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Antidiabetic Potential of Hydromethanolic Extract of *Hyoscyamus albus* in a Streptozotocin-Induced Diabetic Rat Model

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KEYWORDS

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ABSTRACT:

Introduction: Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, action, or both. The search for natural therapeutic alternatives has gained increasing interest due to the side effects associated with conventional treatments. *Hyoscyamus albus*, a medicinal plant known for its diverse pharmacological properties, has been traditionally used for various ailments, including metabolic disorders.

Objectives: This study aimed to evaluate the antidiabetic potential of the hydromethanolic extract from the aerial parts of *Hyoscyamus albus* in streptozotocin-induced diabetic rats. The study also investigated its effects on glucose metabolism and lipid profile.

Methods: Diabetes was induced in rats using streptozotocin, and the animals were subsequently treated with *H. albus* hydromethanolic extract at doses of 250 mg/kg and 500 mg/kg for 21 days. Blood glucose levels and lipid parameters were monitored throughout the experiment. Additionally, an oral glucose tolerance test (OGTT) was conducted to assess the postprandial hypoglycemic effect of the extract.

Results: Oral administration of *H. albus* extract significantly reduced fasting blood glucose levels ($P < 0.05$) and improved glucose tolerance. The treatment also led to a beneficial modulation of serum lipid profiles, including reduced cholesterol and triglyceride levels after 21 days of supplementation.

Conclusions: The findings suggest that the hydromethanolic extract of *Hyoscyamus albus* possesses significant antihyperglycemic and antihyperlipidemic properties. These results highlight its potential as a natural therapeutic agent for diabetes management.

1. Introduction

Diabetes mellitus is a chronic metabolic disorder resulting from insufficient insulin production by the pancreas or an alteration in its peripheral action [1]. This dysregulation leads to persistent hyperglycemia, which can cause severe systemic complications, including cardiovascular, renal, neurological, and ophthalmic disorders [2]. According to data from the International Diabetes Federation, diabetes mellitus is one of the leading causes of morbidity and mortality worldwide. In 2013, 382 million adults were affected, and 5.1 million people died from the disease. Its prevalence is expected to reach 592 million by 2035 [3].

The use of oral antidiabetic drugs is often associated with potentially serious adverse effects, such as lactic acidosis, hypoglycemia, digestive disorders, headaches, and anemia [4].

Given these limitations, modern medicine is exploring alternatives, including phytotherapy, which is recognized for its therapeutic benefits and lower risk of side effects. As medicinal plants are readily available and accessible, they represent a promising substitute. This approach is gaining increasing interest from both health and economic perspectives [5].

Hyoscyamus albus L., a Mediterranean plant belonging to the Solanaceae family, is renowned for its health benefits due to its richness in tropane alkaloids, particularly hyoscyamine and scopolamine. These compounds exhibit anticholinergic, analgesic, antispasmodic, antidiabetic, and sedative properties [6].

2. Objectives

The main objective of this research is to investigate the antidiabetic potential of the hydromethanolic extract obtained from the aerial parts of *Hyoscyamus albus*,

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providing a foundation for its potential use in medical interventions targeting diabetes.

3. Methods

The aerial parts of *Hyoscyamus albus* (H. albus) were collected in June 2021 from the Tlemcen region (Northwest Algeria). The plant was identified and authenticated in collaboration with the Botany Laboratory of Tlemcen University. The samples were cleaned and then dried for two weeks at room temperature in the shade. Afterward, the aerial parts were ground using an electric mill and prepared for extraction.

The dried plant powder was exhaustively extracted using a methanol/water mixture (70/30, v/v) for 48 hours. After filtration and concentration at 60°C under reduced pressure, the extract was evaporated and stored in a refrigerator at 4°C until use [7].

Experimental Animals

Adult male Wistar albino rats, weighing between 200 and 250 g, were obtained from the Pasteur Institute of Algiers, Algeria. The animals were housed in sterile polypropylene cages and maintained under standard laboratory conditions (temperature of 25 ± 2°C with a 12-hour light/dark cycle). They had free access to food and water ad libitum.

Oral Glucose Tolerance Test (OGTT)

The rats were fasted for 12 hours, with free access to water. They were then randomly divided into four groups (n = 5):

Group I (normal control): Received the vehicle (0.9% NaCl).

Groups II and III: Treated with 250 mg/kg and 500 mg/kg of *Hyoscyamus albus* hydromethanolic extract, respectively.

Group IV: Received 5 mg/kg of glibenclamide. Thirty minutes after treatment, all animals received a glucose solution (3 g/kg). Blood samples were collected from the tail vein and measured using a glucometer (Accu-Chek) at baseline (before treatment) and at 30, 60, 120, and 180 minutes after glucose administration [8].

Induction of Diabetes

Diabetes was induced by intraperitoneal (IP) injection of streptozotocin (STZ) at a dose of 45 mg/kg, dissolved in a sodium citrate buffer (0.1 M, pH = 4.6), as a single administration. After an eight-hour fasting period, all experimental rats received the IP injection of STZ, except for the control group, which received only the sodium citrate buffer [9].

Estimation of Blood Glucose in the Diabetic Model

Diabetes in rats was induced by intraperitoneal injection of STZ (45 mg/kg body weight) in experimental groups. The rats were divided into five groups (n = 5 per group):

Group 1: Normal control

Group 2: Diabetic control

Groups 3 and 4: Diabetic rats receiving 250 mg/kg and 500 mg/kg of *Hyoscyamus albus* extract, respectively

Group 5: Diabetic rats receiving glibenclamide (10 mg/kg)

The rats received daily oral treatments for 21 days, and fasting blood glucose levels were measured weekly [10].

Lipid Profile

Total cholesterol (TC), triglycerides (TG), and HDL levels were evaluated using a commercial kit (SPINREACT, Girona, Spain), following the manufacturer's instructions.

Statistical analysis

Statistical analyses were performed using SPSS Statistic version 26 and results are presented as mean ± SD. Statistical comparisons were made using the ANOVA one-way test. Values of $P<0.05$ were considered statistically significant .

4. Results

The antihyperglycemic effect of the hydromethanolic extract of *Hyoscyamus albus* was evaluated in non-diabetic rats using the glucose tolerance test. Before glucose administration, no significant difference in blood glucose levels was observed between the control and treated groups ($P > 0.05$). After 30 minutes, blood glucose levels peaked in all groups. However, rats treated with *H. albus* at doses of 250 mg/kg and 500 mg/kg showed a significant decrease ($P < 0.05$) in blood glucose at 60, 120, and 180 minutes compared to the untreated control group (Figure 1).

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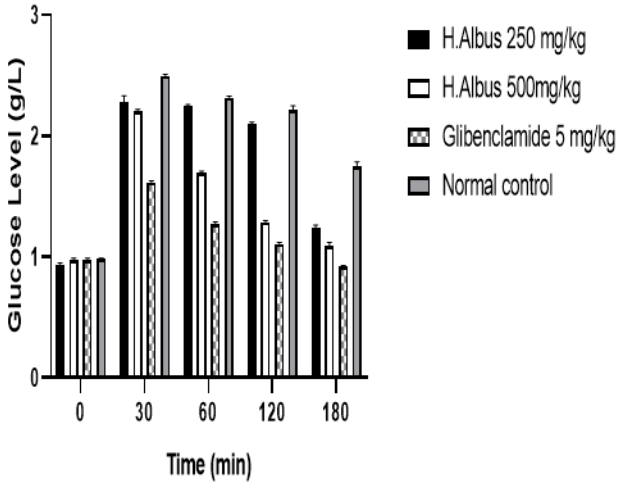

Diabetes induction with streptozotocin (STZ) led to persistent hyperglycemia in diabetic rats. As shown in (Table 1), after diabetes induction, the fasting blood glucose levels of diabetic control rats measured on days 0 and 7 were significantly higher than those of the normal control group ($P < 0.05$).

Table1 : Results of 21 days treatment of Extracts on blood glucose of Streptozotocin induced diabetic rats

Traitment	day0	Day7	Day14	Day 21
Normal control	0.973 ±0.149*	0.911 ±0.185*	1.063±0.14*	1.13±0.12*
Diabetic control	2.65 ±0.987	3.572±1.054	3.7902± 0.75	3.91±0.32
Glibenclamide10mg/kg	3.504± 0.234	3.313±0.37	2.05±0.704*	1.038±0.17*
H.albus 250mg/kg	3.72 ±1.1	3.52±0.32	2.72±0.22*	2.37±0.91*
H.albus 500mg/kg	3.601± 0.45	2.59±0.87*	2.41±1.32*	1,82.±1.14*

Values are Mean±SD; n=5 . *P<0.05 when compared with diabetic control group

Oral administration of the hydromethanolic extract of *H. albus* exhibited dose-dependent antidiabetic activity. At 250 mg/kg, blood glucose levels gradually decreased from 3.72 ± 1.1 g/L (day 0) to 2.37 ± 0.91 g/L (day 21), with a significant reduction from day 7 onward ($P < 0.05$). At 500 mg/kg, the hypoglycemic effect was more pronounced, with blood glucose dropping from 3.601 ± 0.45 g/L to 1.82 ± 1.14 g/L. This higher dose was as effective as glibenclamide (10 mg/kg), highlighting the promising potential of *H. albus* in diabetes management.

Lipid profile evaluation revealed a significant increase in cholesterol, triglyceride, and HDL levels in untreated diabetic rats. After 21 days of treatment, administration of the hydromethanolic extract of *H. albus* led to a significant reduction ($P < 0.05$) in these lipid parameters, suggesting a beneficial effect on lipid metabolism (Table 2).

Table 2 : Results of 21 days treatment of extracts on serum lipid profle of streptozotocin induced diabetic rats

Traitment	Cholesterol (g/L)	HDL (g/L)	Triglyceride(g/L)	VLDL (g/L)
Normal control	1.02±0.11*	0.35±1,12	0.95±0.13*	0.19±0.13*
Diabetic control	2.182±0.24	0.17±0,89	1.4105±0.18	0.28±0.18
Glibenclamide10mg/kg	1.298±0.47*	0.41±0,77	0.95±0.23*	0.19.±0.23*
***H.albus* 250mg/kg**	1.939±0.14	0.554±0,1	1.86±1.18*	0.37± 1.18*
***H.albus* 500mg/kg**	1.478±0.12*	0.384±0,02	0.836±0.23*	0.166±0.23*

Values are Mean±SD; n=5 . *P<0.05 when compared with diabetic control group

5. Discussion

Diabetes mellitus is a metabolic disorder that primarily disrupts the metabolism of carbohydrates, lipids, and proteins, leading to long-term dysfunction of several organs, as well as hyperlipidemia associated with hyperglycemia [11]. Recently, researchers have shown increasing interest in medicinal plants for diabetes management, as plant-derived phytochemicals have strong potential to regulate metabolic imbalances. Numerous phytomolecules, such as flavonoids, phenolic compounds, alkaloids, and polysaccharides, are recognized for their hypoglycemic and antihyperglycemic properties [12].

The improvement in postprandial blood glucose levels is achieved through more efficient glucose utilization by peripheral tissues, promoting glucose tolerance. The digestion and absorption of carbohydrates, which are essential for controlling blood glucose after a meal, depend on the enzymes α-amylase and α-glucosidase. These enzymes break down carbohydrates into glucose, which is then absorbed by intestinal cells [13].

Certain bioactive compounds, including flavonoids and polyphenols, play a key role in blood glucose regulation by inhibiting carbohydrate digestion, stimulating insulin secretion, and modulating glucose absorption, thereby reducing postprandial hyperglycemia. *H. albus* extracts, rich in phenolic compounds with antidiabetic properties, further contribute to this regulation. Specific phenols, such as caffeic acid, quercetin, and tannic acid, have been shown to influence glucose absorption by inhibiting the sodium-glucose transporters SGLT1 and SGLT2 in

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enterocytes, highlighting their potential in blood glucose management [14].

In a study conducted by Lakmin et al. [15], the *H. albus* extract demonstrated strong inhibition of α-amylase and α-glucosidase, underscoring its potential as a natural alternative for modulating these key enzymes involved in carbohydrate metabolism and the regulation of postprandial hyperglycemia.

Streptozotocin is known for its selective cytotoxicity against beta cells in the pancreatic islets. The injection of streptozotocin (STZ) leads to the destruction of pancreatic beta cells in rats, as these cells are particularly vulnerable to damage caused by free radicals and nitric oxide due to their limited capacity to neutralize these molecules [16,17].

Studies have highlighted the antidiabetic potential of Hyoscyamus albus, particularly through the evaluation of its methanolic leaf extract and its specific alkaloids, calystegines. Oral administration of the methanolic extract at doses of 100 and 200 mg/kg for 30 days in streptozotocin-induced diabetic rats resulted in a significant reduction in blood glucose levels and glycated hemoglobin [18]. Furthermore, the measurement of plasma insulin levels after administration of 10 and 20 mg/kg of the extract showed a significant increase ($P < 0.05$), suggesting stimulation of insulin secretion. Histopathological analysis of the pancreas in treated diabetic mice revealed that the calystegines extracted from Hyoscyamus albus seeds exert a protective effect on the β cells of the Islets of Langerhans, reducing streptozotocin-induced damage, stimulating their regeneration, and improving their secretory function. Additionally, these polyhydroxylated alkaloids demonstrated a notable hypoglycemic effect in diabetic mice after 20 days of treatment, bringing blood glucose levels and lipid parameters closer to normal values [19].

The observed beneficial effects could be attributed to a combination of mechanisms, including the protection of pancreatic β cells, improvement of insulin sensitivity, and modulation of metabolic pathways involved in glucose and lipid homeostasis. These findings highlight the therapeutic potential of this plant in diabetes management, paving the way for further research to identify the active compounds responsible for these effects and to better understand their mechanisms of action [20].

Diabetic individuals often present lipid abnormalities such as hypertriglyceridemia and hypercholesterolemia. Reducing lipid levels, whether through diet or medication, lowers the risk of cardiovascular diseases and improves lipid metabolism [21].

Our study, along with previous research, confirms the antidiabetic potential of *H. albus* and supports its role in managing hyperglycemia and lipid disorders. These findings reinforce the importance of further experimental and clinical studies to validate its efficacy and establish its potential as a complementary approach in diabetes treatment.

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