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Research

Exploring the Antidiabetic Potential of *Plumeria Alba* in Type 2 Diabetic Animal Model

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Abstract:
Diabetes mellitus is a metabolic disease characterised by high blood sugar levels. Compared to allopathic medications, plant-based therapies are less harmful. Flavonoids, tannins, and alkaloids are found in the well-known medicinal plant Plumeria alba Linn (Apocynaceae). Antioxidants and terpenoids. However, it is yet unknown if Plumeria alba Linn. leaves have an antihyperglycemic effect. The hypoglycemic effects of ethanolic and aqueous leaf extractives of Plumeria alba were examined in a Streptozotocin-nicotinamide-induced Type II diabetes model and compared to the diabetic control group. The anti-diabetic effect was evaluated in albino Wistar rats. For 21 days, ethanolic and aqueous leaf extracts at 250 mg/kg b.w. and 500 mg/kg b.w. were administered to normal and experimental rats, and the measurement of the impact on blood sugar levels. The ethanolic extract at a dosage of 500 mg/kg b.w. shows a highly substantial ($p<0.001$) decrease in blood glucose levels compared to the diabetes control group.

Keywords: Anti diabetic activity , Blood sugar level, Plant extract *P alba,* STZ-NAD

INTRODUCTION

Diabetes mellitus is a type of disease that can be brought on by insufficient or nonexistent insulin production in the human body. It is a very common disease caused by a person's lack of physical activity due to resources, junk food, obesity, and less nutrient-dense food, and it can also be inherited. Diabetes mellitus encompasses a spectrum of metabolic disorders that affect the metabolism of carbohydrates, lipids, and proteins. This condition is defined by chronic hyperglycemia, stemming from either impaired insulin secretion, insulin action, or a combination of both. Diabetes mellitus is primarily classified into two categories: Type 1 (insulin-dependent) and Type 2 (non-insulin-dependent). Type 1 diabetes is the consequence of the autoimmune destruction of pancreatic islet β-cells, whereas Type 2 diabetes arises from both inadequate insulin secretion and insulin resistance. Contemporary epidemiological findings indicate that 9% of adults aged 18 and older are affected by diabetes mellitus; furthermore, the World Health Organization estimated that 1.5 million fatalities were attributable to the disease in 2012. According to WHO, diabetes will be the 7th leading cause of death in 2030. The renowned Indian surgeon Sushruta used the term "madhumeha" (honey-like pee) to describe diabetes in his work Samhita about the fifth century BC. He noted the urine's sweet taste, sticky texture, and ant-attracting properties (!). Sushruta goes on to say that excessive eating of foods like rice, cereals, and sweets is linked to diabetes, which mostly affects the wealthy castes. (1)

Traditional medicine has relied on plants for generations to heal a variety of illnesses by providing bioactive compounds. Plumeria alba, often known as white frangipani, is widely used for its therapeutic properties in a number of regions. It is commonly found in gardens and temples and serves both decorative and medicinal purposes. Research on phytochemistry and pharmacology has begun to support traditional claims and investigate its application in contemporary treatment. (2)

II. DESCRIPTIONOFBOTANICS

The little ornamental tree P. alba is distinguished by:

Oblong- placed leaves lanceolate, dark green, alternately

Flowers: Strongly fragrant, waxy, white with yellow centers

Latex: possibly with purgative qualities hazardous and milky

Fruit: Follicle, which is rarely seen in cultivation.

Its latex includes substances, and its flowers and leaves are frequently employed in medical formulations. (3)

Pharmacological Activity

1. **Antioxidant Activity**
   Extracts from the plant's leaves and flowers show moderate to strong antioxidant activity. The flower and leaf oils had respective total antioxidant capacities (TACs) of 57 µg/g and 83 µg/g. Due to their higher polyphenol content, leaf extracts often exhibit stronger DPPH radical scavenging than flower extracts. (4)
2. **Analgesic effect**
   Ethanolic extracts of P. alba flowers increased latency time in hot plate tests and considerably decreased writhing caused by acetic acid in animal models. These dose-dependent analgesic effects validated the conventional method of treating pain. These results imply that P. alba flower extracts have both cerebral and peripheral analgesic effects. (5)
3. **Antimicrobial Activity**
   The leaf and flower extracts exhibit a variety of antibacterial qualities against fungus like Candida albicans and bacteria like E. coli and Staphylococcus aureus. (6)
4. **Antiarthritic Activity**
   In Sprague-Dawley rats, P. alba's ethyl acetate and n-butanol fractions have antiarthritic effects.P. Alba provides a scientific justification for the plant's traditional usage in the management of inflammatory diseases like rheumatoid arthritis. (7)

MATERIAL AND METHODS

1. **Animal used in experiment:** Wistar rats of either sex, weighing 150-200 gm will be used for this research. The animals will be maintained in a well-ventilated room with a 12-hour light/dark cycle in standard polypropylene cages under controlled temperature (26 ± 1°C) and humidity (30%–40%). Animals will be allowed of free access to standard laboratory feed and water ad libitum. (8)
2. **Chemical, Drugs and Kits:** Drugs and chemicals that will be used in the experiment such as Streptozotocin, Nicotinamide, Glibenclamide will be purchased from SRL Chemicals Ltd. Glucose and inflammatory markers kits (TNFα and IL6) will be procured from Fischer Scientific Ltd. Additionally, analytical-grade chemicals such as thiobarbituric acid (TBA), trichloroacetic acid (TCA), 5,5-dithiobis, 2 nitrobenzoic acid (DTNB), and other required chemicals and substances will be purchased from certified supplier. (9)
3. **Plant Collection and Authentication:** The leaves of Plumeria alba will be collected and authenticated by a scientifically qualified botanist.
4. **Preparation of the Plumeria Alba extract:** After authentication the collected fresh Plumeria alba Linn. leaves will be air-dried and weighed, followed by grinding into coarse powder using a grinder. The powdered material will be successively extracted in a 500 mL round bottom flask with ethanol and water (70:30). The reflux time of solvents is 40 cycles. Extracts will be allowed to cool down and filtered at room temperature, then the solvents will be evaporated under reduced pressure until dryness. (10)
5. **Induction of Type 2 DM:** Type 2 DM will be induced after single intraperitoneal (i.p.) administration of streptozotocin (50 mg/kg of body weight dissolved in citrate buffer), 15 min after i.p. administratin of nicotinamide (120 mg/kg) to the rats. The desirable hyperglycemia (fasting blood glucose level > 200 mg/dL) will be checked using glucometer after 72 h of Nicotinamide and Streptozotocin injection. (11)

6. **Administration of plant extract:** Plant extract will be administrated intraperitoneally in doses 250 and 500 mg/kg.
7. **Collection of blood and serum p reparation:** Blood will be collected from each rat and centrifuged at 3000 rpm for 10 minutes to obtain clear serum, which will be stored at −20 °C until analysis.
8. **Tissue sampling and homogenate preparation:** After blood collection rats will be euthanized using thiopental (40 mg/kg, i.p.) followed by exsanguination and the pancreas of each rat will be removed for the biochemical estimations. Pancreatic tissue will be homogenized in phosphate buffer solution (pH 7.4) and then it will be 8 centrifuged for 5 minutes at 1000g under a maintained condition of 4 0C. The supernatant formed will be then transferred into another tube, which will be used for LPO and GSH estimation. Remaining supernatant will be recentrifuged for 15 min at 10,500g under 4 0C to get post-mitochondrial supernatant (PMS). The PMS will be used to measure SOD and CAT activity. (12)

RESULT

Percentage yield of extract

In a Soxhlet apparatus, 500g of dried powdered P. alba leaves were extracted in turn using petroleum ether, chloroform, ethyl acetate, ethanol, and distilled water. The yield percentages were determined to be 11.20%, 13.11%, 14.12%, 21.81%, and 19.11%, in that order.

Effect of Plumeria alba leaves extracts on diabetes

The diabetogenic drug streptozotocin (STZ) is commonly administered to rats in order to cause hyperglycemia. Diabetes mellitus can be caused by at least three chemical processes: administration of streptozotocin after nicotinamide administration (STZ-NAD), induction of a high-fat diet (HFD) followed by low-dose streptozotocin administration, and administration of streptozotocin during infancy 11–12, 13–20. When AEPA (250 mg/kg b.w.) was taken orally, the blood sugar level (mgdL-1) was much lower than in the diabetic group. An ethanolic extract of Plumeria alba at a dosage of 500 mgkg-1 b.w. yielded more significant outcomes ($p<0.001$) than the DC.

Effect of various extract of Plumeria alba on lipid profile

The levels of biochemical indicators, such as triglycerides, HDL, LDL, and total cholesterol. LDL levels were 33.14 mg/dL in the normal control group and 43.0 mg/dL in the diabetic control group ($p < 0.001$), cholesterol was 74 mg/dL in the normal control group and 135.83 mg/dL in the diabetic control group ($p < 0.001$), and HDL was 54.44 mg/dL in the normal control group and 27.33 mg/dL in the diabetic control group. In contrast, the groups who took 250 mg/kg or 500 mg/kg of Plumeria alba once daily for 14 days were able to prevent acquiring diabetes in a dose-dependent manner thanks to the ethanolic extract of

The effect of various extract of Plumeria alba on the total cholesterol, triglyceride, and lipid levels in the blood serum after 14 days.

Category	*Normal control group*	*Diabetic control group*	*Gliclazide treated group*	*Diabetic treated dose level 1*	*Diabetic treated dose level 2*
Triglycerides	71.5	115.83	73.66	94.33	88.83
Cholesterol	74	135.83	78.5	100.5	95.5
HDL	56.44	25.33	50.33	34.83	40.66
LDL	33.14	43	26.86	38.66	35.33

The data is represented as the mean ± standard deviation of six rats in one group and seven rats in four groups. Compared to the diabetic control group, $ap<0.05$, $bp<0.01$, and $cp<0.001$. Compared to the control group, $zp<0.001$

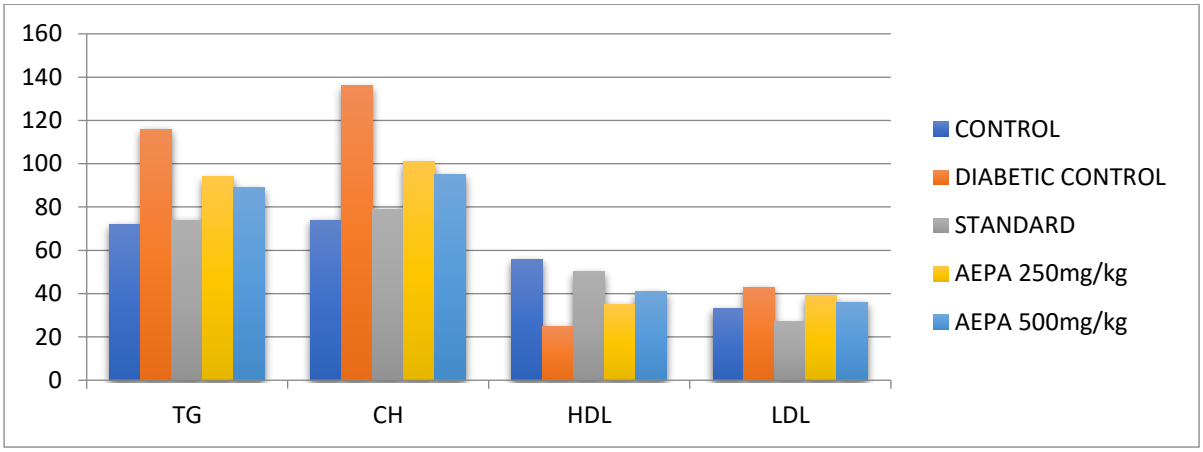

Figure 3.1 Effect of various extract of pulmeria alba on lipid profile

In vivo Antioxidant Activity

Oral administration of Plumeria alba ethanolic and aqueous extracts at dosage levels of 250 mg/kg b.w. and 500 mg/kg b.w., respectively, significantly increased GSH, GST, GPx, and CAT in the liver and kidney of rats with streptozotocin-nicotinamide-induced diabetes. The erythrocytes' SOD level decreased from 5.64 U min/mg Hb to 3.67 U min/mg Hb when diabetes was induced. Nevertheless, the SOD level increased significantly following the administration of ethanolic and aqueous extract, nearly reaching that of the normal control group and demonstrating antioxidant activity.

The Effect of Plumeria alba extracts on in vivo antioxidant enzymes of liver

Category	*Normal control group*	*Diabetic control group*	*Gliclazide treated group*	*Diabetic treated dose level 1*	*Diabetic treated dose level 2*
GSH	123.67	72.67	120.5	105.5	115.83
GST	8.5	5.16	6.5	4.60	5.55
GPx	9.45	7.1	7.0	4.15	4.83
CAT	75.67	37	65.83	58.17	61.67
SOD	5.64	3.50	5.10	5.80	6.75

The data is represented as the mean ± standard deviation of six rats in one group and seven rats in four groups. Compared to the diabetic control group, ap<0.05, bp<0.01, and cp<0.001. Compared to the control group, zp<0.001

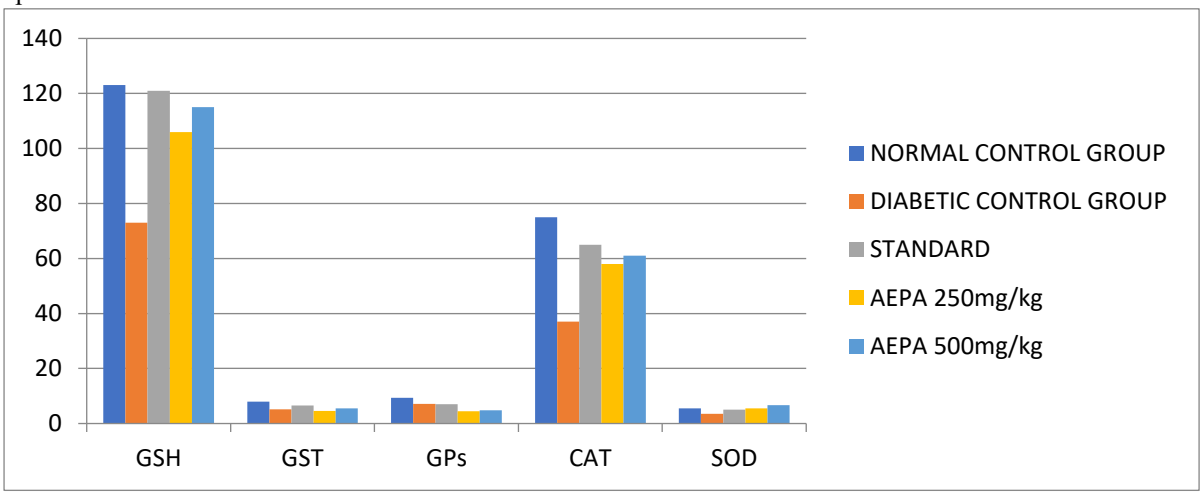

Figure 3.2 ***The Effect of Plumeria alba extracts on in vivo antioxidant enzymes of liver***

The Effect of Plumeria alba extracts on in vivo antioxidant enzymes of kidney

Category	*Normal control group*	*Diabetic control group*	*Gliclazide treated group*	*Diabetic treated dose level 1*	*Diabetic treated dose level 2*
GSH	116.5	44.66	90.83	89.83	94.3
GST	7.25	3.80	4.51	3.0	4.25
GPx	5.78	3.61	5.5	4.4	6.0
CAT	36.50	22.0	37.83	25.5	32.33

The data is represented as the mean ± standard deviation of six rats in one group and seven rats in four groups. Compared to the diabetic control group, ap<0.05, bp<0.01, and cp<0.001. Compared to the control group, zp<0.001

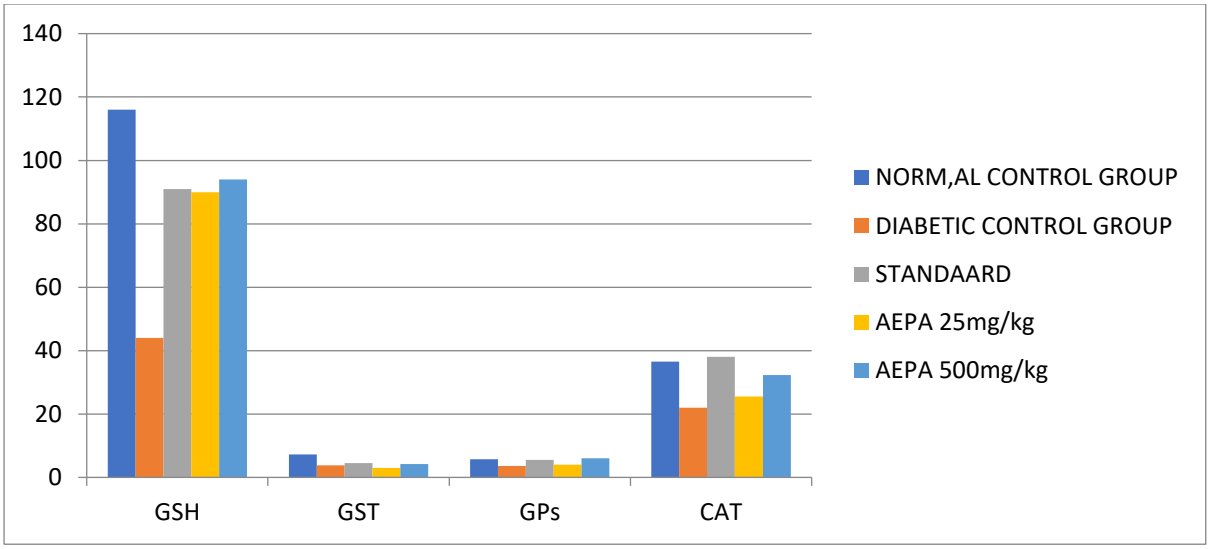

Figure 3.3 ***The Effect of Plumeria alba extracts on in vivo antioxidant enzymes of kidney***

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