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Antidiabetic, Antioxidant, and Antihyperlipidemic Effects of *Benincasa hispida*

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Abstract
The *Benincasa hispida* (wax gourd) is a cucurbitaceous vegetable long used in traditional Asian medicine for metabolic disorders. We conducted a comprehensive review of in vitro and animal studies up to 2020 to evaluate its antidiabetic, antioxidant, and antihyperlipidemic effects. Extracts of *B. hispida* (fruit, peel, seed) consistently lowered blood glucose in diabetic rat models. For example, various studies reported dose-dependent glucose reductions of up to 62% in alloxan-diabetic rats. In high-dose feeding studies, wax gourd powder significantly reduced fasting glucose and improved insulin levels in streptozotocin-diabetic rats. Antioxidant assays and biomarker analyses showed potent free-radical scavenging and upregulation of endogenous antioxidants. In ulcerated rats, *B. hispida* extract significantly decreased malondialdehyde (MDA) and normalized SOD and vitamin C levels. Likewise, extracts enhanced hepatic catalase and glutathione in ischemia-reperfusion models. Lipid profiles improved markedly: diabetic rats treated with B. hispida extract showed lower cholesterol and triglycerides and higher HDL compared to controls. These preclinical findings support the traditional use of *B. hispida* for diabetes and suggest multiple beneficial mechanisms.

Key Words: Antidiabetic, Antioxidant, Antihyperlipidemic, *Benincasa hispida*

Introduction
Diabetes mellitus and hyperlipidemia are major risk factors for cardiovascular disease, often exacerbated by chronic oxidative stress. Management of these metabolic disorders increasingly looks to medicinal plants. *Benincasa hispida* Cogniaux (Thunb.), commonly known as wax gourd or winter melon, is an edible vine crop. Its mature fruit and peel have been used as cooling foods and herbal remedies in Ayurveda and Traditional Chinese Medicine, including for urinary disorders, ulcers, and diabetes. The plant is rich in flavonoids, saponins, steroids, and vitamin C, compounds known to influence metabolism. Although clinical data are limited, numerous preclinical studies have explored *B. hispida's* effects on glycemic control, lipid metabolism, and antioxidant defense. We systematically reviewed peer-reviewed articles up to 2020 focusing on in vitro assays and animal experiments to assess these pharmacological effects. Our aim was to synthesize evidence that *B. hispida* extracts exert antihyperglycemic, antioxidant, and lipid-regulating actions, and to consider the underlying mechanisms.

Methods
A structured literature search was performed in PubMed and related databases up to 2020 using keywords "*Benincasa hispida*," "wax gourd," "ash gourd," combined with "antidiabetic," "antioxidant," "antihyperlipidemic," "streptozotocin," "alloxan," and "rats." Inclusion criteria were original research articles and reviews reporting glucose-lowering, lipid-modifying, or antioxidant outcomes from *B. hispida* extracts or isolates in cell or animal models. We prioritized studies with quantitative results (e.g. blood glucose levels, lipid panels, oxidative biomarkers) and mechanistic insights (enzyme activities, gene expression). Data were extracted from eligible studies to summarize experimental designs and outcomes. As this was a literature-based analysis, no new experiments were conducted.

Results

Antidiabetic Effects: Multiple in vivo studies demonstrate that B. hispida extracts lower blood glucose in diabetic animals. An ethanolic or aqueous fruit extract given to alloxan-induced diabetic rats (50–200 mg/kg, orally) produced dose-dependent reductions in fasting glucose. At 200 mg/kg, the extract achieved approximately 62% glucose reduction within 6 hours, surpassing the effect of tolbutamide. Similarly, B. hispida powder fed at 5–20% of diet to streptozotocin-diabetic rats for 4 weeks significantly decreased fasting blood glucose in all treatment groups versus untreated controls. In that study, the highest-dose group also showed increased insulin and glycogen storage, suggesting improved pancreatic or hepatic function. In vitro, B. hispida peel extracts inhibited α-amylase, implying reduced intestinal carbohydrate absorption. Aqueous, ethanolic, and methanolic fruit-peel extracts showed significant α-amylase inhibitory activity. These findings indicate that B. *Hispida* bioactives exert insulinotropic or glucose-utilizing effects.

Antihyperlipidemic Effects: Preclinical data also reveal favorable lipid-lowering actions. Diabetic rats often exhibit dyslipidemia (elevated triglycerides, cholesterol, LDL; reduced HDL). In the wax gourd feeding study, plasma cholesterol levels were significantly lower in B. hispida–treated diabetics than in diabetic controls. Triglycerides were elevated in untreated diabetic rats but were modestly reduced by B. hispida intake. Correspondingly, a chloroform extract of *B. hispida* fruit ameliorated derangements in lipid metabolism in alloxan-diabetic mice. In another study, the chloroform fruit extract significantly decreased cholesterol, triglycerides, LDL and raised HDL toward normal levels. Such lipid changes imply inhibition of cholesterol synthesis or enhanced clearance. Notably, B. hispida fractions also showed anti-adipogenic effects in vitro: the hexane fraction suppressed 3T3-L1 adipocyte differentiation by downregulating PPAR-γ and C/EBP-α and leptin expression, leading to reduced lipid accumulation. This suggests that *B. hispida* may reduce fat deposition and serum lipids through gene-regulatory mechanisms.

Antioxidant Effects: Rich phytochemicals in *B. hispida* translate into strong antioxidant activity. Several studies measured free-radical scavenging and oxidative stress markers. In a rat model of gastric ulceration, daily oral *B. hispida* juice significantly decreased malondialdehyde (MDA) levels—a marker of lipid peroxidation—in both red blood cells and gastric tissue compared to untreated ulcer rats. Treated rats also showed normalization of the ulcer-induced elevation in superoxide dismutase (SOD) and vitamin C levels, implying that oxidative injury was blunted by the extract. In renal ischemia-reperfusion injury models, B. hispida fruit methanol extract lowered renal MDA and elevated antioxidant enzymes (SOD, catalase, GSH) versus controls. These in vivo effects corroborate in vitro assays: seed and peel extracts exhibit high DPPH and ABTS radical-scavenging capacities, reflecting abundant phenolics. The antioxidant action is attributed to flavonoids (e.g. quercetin glycosides), tannins, and vitamins C and E present in the plant. By neutralizing free radicals, B. hispida extracts protect pancreatic β-cells and vascular tissues from oxidative damage, contributing indirectly to glycemic and lipid control.

Discussion

The preclinical evidence converges on *B. hispida* as a multifaceted metabolic modulator. The potent antihyperglycemic activity may result from several mechanisms: stimulation of insulin release or regeneration of β-cells, enhancement of peripheral glucose uptake, and/or inhibition of intestinal glucose absorption. Flavonoid constituents in B. hispida might mimic sulfonylureas or incretins, explaining the normoglycemic effect in non-diabetic rats and glucose lowering in diabetics. The α-amylase inhibition by peel extracts suggests delayed carbohydrate digestion. Together, these effects are comparable in magnitude to standard drugs in animal models. Concerning lipids, the marked reduction in cholesterol and triglycerides in treated rats indicates that B. hispida influences lipid biosynthesis and clearance pathways. The reported downregulation of adipogenic transcription factors

suggests a direct effect on fat metabolism, which could explain the improved lipid profile and anti-obesity effects noted in animals. Oxidative stress is a common mediator in diabetes complications. *B. hispida's* antioxidant activity is demonstrated both by in vitro free-radical assays and in vivo biomarkers. The decrease in MDA and normalized antioxidant enzymes after extract treatment implies mitigation of lipid peroxidation and preservation of endogenous defenses. Such antioxidant protection can prevent β-cell damage and ameliorate insulin resistance. Indeed, elevated SOD and catalase have been observed in tissues following B. hispida treatment, further confirming this effect. It is noteworthy that most studies used crude extracts (aqueous, ethanolic, chloroform) of the fruit or peel, suggesting that a combination of hydrophilic and lipophilic compounds contributes to activity. The pharmacokinetic bioavailability of these compounds in humans remains to be studied.

The consistency of effects across different studies and models strengthens the case for B. hispida's efficacy. Limitations include variability in extract preparation and doses, and the fact that most data come from acute or short-term rodent studies. No clinical trials in diabetic patients have been reported as of 2020. Nonetheless, the safety profile appears favorable: high-dose *B. hispida* extracts showed no acute toxicity in mice or rats.

Conclusion

Preclinical studies up to 2020 provide robust evidence that *Benincasa hispida* exerts antidiabetic, antioxidant, and antihyperlipidemic effects in vitro and in animal models. Fruit and peel extracts consistently reduce blood glucose, improve lipid profiles, and scavenge free radicals or augment antioxidant defenses. These effects are likely mediated by flavonoids, saponins, and other phytochemicals which act on multiple metabolic pathways. B. hispida shows promise as a nutraceutical or source of lead compounds for managing diabetes and dyslipidemia. Future work should clarify active constituents and mechanisms, and carefully designed clinical trials are warranted to confirm efficacy in humans.

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