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ETHANOLIC EXTRACTS OF *CAESALPINIA BONDUCELLA* LEAVES FOR ANTIDIABETIC ACTION IN ALBINO RATS

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ABSTRACT: Further investigation into the mechanisms underlying the antidiabetic and antihyperlipidemic effects of *Caesalpinia bonducella* leaf extracts is warranted to elucidate its potential as a therapeutic agent for managing metabolic disorders such as hyperglycemia and hyperlipidemia. Future studies could explore the extract's impact on insulin sensitivity, glucose uptake in peripheral tissues, and its influence on key enzymes involved in lipid metabolism. Additionally, assessing the extract's safety profile and potential adverse effects through preclinical and clinical trials will be crucial for its eventual translation into therapeutic use. Understanding the pharmacokinetics and bioavailability of the active compounds within the extract will aid in optimizing dosage regimens and formulation strategies to enhance its efficacy and minimize any potential side effects. Moreover, investigating the long-term effects of *Caesalpinia bonducella* leaf extract supplementation on overall metabolic health, including its potential to prevent or delay the progression of diabetic complications such as cardiovascular disease and nephropathy, would provide valuable insights into its broader therapeutic utility. Collaborative efforts between researchers, clinicians, and pharmaceutical companies will be essential for advancing the development of *Caesalpinia bonducella* leaf extract as a promising therapeutic option for addressing the multifaceted pathophysiology of diabetes and its associated complications.

INTRODUCTION: WHO, 2016, As per IDF rural occurrence of diabetes in 2017 is 146 million people and in 2045 is 156 million. According to WHO projection, India is becoming the "Diabetes capital of the world" (the highest number of diabetics in the world followed by China and then the USA).

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Diabetes Mellitus Classification: Type 1diabetes–TIDM (β-cell destruction), Type 2 diabetes–T2DM (Insulin resistance), Genetic defects (β-cell function), Genetic defects (insulin action), Exocrine pancreatic defects, Endocrinopathy, Infections, Drugs induced diabetes, Genetic syndrome; Gestational diabetes mellitus (GDM).[1]

Etiology of *Diabetes Mellitus:*
Causes of *Diabetes Mellitus* [2]*:*
***Diabetes mellitus* can be divided into two main Categories:**
Type I: Untreated, insulin resistant type 2 diabetes. Further, it is divided into two distinct types:

Type IA: Autoimmune.

Type IB: Idiopathic.

Type II: Diabetic coma caused by lack of insulin (NIDDM)

Type II: Diabetes Mellitus [3].

Walsh, 2002 both overweight and normal-weight adults can develop type II diabetes mellitus, which is characterized by a lack of insulin production. This contributes to around 80% of all cases of diabetes. Lack of glucose receptors or cells could contribute to its onset. In addition to being linked to T2 DM, down regulation of insulin receptors has been linked to obesity.

While insulin has shown to be somewhat beneficial in lengthening diabetes patients 'lives, there are still numerous problems with this treatment; therefore, it is not a long-term fix [4]. Additionally, the treatment with oral hypoglycemia medications is ineffective. So, it would be interesting to look for novel therapeutic agents derived from plants utilized in conventional treatment that have no negative side effects [5].

In the southern regions of India and Sri Lanka, *Caesalpinia bonducella* Roxb. (Fabaceae) is a vast, impenetrable, thorny shrub that is recurrently planted as a hedge plant [6]. It has been shown to have anti-inflammatory and antimalarial properties. It is said to be an aphrodisiac and all-purpose tonic that aids in physical regeneration [7].

Since, in previous studies, the anti-diabetic activity of seed extracts was reported. Hence, it is intended that this study establish scientific evidence for the *Caesalpinia bonducella* leaf extract for anti-diabetic activity [8].

Experimental Work:

Plant Material: The plant's fresh leaves were acquired from Sambhal, Uttar Pradesh, India, during the month of July, and Dr. Sunita Garg, director of the Raw Materials Herbarium & Museum (RMHD), Delhi, validated them. The plant specimen was donated to the National Institute of Science Communication and Information Resources (CSIR-NISCAIR), Raw Materials Herbarium & Museum (RHMD), New Delhi. At the same institution, a voucher specimen number (ARFC/SOP/IAEC/01/18) was given. To eliminate the surface impurities, the gathered leaves were washed under running water from the faucet. Under shade, the plant materials were air-dried.

FIG. 1: *CAESALPINIA BONDUCELLA* LEAVES

Preparation of the Extracts: The dried leaves were ground into a powder and extracted using a Soxhlet device in ethanol at 600–800°C [9]. Finally, a rotating vacuum evaporator was used to evaporate the extracted samples. The sequential solvent extraction procedure produced the extract yield. The yield was discovered to be (12%) for ethanol. For additional research, dried extracts were employed [10].

FIG. 2: SOXHLET DEVICE

Animals: Albino Wistar rats (weighing between 125 and 150g) were purchased and brought to the Animal Research Facility Center of the School of Pharmacy at Monad University in Hapur. The IAEC of the School of Pharmacy at Monad University in Hapur approved the experimental protocol. (Reference number: ARFC/SOP/IAEC/01/18). Rats were kept in polypropylene cages lined with husk under typical ambient conditions (25 5 °C, 55 10% relative humidity). The rats were provided with free access to water and were fed on a typical pellet diet.

FIG. 3: ALBINO WISTAR RATS

Verbal Glucose Patient Test: Normal mice that had been fasted instant (18 hours) underwent the oral glucose tolerance test [6]. The next six groups' groups I, II, III, IV and V were created using rats. Every group contained six animals. Rats from Group I served as the standard (administered only normal saline). Rats from groups II to IV received varying doses of *C. bonducella* ethanolic seed extract (200, 300, and 400 mg/kg, orally), whereas rats from group V received Glibenclamide (0.5 mg/kg b.w. per day p.o.) treatment. 30 minutes following extract administration, the animals from all groups were loaded with 60 percent glucose (3 g/kg p.o.). Before administering the medication, blood was taken from the tail at 0, 30, 60, 90, 120, and 150 minutes after glucose loading. An electronic glucometer was used to estimate the blood glucose levels (Gluco-one, Dr. Morepen) [11].

Streptozotocin Encouraged Hyperglycemia: In instant fasting albino Wistar rats, a single dosage of streptozotocin (60 mg/kg, i.p.) reconstituted in normal saline caused hyperglycemia. On the fifth day of STZ treatment, blood was drawn by a tail vein puncture, and one-touch Glucometer (Gluco-one, Dr. Morepen) strips were used to test blood glucose levels. Rats having a fasting blood sugar level of 250 were deemed to have hyperglycemia [7].

Rats were put into six groups at random (six animals in each group). Only normal saline was given to group (I), the normal control, and 0.25 percent CMC was given to the group (II), the diabetic control. Diabetes group (III) rats were given *Caesalpinia bonducella* ethanolic extract (200 mg/kg, p.o) (EECB). Diabetic rats in the group (IV) were given (400 mg/kg, p.o.) EECB Diabetic rats in the group (V) got the conventional medication glimepiride (10 mg/kg, p.o.). Body weight and blood glucose were monitored using strips on the first, third, fifth, seventh, ninth, eleventh, fifteenth, seventeenth, and twenty-first days of therapy for EECB [12, 13]. At the conclusion of the experiment, blood was drawn for additional biochemical analysis, starved animals were decapitated at the cervical spine, and organs like the pancreas were taken out, cleaned with ice-cold saline, and preserved for additional analysis [14, 15]. Several biochemical markers, including blood glucose level, lipid profile, and oxidative profile, were estimated using serum.

Statistical Analysis: The mean SD is used to express all findings. Graph Pad Prism 5.0 version software was used for the statistical analysis, which was done using the ANOVA (Bonferroni multiple comparison test) method. A result of p 0.05 or above was deemed significant [16].

RESULTS:

Glucose Tolerance Test [17]: In the glucose tolerance test, the ethanolic leaves extract of *C. bonducella* significantly lowered blood glucose levels. This finding suggests that the extracts can effectively prevent the absorption of glucose.

Anti-hyperglycemic outcome: In line with expectations, the diabetic control group's severe hyperglycemia was higher than that of the healthy animals. Following the STZ injection, the blood glucose levels of the STZ-treated group alone dramatically rose from 76.4 to 290.40 mg/dl. From the first day of therapy through day 21, blood glucose levels were substantially lower in the extract-treated groups [18]. When compared to the STZ-treated control group, all extract-treated groups showed a significant lowering impact (p 0.05) on blood glucose levels. According to **Table 1**, the greatest concentration of *C. bonducella's* ethanolic leaf extract (600 mg/kg) was shown to be more efficient than the lower concentration (200 mg/kg) at lowering blood glucose levels. The high dose (600 mg/kg of body weight) of the ethanolic leaves extract of *C. bonducella* has blood glucose-lowering properties that were comparable to those of the medication Glibenclamide. On day 21, an ANOVA comparison indicated that the high dosage (600 mg/kg) of *C. bonducella* ethanolic leaves extract had a very significant effect compared to the low dose of the extract. When compared to the diabetic control group, oral treatment of EECB

(600 mg/kg) significantly (p0.001, n=6, one-way ANOVA with Bonferroni multiple comparison test) decreased blood glucose levels. Maximum antihyperglycemic action was shown by EECB (600mg/kg). The blood glucose level was significantly reduced in the group receiving the standard treatment (Glibenclamide, 10mg/kg, p.o.) from 289.603.11 to 160.23.0 (p0.001, n=6). However, leaf extracts from the studied groups demonstrated the following antidiabetic efficacy.

TABLE 1: EFFECT OF EECB ON STREPTOZOTOCIN -INDUCED DIABETIC RATS' BLOOD GLUCOSE LEVEL (MG/DL)

S. no.	Treatment	Blood Glucose Level (mg/dl)			
		1st day	7th day	14th day	21th day
1	Normal control (10 ml/kg vehicle control)	89.75± 6.3	94±3.44	96.5±4.18	99.5±2.9
2	Diabetic control (60mg/kg STZ control)	290.4±2.9	302.8±2.9	312.2±4.6	321.8±2.4
3	STZ+EECB leaves (600mg/kg)	260.5±2.4	222.1±4.1*	193.4±3.1*	152.8±1.9
4	STZ + Glibenclamide (0.5mg/kg b.w perday p.o)	289.6±3.1	251.4±2.0	198.5±1.9	160.2±3.0

Effect of EECB Leaves on Diabetic Rats' Lipid Profile: In **Table 2,** the outcomes of the lipid profile of the diabetes control and treatment groups are shown. EECB (200, 400 mg/kg, p.o.) administration resulted in a substantial (p0.05, p0.001, n=6, one-way ANOVA with Bonferroni multiple comparison test) decrease in TC, TG, LDL, and VLDL when compared to diabetes control [19, 20]. Additionally, one-way ANOVA with Bonferroni multiple comparison test revealed that EECB (400 mg/kg) and Glibencl amide (10 mg/kg, p.o.) significantly improved HDL levels (p0.05, p0.001 n=6) [21].

TABLE 2: *CAESALPINIA BONDUCELLA* DOSE EFFECT ON LIPID PROFILE IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

S. no.	Treatment	Total Cholesterol	Triglyceride	HDL	LDL	VLDL
1.	Normal control (10 ml/kg vehicle control)	79.65±5.12	61.5±6.55	39.85±3.30	30.1±1.36	10.3±0.29
2.	Diabetic control (60mg/kg STZ control)	196±12.05	164.5±6.75	27.65±3.5	138.15±2.19	31.1±1.08
3.	STZ+EECB leaves (200mg/kg)	168±8.97***	149±4.98***	29.55±2.37	119.45±1.39***	34±1.73
4.	STZ+EECB leaves (400mg/kg)	147.33±2.43***	130.66±3.35***	33.11±2.55*	87.29±1.06***	24.6±1.18***
5.	STZ + Glibenclamide(0.5mg/kgb. wperdayp.o)	133.5 ±4.20***	121.25±4.75***	36.75±2.21***	77.5±2.08***	20.25±1.96***

CONCLUSION: Long standing diabetes mellitus is related to several problems, including atherosclerosis, myocardial infarction, neuropathy, and nephropathy. Previous research conducted in our lab demonstrated that *Caesalpinia bonducella* leaf extracts may produce strong *in-vivo* antioxidant activity. Other researchers assessed various plants for their anti-diabetic properties as well as their relationship to antioxidant activity. In the recent examination, larger dosages (600 mg/kg) of *Caesalpinia bonducella* ethanolic leaf extracts were able to significantly lower blood glucose levels in diabetic rats after 2 hours of therapy, with no discernible changes in body weight. Other researchers noticed related results. Therefore, unlike insulin and other manufactured medicines, ethanolic leaf extracts from *Caesalpinia bonducella* may be deemed to have good antidiabetic principles. In the current investigation, *Caesalpinia bonducella* leaf extracts were shown to be as efficacious equally glimepiride at lowering blood glucose levels in STZ-induced diabetic rats. However, the *Caesalpinia bonducella* plant's mechanism has been precisely identified. By increasing the production of free radicals by glucose auto-oxidation, hyperglycemia raises the risk of cell damage. The actions of the diabetogenic drug STZ and the rise in blood glucose levels may both contribute to the increase in oxygen-free radicals in diabetes. Since *Caesalpinia bonducella* is an active antioxidant and was discovered to be the most effective anti-diabetic medication to lower blood glucose levels, *Caesalpinia bonducella* leaf

extract exhibited considerable suppression of STZ-induced diabetes in experimental mice.

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