Turkish Journal of Agriculture - Food Science and Technology, 11(10): 1905-1916, 2023
DOI: https://doi.org/10.24925/turjaf.v11i10.1905-1916.6212

Turkish Journal of Agriculture - Food Science and Technology

Available online, ISSN: 2148-127X | www.agrifoodscience.com | Turkish Science and Technology Publishing (TURSTEP)

Comprehensive Evaluation of the Clinical Efficacy of an Anti-Diabetic Polyherbal Formulation

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ARTICLE INFO

Research Article

Received : 03-07-2023
Accepted : 20-10-2023

Keywords:
Polyherbal formulation
Hyperglycemia
Fasting glucose
2 hours PP glucose HbA1c
Insulin.

ABSTRACT

Background: There are several clinical studies examining the health advantages of several single medicinal herbs utilized in traditional blood glucose-lowering treatments. But very few or no studies on herbal formulations were made as Polyherbal for the same goal. As a result, it is now necessary to confirm that patients with hyperglycemia can benefit from such Polyherbal medicines as Dolabi. *Methods:* This prospective open-label, herbal coded test drug-controlled, randomized trial was conducted at the Munshiganj and Dhaka area in Bangladesh. We enrolled 108 male and 104 female patients of 30-70 years with primary and moderate hyperglycemia. They were recruited from the OPD of an Unani & Ayurvedic hospital in Munshiganj and different Unani clinics in Dhaka, Bangladesh after fulfilling the inclusion criteria. Patients were randomly assigned to receive metformin hydrochloride 500 mg two times daily and 2 tablets of Dolabi two times daily by using a random numbers table with the help of an assistant. Blood samples, height, weight, blood pressure, and personal data were recorded—laboratory results were obtained at the study baseline, after 1.5 months and after 3 months of intervention. *Results:* In the case of the test drug, results showed a significant decrease in blood glucose level between the baseline and after 3 months, in males, it was from 9.83±1.17 to 7.72±1.06 mg/dL for fasting glucose, from 16.60±2.35 to 8.23±1.17 mg/dL for 2 hours PP glucose, from 9.33±1.17 to 7.45±2.03 percent for HbA1c and for Insulin it reduces from 183.10±27.59 to 168.10±29.59 pmol/ L. The control drug metformin hydrochloride also showed a significant decrease in blood glucose level between baseline and after 3 months, in the case of males it was from 9.99±2.52 to 6.97±1.76 mg/dL for fasting glucose, from 17.43±5.05 to 7.89±2.42 mg/dL for 2 hours PP glucose, from 10.43±2.36 to 6.87±1.18 percent for HbA1c and for Insulin it reduces from 198.75±30.61 to 183.75±30.61p mol/L. In the case of females the test drug showed a significant reduction in fasting glucose, 2 hours PP glucose, HbA1c and Insulin between the baseline and after 3 months, it was from 10.02±1.11 to 7.78±0.93 mg/dL, from 16.88±2.21 to 8.16±1.11 mg/dL, from 9.84±1.04 to 7.45±1.03 percent and from 199.47±30.90 to 173.47±30.90 mg/dL respectively. In the case of females, the control drug showed a significant reduction in fasting glucose, 2 hours PP glucose, HbA1c and Insulin between baseline and after 3 months, it was from 10.18±1.92 to 6.71±1.59 mg/dL, from 18.70±3.88 to 7.60±3.74 mg/dL, from 10.58±1.08 to 6.98±1.08 percent and from 200.00±31.83 to 188.00±31.83 mg/dL respectively. *Conclusions:* We can infer the following from the present study's findings: The polyherbal formulation Dolabi is able to reduce the blood glucose level. It can be an effective drug for primary hyperglycemic patients.

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Introduction

Patients who have diabetes are at a greater risk of developing chronic metabolic disorders, including high blood glucose (also known as blood sugar) levels, which over time can have a detrimental effect on their hearts, blood vessels, eyes, kidneys, and nerves. According to the Global Burden of Disease Collaborative Network 2020, type 2 diabetes is the most prevalent form of the disease and develops when the body either stops producing enough insulin or becomes insulin resistant (Global Burden of Disease Collaborative Network 2020). This form of diabetes most commonly affects adults. Over the past three decades, there has been a marked increase in the prevalence of type 2 diabetes in nations with incomes ranging from very low to very high. When the pancreas produces very little or none of its own insulin, a person is said to have the chronic illness known as diabetes type 1. Juvenile diabetes or insulin-dependent diabetes where its earlier titles (Diabetes, 2023). It is essential for diabetes patients to have

access to reasonably priced medical treatment, particularly insulin, in order for them to have any chance of survival. According to 'Diabetes- Overview' (n.d.), all parties have reached a consensus that an end must be put to the rise of diabetes and obesity by the year 2025 ('Diabetes- Overview' n.d.). The bulk of the world's 422 million diabetics, who together live in low- and middle-income nations, are afflicted with the disease, which is directly responsible for 1.5 million deaths each year. Over the course of the last few decades, both the incidence of diabetes and the prevalence of diabetes have seen a steady increase ('Diabetes- Overview' n.d.).

Diabetes affected 8.5% of those aged 18 and older in 2014 in the United States. In 2019, diabetes was directly responsible for the deaths of 1.5 million individuals over the world, with those under the age of 70 accounting for 48 percent of these fatalities. According to the Global Burden of Disease Collaborative Network 2020, hyperglycemia is responsible for twenty percent of all fatalities from cardiovascular disease, and diabetes is responsible for an additional four hundred and sixty thousand deaths from renal sickness. The age-standardized death rates for diabetes have increased by 3% between the years 2000 and 2019. According to Diabetes, 2023, nations with lower-middle incomes had a 13% rise in the death rates caused by diabetes. On the other side, the risk of dying between the ages of 30 and 70 from any of the four most common noncommunicable illnesses (cancer, chronic respiratory diseases, diabetes, or cardiovascular diseases) reduced by 22% throughout the globe between the years 2000 and 2019 (Diabetes, 2023).

According to the International Diabetes Federation (IDF), Bangladesh ranked seventh globally in 2021 with 13.1 million cases of adult diabetes (ages 20-79) (International Diabetes Federation, 2019) Our forecasts indicate that Bangladesh will hold the seventh position in the world by the year 2045.

One of the seven countries that make up the IDF SEA area, Bangladesh is one of them. According to 'The International Diabetes Federation (IDF) Bangladesh, the number of people living with diabetes is expected to rise to 151.5 million by the year 2045(The International Diabetes Federation (IDF)Bangladesh, n.d.). There are now 537 million people living with diabetes in the world. According to the findings of the study, the number of diabetics in Bangladesh would rise to over 7.9 million by the year 2020, which is about one in ten adults in the country. It should be underlined that our data included a younger demographic than the estimates provided by the IDF; as a result, the total case count is inflated due to the fact that diabetes is less prevalent in the younger age range. Despite this, there is an immediate need for policies that will support the implementation of diabetes prevention programs in this country. This is due to the high incidence of diabetes cases in Bangladesh, which places it among the nations of Southeast Asia with the largest burden of the illness (Hossain et al., 2022). Both diabetes and its precursor, prediabetes, affect a sizeable percentage of the population in Bangladesh. According to the numbers from the most recent BDHS 2017–18 survey, in the year 2020, more than 19 million Bangladeshis who were 18 years of age or older will have diabetes or prediabetes. Diabetes was connected with age, sex, body mass index (BMI), income quintile, job status, hypertension, and the administrative division of the nation; however, it was not associated with either location of residence (urban or rural) nor degree of education. These findings provide further evidence that diabetes and prediabetes continue to have a pervasively high incidence in Bangladesh (Hossain et al., 2022).

Throughout the course of human history, several communities have placed a significant amount of their medicinal reliance on plants and herbs (''Medicinal Plants and Herbs for Diabetes. n.d.). The treatment and management of diabetes is now the focus of research in contemporary medicine, which is looking at the viability of using traditional remedies either on its own or in conjunction with conventional pharmaceuticals. It is imperative that the origin and purity of a plant be established before determining whether or not it is effective and whether or not it may mitigate any potential adverse effects. Nazamuddin et al. (2014), state that if employing herbal medications, one should always seek the opinion of a qualified specialist (Nazamuddin et al., 2014).

In the polyherbal Unani preparation Tablet DOLABI®, Have a combination of three great antidiabetic herbs as well as one mineral. In addition to Gymnema *(Gymnema sylvestre)*, Bamboo Manna *(Bambusa bambos)*, Bladder Dock *(Rumex vesicarius)*, and Mineral Pitch (Shilajit), the anti-diabetic mixture also contains Bladder Dock *(Rumex vesicarius)*. Dolabi is a research product that is manufactured by Hamdard Laboratories. It is a tried-and-true cure for diabetics that comes from the Unani tradition. The most important ingredient in Dolabi is gymnema, also known as Gymnema sylvestre. Additionally, it is referred to as gurmar, which is a Hindi word that literally translates as "destroyer of sugar" (Tiwari et al., 2017). Insulin secretion is improved with dolabi, and the drug also improves pancreatic function. It does this by aiding in inhibiting the absorption of sugar from the gastrointestinal tract (''Tablet Dolabi-Description'' n.d.). This helps to keep a normal blood sugar level, which is beneficial to overall health.

Gymnema (Gymnema sylvestre)

There is a kind of woody climbing plant known as Gymnema sylvestre that is native to the tropical woods in the middle and southern parts of India. In the production of herbal treatments, the leaves constitute an essential component. Meshasringi is the Sanskrit name for G. sylvestre, which translates to "ram's horn" in English and "periploca of the woods" in Spanish. Both of these names relate to the same plant. The chewing of the leaves affects one's capacity to sense sweetness, which is where the Hindi word gurmar, which translates to "destroyer of sugar," comes from (Tiwari et al., 2017).

It wasn't until the late 1920s that researchers discovered the hypoglycemic (or blood sugar-lowering) properties of gymnema leaves (Mhaskar and Caius, 1930). It is assumed that compounds belonging to the chemical family known as gymnemic acids are the ones responsible for the pharmacological action. According to research conducted by Sugihara et al. (2000) on healthy participants, gymnema leaves cause a rise in insulin levels (Sugihara et al., 2000). Research conducted on animals suggests that this might be occurring for one of two reasons: either the insulin-secreting cells in the pancreas are renewing (Shanmugasundaram et al., 1090; Prakash et al., 1986) or the insulin flow from these cells is growing.

Figure-1. *Gymnema sylvestre* fresh leaf. source. Wikipedia

Figure-2. *Gymnema sylvestre* dry leaf.

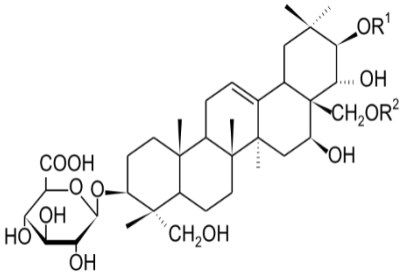

Figure-3. Gymnemic Acids source. Wikipedia

Figure-4. *Bamboo Manna (Bambusa bambos)* Tree. Source. Wikipedia

Figure-5. Bamboo shoot Source. Wikipedia

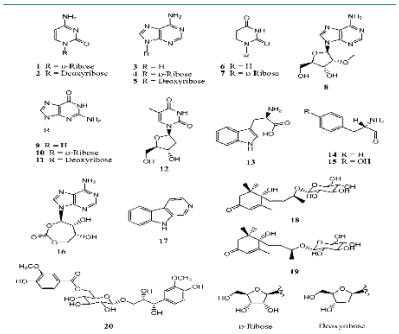

Figure-6. Chemical Constituents of *Bamboo Manna* source. (Sun, J et al.,2016).

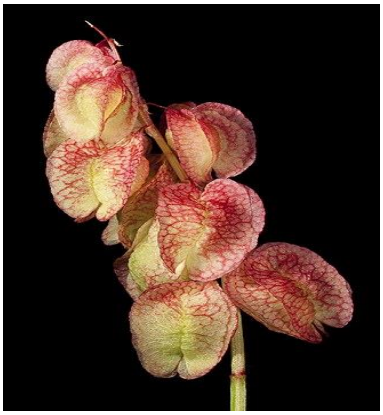

Figure-7. Bladder Dock (Rumex vesicarius) flower Source. Wikipedia

Figure-8. Bladder Dock herb Source. Wikipedia

Figure-9. Structures of Luteolin source. (Al-Masri, A. A et al.,2023)

Figure-10. Mineral Pitch (Shilajit) In mountain source. https.//mapi.com

Figure-11. Mineral Pitch (Shilajit) Rock source.https.//www.tattvasherbs.com

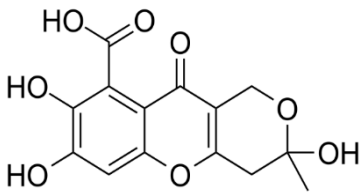

Figure-12. Fulvic Acid source. Med Chem Express

According to other animal research (Gholap and Kar, 2003, Shimizu et al., 1997), gymnema has the ability to bring blood sugar levels down by increasing the amount of glucose that is taken up into cells, preventing adrenal hormones from stimulating the liver to produce glucose, and reducing the quantity of glucose that is absorbed from the stomach. In the clinical studies, the use of gymnema sylvestre as an anti-diabetic medication was proven to be successful. The action that is insulinotropic Adult human volunteers (25–40 years old) displayed activity after taking two doses of 2 g/day of Gymnema sylvestre (Shanmugasundaram et al., 1981). When given to ten healthy subjects over the course of ten days and to six diabetics over the course of fifteen days, a water-based Gymnema sylvestre leaf extract may have decreased fasting and oral glucose tolerance test (OGTT) glucose

intensity (Khare et al., 1983). The only exception to this was the OGTT in the normal cluster. It has been established that a diabetic patient's HbA1C level may be lowered by ingesting 400 mg of the leaf extract of Gymnema sylvestre twice a day (Joffe and Freed, 2001). Figure 1, 2 and 3 is showing the picture of: fresh leaf of Gymnema sylvestre, Gymnema sylvestre dry leaf, Gymnemic Acids.

***Bamboo Manna* (*Bambusa bambos*)**

Bambusa bambos is a species of clumping bamboo that is endemic to Southern Asia. It is also known as the huge thorny bamboo, Indian thorny bamboo, spiny bamboo, and thorny bamboo. It may be found in India, Bangladesh, Sri Lanka, and Indochina. In addition to this, it has been granted citizenship in the countries of the Seychelles, the Philippines, Java, Malaysia, Maluku, Central America, and the West Indies. (Ohrnberger, 1999). Figure 4, 5 and 6 is the picture of: *Bamboo Manna (Bambusa bambos)* Tree, Bamboo shoot and, Chemical Constituents of Bamboo Manna.

In yet another study, streptozotocin-induced diabetic rats were given bambusa arundinacea, which was reported to have hypoglycaemic effects (Nazreen et al., 2011). They found in their research that treating rats resulted in a significant decrease in blood sugar levels, as well as a fall in glutathione and lipid peroxidation levels, and an increase in enzyme activity. These changes were all brought about by the treatment. According to their results, diabetic mice are susceptible to oxidative stress, and the leaf extract of B. balcooa has the potential to aid in reestablishing a healthy balance between the processes that lead to the production of reactive oxygen species and the activity of enzymes that assist scavenge them. (Goyal et al., 2017).

***Bladder Dock* (*Rumex vesicarius*)**

Rumex vesicarius is a species of perennial flowering plant that belongs to the family Polygonaceae. It is also known by the common name's bladder dock and Ruby dock, among other names. Rumex vesicarius is an indigenous plant that may be found in tropical and temperate regions of Asia, Africa, and Western Australia, according to Plants of the World Online. (Rumex vesicarius L, 2020). Figure-7, 8 and 9 is the picture of: *Bladder Dock (Rumex vesicarius)* flower, Bladder Dock herb and Structures of Luteolin.

The leaves of Rumex vescarius L. are used to provide local treatment for diabetes, a disease that is chronic. The flavonoid luteolin from Rumex vescarius was chosen to study for the possibility of acting as an anti-diabetic agent through the use of an in vivo test against male albino Wistar rats. These rats had been fed alloxan to induce diabetes. Interaction with the enzyme alpha-glucosidase may be responsible for the potent anti-diabetic properties of the plant and the flavonoid luteolin that the plant has (Al-Masri et al., 2023).

***Mineral Pitch* (Shilajit)**

It is an exudate that is frequently found in the Himalayas, Badakhshan in Afghanistan, the Karakoram, Gilgit-Baltistan in Pakistan, Nepal, Bhutan, Russia, Central Asia, Iran, Mongolia, and the south of Peru, where it is known as Andean Shilajit. Shilajit is also known as Mumijo (Wilson et al., 2011). Shilajit is also known as Mumijo. Mumijo is another name for Shilajit. (Hill and Forti, 1997). Figure-10,11 and 12 is showing the picture of: Mineral Pitch (Shilajit) In mountain, Mineral Pitch (Shilajit) Rock and chemical structure of Fulvic Acid.

The effects of Shilajit extract on diabetic neuropathy in streptozotocin-induced diabetic male rats were explored utilizing behavioral and cytotoxic activities. The doses used were fifty, one hundred, and two hundred milligrams per kilogram. After administering Shilajit injections at a dose of 100 milligrams per kilogram per day for a period of four weeks, researchers (Trivedi et al., 2004) discovered that blood sugar levels fell as a result of the treatment. Shilajit, at a dose of 100 mg/kg, was orally administered to the animals, and it was determined that this resulted in lower levels of blood sugar (Bhattacharya, 1995). This finding was made in comparison to the group that served as the control. According to the findings of a study carried out by Trivedi et al. (2004), reactive oxygen species have a substantial role in the progression of diabetic neuropathy. Shilajit has the capacity to scavenge free radicals, which decreases the harmful impact that accumulated free radicals can have on pancreatic cells (Bhattacharya, 1995). According to the findings of an experiment (Bhattacharya, 1995), Shilajit has the ability to scavenge free radicals.

Methods

Type of the study: In this prospective, open-label, herbal coded test drug-controlled, parallel trial, allopathic (Metformin HCL 500mg) and herbal coded test drug groups (Tablet DOLABI®) were allocated in a 3:1 ratio.

Study population: Participants in the research must be between the ages of 30 and 70, be of both sexes, have fasting blood glucose (FBG) > 5.6 mmol/L or HbA1c > 7%, and have been using oral hypoglycaemic medications (metformin and/or glibenclamide) for more than three months.

Sample size: Patients were picked and registered by a process known as random sampling. Screening tests, such as blood sugar levels while the patient was fasting and lipid profiles, were performed on an average of two to three patients every clinic day. The clinical experiment had a total of 212 participants' participation. Following the completion of the inclusion and exclusion procedures, the test and positive control groups comprised a total of 159 patients and 53 patients, respectively.

Sampling technique: Respondents were randomly assigned to receive either the herbal product or the intervention. Participants were randomly assigned to receive either the Dolabi or the Metformin HCL formulation using computer-generated randomization. Each supplement has a code correlating to the trade name box. Each and every supplement was enclosed in a set of uniform, transparent capsules created by the respective pharmaceutical firm. Participant recruitment, gathering information, and analysis (MM), as well as the supplements each participant gets, were all known to the participants and investigator.

Inclusion criteria: Participants in this research have to meet the requirements listed below: (1) Were diagnosed as T2D at least for 2 years duration; (2) Were > 30 years old; (3) Had low density lipoprotein (LDL100 mg/dL; (4) Triglycerides 150 mg/dL; (5) Had been receiving hypolipidemic (statins) drugs for over three months; (6) Had fasting blood glucose (FBG) > 5.6 mmol/L or HbA1c > 7% (53 mmol/mol); (7) Had been receiving oral hypoglycaemic drugs (metformin and/or glibenclamide) for over three months.

Exclusion criteria: Participants were deemed ineligible if they fulfilled any one of the following requirements: (1) They had type 1 diabetes, gestational diabetes, or another specific type of diabetes; (2) They were candidates for insulin therapy; (3) They had used other herbal supplements for diabetes control during the course of the study; (4) They had severe renal or hepatic impairment; (5) They had severe infection; (6) They had a history of allergies to PHF plants; (7) They were addicted to alcohol or drugs; and (8) They were pregnant or nursing.

Data analysis: In addition to descriptive statistics, mean and standard deviation calculations were performed. The identification of connections between socio-demographic parameters was accomplished through the use of cross tabulation and chi square statistics. The data were analyzed with SPSS (version 18, SPSS, Chicago, Illinois, USA), and a two-sided P value of 0.05 was considered to be significant. SPSS was distributed in the United States. In order to measure parameters of metabolic profiles, blood samples were obtained at the beginning of the experiment to establish a baseline, after 1.5 months of intervention, and after 3 months of intervention. A two-tail paired t-test was carried out as part of the main effect research in order to evaluate the usefulness of both the baseline data and the data collected after three months of blood glucose monitoring. In order to investigate the overall characteristics of the baseline, a Chi-square test was carried out on the categorical data. After obtaining a significant result from the two-tail paired t-test, we carried out Tukey's post hoc comparisons in order to establish whether or not there were pairwise differences.

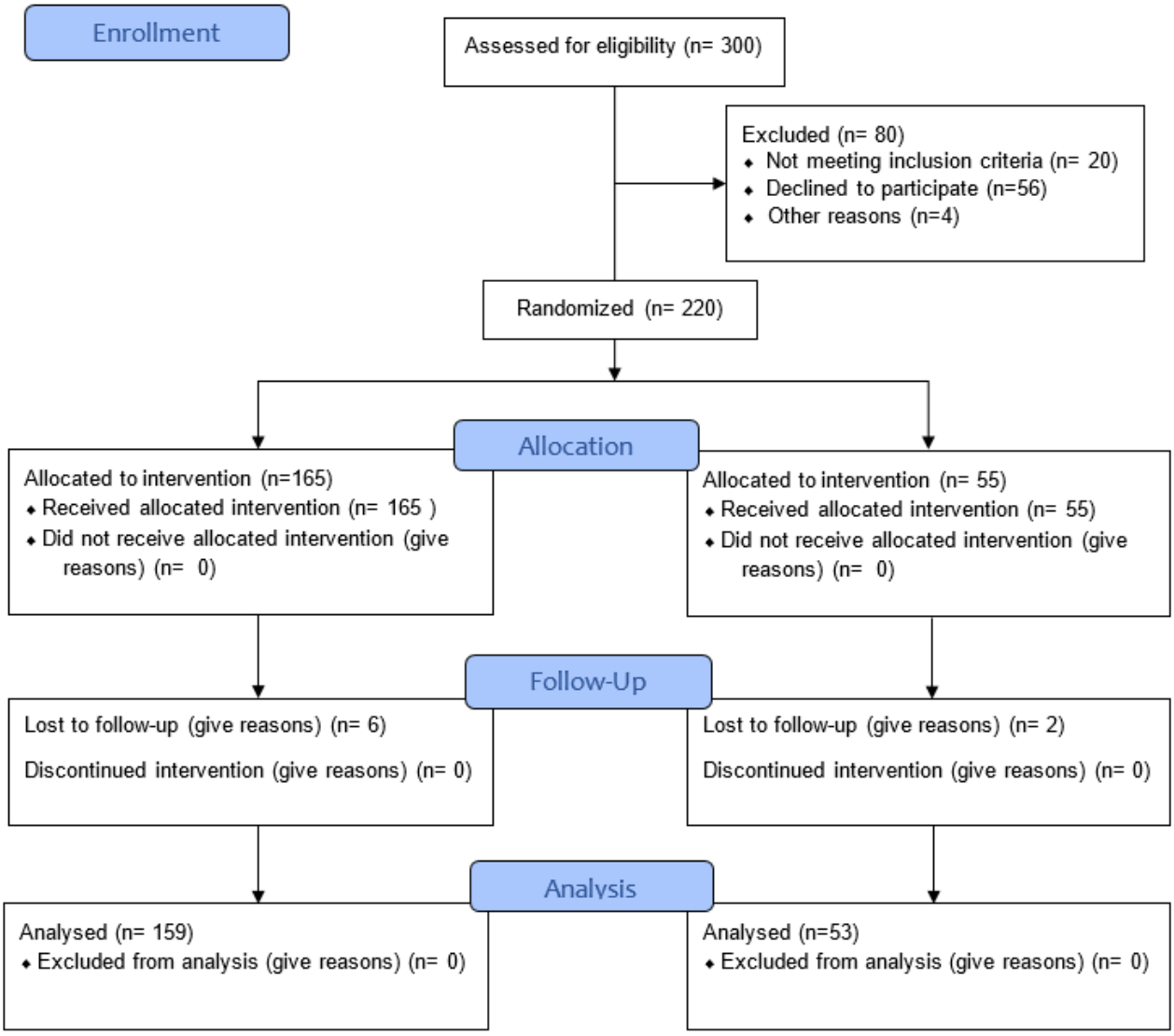

Figure 13: RCT Flowchart

Results

According to the results of our recent study, the majority of male diabetes patients of test group are in 36 and 45 class and for positive control group the class is 46-55 years, in case of female respondents' majority of diabetes patients in both groups are between the ages of 36 and 45 showed in Table 1. Participants are a sizable number of service bearers 45 showed in Table 2. The majority of participants in both groups had comorbid conditions 45 showed in Table 3. The majority of the study group was overweight, with a BMI between 23.0 and 27.5, and they had a history of diabetes in their families 45 showed in Table 4 and 5. From 1 to 5 years, the majority of the population is suffering from diabetes 45 showed in Table 6. Table 7 shows that, among 80 male respondents of test group and 28 male respondents of positive control group, mean of fasting glucose level at baseline were 9.83±1.17 and 9.99±2.52 respectively, after 1.5- month the mean was 8.61±1.07 in test group and 8.98±2.52 in positive control group and after 3 months mean was in test group 7.72±1.06 and in positive control group 6.97±1.76. Regarding 2 hours PP glucose level, among 80 respondents of test group and 28 respondents of positive control group, mean at baseline were 16.60±2.35 and 17.43±5.05, after 1.5-month mean was in test group 10.00±1.17 and in positive control group 8.29±2.42, after 3 months mean was in test group 8.23±1.17 and positive control group 7.89±2.42. Regarding HbA1c level, the mean was 9.33±1.17 and 10.43±2.36 at baseline, 8.43±1.17 and 8.35±2.03 after 1.5-month and 7.45±2.03 and 6.87±1.18 after 3 months in test and positive control group respectively. Regarding insulin level, at baseline the mean were 183.10±27.59 and 198.75±30.61. After 1.5-month they were 175.10±27.59 and 190.75±30.61 and after 3 months they were 168.10±29.59 and 183.75±30.61 in test and positive control group respectively. Comparison between baseline and after 12 weeks test data were statistically significant in case of diabetic parameters regarding male test group. Table 8 shows that, among 79 female respondents of test group and 25 female respondents of positive control group, mean of fasting glucose level at baseline were 10.02±1.11and 10.18±1.92, after 1.5- month the mean was test group 8.92±0.91and positive control 8.83±1.79 and after 3 months mean was in test group 7.78±0.93 and positive control group 6.71±1.59. Comparison test data between base line and after 3 months were statistically significant. Regarding 2 hours PP glucose level, among 79 respondents of test group and 25 respondents of positive control group, mean at baseline were 16.88±2.21 and 18.70±3.88, after 1.5-month mean was in test group 10.73±1.18 and in positive control group 8.80±3.88, after 3 months mean was in test group 8.16±1.11 and positive control group 7.60±3.74. Regarding HbA1c level, the mean was 9.84±1.04 and 10.58±1.08 at baseline, 8.57±.92 and 8.38±1.08 after 1.5-month and 7.45±1.03 and 6.98±1.08 after 3 months in test and positive control group respectively. Regarding insulin level, at baseline the mean were 199.47±30.90 and 200.00±31.83. After 1.5-month they were 189.34±30.92 and 193.00±31.83 and after 3 months they were 173.47±30.90 and 188.00±31.83 in test and positive control group respectively. Comparison between baseline and after 12 weeks test data were statistically significant in case of diabetic parameters regarding female test group.

Table 1. Age distribution by treatment group according to gender

	Age	Treatment Group			
		Test group		Positive control group	
		N	(%)	N	%
Male	≤35 years	17	21.25	04	14.29
	36-45 years	28	35.00	07	25.00
	46-55 years	20	25.00	10	35.71
	56-65 years	14	17.50	06	21.43
	>65 years	01	1.25	01	3.57
	Total	80	100.0	28	100.0
Female	≤35 years	19	24.05	06	24.00
	36-45 years	34	43.04	13	52.00
	46-55 years	17	21.51	04	16.00
	56-65 years	08	10.13	02	8.00
	>65 years	01	1.27	00	0.00
	Total	79	100.0	25	100.0

Table 2. Distribution of treatment group according to Occupation

Occupation	Treatment group			
	Test group =159		Positive control group=53	
	N	%	N	%
Unemployed	03	1.9	-	-
Service holder	70	44.0	26	49.1
Agricultural work	13	8.2	02	3.8
Business	09	5.7	02	3.8
Day laborer	03	1.9	-	-
House wife	49	30.8	17	32.1
Retired	12	7.5	06	11.3
Total	159	100.0	53	100.0

Table 3. Distribution of treatment group according to presence of comorbidity

Comorbid condition	Treatment group			
	Test group =159		Positive control group=53	
	N	%	N	%
Yes	73	45.9	26	49.1
No	33	20.8	14	26.4
Don't know	53	33.3	13	24.5
Total	159	100.0	53	100.0
If yes, Name of the condition				
Hypertension	60	82.2	21	80.8
Cardiovascular disease	11	15.1	05	19.2
Hypothyroidism	02	2.7	-	-
Total	73	100.0	26	100.0

Table 4. Distribution of treatment group according to BMI (Body Mass Index)

BMI classification (Asian)	Treatment group			
	Test group		Positive control group	
	N	(%)	N	%
Underweight <18.5	-	-	-	-
Normal range 18.5-22.9	69	43.4	14	26.4
Overweight 23.0-27.5	89	56	36	67.9
Obese c ≥ 27.5	01	0.6	03	5.7
Total	159	100.0	53	100.0

Table 5. Distribution of treatment group according to family history of Diabetes

Family history	Treatment group			
	Test group =159		Positive control group=53	
	N	%	N	%
Yes	115	72.3	42	79.2
No	44	27.7	11	20.8
Total	159	100.0	53	100.0

Table 6. Distribution of treatment group according to duration of Diabetic condition

Duration of diabetes	Treatment group			
	Test group =159		Positive control group=53	
	N	%	N	%
1-5 years	94	59.1	28	52.8
6-10 years	36	22.6	11	20.8
>10 years	29	18.2	14	26.4
Total	159	100.0	53	100.0

Table 7. Distribution of treatment group according to Diabetic parameters (Male)

Diabetic Parameter Male	Test group=80	Positive Control group=28	P value of baseline and after 3 months of test group
Fasting glucose (mgdL-1)			
Baseline data	9.83±1.17	9.99±2.52	
After 1 and half month	8.61±1.07	8.98±2.52	.000
After 3 months	7.72±1.06	6.97±1.76	
2 hours PP glucose (mgdL-1)			
Baseline data	16.60±2.35	17.43±5.05	
After 1 and half month	10.00±1.17	8.29±2.42	.000
After 3 months	8.23±1.17	7.89±2.42	
HbA1c (%)			
Baseline data	9.33±1.17	10.43±2.36	
After 1 and half month	8.43±1.17	8.35±2.03	.000
After 3 months	7.45±2.03	6.87±1.18	
Insulin (p mol L-1)			
Baseline data	183.10±27.59	198.75±30.61	
After 1 and half month	175.10±27.59	190.75±30.61	.000
After 3 months	168.10±29.59	183.75±30.61	

Table 8. Distribution of treatment group according to Diabetic parameters (Female)

Diabetic Parameter Female	Test group=79	Positive Control group=25	P value of baseline and after 3 months of test group
Fasting glucose (mgdL-1)			
Baseline data	10.02±1.11	10.18±1.92	
After 1 and half month	8.92±0.91	8.83±1.79	.000
After 3 months	7.78±0.93	6.71±1.59	
2 hours PP glucose (mgdL-1)			
Baseline data	16.88±2.21	18.70±3.88	
After 1 and half month	10.73±1.18	8.80±3.88	.000
After 3 months	8.16±1.11	7.60±3.74	
HbA1c (%)			
Baseline data	9.84±1.04	10.58±1.08	
After 1 and half month	8.57±.92	8.38±1.08	.000
After 3 months	7.45±1.03	6.98±1.08	
Insulin (p mol L-1)			
Baseline data	199.47±30.90	200.00±31.83	
After 1 and half month	189.34±30.92	193.00±31.83	.000
After 3 months	173.47±30.90	188.00±31.83	

Discussion

Although type 2 diabetes is more common in those over the age of 45, the CDC reports that it is also becoming more common in younger age groups including children, teenagers, and young adults (CDC, 2023). According to the findings of the current investigation that we have conducted, the majority of diabetes patients, regardless of gender or demographic, are between the ages of 36 and 45 approximately. It has been projected that the prevalence and incidence of diabetes would both increase in the United States (Geiss et al., 2006; CDC, 2011). These projections are based on figures obtained from earlier national surveys. According to the CDC a disruption in the normal balance of glucose in the body is presently one of the leading causes of mortality in the United States (CDC, 2011). Obesity has been identified as a significant factor in the development of type 2 diabetes as well as prediabetes (Geiss et al., 2006). This is the outcome of the growing obesity epidemic that is occurring all over the world. According to the IDF, Bangladesh had 13.1 million cases of adult diabetes (20-79 years) in 2021, placing it eighth overall. Based on our projections, Bangladesh will be ranked seventh in 2045 (International Diabetes Federation, 2019). Bangladesh is one of the seven countries in the IDF SEA region. 90 million individuals in the SEA Region and 537 million people worldwide have diabetes; by 2045, this number will increase to 151.5 million (‘The International Diabetes Federation (IDF)Bangladesh, 2013.). Analysis revealed that almost 1 in 10 persons (18+) in Bangladesh had diabetes, or more than 7.9 million people by the year 2020. It should be emphasized that our data encompassed a younger demographic than the IDF estimates, hence the overall cases are exaggerated because diabetes is less common in the younger group. Nevertheless, policies supporting the implementation of diabetes prevention programs in this country are urgently needed given the high incidence of cases of diabetes in Bangladesh, which positions it among the Southeast Asian nations with the largest burden of the illness (Hossain et al., 2022). Diabetes and prediabetes affect a substantial portion of the Bangladeshi population. In 2020, more than 19 million Bangladeshis who were 18 years of age or older will have diabetes or prediabetes, according to statistics from the most current BDHS 2017–18. Diabetes was associated with age, sex, BMI, income quintile, employment status, hypertension, and the administrative division of the nation; however, neither place of residence (urban/rural) nor level of education were. These findings confirm the persistently high prevalence of diabetes and prediabetes in Bangladesh (Hossain et al., 2022). Approximately 60% of the global population utilizes traditional medicines derived from medicinal plants (Grover et al., 2002). This review centers on the utilization of Indian Herbal drugs and plants for the management of diabetes, with a particular emphasis on their application within the Indian subcontinent.

Numerous studies have shown associations between obesity, dyslipidemia, and hypertension with insulin resistance and hyperinsulinemia, two diseases that are key components of the metabolic syndrome in individuals with diabetes (Makaryus et al., 2009). Furthermore, impaired glucose homeostasis in offspring of type 2 diabetic mothers who were diagnosed at a young age has been connected to prenatal exposures and the rise in diabetes risk associated with them (Meigs et al., 2000). The best method for preventing type 2 diabetes is to be aware of its modifiable cardiometabolic risk factors (Makaryus et al., 2009). The bulk of type 2 diabetes prevalence studies, however (Nguyen et al., 2008; Srinivasan et al., 2003), only employed one baseline evaluation at middle and later years (Lyssenko et al., 2005; Wilson et al., 2007). There is a dearth of data on the correlates of type 2 diabetes' age of onset in a community among relatively young people. The current research looks at the prevalence of diabetes as people age in the Bogalusa Heart Study, a biracial (black and white) community-based examination of the development of cardiovascular disease risk commencing in infancy (Pickoff et al., 1995).

Patients with diabetes who take G. sylvestre in pill form had decreased levels of glucose in their urine (Gharpurey, 1926) reduces adrenohypophyseal activity (Gupta, 1961), as well as the hyperglycaemic response of epinephrine

(which is known to be mediated by phosphorylase and the gluconeogenetic activity), which leads to a decrease in blood sugar levels. (Gupta and Seth, 1962). It is generally known that the herb has hypoglycemic effects on people with normal diabetes Khare et al (1983), Singh et al. (2008). Shumugasundaram (1983) found that the activity of insulin-dependent enzymes such as hexokinase, glycogen synthetase, glyceraldehydes 3-phosphate dehydrogenase, and glucose 6-phosphate dehydrogenase was reduced in the diabetic tissues of rabbits, whereas the activity of insulin-independent enzymes such as glycogen phosphorylase, gluconeogenic enzymes Treatment with G. sylvestre leaves helped maintain blood glucose in the beryllium nitrate–treated rats with disturbed carbohydrate metabolism leading to liver damage (Prasad et al., 2009) and inhibited hexokinase activity in liver (Groth, 1980). In rats with diabetes caused by exposure to alloxan (Mainigi and Bresnick, 1969). In both rabbits and dogs (Prakash et al., 1986; Kar et al., 2003), the treatment led to a balance in blood glucose levels as well as serum insulin levels. This might have been caused by the repair or regeneration of the islets of Langerhans cells in the pancreas. The water-soluble extract of G. sylvestre (GS4) did not improve insulin release in normal rats when the blood sugar was maintained at 100 mg/dl; however, it did boost hormone release in diabetic rats' islets. According to Shanmugasundaram et al. (1990a), the anti-diabetic activity needed the pancreatic function that was still present. When administered to IDDM patients who were already receiving insulin treatment, the extract (GS4) decreased insulin requirements by lowering fasting blood glucose levels, glycosylated hemoglobin levels, and glycosylated plasma protein levels, while serum lipid levels virtually recovered to normal levels. (Shanmugasundaram et al., 1990a) discovered that therapy with GS4 enhanced endogenous insulin in individuals with IDDM. This was apparently accomplished by rebuilding the patients' surviving beta cells. (Shanmugasundaram et al., 1990b) In patients with type II diabetes who did not have IDDM, using the medicine GS4 for 18 to 20 months resulted in a significant reduction in plasma lipids (cholesterol, triglycerides, phospholipids, and free fatty acids). In contrast, anti-hyperglycemic drugs like sulfonylureas and biguanides work to manage blood glucose homeostasis by stimulating insulin synthesis from the pancreas (Efendi et al., 1979) and blocking gluconeogenesis (Baskaran et al., 1990), respectively. Both of these drugs are known to cause serious side effects, the most common of which is an increase in plasma levels of cholesterol, triglycerides, and free fatty acids. Additionally, the effectiveness of these medications to regulate lipid metabolism decreases over time. During a period of ten weeks, rats that were fed a high-fat diet were administered gymnema extract in order to reduce plasma triglycerides, restrict the rise in body weight, and prevent the accumulation of intraperitoneal fat and liver lipids (Shigematsu et al., 2001a, Shigematsu et al., 2001b). Activated macrophages and lymphocytes are thought to infiltrate the inflammatory focus after the first islet inflammation, which is thought to cause experimental diabetes. These cells may be where the cytotoxic oxygen radicals come from. As part of its immunomodulatory effect, shilajit has been shown to lessen macrophage and lymphocyte activation and migration. (Bhattacharya, 1995) Additionally, because it is an antioxidant, it will guard against harm from cytotoxic oxygen radicals to the pancreatic islet cell (Bhattacharya, 1995, Ghosal et al., 1995).

In one research (Trivedi et al., 2004), shilajit (100 mg/kg) administration in euglycemic rats resulted in significant hypoglycemia. According to Gupta (1966) long-term shilajit administration increases the number of pancreatic beta cells, or pancreatotrophic activity, which may lead to improved pancreatic beta cell sensitivity and quick production of a significant amount of insulin in response to hyperglycemia. Shilajit and glibenclamide together significantly reduced blood glucose levels, which is more than either medication alone did. Therefore, it is plausible that shilajit may have extrapancreatic activity in addition to its pancreatic action, which may have contributed to its hypoglycemic effect. Shilajit (100 mg/kg) has a much greater hypoglycemic impact than metformin (500 mg/kg). Shilajit alone (100 mg/kg) reduced blood sugar levels significantly, however when combined with metformin, this effect was not further enhanced. Shilajit, in all three dosages, significantly improved the lipid profile of rats with diabetes brought on by alloxan. According to reports, hyperlipidemia develops as a result of the disruption of glucose, fat, and protein metabolism that occurs with diabetes. Shilajit's advantageous effects on the lipid profile in alloxan-induced diabetic rats may be related to improved glycemic control (Austin and Hokanson, 1994; Kraus-Friedmann, 1984; Brown and Goldstein, 1983)

The lipid profile was not significantly improved by the addition of glibenclamide to shilajit (100 mg/kg) compared to shilajit alone. This might be explained by the idea that glibenclamide's improvement of the lipid profile in diabetic rats may be secondary to improved glycemic control (Chehade and Mooradian, 2000). Because glibenclamide works through a secondary mechanism, using shilajit did not result in additional improvement in the lipid profile. Combination therapy considerably ($P<0.01$) outperforms glibenclamide alone in terms of its impact on lipid profile.

Metformin improves the lipid profile primarily by reversing impaired glucose metabolism. In addition, it causes a slight drop in triglyceride levels due to a reduction in the production of very low-density lipoprotein in the liver (DeFronzo, 1995). In our investigation, a comparable finding was observed. Additionally, postprandial hyperlipoproteinemia of intestinal origin has been reported to be considerably reduced by metformin. (Chehade and Mooradian, 2000). It is hypothesized that shilajit may operate on lipid metabolic pathways via a different method than metformin because the combination of shilajit and metformin improved the lipid profile, with the exception of TG, more than either metformin or Shilajit alone.

Using alloxan-induced diabetic rats as test subjects, aqueous ethanolic solvent extracts of the stem of Bambusa Arundinaceae (Bambsaceae) were evaluated for their ability to treat diabetes. The findings indicated that aqueous ethanolic extracts had demonstrated notable protection, and that alloxan-induced diabetic rats had the greatest drop in blood glucose. According to the findings of this thorough investigation, Bambusa arundinaceaes stem shown statistically significant anti-diabetic effect when compared to the widely used glibenclamide (Macharla et al., 2012).

The DPPH test is the easiest and most reliable method for assessing the antioxidant capabilities of herbal products.The polyphenol-rich R. vesicarius (ArOH) lowers the rates of oxidation of organic materials by adding a hydrogen atom to the chain-carrying ROO* radicals (Gaurav et al., 2020). Polyphenols play a key role in the biological system's metabolism of reactive oxygen species (ROS) by preventing the generation of free radicals. According to earlier experimental and clinical investigations, it may be possible to halt the progression of diabetes by blocking carbohydrate hydrolyzing enzymes such glucosidase and amylase (Francoet al., 2020). For both human and animal species, starch serves as the main source of carbohydrates. Salivary and pancreatic -amylase randomly converts the starch into simple saccharides, resulting in smaller molecules like glucose that are absorbed into the bloodstream. According to Gaurav et al. (2020), the -amylase and -glycosidase inhibitors either stop the digestive tract from absorbing sugar or postpone the breakdown of starch into simpler sugars. Our results demonstrated that R. vesicarius might delay the breakdown of carbohydrates.

Dry extracts of Gymnema (*Gymnema sylvestre*), Bamboo Manna (*Bambusa bambos*), Bladder Dock (*Rumex vesicarius*), and Mineral Pitch (Shilajit) were given to research participants. But other than a basic spoken explanation regarding carbohydrates and sugary foods, no specific diet or exercise regimen was suggested. When assessing the study's findings, this constraint must be considered.

Conclusions

In conclusion, those with hyperglycemia have increased glucose levels, showed a positive effect and reduced blood glucose level after taking a combination of dry extracts from the following plants: Gymnema (*Gymnema sylvestre)*, Bamboo Manna (*Bambusa bambos*), Bladder Dock (*Rumex vesicarius*), and Mineral Pitch (Shilajit). To determine the appropriate diet and nutritional state of patients, more study is required. Additionally, depending on how severe the diabetic's condition is, the effects of a combination of dry extracts from the following plants may be used: Gymnema (*Gymnema sylvestre*), Bamboo Manna (*Bambusa bambos*), Bladder Dock (*Rumex vesicarius*), and Mineral Pitch (Shilajit).

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