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Case Report

Why do they use bhat chew sticks? An experiment to demonstrate the antihyperglycemic activity of *Clerodendrum infortunatum* Linn.

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Abstract

Introduction: The rise in blood glucose than the recommended level is called hyperglycemia, mainly caused by diabetes mellitus (DM). DM is in turn a consequence of decreased insulin secretion or action or both. This experiment is intended to evaluate the effect of *Clerodendrum infortunatum* Linn. (bhat) chew sticks in controlling diabetes in humans. **Method**: The fasting blood sugar was measured twice with the help of a glucometer. First, all participants were requested to measure their blood sugar on an empty stomach in the morning without using a bhat chew stick. The next morning, their fasting plasma sugar was again accessed after the use of the bhat chew sticks as a toothbrush. The fall in blood sugar value was recorded and the efficiency of the stimulus was tested using student t-test at α level of significance and n-1 degree of freedom. **Result**: A total of 27 individuals participated in the study and all responded to the stimulus. A fall in blood glucose was observed between 3-59 mg/dL and the response was not found to be significant at 0.05 level of significance. **Conclusion**: Rural people use chew sticks as toothbrushes and prefer *C. infortunatum* twigs to control diabetes. The present experiment shows that bhat lowers the blood sugar level in both diabetic and non-diabetic individuals. However, chronic impacts should also be monitored by conducting large-scale studies on humans to establish proper dosage, indications, and side effects of *C. infortunatum*.

Keywords: *Clerodendrum infortunatum*, diabetes, hyperglycemia, random blood sugar, chew stick.

Introduction

Glucose is a monosaccharide which is the main source of energy in the body. Excess glucose is converted into glycogen, a polysaccharide, and stored in the liver and again converted back into glucose when necessary to be used as a fuel in cellular respiration [1]. Hyperglycemia, Greek hyper (elevated) + glykys (sugar) + haima (blood), is a medical condition where 2 hours postprandial plasma glucose is higher than 180 mg/dL and fasting blood glucose is more than 125 mg/dL. A person is said to be pre-diabetic if the fasting plasma glucose level is between 100-125 mg/dL[2, 3]. Individuals with decreased physical activity are more susceptible to developing hyperglycemia [4]. Moreover, its prevalence is lower in higher-income groups due to better access to education, healthcare, and healthy food options [5].

The major culprit behind hyperglycemia is insulin. Its secretion, its action, or both causes hyperglycemia [6]. Glucose homeostasis, which plays an important role in maintaining blood glucose levels, is a balance between hepatic glucose production by glycogenolysis and peripheral glucose uptake for cellular respiration. Insulin is the most important regulator of glucose homeostasis [7, 8]. Other than diabetes, it may also be caused by several factors like pituitary, thyroid, adrenal, and pancreatic disorders, sepsis, intracranial diseases like encephalitis, meningitis, and brain haemorrhages, convulsions, major surgeries, and end-stage terminal diseases [9].

Diabetes causes chronic hyperglycemia and in turn, it causes metabolic abnormalities affecting adipose tissue, skeletal muscle, and liver. The children with a complete lack of insulin, in type 1 diabetes, may experience increased appetite, excessive thirst, painful urination, weight loss, and vision impairment. However, adults with type 2 diabetes may not experience any of these symptoms, especially in their early stages [10]. DM causes many well-known classic complications. It causes microvascular complications such as retinopathy, nephropathy, and neuropathy. It also causes macrovascular complications like coronary artery disease, cerebrovascular disease, and peripheral arterial disease. All these complications cause direct or indirect impacts to the individual, family, society, and public health programs [11]. Uncontrolled diabetes may cause death due to ketoacidosis if not treated properly [12].

The increased calorie intake causes hyperglycemia which is a main symptom of DM and has affected a remarkable population [13]. Type 1 diabetes mellitus (T1DM) accounts for only 10% of all diabetes and the remaining goes to

type 2 diabetes mellitus (T2DM) which in turn is caused by obesity and demographic shifts. The prevalence of diabetes in 2021 was about 529 million which is expected to rise to 1.31 billion by 2050 [14]. The DM has become a fast-growing global problem with huge socioeconomic consequences. The real prevalence should be rather high because nearly half of diabetics are not diagnosed until 10 years after the onset of the disease [15].

Treatment options are available in both Allopathy and Ayurveda. Several classes of antidiabetic drugs are in allopathy practice including Sulfonylureas, Meglitinides, Thiazolidinediones, Alpha-glucosidases inhibitors, Dipeptidyl-peptidase-4 inhibitors, Glucagon-like peptide-1 agonists, and Sodium-glucose co-transporter - 2 inhibitors. But they possess a long list of adverse effects such as nausea, vomiting, diarrhea, hypoglycemia, metallic aftertaste, bloating and flatulence, polyuria, headache, urinary tract infection (UTI), pharyngitis, and increased risk of heart attack and bladder cancer. World Health Organization (WHO) has listed 15 medicinal herbal plants used in the treatment of DM. They include *Allium sativum*, *Trigonella foenum graecum*, *Aloe barbadensis*, *Tinospora cordifolia*, *Allium cepa*, *Cinnamomum cassia*, *Zingiber officinalis*, *Carica papaya*, *Gymnema sylvestre*, *Azadirachta indica*, *Eugenia jambolana*, *Mangifera indica*, *Momordica charantia*, *Ocimum sanctum*, and *Brassica juncea* [16]. However, insulin therapy has been proven to be the bedrock for the management of hyperglycemia in hospitals for the last two decades [17].

Clerodendrum infortunatum Linn. (Family: Verbanaceae) also called Bhat in Hindi, is a terrestrial shrub with a slightly woody square stem and simple, opposite, decussate, petiolate, exstipulate, coriaceous, and serrate hairy leaves. Its leaves have a typical unpleasant odour. The plant is 2-4 feet tall. Flowers are bluish purple often white and arranged in a branched raceme inflorescence called panicle. Fruits are quadrilobed drupe [18]. The easy availability and extensive use of its parts by local healers against various diseases make *C. infortunatum* one of the most studied species in the family Verbenaceae [19, 20]. However, the genus *Clerodendrum* has been recently classified as a member of the family Lamiaceae [21]. *C. infortunatum* is known as Bhanth in the local Tharu language.

C. infortunatum is a widely used medicinal plant and is used in Ayurveda, Homeopathy, and Unani systems of medicine. It possesses anthelminthic, antimicrobial, antioxidant, hepatoprotective, anticonvulsant, wound healing, and analgesic properties [22]. Different parts of the plant are used in fever, diarrhea, fever, headache, skin diseases, scorpion stings, and snake bites [23]. Many traditional practitioners use it against hyperglycemia [24].

Research questions

1. Why do locals use *C. infortunatum* chew sticks?
2. Does *C. infortunatum* tend to decrease the blood sugar level in humans?
3. Is the decrease in blood sugar by *C. infortunatum* significant?

Objective: To find the effect of *C. infortunatum* chew sticks on the blood sugar levels in human beings.

Figure 1: *Clerodendrum infortunatum* shrub with simple, petiolate, and opposite decussate leaves with serrate margins.

Experimental method

This case study was conducted among individuals of both sexes inhabiting Harnaiya village of Siyari Rural Municipality, Rupandehi district, Nepal. To observe the effect of *C. infortunatum* two readings of random blood sugar (RBS) were taken, one without the use of bhat chew sticks and another with its use. After obtaining consent from each participant fasting blood sugar was measured one hour after the use of an ordinary plastic toothbrush and toothpaste and a glucometer (**Dr. Morepen Gluco One** blood glucose monitoring system, India. Model BG - 03) was used following the manufacturer's guidelines and using a sterile technique. All participants were told to use chew sticks made from fresh twigs of *C. infortunatum* the next morning. Participants chewed one end of the twig, brushed their teeth by the chewed end, and the saliva secreted was swallowed immediately preventing spitting. Then again their RBS was accessed after one hour of brushing their teeth. A commonplace was selected where villagers gathered for the glucose measurement.

Statistical method

Null hypothesis H_0: $\mu = \mu_0 = 0$. That is, there is no significant decrease in the blood sugar by the stimulus.

Alternative hypothesis H_1: $\mu > 0$. That is, there is a significant decrease in the blood sugar value after the stimulus.

The change in the blood sugar value was noted for each individual and the standardized normal variate was calculated manually under the null hypothesis.

The test statistics used was,

$|t| = (\bar{x} - \mu)/ (s\sqrt{n})$ at α level of significance and n-1 degree of freedom.

Where, $\bar{x}$ = observed mean of the sample, μ = assumed mean, s = sample standard deviation, and n = sample size.

Result

A total of 27 individuals (26 – 83 years) of both sexes (21 male and 6 female) took part in the study. Their blood sugar value before and after the use of the *C. infortunatum* toothbrush was recorded as RBS1 and RBS2 respectively. The difference between these two variables was denoted as x. A fall in the blood sugar value was observed in all participants ranging from 3mg/dL to 59 mg/dL.

Table 1: Observation table showing the antihyperglycemic effect of C. infortunatum.

S,N.	RBS1	RBS2	x (RBS1 – RBS2)	$(x - \bar{x})^2$
1	68	51	17	0.068
2	111	79	32	202.265
3	97	91	6	138.721
4	84	63	21	10.381
5	88	71	17	0.608
6	129	97	32	202.265
7	137	110	17	85.026
8	88	82	6	138.721
9	96	78	18	0.049
10	73	58	15	7.717
11	63	60	3	218.389
12	75	61	14	6.605
13	113	89	24	38.713
14	91	81	10	60.497
15	104	95	9	77.070
16	185	126	59	1699.253
17	76	71	5	163.277
18	85	67	18	0.049
19	86	72	14	14.273
20	126	107	19	1.493
21	68	53	15	7.717
22	83	62	21	10.321
23	90	73	17	0.608
24	86	76	10	60.497
25	117	91	26	67.732
26	80	73	7	116.165
27	79	61	18	6.640
			$\bar{X} = \sum x/n$ = 17.778	$\sum(x-\bar{x})^2$ = 3329.72

The working table with raw data taken during the administration of *C. infortunatum* toothbrush among old individuals (51-83 years) of both sexes to find its anti-glycemic effect. RBS1 is the random blood sugar before meal measured in mg per deciliter without the use of the herbal toothbrush and RBS2 is its value after using an herbal toothbrush made from the fresh stem of *C. infortunatum*.

From the above working table and using the statistical relation given above, the test statistics was found to be 0.302 which is less than the tabulated value at 26 degree of freedom for a one-tailed test finding no reason to reject the null hypothesis. Hence it can be concluded that the use of *C. infortunatum* stem toothbrush does not show a significant decrease in the fasting blood sugar level at 0.0005 level of significance.

Conclusion and Discussion

Before the invention of artificial plastic toothbrushes, everyone used chew sticks made from various plant stems. Despite modernization, some old-generation individuals, especially from the countryside, prefer chew sticks to clean their teeth and oral hygiene. They believe that these herbal toothbrushes prevent pyorrhea, make teeth strong, manage toothache, stimulate appetite, and treat various systemic diseases such as diabetes. Unlike in the case of artificial toothbrushes with toothpaste, the users are not required to spit the saliva. Moreover, the users can save money since buying toothbrushes and toothpaste becomes unnecessary. They are safe from germs collected in artificial brushes and harmful ingredients found in toothpastes which are sometimes found to be carcinogenic. They use different plants as chew sticks for each type of ailment to be addressed.

Several efforts have been made to establish the antihyperglycemic effect of C. *infortunatum*. Unfortunately, all of them are found to be conducted on mice. Das et al. (2011) used methanol extract of C. *infortunatum* leaves in streptozocin (STZ)-induced rats at doses of 250 and 500 mg/kg body weight per day intraperitoneally. The control group was given a reference drug called Glibenclamide at 0.5 mg/kg/day dose orally. They measured fasting blood glucose levels every fifth day during the 15 days of treatment. The leaf extract of bhat at the doses of 250 and 500 mg/kg significantly (P<0.001) and dose-dependently reduced and normalized blood glucose levels as compared to that of the control group [25]. Baid (2013) also tested the antihyperglycemic and hypolipidemic activities of chloroform extract of bhat in streptozocin-induced diabetic Wistar rats. The diabetic rats were divided into five groups (I-V). Group I - normal control received buffer solution (10 ml/kg per oral); Group II - diabetic control received only STZ injection, Group III & IV- diabetic rats received chloroform leaf extract of *C. infortunatum* (200 and 400 mg/kg per oral).; Group V - Diabetic rats received Metformin 100 mg/kg per oral as a reference drug for 28 days. She measured the fasting blood glucose levels of rats on 0, 7th, 14th, 21st, and 28th day of post-treatment. The blood samples were taken also for the estimation of serum biochemical parameters like triglycerides (TG), high-density lipoprotein (HDL), low-

density lipoprotein (LDL), and very low-density lipoprotein (VLDL) at the end of the study. The chloroform extract significantly ($P < 0.05$) and dose-dependently reduced and normalized the blood glucose level in comparison to that of the STZ control. The serum biochemical parameters were also significantly ($P < 0.05$) restored to the normal value in the experimental group in comparison to the STZ control [26].

Similarly, Yasmeen et al. (2015) came up with a similar conclusion. They selected alloxan-induced diabetic albino rats for the experiment and divided them into six groups (1-6). Group 1 was taken as non-diabetic control, group 2 was considered as diabetic control, and group 3 as standard and was treated with 0.1 mg/kg/day of Glibenclamide. The remaining three groups (4, 5, and 6) were taken as experimental groups and were treated with 200 and 400 mg/kg of ethanolic extract of *C. infortunatum*. They analyzed blood samples for blood glucose on days 1, 3, 7, 14, 21, and 28 and lipid profile on day 28. In the result, it was found that the extract showed a significant ($P< 0.001$) reduction in blood glucose and serum profile level than in control at 40 mg/kg dose [27]. All related experiments found in the literature so far are found to be performed in model animals, not humans.

Recommendations

- The study of antihyperglycemic activities of organic solvent extract of bhat should be conducted in humans.
- The impact of long-term administration of *C. infortunatum* should be evaluated for RBS and HbA1c levels.
- The plant extract dosage should also be decided by mass study in humans.
- Its side effects should be identified by mass clinical studies.

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Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Abbreviations:

DM … diabetes mellitus

T1DM … type 1 diabetes mellitus

TG …triglyceride

T2DM … type 2 diabetes mellitus

STZ … Streptozocin

RBS … random blood sugar

LDL … Low-density lipoprotein

HDL … high-density lipoprotein

VLDL … very low-density lipoprotein

UTI … urinary tract infection

WHO … World Health Organization

HbA1c … Haemoglobin A1c

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