that simultaneous attempts have been made to identify a local herbal remedy that corrects both pancreatitis and diabetes. When studying the effect of corrective drugs from several tested drugs (dihydroquercetin, rutin, chresariol, cinnarizine, *Ferula foetida* resin), a positive effect of dihydroquersitin and rutin on both the secretion and excretion of the pancreas have been determined.This means that in combination with various surgical and therapeutic agents, it is possible to use drugs derived from local plants, including flavonoids, in the treatment of pancreatitis. The advantage of these is that not only drugs are antioxidants, but alsothey can have a general healing effect on the body, in addition to pancreatic pathologies.

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