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Crude Plant Extracts with Anti-Diabetic Potential: Revisiting Traditional Herbal Remedies for Diabetes Care

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Abstract
Background: The objective of this investigation was to assess the anti-diabetic properties of the aqueous and alcoholic extracts in diabetic rodents that had been induced with alloxan.
Approaches: Following an acute toxicity test, alloxan was implemented to induce diabetes in Swiss albino rodents for scientific purposes. The two-week fasting mean blood glucose level in normal, diabetic mice that were not treated, and diabetic mice that were treated with alcoholic and aqueous extracts was the subject of the investigation. The Statistical Package for the Social Sciences, Version 20, was employed to conduct a statistical analysis of the data. Statistically significant was defined as a P-value that was less than 0.05.
Results: The extracts were found to contain steroids, phenolic compounds, flavonoids, and terpenes following phytochemical screening. These substances may have an effect on the extracts' anti-diabetic properties. Nevertheless, the preparations were devoid of anthraquinones and alkaloids.
Conclusion: The Alcohalic extract (200 mg/kg) exhibited the highest percentage reduction in blood glucose levels, and the ability of Hibiscus syriacus extracts to reduce blood glucose levels is likely due to the presence of antioxidant constituents, such as flavonoids.
Keyword-Hibiscus syriacus, Diabetes

1. Introduction

The significance of medicinal plants in drug development is well-established, as humans have utilized them for various ailments since the dawn of history. Traditional folk remedies derived from wild plants have consistently directed researchers in their pursuit of innovative medications to promote health in humans and animals. Moreover, certain medicinal plants remain undiscovered within the flora and require scientific assessment. Hibiscus syriacus, commonly known as the Korean rose, is a notable flowering shrub belonging to the Malvaceae family. Native to Asia, it is widely cultivated for ornamental and medicinal purposes. The plant exhibits large, vibrant flowers in a spectrum of colors, including pink, purple, white, and blue. In addition to its aesthetic appeal, Hibiscus syriacus possesses notable therapeutic properties. In traditional herbal medicine, both the flowers and leaves are utilized to treat various health conditions such as fever, inflammation, and digestive disorders. Research has demonstrated that Hibiscus syriacus is abundant in bioactive constituents such as flavonoids and phenolic acids, which contribute to its therapeutic effects. These elements exhibit both antioxidant and anti-inflammatory properties, positioning the plant as a valuable resource in herbal medicine. [3]

Plants have been employed for their therapeutic properties since antiquity. Various plant components, such as leaves, stems, roots, flowers, and fruits, encompass a diverse array of active compounds. These active compounds, referred to as phytochemicals, have garnered considerable attention recently due to their potential health advantages. Phytochemicals are natural compounds found in plants that exhibit antioxidant, anti-inflammatory, anti-cancer, antimicrobial, and immunomodulatory properties. To effectively harness the therapeutic potential of these phytochemicals, it is imperative to utilize appropriate extraction methods to obtain them from plant materials. The extraction process is essential for utilizing the beneficial healing properties found in bioactive compounds derived from plants. [5] Soxhlet extraction entails a continuous cycle of solvent extraction and subsequent evaporation. This technique entails positioning the plant material within a permeable extraction thimble and continuously circulating a solvent through it. The vaporized solvent condenses in a distinct flask and subsequently returns to the extraction chamber, facilitating the efficient extraction of bioactive compounds. [6, 7] Phytochemical analysis involves the examination of plant chemistry to identify and quantify bioactive compounds found in plants. These bioactive compounds, known as phytoconstituents, may include alkaloids, flavonoids, terpenes, saponins, steroids, glycosides, and various other secondary metabolites. [8] Diabetes mellitus is a chronic condition that affects the body's capacity to metabolize food into energy. It includes multiple forms, namely type 1, type 2, and gestational diabetes. In these various forms of diabetes, there is either inadequate insulin production or ineffective utilization of the produced insulin by the body [9]. Research has shown that certain natural compounds and plant extracts may have properties that can counteract diabetes. Substances like berberine, curcumin, and resveratrol have shown potential in modulating blood glucose levels and improving insulin sensitivity. Preclinical investigations into the efficacy of natural compounds and botanical extracts in modulating blood glucose levels and improving insulin sensitivity utilize diverse methodologies. Animal models with induced diabetes, such as streptozotocin or alloxan-induced diabetic mice, are frequently utilized to evaluate the safety and efficacy of these substances prior to progressing to human clinical trials. Researchers can subsequently examine the effects of administering natural compounds or plant extracts on glucose metabolism, insulin production, and other relevant factors utilizing these models [11].

2. Materials and ethods Animals

They were obtained from the animal home and were adult male Swiss albino mice weighing between 25 and 35 grams. The mice were given unrestricted access to water and the standard rodent diet at all times. Humane treatment was provided to each and every animal in accordance with the recommendations of the Institutional Animal Ethical Committee (IAEC), which was established in accordance with the Prevention of Cruelty to Animals Act of 1960. Before the experiment began, the animals were placed in quarantine for a period of seven days so that they could become accustomed to the environment of the laboratory. During the entirety of the trial, the animals were housed in cages made of polypropylene (each cage contained) home to three different creatures). Both the temperature (25 ± 1°C) and humidity (50 ± 15%) of the animals, as well as their photoperiod (light-dark cycles ranging from 12 to 12 hours), were carefully monitored and controlled.

Acute toxicity studies(LD50)

The acute oral toxicity evaluation of both alcoholic and aqueous extracts of *Hibiscus syriacus*, conducted in accordance with the OECD 423 guideline, revealed no mortality or significant toxic effects at the tested dose levels of 5, 50, 300, and 2000 mg/kg in mice. Throughout the 14-day observation period, no major behavioral or physiological abnormalities such as restlessness, tremors, diarrhoea, sluggishness, weight loss, or paralysis were observed. These findings suggest that both extracts exhibit a high margin of safety when administered orally and can be classified as **low-toxicity substances**. Based on the absence of mortality and serious adverse effects up to 2000 mg/kg, the **LD50 cut-off value** is presumed to be **greater than 2000 mg/kg**, placing the extracts in **GHS Category 5 or unclassified**, indicating relatively low acute oral toxicity.

Induction of diabetes

An intraperitoneal injection of newly synthesized alloxan (80 mg/kg body weight; B.W.) dissolved in 0.1M sodium citrate buffer (pH 4.5) was administered to mice after they had fasted for a full 24 hours from the time they were born. Mice that served as controls were given an equivalent amount of citrate buffer by themselves. The development of hyperglycemia in mice was confirmed by measuring the glucose levels in their blood while they were fasting using fine test strips and a glucometer (Accu-Chek, Roche, Germany) 48 hours after the injection of alloxan. Those mice who had fasting blood glucose levels that were more than 11.0 mmol/L were classified as diabetic.

Experimental design

In order to analyze the animals' oral glucose tolerance and fasting blood glucose levels, the animals were divided into seven groups, with five animals in each group before the tests were administered.

Group 1 consisted of mice that were given an intraperitoneal injection of 1% Tween 80; Group 2 consisted of mice that were rendered diabetic with a single intraperitoneal injection of alloxan (80 mg/kg body weight); and Group 3 consisted of diabetic mice that were given glibenclamide (10 mg/kg body weight) to be taken orally on a daily basis for a period of two weeks. Group 4 consisted of diabetic mice that were given an alcoholic extract of Hibiscus syriacus (100 mg/kg body weight) on a daily basis through oral administration for a period of two weeks. Group 5 consisted of diabetic mice that were given an alcoholic extract of Hibiscus syriacus (200 mg/kg body weight) on a daily basis through oral administration. Group 6 consisted of diabetic mice that were given an aqueous extract of Hibiscus syriacus (100 mg/kg b.w.) on a daily basis through oral administration for a period of two weeks. Group 7 consisted of diabetic mice that were given an aqueous extract of Hibiscus syriacus (200 mg/kg b.w.) daily through oral administration for a period of two weeks. The alcohol extract of the plant was dissolved in one drop of Tween (80%, Prolabo, France) and distilled water.

Samples

They were treated with plant extracts two days after receiving alloxan injections, with the exception of diabetic control groups. Blood samples were obtained from each group on days 1,7,and14of the study period to measure blood glucose levels[12].Changes in bodyweight were also documented.

Oral glucose tolerancetest

After two weeks of treatment with plant extracts, the animals were fasted for 12-14 hours while having unrestricted access to water, and their fasting blood glucose levels were assessed four times. Glucose solution (2 g/kg bodyweight) was given orally in a volume of 1 mL/kg.Blood samples were taken 30, 60, and 120 minutes after glucose injection [13].

Statistical analysis

Data are presented as mean ± standard deviation. Two-way analysis of variance (ANOVA) was used to compare treatment group means, and P-values < 0.05 indicated significant differences. Data were statistically analysed using the Statistical Package for the Social Sciences (SPSS) version 20.0 software. Bar and line charts were created with Excel2007.

3. Results and discussion Acute toxicity test

The acute toxicity investigation revealed that delivering incremental dosages of both aqueous and alcoholic extracts of Hibiscus syriacus did not elicit any discernible indicators of toxicity up to a dosage of 2000 mg/kg. This was confirmed by the absence of significant alterations in behaviors like alertness, motor activity, weight loss, lethargy, paralysis, respiration, restlessness, diarrhea, convulsions, and coma. Furthermore, no fatalities were recorded during the span of two weeks, and the individuals remained physically active. The results indicate that the plant extracts exhibited no significant harmful effects at the evaluated concentrations, suggesting that the median lethal dosage (LD50) in mice exceeds 2000 mg/kg body weight. The extract of Hibiscus syriacus is non-toxic, since its median lethal dosage (LD50) exceeds 2000 mg/kg [14].

Effect of *Hibiscus syriacus* extracts on fasting blood glucose level

*Hibiscus syriacus*extracts, both aqueous and alcoholic, were given orallytoAlloxan-induced diabetic mice once a day for a period of 14 days. Fig. 2 shows the impact of various dosages of *Hibiscus syriacus* extracts on fasting blood glucose levels.

This study aimed to examine the possible anti-diabetic activities of extracts from the leaves and flowers of Hibiscus syriacus. Dosages of Hibiscus syriacus at 100 and 200 mg/kg body weight were selected based on prior studies of the Hibiscus species [15]. Diabetes mellitus has been generated in experimental mice using alloxan monohydrate [46, 47]. Mice were administered a single intraperitoneal injection of a 80 mg/kg body weight alloxan monohydrate solution to induce diabetes mellitus. The elevated fasting blood glucose levels in the animals, assessed 48 hours post-injection, served as validation for this observation. Alloxan induces diabetes by preferentially annihilating pancreatic β-cells responsible for insulin secretion, a consequence of accumulation via the glucose transporter 2 (GLUT2), which diminishes glucose absorption in

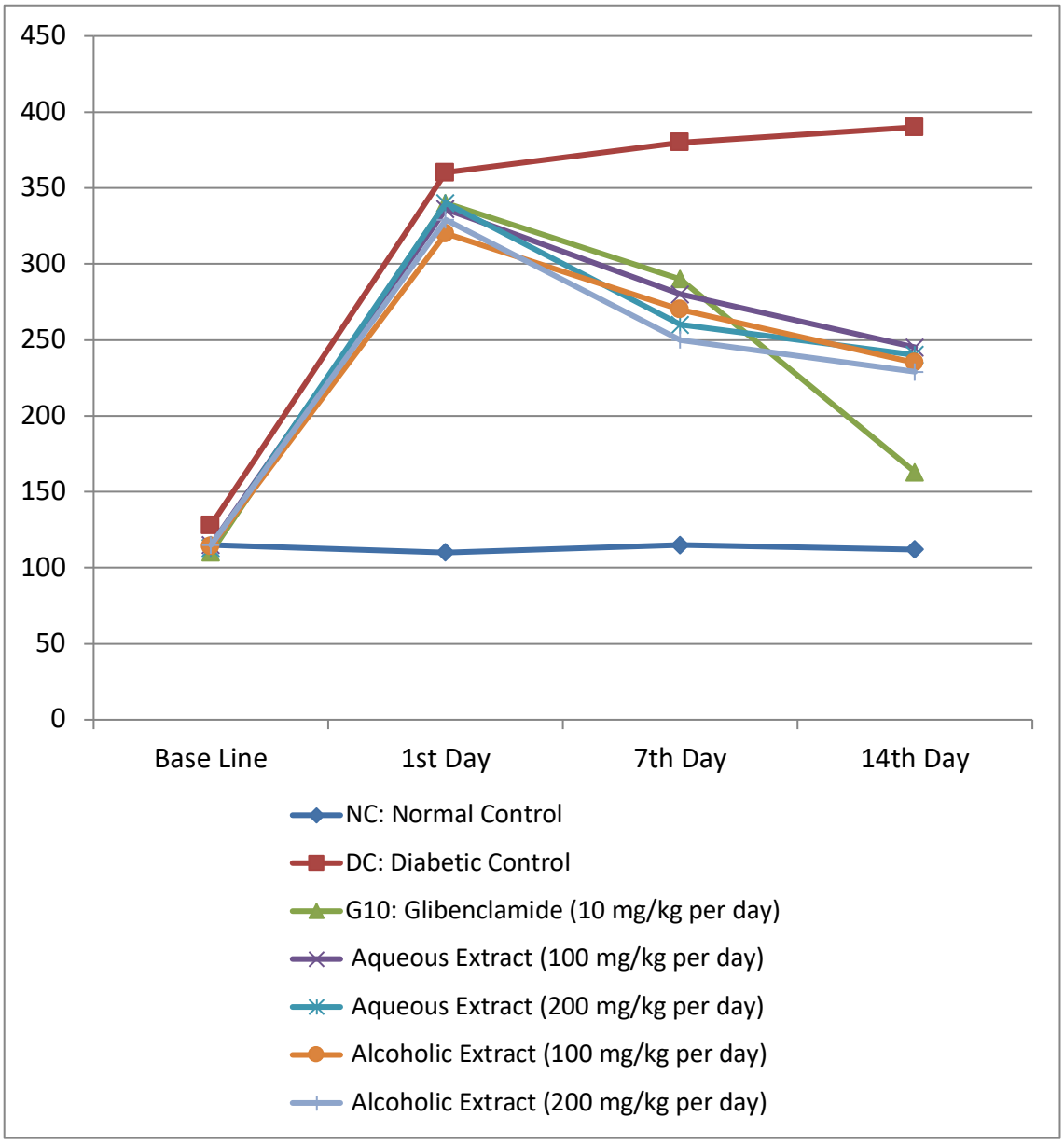

Fig.2Effect of extracts of Hibiscus syriacus on fasting blood glucose level in normal control and alloxan-induced diabetes mice.

peripheral organs. Alloxan is recognized for inducing free radical formation via redox reactions that result in tissue damage, degranulation of ß-cells, and eventual degeneration.

Table2Average Percentage Decrease of Blood Glucose Level

Group of Treatments	DBGL(%)
Diabetic+ Aqueous Extract of *Hibiscus Syriacus* (100mg/kg bodyweight)	27.12 ± 1.58
Diabetic+Aqueous Extract of *Hibiscus Syriacu* (200mg/kg bodyweight)	29.37 ± 1.21

Diabetic+ Alcoholic Extract of *Hibiscus syriacus*(100mg/kg bodyweight)	26.79 ± 2.84
Diabetic+ Alcoholic Extract of *Hibiscus Syriacus* (200mg/kg bodyweight)	30.38 ± 1.93
Diabetic+ Glibenclamide (10mg/kg body weight)	51.96 ± 1.12

The average percentage reduction in blood glucose levels (Table 2) escalated with the increasing relative dosage of Hibiscus syriacus extract administration. Following 14 days of therapy, the alcohalic extract of Hibiscus syriacus at a dosage of 200 mg/kg body weight shown a greater percentage reduction (30.38 ± 1.93) than any other extract. Diabetic mice administered glibenclamide (10 mg/kg body weight) exhibited a decrease of 51.96 ± 1.12 percent as a positive control.

Extracts from Hibiscus syriacus leaves and flowers reduced elevated fasting blood glucose levels. The presence of recognized antioxidant phytochemicals such as flavonoids, polyphenols, and terpenes, which serve as free radical scavengers, may elucidate the anti-diabetic properties of Hibiscus syriacus leaf and flower extracts [17].

The antioxidants were believed to function by imitating insulin's effects on peripheral tissues, either by facilitating regeneration or by stimulating insulin release from the pancreas' existing β-cells. Besides this technique, other mechanisms also have a crucial role in reducing blood glucose levels, rendering them attractive anti-diabetic plants. Among the others include enhancing glucose release by better metabolism or incorporation into adipose tissue, a mechanism linked to pancreatic insulin secretion, and accelerating glucose release from circulation by expediting filtration and renal excretion [18].

The study's results validated the assertions of Indian traditional healers on the application of the plant extract in diabetic therapy. The mechanism by which the extracts exert their anti-diabetic action remains unknown to us, however. Therefore, further investigation is necessary.

Oral glucose tolerance test

Figure3 shows the mean blood glucose levels of diabetic mice treated with *Hibiscus syriacus* extracts, diabetic mice left untreated (positive control), and normal mice (negative control) after two weeks of the mice being tested for glucose tolerance.

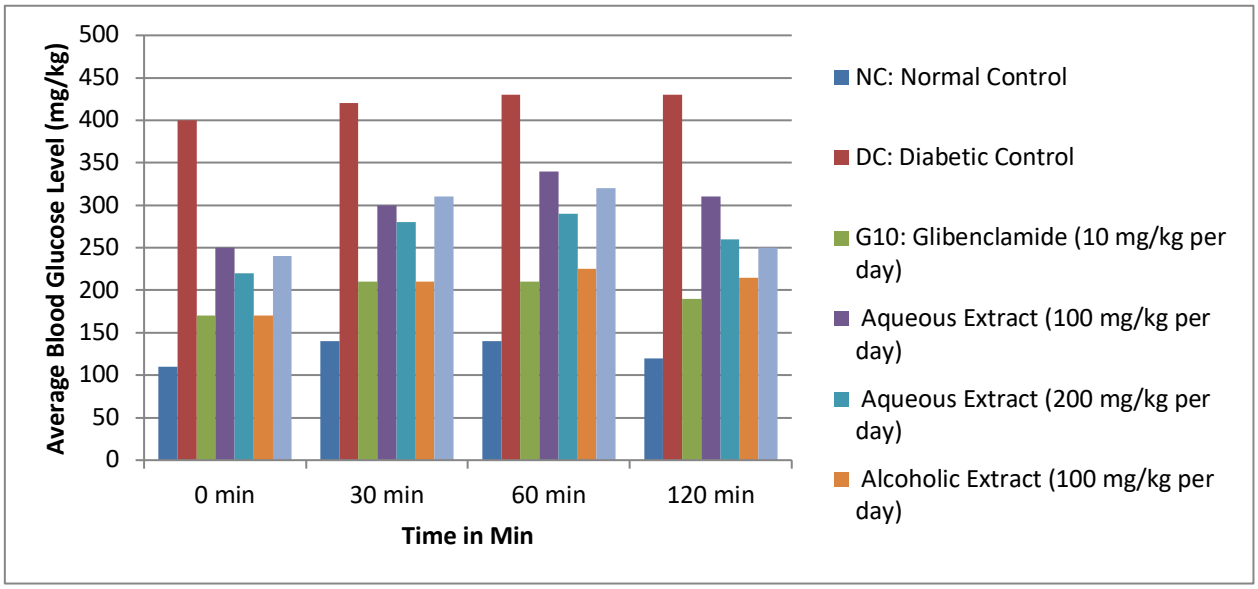

Figure.3Glucose tolerance testof *Hibiscus syriacus* extracts on alloxan-induced diabetic mice.

Following a 12–14 hour fasting period for each group of animals (n = 5), oral glucose (2 g/kg body weight) was administered as a baseline, and the mean fasting blood glucose level was evaluated. Following a 60-minute glucose administration, the average blood glucose concentration in the normal control mice rose to a peak and subsequently declined to a nearly normal level after 120 minutes. As anticipated, the glucose levels in diabetic control mice peaked after a 60-minute glucose load and remained elevated for the subsequent 60 minutes. Following 60 minutes of glucose administration, the subjects that received the extracts exhibited a reduction in their average blood glucose levels. The blood glucose concentration in both aqueous extracts reached its maximum at 60 minutes. The research article, indicating the presence of phenolic compounds, flavonoids, and terpenes. This result aligned with previous studies. Anthraquinones and alkaloids were not present in the extracts. Numerous compounds have been isolated from the plant that possess the capacity to reduce blood glucose levels. [19-25]. The pronounced anti-diabetic action of Hibiscus syriacus extracts may be attributed to the aforementioned components, which might function synergistically and/or independently to augment the activity of glycolytic enzymes.

Conclusion

The extracts were administered orally to mice in doses ranging from 1000 to 3000 mg/kg/day, and no noticeable behavioral changes were observed, indicating the extracts were non-toxic under the tested conditions. Analysis of *Hibiscus syriacus* flower extracts revealed the presence of flavonoids, phenolic compounds, and terpenes—compounds believed to possess bioactive properties relevant to diabetes treatment. In Swiss albino mice with alloxan-induced diabetes, doses of 100 and 200 mg/kg body weight of the *Hibiscus syriacus* extracts showed significant anti-diabetic effects. Specifically, the aqueous and alcoholic extracts reduced blood glucose levels by 27.12 ± 1.58%, 29.37 ± 1.21%, 26.79 ± 2.84%, and 30.38 ± 1.93%, respectively as compare to glibenclamide (10 mg/kg body weight) exhibited a decrease of 51.96 ± 1.12 percent as a positive control These findings suggest that the plant's chemical constituents may help

prevent diabetic complications and potentially serve as alternatives to existing anti-diabetic drugs. However, further studies are recommended to validate the plant's therapeutic potential in diabetes management.

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