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A Review On Antidiabetic Activity Of Phyrus Pashia In Pharmaceutical Research

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Abstract

This review explores the antidiabetic mechanisms of *Pyrus pashia*, such as the inhibition of key carbohydrate-hydrolysing enzymes (α-amylase and α-glucosidase), enhancement of insulin secretion, and potent antioxidant and anti-inflammatory effects. In vitro and in vivo studies have demonstrated the plant's ability to lower blood glucose levels, improve glucose tolerance, and protect pancreatic β-cells from oxidative damage.Pear fruits have been reported to contain abundant bioactive compounds and exhibit antidiabetic activity. In this study, pear (*Pyrus pashia)* fermentation broth was sequentially extracted by five solvents with increasing polarity (petroleum ether, chloroform, ethyl acetate, n-butanol, and water) to evaluate its antioxidant and hypothermic activities, and then the main compounds of the fraction with the highest activity were assessed, which might be responsible for such activities.Eleven monomeric compounds were seriatim examined for α-glucosidase inhibitory activity to fish out anti-diabetic components. For the first time, this study delineated pear peel's anti-diabetic prospect of treatment for type 2 diabetes.

Keywords: Pyrus pashia, antidiabetic, diabetes

Introduction

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces [1]. Insulin is a hormone that regulates blood glucose. Hyperglycaemia, also called raised blood glucose or raised blood sugar, is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body's systems, especially the nerves and blood vessels [2].Diabetes is a metabolic disease with multiple etiologies, mainly manifested by an increase in blood glucose levels and disordered glucose metabolism, followed by disorders of protein and fat metabolism, leading to cardiovascular and cerebrovascular diseases, renal failure, retinopathy, etc. [3-4]. The chemical drugs commonly used to treat diabetes have been reported to show certain toxic and side effects on the human body, such as inducing liver and kidney damage and intestinal discomfort [5]. In recent years, anti-diabetic functional foods and drugs that contain natural active ingredients with little or no side effects have attracted widespread attention. These natural active ingredients show mild and durable effects on blood glucose and lipids reduction, and glucose tolerance improvement. In 1985, 30 million people suffered from diabetes, and by 2010 that figure increased to 285 million. Furthermore, antioxidant (reducing power and DPPH assay) and anti-inflammatory (xylene-induced mouse ear edema assay) activities were comparatively evaluated, and correlation analysis and principal component analysis (PCA) were carried out to seek the bioactive components in antioxidant and anti-inflammatory capacities [6-7]. According to the latest global estimate from the International Diabetes Federation that number of affected patients in 2019 stands at 463 million. α-amylase and α-glucosidase are the key enzymes that affect the digestion and absorption of carbohydrates in

the diet. Inhibiting their activities can delay the degradation of carbohydrates and the absorption of glucose by the human body, thus inhibiting the rapid postprandial rise in blood glucose. pear fruits have been reported to contain abundant vitamins, minerals, polyphenols, flavonoids, anthocyanins, and triterpenes, and thus exhibit a broad spectrum of pharmacological activities, such as antioxidant, hypoglycemic, anti-inflammatory, antiulcer, anti-cancer, cardiovascular, and cerebrovascular effects.Meanwhile, polyphenol plant extracts possess potential key enzyme inhibitory activity of type 2 diabetes (α-glucosidase and α-amylase), as well as hypertension disease[8](angiotensin I converting enzyme) (Boath et al, 2012, Oboh et al, 2012, Zhang et al, 2011).Recently, retardation of carbohydrate-hydrolyzing enzymes, such as α-glucosidase and α-amylase, are becoming a promising effective approach to control type 2 DM through the mechanism of preventing the absorption of glucose [9]

Types of Diabetes

Based upon the etiology, diabetes mellitus can be divided into two main types, Type 1, "Juvenile Diabetes Mellitus" (Insulin Dependent Diabetes Mellitus) and Type 2, "Adult type" (Non-Insulin Dependent Diabetes Mellitus [10-11]

Type 1 diabetes, once known as juvenile diabetes or insulin-dependent diabetes, is a chronic condition.[12] In this condition, the pancreas makes little or no insulin. Insulin is a hormone the body uses to allow sugar (glucose) to enter cells to produce energy occurs in childhood, mainly due to destruction of pancreatic β-cell islets through autoimmune-mediated, resulting in absolute insulin deficiency.[13]

Symptoms:

Type 1 diabetes symptoms can appear suddenly and may include:

- Feeling more thirsty than usual
- Urinating a lot
- Bed-wetting in children who have never wet the bed during the night
- Feeling very hungry
- Losing weight without trying
- Feeling irritable or having other mood changes
- Feeling tired and weak
- Having blurry vision

Type 2 is more associated with an adulthood and elderly people, which are mainly due to insulin resistance or abnormal insulin secretion [14]. The exact causes of pancreatic failure and insulin resistance are unknown, but they are associated with disease state, environmental impact, and food habit. Diabetic patients are more susceptible to various type of infection such as skin diseases and carbuncles [15]. The pancreas does not produce enough insulin hormones that regulate the movement of sugar into the cells. And cells respond poorly to insulin and take in less sugar.

Symptoms: Symptoms of type 2 diabetes often develop slowly. In fact, you can be living with type 2 diabetes for years and not know it. When symptoms are present, they may include:

- Frequent urination
- Increased hunger
- Unintended weight loss
- Fatigue
- Blurred vision
- Slow-healing sores
- Frequent infections
- Numbness or tingling in the hands or feet
- Areas of darkened skin, usually in the armpits and neck

Other types of diabetes:

- Gestational diabetes
- Maturity onset diabetes of the young (MODY)
- Neonatal diabetes
- Latent Autoimmune diabetes in Adults (LADA]

Common Symptoms of Diabetes

- Increased thirst
- Frequent urination
- Extreme fatigue
- Blurred vision
- Slow-healing sores or frequent infections

Treatment of Diabetes

Depending on what type of diabetes you have, blood sugar monitoring, insulin and oral drugs may be part of your treatment. Eating a healthy diet, staying at a healthy weight and getting regular physical activity also are important parts of managing diabetes [16].

1 Insulin People with type 1 diabetes must use insulin to manage blood sugar to survive. Many people with type 2 diabetes or gestational diabetes also need insulin therapy. Insulin cannot be taken orally to lower blood sugar because stomach enzymes interfere with insulin's action [17] .Insulin is often injected using a fine needle and syringe or an insulin pen — a device that looks like a large ink pen.

2 Corticosteroids

As exposed in the RECOVERY study, the use of dexamethasone is recommended for patients using oxygen, being able to reduce mortality, mainly in critically ill patients. The use of glucocorticoids should be done with attention to the possible adverse effects, such as hyperglycemia, an increased risk of infections (bacterial, fungal and Strongyloidiasis infections), [18] hyperglycemic hyperosmolar, and mainly in diabetic patients,

life threatening diabetic ketoacidosis. Knowing that dexamethasone/ glucocorticoids can complicate glycemic control, it is reasonable to individualize the choice of use of these drugs in diabetic patients.

3.Metformin

It is known that metformin has immunomodulatory effects, with some reports studying antibody titres in a small number of individuals suggesting that immune responses to influenza vaccination is modestly impaired; however, it is not possible to know its clinical significance.

4. Sulfonylureas

Sulfonylureas increase the risk of hypoglycemia and should be avoided in hospitalized patients with severe medical illness

1. Inhibition of Carbohydrate-Hydrolyzing Enzymes

- **α-Amylase and α-Glucosidase Inhibition**: The fruit of *Pyrus pashia* contains compounds that inhibit the activity of α-amylase and α-glucosidase, enzymes responsible for breaking down carbohydrates into glucose. By inhibiting these enzymes, the fruit slows the digestion and absorption of carbohydrates, leading to lower postprandial (after eating) blood glucose levels.[19] This is similar to the mechanism of action of some pharmaceutical antidiabetic agents, such as acarbose

Potential Role in Weight Management

- Obesity is a significant risk factor for type 2 diabetes. The fruit is low in calories and high in fibre, which may aid in weight management by promoting satiety and reducing overall caloric intake. Managing body weight is an important aspect of diabetes control.

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Pathophysiology

Identification of β-cell Dysfunction and Insulin Resistance

Development of the insulin radioimmunoassay led to the identification that individual with "early maturity onset diabetes" produced insulin and secreted this hormone in response to nutrient ingestion. Subsequently, it was shown that these individuals manifest a defect in the ability of the islet β-cell to respond to intravenous secretagogues including glucose. It was subsequently shown that this contributed to increased glucose production by the liver and decreased glucose uptake in muscle and adipose tissue

Roles of Reduced β-cell Number and α-cell Dysfunction

A reduced number of β-cells is a longstanding observation in type 2 diabetes, and this has recently again become of interest. The basis for this loss is multifactorial, and includes glucolipotoxicity and amyloid deposition that result in β-cell apoptosis through oxidative as well as endoplasmic reticulum stress.[20] This loss is not counterbalanced by the development of new β-cells as the human pancreas appears incapable of renewing these cells beyond the age of 30. the relative importance of β-cell function versus mass could have

important implications for the development of approaches to preserve β-cells and help maintain or improve glucose tolerance.It is known that islet blood flows from the β- to the α-cell and then to the somatostatin producing δ-cell, and that the high concentrations of insulin bathing the α-cell are capable of suppressing glucagon release.

Diagnosis

Diabetes symptoms often start suddenly and are often the reason for checking blood sugar levels. Because symptoms of other types of diabetes and prediabetes come on more gradually or may not be easy to see, the American Diabetes Association (ADA) has developed screening guidelines. The ADA recommends that the following people be screened for diabetes.

- Anyone with a body mass index higher than 25 (23 for Asian Americans), regardless of age, who has additional risk factors. These factors include high blood pressure, non-typical cholesterol levels, an inactive lifestyle, a history of polycystic ovary syndrome or heart disease, and having a close relative with diabetes.
- Anyone older than age 35 is advised to get an initial blood sugar screening. If the results are normal, they should be screened every three years after that.
- Women who have had gestational diabetes are advised to be screened for diabetes every three years.
- Anyone who has been diagnosed with prediabetes is advised to be tested every year.
- Anyone who has HIV is advised to be tested

Etiology and Risk Factors

The etiology of diabetes mellitus involves a combination of genetic and environmental factors. Type 1 diabetes is primarily an autoimmune disease characterized by the destruction of pancreatic beta cells. Genetic susceptibility, viral infections, and environmental triggers contribute to its development [21]. Type 2 diabetes is strongly associated with obesity, sedentary lifestyle, and genetic predisposition. Gestational diabetes is influenced by hormonal changes during pregnancy and is associated with increased maternal and fatal risks.

Technologies And Devices

1. Continuous Glucose Monitoring (CGM)

CGM systems use a sensor placed under the skin to measure glucose levels continuously throughout the day. They provide real-time glucose readings and trends, helping individuals make informed decisions about insulin dosing, diet, and physical activity. CGM systems can also alert users to high or low glucose levels, reducing the risk of severe hypoglycemia or hyperglycemia.

2. Insulin Pumps

Insulin pumps are small devices that deliver insulin continuously through a thin tube (catheter) inserted under the skin.[22] They provide a convenient alternative to multiple daily injections, allowing for precise insulin dosing and flexibility in basal and bolus insulin delivery. Some advanced insulin pumps integrate with CGM systems, creating closed-loop systems that automatically adjust insulin delivery based on glucose readings.

3. Closed-Loop Systems (Artificial Pancreas)

Closed-loop systems, also known as artificial pancreas systems, combine CGM technology with insulin pumps to automate insulin delivery. These systems use algorithms to adjust basal insulin rates and deliver bolus doses based on real-time glucose readings, reducing the burden of manual insulin management, and improving glucose control.

4. Insulin Pens

Insulin pens are portable devices that allow for the convenient and accurate delivery of insulin. They come prefilled with insulin cartridges and are discreet and easy to use, making them popular among individuals who require insulin injections.

Conclusion

Various parts of the P. pashia tree have long been used traditionally in the Indian medicinal system, particularly in the Himalayan region. The fruit is edible and represents a source of high nutritional value. Various phytochemicals have been reported in the fruit, owe, leaves and bark portion of the plant. However, research on P. pashia for pharmacological properties is minimal due to the limited information availableregarding different plant parts. The fruit is edible and represents a source of high nutritional value. The various phytochemicals reported from the fruit, owner, bark and leaves may be used to develop a novel drug by using the reverse pharmacological approach to curing various diseases .its mechanism of action, as well as the synergy among different bioactive compounds, should be further studied to develop functional edible products with antidiabetic effects.

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