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Alternative Treatment Approaches For The Management Of Diabetes: Role Of Soursop Leaves And Spirulina As Antidiabetic Agents

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Abstract

Diabetes mellitus (DM) is a metabolic disorder characterized by blood glucose levels that are consistently high. Different medicinal approaches may be used to address this complex medical condition. Herbal formulations and extracts are gaining popularity as a means of treating type 2 diabetes (T2DM). Therefore, the purpose of this research is to examine the efficacy of spirulina and powdered soursop leaves as dietary supplements for the treatment of diabetes. Thirty individuals with type 2 diabetes mellitus were randomly assigned to one of three groups: Experimental Group I (SP), which received Spirulina powder (SP), Experimental Group II (SLP), which received Soursop leaves powder (SLP), and Control Group (placebo). There were several preexisting similarities between the control and research groups. Multiple criteria were used to evaluate the efficacy of administering 2 grams of supplementations twice a day for three months. A nutritional study of the supplements showed that the powdered spirulina is high in calories, carbohydrates, proteins, lipids, iron, and magnesium, whereas the powdered soursop leaves had a high moisture content, ash content, and crude fiber content. The microbiological analysis discovered no significant differences between the two supplements. The phytochemical analysis revealed a high phenolic and flavonoid content in the soursop leaf powder. The anthropometric study yielded similar results for SP and SLP. Diabetic subjects' lipid profiles (TCH, HDL, LDL, VLDL, and TGL) and blood glucose levels (FBG, PPBGC, and glycosylated hemoglobin, HbA(1c)) were measured before and after the supplementation. After 3 months of supplementation with powdered soursop leaves, both fasting and postprandial blood glucose levels were considerably reduced. The HbA(1c) level also decreased significantly, which is indicative of better long-term glucose management. Triglyceride levels dropped significantly compared to lipid levels. The participants who were given spirulina powder had substantial increases in high-density lipoprotein (HDL) and decreased levels of total cholesterol (TC), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL). Evaluation of clinical symptoms and problems post-intervention revealed that spirulina supplementation successfully reduced symptoms and complications. These findings provide evidence in favor of the effectiveness of spirulina powder in improving the lipid profile and soursop leaf supplementation in decreasing blood glucose levels in individuals with type 2 diabetes mellitus.

Keywords: Diabetes, Antidiabetic, Type 1 diabetes, Type 2 diabetes, MODY, HDL, VLDL

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1. Introduction

The term "diabetes mellitus" originates from the Greek word "diabetes," which translates to "siphon" or "to pass through," and the Latin word "mellitus," which means "sweet." An examination of historical records reveals that the designation "diabetes" was first used by Apollonius of Memphis during the period of 250 to 300 BC. The civilizations of Ancient Greece, India, and Egypt were among the early societies to recognize the presence of sweetness in urine as a characteristic of a particular medical illness. Consequently, the term "Diabetes Mellitus" emerged as a result of their observations and understanding. In 1889, Mering and Minkowski made a significant discovery on the involvement of the pancreas in the pathophysiology of diabetes. The hormone insulin was isolated from the bovine pancreas by Banting, Best, and Collip in 1922 at the University of Toronto, resulting in the subsequent development of a viable therapy for diabetes. Over the course of time, significant endeavors have been undertaken, resulting in several breakthroughs and the development of various approaches to address this escalating issue. Regrettably, diabetes continues to be prevalent as a chronic ailment both nationally and globally. In the United States, it continues to be ranked as the seventh most prevalent cause of mortality (Sapra & Bhandari, 2023).

Diabetes mellitus (DM) is a metabolic disorder characterized by abnormally high amounts of glucose in the bloodstream. It encompasses many categories, including type 1 and type 2 diabetes, maturity-onset diabetes of the young (MODY), gestational diabetes, neonatal diabetes, and secondary causes attributed to endocrinopathies, steroid use, and other related factors. The primary subcategories of diabetes mellitus (DM) consist of Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM), which are often characterized by impaired insulin production (T1DM). Type 1 diabetes mellitus (T1DM) often manifests in the pediatric or teenage population, but type 2 diabetes mellitus (T2DM) is commonly associated with middle-aged and older persons who have had persistent hyperglycemia as a result of unfavorable lifestyle and dietary habits. The etiology of Type 1 Diabetes Mellitus (T1DM) and Type 2 Diabetes Mellitus (T2DM) exhibits significant differences, resulting in distinct aetiologies, manifestations, and therapeutic approaches for each type (Genuth et al., 2014).

The anticipated worldwide prevalence of diabetes in 2019 is 9.3%, corresponding to around 463 million individuals. This figure is projected to increase to 10.2% (equivalent to 578 million people) by the year 2030, and further rise to 10.9% (almost 700 million individuals) by 2045. The prevalence of the condition is found to be greater in urban regions (10.8%) compared to rural areas (7.2%), as well as in high-income nations (10.4%) in contrast to low-income countries (4.0%). Approximately half (50.1%) of individuals who have diabetes are unaware of their condition. The estimated worldwide prevalence of impaired glucose tolerance in 2019 was 7.5%, equivalent to 374 million individuals. Projections indicate that this prevalence is expected to increase to 8.0% (454 million) by 2030 and further to 8.6% (548 million) by 2045 (Saeedi et al. 2019).

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, Iss 12, Dec 2022

Within the pancreatic islets of Langerhans, two primary subcategories of endocrine cells may be identified, namely beta cells responsible for insulin production and alpha cells responsible for the secretion of glucagon. Beta and alpha cells exhibit dynamic variations in their hormone releases in response to changes in the glucose environment. In the absence of a proper equilibrium between insulin and glucagon, the levels of glucose become imbalanced in an improper manner.

Type 1 diabetes

In T1DM, beta cells in the pancreas are frequently destroyed as a result of an autoimmune process. As a result, there is no or very little insulin in the body. A significant risk factor for both kinds is the genetic background. Numerous loci have been discovered that increase the risk for DM as the human genome is studied more thoroughly. Major Histocompatibility Complex (MHC) and Human Leukocyte Antigen (HLA) polymorphisms have been shown to affect T1DM risk (Rajaei et al., 2019).

Type 2 diabetes

The development of T2DM is more subtly manifested, with an insulin functional deficit brought on by an imbalance between insulin levels and insulin sensitivity. Although insulin resistance has several causes, fat and aging are the most frequent ones. Genetics and lifestyle play a more intricate role in T2DM. There is unmistakable evidence that T2DM has a greater hereditary profile than T1DM. According to Roden and Shulman (2019), the majority of individuals with the condition have at least one parent who also has T2DM.

Gestational Diabetes

As the name suggests, gestational diabetes is diabetes discovered during pregnancy. Between 3% and 9% of all pregnancies are impacted by it. In most instances, the development of diabetes during pregnancy is brought on by an inability of the body to produce enough insulin to counteract the significant rise in insulin resistance that results from pregnancy, particularly in the second and third trimesters. These women are known to have an underlying beta cell lesion when they acquire gestational diabetes, and over time, they have a very high chance (>50%) of permanently acquiring type 2 diabetes (Petry, 2014).

Secondary or other particular kinds of diabetes make up the fourth group of diabetes. Monogenic deficiencies of beta cell function, genetic defects of insulin action, exocrine pancreatic illness, endocrinopathies, and chemically or drug-induced, infectious, and unusual immune-mediated and genetic diseases linked to diabetes are the primary groups.

MODY

Maturity-onset diabetes of youth (MODY) is the term used to describe the monogenic abnormalities in beta cell activity. Many of the individual gene abnormalities have just lately been discovered and named. For instance, MODY1 includes the glucokinase gene on chromosome 7 and MODY2 involves the hepatocyte nuclear factor 4-alpha (HNF4-) gene on chromosome 20 (ADA, 2012).

To control T2DM, weight reduction, and lifestyle modifications may partially decrease hyperglycemia. However, certain anti-diabetic medications are necessary to manage glycemic levels. Oral anti-diabetic medications have certain unfavorable side effects, such as hypoglycemia, fluid retention, osteoporosis, and heart failure, which restricts their clinical use. In order to treat hyperglycemia, hyperinsulinemia, and hypertriglyceridemia, it is required to create novel anti-diabetic options with low adverse effects (Ghosh & Parida, 2016).

Recent research, as reported by McCoy et al. 39, shows that young individuals have difficulty controlling their diabetes, particularly when it comes to their food. Young people have life-stage pressures related to managing their nutrition, medications, and insulin regimens as well as checking their blood sugar levels. Additionally, diabetes management may be increasing their professional, educational, and other obligations, which sometimes may conflict with the best diabetic care. Young individuals with T2DM are growing more likely to have numerous diabetes complications due to the early beginning of the disease.

Additionally, recent research showed that consuming a lot of antioxidants, polyphenols, and dietary fiber prevents the development of T2DM and reduces oxidative stress since they have a low glycaemic index and maintain healthy blood sugar levels (McCoy et al. 39, 2019).

However, there hasn't been much research that has looked into the value of dietary supplements that include polyphenols and antioxidants in regulating blood sugar levels and enhancing health. Additionally, it has not been well-researched how antioxidant-rich dietary supplements could prevent the development of T2DM. In light of this, the current research aims to explore the effectiveness of dietary supplements in the efficient treatment of diabetes, since young individuals with diabetes find it challenging to control their diets in addition to their prescriptions and insulin injections.

For thousands of years, natural products (NPs), such as herbal formulations and their extracts, have been utilized to treat human illnesses with a distinct system of ideas and treatments. These NPs are now increasingly being used to treat T2DM (Pang, 2014). The impacts and processes of NPs have drawn increasing amounts of interest in recent years (Salimifar et al., 2013).

The current research will supplement the body of knowledge on diabetes and its prevalence globally. The significance of managing diabetes with dietary and lifestyle changes is discussed in this research. Additionally, the study will discuss dietary supplements that can support maintaining body weight and glycaemic levels, as well as existing research on the benefits of

ISSN PRINT 2319 1775 Online 2320 7876

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antioxidants and phytochemicals for T2DM self-management and their role in regulating blood sugar levels and maintaining weight. Natural dietary supplements may be effective in managing T2DM and are safe to use. In order to minimize morbidity and associated difficulties in young people during their most productive years of life, natural dietary supplements may serve as supportive therapy.

1.1 Objectives of the Study

- To identify the early adult diabetic subjects (20 to 40 years of age).
- To develop and standardize natural substance powders (Spirulina powder and Soursop leaves powder) for selected early adult diabetic subjects.
- To assess Nutritional Status (ABCD technique) of all selected Early adult diabetic subjects.
- To assess the effectiveness of the developed product on selected early adult diabetic subjects.
- To make the comparison between control and experimental groups before and after supplementation.

2. Materials and methods

Spirulina powder, Soursop leaves powder, Bengal gram dal, black gram dal, red chilies, cumin seeds, coriander seeds, wheat flour, and buttermilk. The different parameters are investigated are the nutritional content of the developed products, demographic and anthropometric analysis, pre and post-collection of data regarding the blood glucose levels, and lipid profiles, and the changes in clinical symptoms and complications.

2.1. Study Design

The current study uses a case study design. The subjects were divided into 2 case study groups and 1 control group. In each case study group, there were 30 subjects totaling 60 subjects in 2 experimental groups and an additional 30 subjects for the control group making a total of 90 subjects.

2.1.2 Size and Duration

A total number of 90 early adult diabetic subjects were selected and the study was performed for a duration of three months. The sample size was selected after the consent and patient information sheet. Below are the criteria for the groups. Before conducting the study, ethical approval was obtained from the Institutional Ethics Committee from SPMVV and St John's Hospital and Medical College, Bangalore, Karnataka. Insurance from Bajaj Alliance was also obtained as per the requirement of St John's Hospital and Medical College, Bangalore, Karnataka.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, Iss 12, Dec 2022

Group	Intervention
Control Group	-
Experimental Group -1	Spirulina powder
Experimental Group –II	Soursop leaves powder

2.1.3 Inclusion criteria

As per the requirement of the study, subjects diagnosed with Type 2 diabetes and within the age group of 20-40 years were selected for the intervention/study.

2.1.4 Exclusion criteria

Since the intervention/study is intended for the age group of 20-40 years, other ages of people who were below 20 and above 40 years were not considered and people who are dependent on insulin were also not considered for the intervention/study.

2.1.5. Area of the Sample Collection

The study was conducted at St John's Hospital and Medical College, Bangalore, Karnataka. The primary reason for selecting St John's Hospital and Medical College, Bangalore, Karnataka is that we can recruit many subjects for study from various income/economic backgrounds.

2.1.6 Tools used for data collection

- The study used an interview schedule process and segregated only relevant questions and a standardized questionnaire was prepared with questions related to Demographical characteristics and "Nutritional Status Assessment (ABCD)".
- Under demographical data, the data regarding the name, age, gender, education, occupation, monthly income, and personal habits were collected.
- The anthropometric data such as the height, weight, and body mass index (BMI) of the subjects before and after intervention were collected.
- "Pre and Post collection of the data for biochemical investigations are Fasting blood glucose (FBG), Postprandial blood glucose (PPBG), Glycosylated hemoglobin (HbA1c), and lipid profile (Total cholesterol, LDL, HDL, VLDL, and Triglycerides)" from the subjects who participated in the study.
- Attributes regarding the history of the subject's health, and their present health condition with respect to "excessive thirst, excessive hunger, frequent urination, weight

ISSN PRINT 2319 1775 Online 2320 7876
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loss, weakness, decreased wound healing, excessive sweating, numbness, blurred vision, fatigue, etc. were collected. Information on the subject's Comorbid factors such as heart diseases, diabetic neuropathy, nephropathy, retinopathy, diabetic ketoacidosis, etc., and associated medical illnesses like hypertension and asthma were collected".

- The assessed dietary patterns and the food frequency consumption of the subjects were recorded by the 24-hour recall method.

2.1.7 Selection of supplementation products and method of preparation for supplementation

The current study used natural resources such as Spirulina and Soursop leaves which were blended. The primary reason for selecting these substances is because these supplements do not have adverse effects like traditional medications.

- **"Spirulina (*Arthrospira platensis*)** - Spirulina contains protein, essential fatty acids such as GLA (gamma-linolenic acid), Omega 3, 6, and 9, Chlorophyll, Phycocyanin, Iron, Vitamins A, B, C, D, and E, Calcium, Potassium, Copper, Magnesium, Selenium and Zinc. Spirulina helps in synthesizing natural insulin. The organic powder was sourced from the vendor for intervention.

- **Soursop leaves (*Annona muricata*)** - Soursop leaves contain various vitamins, and minerals viz., Beta carotene, Vitamins B, C, E, Potassium, Magnesium, Copper, Manganese, Chromium, Calcium, Iron, Protein, Fibre, and phyto nutrients that are rich in antioxidant compounds including Alkaloids, Flavonoids, Lactones, Saponins, Tannins, Phenols, Phytosterols and Acetogenin. Soursop leaf can help in improving the function of pancreatic beta cells that produce insulin". The leaves were washed thoroughly in cold water and dried under a sunshade for 8 days. The dried leaves were then made into fine powder for intervention.

The powders that were developed underwent a selection process and were afterward standardized to assess their anti-diabetic characteristics. Additionally, a nutritional analysis of the powders was conducted in the laboratory using established protocols. The powders have a high content of dietary fiber, magnesium, zinc, iron, and phytochemicals. A sensory examination was carried out at the laboratory of the SPMVV department.

2.1.8 Intervention Program

For the intervention program, the following products were used

(a) Spirulina powder and
(b) Soursop leaves powder

ISSN PRINT 2319 1775 Online 2320 7876

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Note - Patients were given 2 grams of the above powders per day

Using the above powders three separate products were prepared namely,

- **Rice & Dal Spice Mix Powder** (Ingredients roasted Bengal gram dal, black gram dal, red chilies, cumin seeds, and coriander seeds). Both the dietary supplement powders were individually mixed with Rice and the Dal Spice Mix Powder.

- **Wheat Flour**: Both the dietary supplement powders were individually mixed with the Wheat Flour and served as Chapati/Rotis.

- **Butter Milk:** Both the dietary supplement powders were individually mixed and served with Butter Milk.

2.1.9 Statistical analysis

The SPSS package program was used for the statistical analysis of the data. Mean. Standard deviation, ANOVA, t-test, and chi-square test were used to verify the significant differences between control and experimental groups before and after interventions.

3. Results

3.1 Analysis of the nutrient composition of the developed products

The below table shows the nutrient composition of Spirulina and Soursop leaves powder. From the results, it is evident that Spirulina powder is higher in energy with 290 K calories than Soursop leaves powder. It also showed higher amounts of carbohydrates (23.9g), crude protein (57.5g), crude fat (7.7), iron (28.5 mg), and magnesium (195mg) than Soursop leaf powder. Whereas, Soursop leaves powder is high in moisture content (7.8 g), Ash (14.9g), and crude fiber (9.3g).

Table 1: Analysis of Nutrient Composition of the Developed Products

Sl. No.	Nutrient	Spirulina Powder	Soursop Leaves Powder
1	Energy(Kcal)	290	66
2	Carbohydrates (grams)	23.9	16.6
3	Crude Protein(grams)	57.5	1.0

ISSN PRINT 2319 1775 Online 2320 7876
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4	Crude Fat(grams)	7.7	0.3
5	Moisture (grams)	4.68	7.8
6	Ash(grams)	6.23	14.9
7	Crude Fibre(grams)	3.6	9.3
8	Iron(mg)	28.5	0.6
9	Zinc(mg)	2	0.1
10	Magnesium (mg)	195	21

3.2 Microbiological Evaluation of the Developed Products

Next, the microbiological analysis of the developed products was conducted and the parameters used were Yeast and Mould, Total Plate Count, and Coliform. The results are expressed in Table 2. It was found that yeast and mold and Coliform for Spirulina powder were absent during the initial analysis as well as after 15, 30, 45, 60, 75, and 90 days of shelf-life testing frequency. The total plate count was found to be less than 1 during the initial analysis and remained the same throughout the shelf-life testing frequency after 15, 30, 45, 60,75, and 90 days. A similar result was observed in soursop leaf powder.

Table 2: Microbiological Evaluation of the Developed Products

Product	Sl. No.	Parameters	UOM	Initial Analysis	Shelf-Life Testing Frequency					
					After 15 Days	After 30 Days	After 45 Days	After 60 Days	After 75 Days	After 90 Days
Spirulina Powder	1	Yeast and Mould	PR/AB/Gram	Absent	Absent	Absent	Absent	Absent	Absent	Absent
	2	Total Plate Count	CFU/Gram	<1	<1	<1	<1	<1	<1	<1
	3	Coliform	PR/AB/Gram	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Soursop Leaves Powder	1	Yeast and Mould	PR/AB/Gram	Absent	Absent	Absent	Absent	Absent	Absent	Absent

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	2	**Total Plate Count**	**CFU/Gram**	**<1**	**<1**	**<1**	**<1**	**<1**	**<1**	**<1**
	3	**Coliform**	**PR/AB/Gram**	**Absent**	**Absent**	**Absent**	**Absent**	**Absent**	**Absent**	**Absent**

3.3 Phytochemical Analysis of Developed Products

Table 3 shows the phytochemical content present in Spirulina powder and Soursop leaves powder. The phytochemicals that were checked for are Phenolic and Flavanoid contents. The results showed that higher phenolic (75.99 mg of GAE/100g) and flavonoid content (7.79 mg of quercitin/100g) was found in Soursop leaves powder than in Spirulina powder which showed 25.05 mg of GAE/100g of phenolic content and 6.01mg of quercitin/100g of flavonoid content.

Table 3: Phytochemical Analysis of Developed Products

Sl. No.	Products	Total Phenolic content mg of Gallic acid equivalent(GAE)/100g	Total Flavonoid content mg of Quercetin/100g
1	Spirulina powder	25.05	6.01
2	Soursop leaves powder	75.99	7.79

3.4 Effect of Interventions on Anthropometric Measurements

The next step was to investigate the anthropometric measurements of two treatment groups before and after intervention when compared with the control group. The parameters checked were weight and BMI. According to the results, the mean weight of the experimental group that received spirulina powder before intervention was 70.97 whereas the control group was 72.58kgs. The mean weight after intervention was 70.33 and the mean weight of the control group was 72.92kg. The results were found to be statistically significant as the p-value was less than 0.01. Similarly, the mean weight of the second experimental group treated with Soursop leaf powder was 72.13 similar to that of the control group (72.58) before intervention. After the intervention, the EG-II showed a mean decrease in weight to 71.43 when compared to the control group (72.92). As for the BMI, the experimental group I provided with spirulina powder showed a BMI of 26.39 before intervention when compared to that of the control group (25.91). Whereas after intervention the mean BMI remained the same with 26.17 comparable with the mean BMI of the control group. The results were found to be statistically significant as the p-value was less than 0.01. The BMI of the EG-II before intervention showed a mean BMI of 26.79 similar to that of the EG-I. The mean value after the intervention was also found to be similar to the control and EG-I with a value of 26.5. However, the results were found to be statistically significant.

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Table 4: Effect of interventions on Anthropometric Measurements

Parameters		Weight (kg)					BMI (kg/m2)				
Sl. No.	Groups	Before		After		P-value	Before		After		P-value
		Mean	±sd	Mean	± sd		Mean	±sd	Mean	±sd	
1	Control (CG)n=30	72.58	7.76	72.92	7.15	0.269	25.91	2.43	26.05	2.14	0.249
2	EG – I (SP)n=30	70.97	7.07	70.33	6.74	0.002	26.39	2.35	26.17	2.34	0.005
3	EG – II (SLP)n=30	72.13	11.47	71.43	10.75	0.001	26.79	3.81	26.5	3.66	0

3.5 Effect of interventions on Biochemical Parameters: Blood Glucose Levels

The experimental groups I and II were further investigated for biochemical parameters such as fasting blood sugar, post-prandial blood sugar, and HbA1c before and after the intervention when compared to the control group as reported in Table 5. The mean FBG of EG-I showed 171.63 before intervention and was reduced to 156.17 after intervention, whereas EG-II showed 162.73 before intervention and reported a drastic decrease to 144.63mg/dl after intervention. Whereas the control group showed 189.23mg/dl before and 196.33 after the intervention. This shows that Soursop leaves powder is more effective in reducing FBS than spirulina powder. When checked for PPBG the EG-I showed a mean value of 280.97 before intervention and a decreased value of 258.7 after intervention. The EG-II showed 260.17 before intervention and a drastic fall to 237.93 after intervention. The values were compared to the control value which was 307.47 before the intervention and 318 after the intervention. Similarly, the EG-I showed a mean HbA1c value of 8.59 before intervention and 8.08 after intervention whereas the EG-II showed 8.66 before intervention and 8.22 after the intervention. These values were compared with that of the control which showed 9.72 and 9.76 before and after intervention. The overall results show that the EG-II provided with soursop leaves powder showed beneficial effects in lowering the blood glucose level.

Table 5: Effect of interventions on biochemical parameters: Blood glucose levels

Groups	FBG(mg/dl)	PPBG(mg/dl)	HbA1c (%)

ISSN PRINT 2319 1775 Online 2320 7876

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	Before		After		P-value	Before		After		P-value	Before		After		P-value
	Mean	±sd	Mean	±sd		Mean	±sd	Mean	±sd		Mean	±sd	Mean	±sd	
Control (CG) n=30	189.23	57.17	196.33	65.62	0	307.47	76.15	318	76.05	0.156	9.72	2.06	9.76	2.11	0.738
EG – I (SP) n=30	171.63	67.7	156.17	60.86	0	280.97	46.13	258.7	46.27	0	8.59	1.6	8.08	1.45	0
EG – II (SLP) n=30	162.73	55.51	144.63	47.53	0	260.17	47.66	237.93	45.3	0	8.66	1.43	8.22	1.3	0

3.6 Effect of interventions on Biochemical Parameters of all the subjects – Lipid Profile

The biochemical parameters such as the lipid profile were investigated in EG-I and EG-II before and after the intervention. The parameters checked were Total cholesterol (Tch), High-density lipid (HDL), and Low-density lipid (LDL). Before the intervention, the EG-I and EG-II showed 210.8 and 193.4 mg/dl TCH before intervention it was reduced to 189.87 and 178.07mg/dl. It is evident that EG-I showed a significant decrease after intervention. The HDL value for EG-I and EG-II before intervention was 39.7 and 42.27 mg/dl and 43.8 and 43.4mg/dl after the intervention. These results clearly indicated that the HDL was effectively increased in EG-I. The LDL values for EG-I and EGII before intervention were 137.67 and 150.43mg/dl and after intervention, it was reduced to 126.6 and 143.6mg/dl. Here again, the EG-I provided with spirulina powder showed good effects in reducing the LDL. All the results were compared to the control group.

Table 6: Effect of interventions on Biochemical Parameters of all the subjects –Lipid Profiles

Groups	TCH(mg/dl)					HDL(mg/dl)					LDL(mg/dl)				
	Before		After		P-value	Before		After		P-value	Before		After		P-value
	Mean	±sd	Mean	±sd		Mean	±sd	Mean	±sd		Mean	±sd	Mean	±sd	

Control (CG) n=30	**213.27**	**21.12**	**204**	**20.46**	**0**	**43.8**	**6.51**	**44.27**	**6.34**	**0.36**	**133.37**	**30.54**	**133.9**	**29.13**	**0.779**
EG – I (SP) n=30	**210.8**	**33.02**	**189.87**	**31.01**	**0**	**39.7**	**4.84**	**43.8**	**5.99**	**0**	**137.67**	**34.87**	**126.6**	**27.28**	**0**
EG – II (SLP) n=30	**193.4**	**31.74**	**178.07**	**29.87**	**0**	**42.27**	**5.84**	**43.4**	**5.59**	**0.002**	**150.43**	**36.24**	**143.6**	**31.2**	**0**

3.8 Effect of interventions on biochemical parameters of all the subjects –Lipid Profiles

The experimental groups EG-I and EG-II were also checked for the decrease of VLDL and TGL after the intervention. It was found that before intervention the mean VLDL values of EG-I and EG-II were 45.03 and 42.13mg/dl and 40.33 and 39.3mg/dl after the intervention. Whereas EG-I and EG-II showed the TGL values as 199.87 and 185.83mg/dl before intervention and 174.43 and 169.67mg/dl after intervention. The results were compared to the control values. Clearly, the EG-I showed as a potent product in reducing the VLDL and TGL effectively.

Table 7: Effect of interventions on Biochemical Parameters of all the subjects –Lipid Profiles

Groups	**VLDL(mg/dl)**					**TGL(mg/dl)**				
	Before		**After**		**P-value**	**Before**		**After**		**P-value**
	Mean	**±sd**	**Mean**	**±sd**		**Mean**	**±sd**	**Mean**	**±sd**	
Control (CG)n=30	**50.83**	**14.6**	**52.9**	**14.9**	**0.04**	**201.13**	**37.65**	**194.9**	**40.05**	**0.164**
EG – I (SP)n=30	**45.03**	**11.9**	**40.33**	**12.11**	**0.002**	**199.87**	**26.78**	**174.43**	**20.11**	**0**
EG – II (SLP)n=30	**42.13**	**11.54**	**39.3**	**9.75**	**0.001**	**185.83**	**14.89**	**169.67**	**15.01**	**0**

3.9 Effect of intervention on clinical symptoms and complications of Diabetes among the subjects of all the groups

The study further investigated the clinical symptoms and complications of diabetes among both the EG-I and EG-II groups before and after interventions and was compared with that of the control group. It was found that the highest subjects (50%) of the EG-I were found with polyphagia next to blood pressure (46.7) before intervention. However, after intervention, the number reduced to 33.3% each for polyphagia and blood pressure. Similarly, the highest

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Research paper UGC CARE Listed (Group -I) Journal Volume 11, Iss 12, Dec 2022

number of subjects from EG-II suffered from Polyphagia (50%) next to blood pressure (43.3%) before intervention and the percentage reduced to 43.3 and 33.3 % respectively. The results were compared to the control group. From the results, it is clear that the EG-I group treated with spirulina powder showed an effective decrease in clinical symptoms and complications of diabetes after interventions.

Table 8: Effect of Intervention on Clinical Symptoms and Complications of Diabetes among the subjects of all the groups

Sl. No.	Clinical Symptoms and Complications	Groups											
		Control(CG)(n=30)				EG – I (SP)(n=30)				EG – II(SLP) (n=30)			
		B		A		B		A		B		A	
		N	%	N	%	N	%	N	%	N	%	N	%
1	Polyuria	18	60	17	57.6	11	36.7	9	30.0	11	36.7	10	33.3
2	Polydipsia	18	60.0	17	56.6	7	23.3	7	23.3	14	46.7	12	40.0
3	Polyphagia	21	70.0	22	73	15	50.0	10	33.3	17	56.7	13	43.3
4	Excessive Sweating	12	40.0	12	40.0	9	30.0	8	26.7	13	43.3	9	30.0
5	Weakness	11	36.7	12	40.0	10	33.3	6	20.0	9	30.0	7	23.3
6	Loss of Weight	6	20.0	8	26.7	9	30.0	7	23.3	6	20.0	4	13.3
7	Decreased Wound Healing	7	23.3	7	23.3	6	20.0	4	13.3	4	13.3	2	6.7
8	Blurred Vision	7	23.3	8	26.7	5	16.7	1	3.3	4	13	2	6.7
9	Skin Problems	6	20.0	6	20.0	3	10.0	1	3.3	4	13	1	3.3
10	Foot Problems	4	13.3	4	13.3	4	13.3	1	3.3	3	10.0	-	-
11	Blood Pressure	12	40.0	11	36.7	14	46.7	10	33.3	13	43.3	10	33.3
12	Kidney Problems	-	-	-	-	-	-	-	-	-	-	-	-
13	Cardiac Problems	-	-	-	-	-	-	-	-	-	-	-	-

4. Discussion

Over the ages, plants have been crucial in generating products that have been used to treat illnesses and disorders. In both traditional and contemporary medicine, a variety of items made from fresh or dried plant components or extracts are used as communal remedies. In recent years, there has been a notable increase in scientific interest in the use of soursop leaf and spirulina as functional components for the treatment of diabetes mellitus (Zubaidi et al., 2023; Parikh et al., 2001). The goal of the present study was to evaluate the effectiveness of powdered soursop leaf and spirulina supplementation. First, the nutritional analysis was evaluated for both powders. Consistent with our findings, Kulshreshtha et al.'s (2008) research revealed that spirulina has a high protein content (60–70% of its dry weight), lipid content (4-6%), and carbohydrate content (13.5%). It also includes antioxidants, iron, calcium, and B vitamins, among other things.

Spirulina has been authorised by the Food and Drug Administration (FDA) as a food that is generally recognised as safe (GRAS) and has no toxicological effects on human health (GRAS, 2002). It includes a compound of vitamins A, B, D, E, and K among the micronutrients. In addition to carotenoids and essential fatty acids (α- and γ-linolenic acid, stearidonic acid, eicosapentaenoic acid, docosahexaenoic acid, and arachidonic acid), spirulina is rich in minerals like calcium, potassium, iron, nickel, chromium, magnesium, manganese, copper, sodium, zinc, selenium, and lead that are needed for a well-balanced diet. Furthermore, the human body can get all necessary amino acids from spirulina, which is the most abundant natural source of digestible protein (Masten Rutar et al., 2022). According to our investigation, the soursop leaves had a high moisture content, which is consistent with a study's findings that the fruit had the greatest moisture content and the leaf came in second. Contrary to what we have reported, the same research revealed that the leaf's lipid content was most significant and its crude fibre content was lowest (Agu & Okolie, 2017).

According to the phytochemical examination, soursop leaves had greater levels of phenolic and flavonoid content than spirulina. Our outcomes matched those of research conducted by Agu et al. (2017). The results of the microbiological analysis revealed that the powdered soursop and spirulina were free of coliform, yeast, and mould, as well as total plate count. This is explained by both supplements' potent antibacterial qualities. As reported by Abdel-Moneim et al. (2022), spirulina shows dose-dependent antibacterial activity against ileal counts of total bacteria, total moulds and yeast, coliform, E. coli, Salmonella spp., and Enterococcus spp. These findings corroborate our hypothesis. Similar research revealed that Soursop leaf has antibacterial efficacy against Bacillus cereus, Escherichia coli, Staphylococcus aureus, and Serratia marcescens (Balderrama-Carmona et al., 2020). According to different research, soursop leaves have strong antifungal properties that inhibit the development of fungi, particularly Candida albicans (Campos et al., 2023).

The research observed no statistically significant change in the weight and BMI of either of the experimental groups when anthropometric examination was performed before and after the intervention. But according to research, there has been a noticeable decline in BW, WC, BMI, and body fat (BF), especially in obese individuals treated with spirulina supplements (Yousefi et al., 2018). According to our findings, the group that received soursop leaf powder treatment had lower levels of FBS, PPBG, and HbA1c. Similarly, soursop leaves are particularly helpful

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in managing diabetes since they stabilize blood sugar levels within the usual range, according to research done on diabetic rats. In stained pancreatic sections of diabetic rats, the research demonstrated antihyperglycemic action and suggested pancreatic islet regeneration (Adewole & Caxton-Martins, 2009). Nonetheless, another investigation showed that a two-month Spirulina supplementation led to a noteworthy reduction in both fasting and postprandial blood glucose levels (Parikh et al., 2001).

When the lipid profiles of the experimental groups were compared before and after the intervention, it was discovered that the group treated with spirulina powder had significantly higher levels of HDL and significantly lower levels of TCH, LDL, VLDL, and TGL. Our findings are consistent with those of another study (Hamedifard et al., 2019) that found that patients with metabolic syndrome and related disorders who were given spirulina experienced significant reductions in fasting blood sugar, total cholesterol, low-density lipoprotein cholesterol, insulin, and very low-density lipoprotein cholesterol, and increase in high-density lipoprotein cholesterol. While HDL-C levels were significantly increased, LDL-C, TC, and TG levels were significantly decreased by the Spirulina intervention, according to a systematic review and meta-analysis of data from randomized controlled trials that pooled results from 20 studies (with 23 arms and 1076 participants) (Rahnama et al., 2023).

Current results demonstrate the value of Spirulina supplementation in lowering total cholesterol, triglycerides, and low-density lipoprotein cholesterol, and increasing high-density lipoprotein cholesterol in the blood. The presence of clinical symptoms and consequences after intervention were also examined in this investigation. Spirulina powder therapy was shown to significantly reduce the proportion of participants experiencing polyphagia and high blood pressure. Zeinalian et al. (2017) conducted a study on 62 obese people and found that after receiving 1 g of spirulina for 12 weeks, there was a substantial decrease in appetite of −4.16%. An improvement in leptin resistance in the arcuate nucleus may be the cause of the decrease in appetite. Spirulina supplementation considerably lowers both systolic and diastolic blood pressure, according to a recent systematic review and meta-analysis (Machowiec et al., 2021).

5. Conclusion

The findings of the present research show that Spirulina supplementation, in comparison to soursop leaves powder supplementation, may have a helpful effect in positively modifying lipid profiles in type 2 diabetes patients. Comparing soursop leaf powder to spirulina supplementation, however, revealed benefits in long-term glycemic control. However, supplementing with spirulina powder showed a significant decrease in the participants' clinical symptoms and consequences. However, there is still a large knowledge vacuum, thus further in-depth studies are needed to learn more about Spirulina's anti-diabetic potential. For this possible impact, a comprehensive metabolomic investigation must be conducted. Identification of the metabolite modifications that emerge from the influence of bioactivities is also necessary. Nonetheless, significant efforts are required to carry out further metabolomic research in order to support drug development.

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