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HERBAL BASED ANTIDIABETIC DRUG DELIVERY SYSTEM OF [TRIGONELLA FOENUM-GRAECUM, NIGELLA SATIVA] AND [CASSIA AURICULATA]

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ABSTRACT
According to the World Health Organisation, oral antidiabetic drugs are the main treatment for type 2 diabetes mellitus, which is the most prevalent endocrine disease. However, these drugs have adverse effects, which is why 80% of people prefer traditional medications made from therapeutic plants. Scientists, researchers, and pharmaceutical companies worldwide are increasingly embracing plants and herbal sources as potential bioactive compounds for novel, targeted antidiabetic drugs that may control diabetes with fewer side effects than traditional anti-diabetic medications. This study focuses on identifying the most effective herbs in reducing blood sugar levels in type 2 diabetes. Medicinal plants are the most abundant bio source of medications for traditional systems of medicine, nutraceuticals, food supplements, modern medicines, pharmaceutical intermediates, and chemical entities for synthetic drugs. Over a 30-day period, this research evaluated the efficacy of herbal tea, combining fenugreek (Trigonella Foenum-graecum) and black cumin seed (Nigella sativa), versus aavaram flower (Cassia auriculata) in reducing blood sugar levels among highly diabetic family members. FTIR and XRD was used to determine the chemical composition and crystallographic structure of the herbal tea, and the antimicrobial testing was conducted against gram (+) ve bacteria, gram (-) ve bacteria and fungi. Results indicate that the fenugreek and black cumin seed combination is more effective in lowering blood sugar levels than the avaram flower.

KEYWORDS: Type 2 diabetes mellitus, Herbal medicine, Fenugreek, Avaram flower and Black cumin.

INTRODUCTION
Herbal products are not only used for dietary purposes such as food, nutrition, and so on; they also play an important part in the treatment of numerous disorders. The use of various plant components, including flowers, fruits, seeds, leaves, berries, bark, and roots for therapeutic purposes is known as herbal medicine, often referred to as phytomedicine or botanical medicine. World Health Organisation has also reported that traditional medicine is used for primary health care in the majority of countries. The goal of this study is to highlight potential herbal treatments for diabetes as an efficient and long-lasting alternative. Diabetes mellitus (DM) is a metabolic condition that is one of the most prevalent lifestyle conditions. The World Health Organisation (WHO) estimates that more than 347 million people around the world have diabetes mellitus (DM). Chronic hyperglycaemia, elevated blood sugar, increased insulin production, increased insulin resistance, and glucose or insulin intolerance are all symptoms of diabetes mellitus. It is still one of the world's leading causes of mortality and the fastest-growing disease. Type 2 Diabetes Mellitus (T2DM) is the most common type of diabetes, accounting for around 90% of cases Global prevalence of type 2 diabetes was predicted to be 2.8% in 2000; by 2030, it is anticipated to increase to 4.4%. Current diabetes treatments typically involve insulin injections and oral anti-diabetic drugs; however, these therapies have side effects and toxicity and are limited in terms of pricing, accessibility, and acceptance. Herbal-based therapy is the best option to overcome the adverse effects of conventional treatment. Herbs and plants are newly discovered medicinal agents with hypolipidemic effects in the treatment of type 2 diabetes. Herbs and plants are chosen over medications for treatment because they are more readily available, have lower toxicity, have fewer adverse effects, and are easier to consume. Phytochemicals like flavonoids, tannins, phenols, steroids, alkaloids, and terpenoids, which are responsible for medicinal plants biological actions, have always been produced in significant quantities by medicinal plants. Herbal medicine plays a vital role in the treatment of diabetes. The literature survey shows that the seed of fenugreek (Trigonella Foenum-graecum), the seed of black cumin (Nigella sativa), and the bud & flower of aavaram poo (Cassia auriculata) have been used as

sources of antidiabetic compounds. Fenugreek belongs to the Fabaceae family and is known as Trigonella in Latin, which means "little triangle" because of its yellowish-white triangular blooms. The pharmacological benefits of fenugreek are linked to a variety of bioactive substances, including polyphenols, steroids, lipids, alkaloids, saponins, flavonoids, hydrocarbons, carbohydrates, galactomannan fibre, and amino acids. Hence, several research groups looked into its anti-diabetic properties. Fenugreek's ability to lower cholesterol has been linked to enhanced hepatic cholesterol conversion to bile acids and the excretion of complexes of these compounds with fenugreek saponins and fibre. Administration of fenugreek has not been linked to any toxicological side effects. It has galactagogic, antibacterial, antifungal, anti-inflammatory, anti-hyperlipidemic, antioxidant, and other activities. Fenugreek will also improve the blood lipid profile by lowering serum triglycerides, total cholesterol, LDL, and VLDL cholesterol. Several studies show that it is traditionally used to treat a wide range of diseases, including diabetes and obesity, and that regular consumption of fenugreek may be helpful in the management of diabetes as well as the prevention of atherosclerosis and coronary heart disease. Black cumin (Nigella sativa), is a spice plant belonging to the Ranunculaceae family and it is an herbaceous annual plant that grows upright. It grows in Mediterranean and Asian countries such as India, Pakistan, Indonesia, Italy, and Afghanistan. In China, it is referred to as Hak Jung Chou, whereas it is known in India as Kalonji or Kalajeera. Cassia auriculata L. (Family: Caesalpiniaceae) is a shrub with big bright yellow blossoms that grows in India's hot deciduous forests and maintains a very important position in the Ayurvedic and Siddha systems of medicine. The plant has been shown to have antipyretic, hepatoprotective, antidiabetic, antiperoxidative, antihyperglycemic, and microbicidal properties. Avarai panchaga chooranam, also known as Kalpa herbal tea, is a type of herbal tea made from the five plant parts: roots, leaves, flowers, bark, and unripe fruits. This tea is mostly consumed by people in Asian nations to lower blood sugar levels and regulate diabetes symptoms. The purpose of the current research is to determine which herbal tea, combination of fenugreek & black cumin seed or avaram flower, will lower diabetes most effectively. The investigation lasted 30 days, and the characterisation and antibacterial activity of herbal extracts were also studied using FTIR, XRD, and well diffusion methods.

MATERIALS AND METHEDOLOGY

Raw materials

Fenugreek (Trigonella Foenum-graecum), aavaram poo (Cassia auriculata), Black cumin seed (Nigella sativa) were purchased from local market.

Methodology

Pilot study of the antidiabetic effect of herbs (FBC herbal Tea and Avaram herbal tea)

The study began with the selection of two diabetes patients from our family and lasted for 30 days. During the study, factors such as food consumption, water intake, blood sugar level, and body weight were recorded. They also followed a separate diet throughout the study period, including the 30 minutes of walking per day shown in Table 7. Patient 1 received a mixture of fenugreek and black cumin seed, whereas patient 2 received avaram poo. The herbal tea was made by adding 1 tea spoon of the sample to 2 cups of water and boiling it down to 1 cup.

A **B**

Figure 1: A) FBC herbal tea (Fenugreek + black cumin powder), B) Aavaram flower herbal tea.

Preparation of FBC Extract and Avaram flower extract

Fenugreek and black cumin seed were combined, dried, and ground into a fine powder (FBC powder). In order to make the herbal extract, 50 ml of double-distilled water was combined with 1 g of FBC powder, and the mixture was heated for 4 hours at 50 °C. The heating process was repeated for 5 days to extract its chemical content, and this method is known as the infusion method. Finally, the extracted sample were stored in a cool place for further analysis.

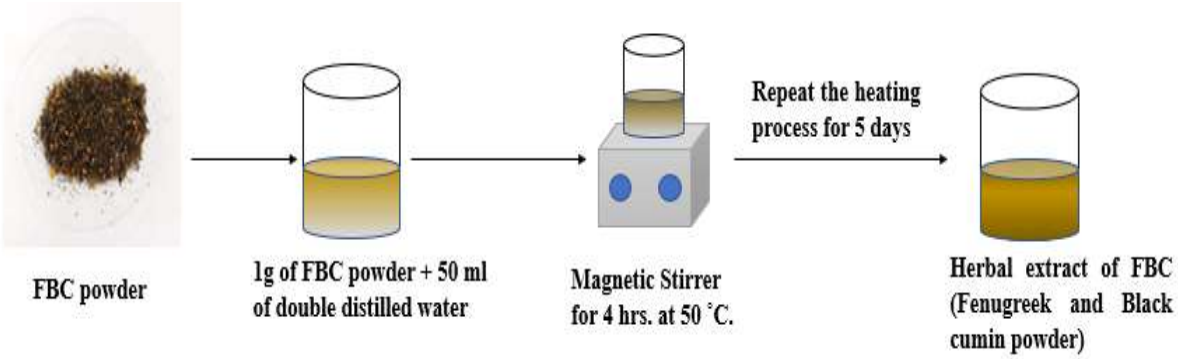

Figure 2: Synthesis of FBC (Fenugreek + Black cumin powder) herbal extract.

Phytochemical analysis of fenugreek seed

Fenugreek (Trigonella foenum-graceum) is one of the oldest medicinal plants in Asia, and its seeds contain a significant number of fibres and are extremely nutritious. The phytochemicals present in fenugreek seeds are Tannins, Anthraquinones, Flavanoides, Alkaloids, Terpenoids, Saponins, Cardiac glycosides, Glycosides, Steroids, Phenolic, Amino acids, Proteins, and Quinones. The main bioactive fenugreek component which acts against diabetes is diosgenin saponin. It has antioxidative properties and contributes significantly to reducing the consequences of diabetes in a number of ways. The mechanisms include stimulation of insulin secretion and cell renewal.

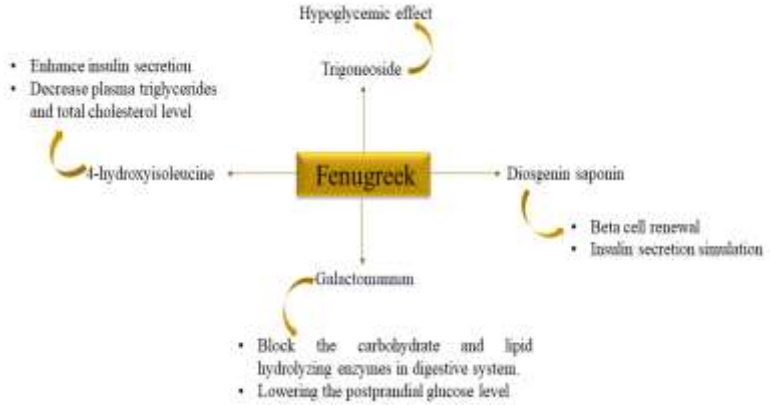

Figure 3: Antidiabetic mechanism of fenugreek seed.

Phytochemical analysis of black cumin seed

The seeds of Nigella sativa, commonly referred to as black seeds because of their strong phytoconstituent content, are one of the medicinal plant species that have become popular for a variety of medical uses. According to a number of studies, thymoquinone is the main component of N. sativa seeds and is responsible for antidiabetic activity. Thymoquinone (30%–48%), thymohydroquinone, dithymoquinone, p-cymene (7%–15%), carvacrol (6%–12%), 4-terpineol (2%–7%), t-anethol (1%–4%), sesquiterpene longifolene (1%–8%), -pinene, and thymol are the main active ingredients of black cumin.

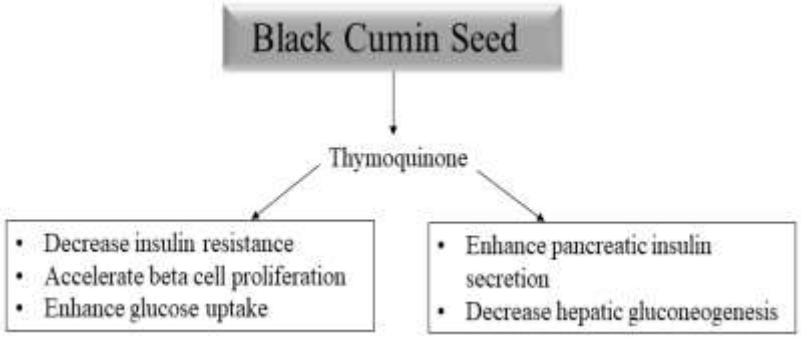

Figure 4: Antidiabetic mechanism of black cumin seed.

Preparation of Aavaram, flower extract

The herbal extract of avaram flower was produced using infusion method. We cleaned, dried, and ground 50g of flower. Then, 1 g of avaram poo powder and 50 ml of double-distilled water were combined, and the solution was heated for four hours at 50 °C. To remove the chemical content, the heating process was performed continuously for five days. Finally, the extracted sample were stored in a cool place for further analysis.

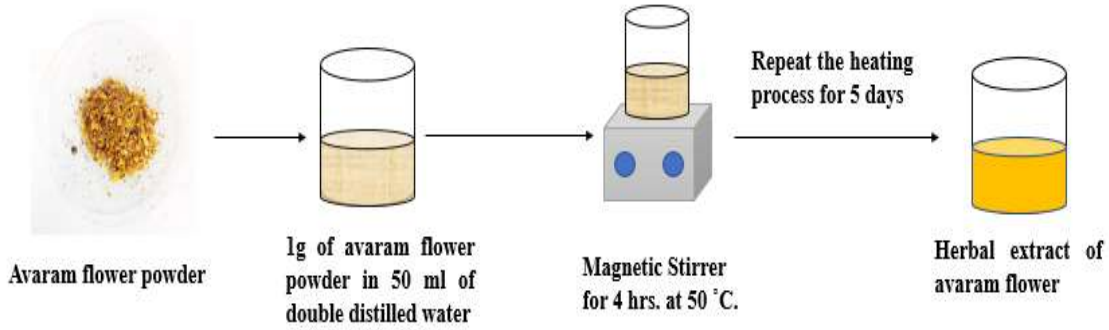

Figure 5: Synthesis of avaram flower herbal extract

Phytochemical analysis of aavaram flower

Alkaloids, phenols, glycosides, flavonoids, tannins, saponins, proteins, carbohydrates, and anthraquinone derivatives are the primary phytochemical components in avaram flowers and are what give it its pharmacological activity. Aavaram flower extract is beneficial in the treatment of diabetes due to its strong carbohydrate hydrolyzing enzyme inhibitor activity, which is responsible for the slow conversion of starch into glucose in our bodies.

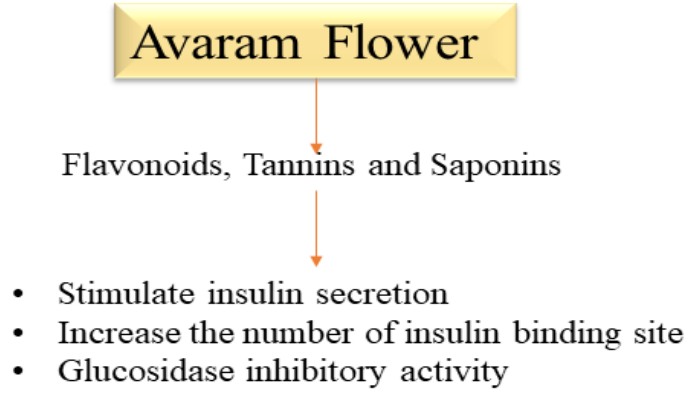

Figure 6: Antidiabetic mechanism of avaram flower

Characterization of herbal extracts

FTIR (Fourier transform infrared spectroscopy) was used to identify the functional group in avaram flower, fenugreek, and black cumin. The quality and purity of the herbal extracts can also be determined via FTIR analysis. It is possible to identify contamination, or the presence of unwanted substances by comparing the FTIR spectra of the extracts with reference spectra. The crystallographic structure, chemical composition and physical properties of herbal extracts were also studied by using X-Ray diffraction analysis.

Invitro antimicrobial analysis

Antimicrobial activity of fenugreek, avaram poo (Cassia auriculata), and black cumin seed herbal extract were investigated. These tests help to identify whether these herbal extracts have antibacterial activity against specific pathogens. The extract was tested against bacteria and fungi using disk diffusion method.

RESULT AND DISCUSSION

Fenugreek, black cumin seed powder, and avaram flower powder were investigated for their possible anti-diabetic properties. Fenugreek's anti-diabetic effect is due to the presence of diosgenin saponin, galactomannan, trigoneoside's, and 4-hydroxyisoleucine, while black cumin seeds anti-diabetic effect is related to the presence of thymoquinone. According to studies, taking black cumin seed and fenugreek in our daily diet can help improve glucose tolerance, boost insulin production, and improve insulin sensitivity. It may also have protective benefits on pancreatic beta cells, which create insulin. In Ayurvedic medicine, the aavaram flower is typically used to cure diabetes. According to studies, avaram flower has hypoglycaemic properties because it contains flavonoids, tannins, and other bioactive compounds. It lowers blood sugar levels by promoting pancreatic beta cell insulin release and improving peripheral glucose uptake.

Ratio for sample preparation

Herbal therapy emerges as a potential nutrient to diabetes management, combining traditional knowledge with cutting-edge scientific research. With rising diabetes incidence and limitations in traditional treatments, herbal interventions provide a more comprehensive approach to care. Herbs such as fenugreek and bitter melon, which have been used for thousands of years to boost insulin sensitivity and modify glucose metabolism, have gained attention. As shown in table 1, three samples (S1, S2, S3) with different ratios of fenugreek, black cumin infused plant extract were prepared to standardize the herbal tea using titration method. Among the samples used to prepare the herbal tea sample S2 exhibited a perfect combination than the other. Hence S2 sample ratio was considered combination for the preparation of herbal tea for dietetic. Therefore, S2 sample was subjected to further characterization studies. The homogenous mixture was obtained using this method for Herbal tea. The standardized ratio of herbal tea preparation is given in table 1.

A B

Figure 7: A) FBC extract, B) Aavaram flower extract

Table 1: Ratio for combination of fenugreek and black cumin seed powder

Sample	Fenugreek (Trigonella foenum-graceum)	Black cumin seed (Nigella sativa)	Double distilled water
S1	1g	1g	50 ml
S2	0.5g	0.5g	50 ml
S3	1.5g	1.5g	50 ml

Each ratio of hydrogel beads preparation was performed five times.

Table 2: Ratio avaram flower powder

Sample	Aavaram flower (Cassia auriculata)	Double distilled water
A1	1g	50 ml
A2	0.5g	50 ml
A3	1.5g	50 ml

Each ratio of hydrogel beads preparation was performed five times.

As shown in table 2, three samples (A1, A2, A3) with different ratios of avaram poo plant extract were prepared to standardize the herbal tea using titration method. Among the samples used to prepare the herbal tea sample A2 exhibited a perfect combination than the other. Hence A2 sample ratio was considered combination for the preparation of herbal tea for dietetic. Therefore, A2 sample was subjected to further characterization studies. The homogenous mixture was obtained using this method for Herbal tea. The standardized ratio of herbal tea preparation is given in table 2.

Functional characterization

The Fourier transform infrared spectrum of the Cassia auriculata flower extract was recorded in the range of 400-4000cm-1, Model FT/IR-4100typeA and is shown in Figure 8 In this research work the recorded spectrum was used to study the different modes (stretching /bending) of vibrations involving chemical bonds present in the compound.

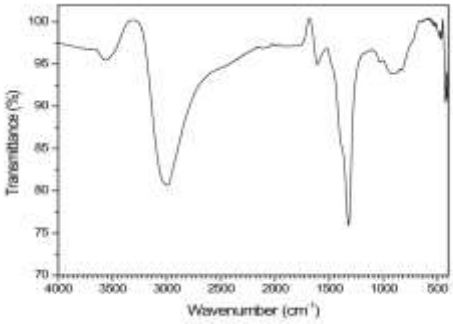

Figure 8: FTIR Analysis of Cassia auriculata flower extract.

Table 3: FTIR spectroscopy of auriculata flower extract.

Wavelength	Chemical Bond	Functional Group
3400–3250	N–H stretch	1˚, 2˚ amines, amides
3100–3000	C–H stretch	Aromatics
1710–1665	C=O stretch	α, β–unsaturated aldehydes, ketones
1250–1020	C–N stretch	aliphatic amines
1320–1000	C–O stretch	alcohols, carboxylic acids, esters, ethers

Different peaks of functional groups in the extract of the plant. The broad peak of the O-H and N-H bond at 3000 cm−1 indicates alcohols and secondary amines.

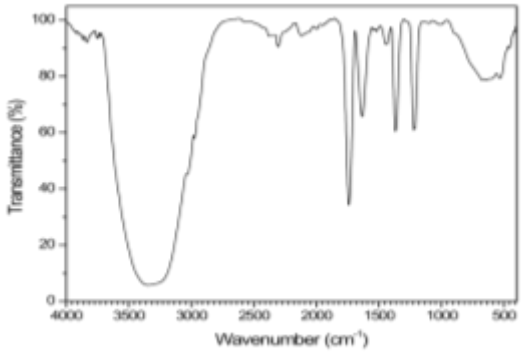

Figure 9: FTIR Analysis of FBC.

Table 4: FTIR spectroscopy of auriculata flower extract.

Wavelength	Chemical Bond	Functional Group
3500-3200	O–H stretch, H–bonded	alcohols, phenols
2260–2100	–C≡C– stretch	Alkynes
1760–1665	C=O stretch	Carbonyls
1650–1580	N–H bend	1˚ amines
1250–1020	C–N stretch	aliphatic amines

Peaks at 1434 cm−1 as well as 990.5 cm−1 and 1780.0 cm−1 elucidate alkenes and alkanes, which projected plane bending due to =C-H and stretching of CH2, respectively. Three functional groups were identified at intermediate peak, four strong peak and one functional group ranges at 1000–3000. In medium peak type C-H, N-H, and C=O functional groups were identified at peaks 3100, 1710, 1250, respectively, whereas in strong peak type functional groups O-H, –C≡C– , C=O, N-H were determined at peaks 3200,2260,1665 and 1580, respectively. This data indicated the presence of aliphatic amine, alcohols, and carboxylic compounds. In a previous study, C-N functional groups were identified at 1250 cm−1.

Crystallographic studies

The XRD analysis of the synthesized plant extract showed the mixed structure due to the combination of the plant cellulose. The XRD of FENUGREEK **(TRIGONELLA FOENUM-GRACEUM) & BLACK CUMIN SEED (NIGELLA SATIVA), AAVARAM FLOWER (CASSIA AURICULATA)** revealed the typical XRD pattern of crystalline black cumin structure with different peaks at $2\theta^{o}$ values. Shi, et al., suggested that the characteristic XRD peaks observed for CuO NPs

prepared using C. auriculata extract shows an intense diffraction peak at 32.54°, 35.56°, 38.77°, 48.74°, 53.53°, 58.37°, 61.56°, 66.29° and 68.17°, corresponding to 110, 0 02, 111, 202, 020, 202,113, 311 and 113 planes, respectively, indicated the formation of a typical monoclinic CuO NP structure without impurities. Patience Mapule Thabede et al., suggested that the pattern showed broad peaks between (2θ) of 17 and 21° which represented cellulosic content in the adsorbent material. Other peaks at 44° and 75° were assigned to the amorphous nature of the adsorbent. The degree of crystalline structure is increased along with the original cellulose content in the hydrogel beads.

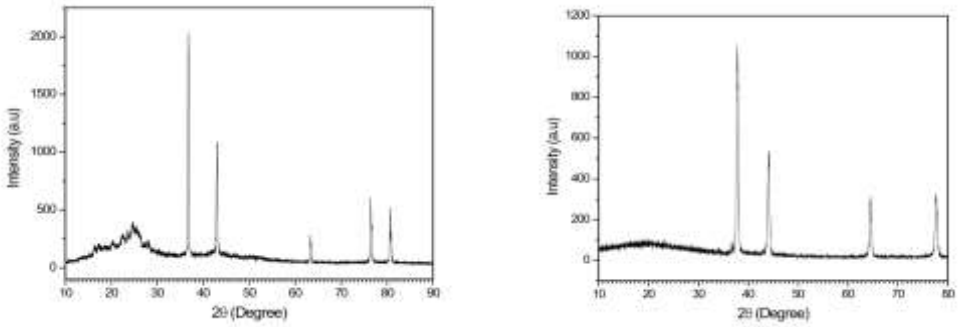

Figure 10: XRD analysis of the synthesized plant extract.

Invitro antimicrobial analysis

Agar well diffusion method is widely used to evaluate the antimicrobial activity of plants or microbial extracts. Similar to the procedure used in disk-diffusion method, the agar plate surface is inoculated by spreading a volume (500ul) of the microbial inoculum over the entire agar surface. Then, a hole with a diameter of 6 to 8 mm is punched aseptically with a sterile 1000ul tip, and 100 µL of the antimicrobial agent or extract solution at desired concentration is introduced into the well. Then, agar plates are incubated at 37°C / 30°C under suitable conditions depending upon the test microorganism.

Table 5: Zone of Inhibition sizes (in mm) average for triplicate samples determined by Agar diffusion method.

S.No	SAMPLE (100ul)	Zone of Inhibition for Microorganism (in mm)			
		Staphylococcus aureus			
		Gentamycin	1	2	3
1	Sample A2	28mm	15mm	16mm	13mm
2	Sample S2	22mm	18mm	16mm	15mm

S.No	SAMPLE (100ul)	Zone of Inhibition for Microorganism (in mm)			
		Candida albicans			
		Gentamycin	1	2	3
1	Sample A2	24mm	15mm	16mm	16mm
2	Sample S2	20mm	15mm	15mm	15mm

The antimicrobial agent diffuses in the agar medium and zone of inhibition checked after incubation period. Here gentamycin is used as a control for bacterial culture and clotrimazole is used as antibiotic control for Yeast culture. Two bacterial strains (E. coli, S. aureus-Gentamycin used as control antibiotics) and one yeast strain candida albicans (clotrimazole used as control antibiotics) were used for the study. Three wells (triplicates) for each sample in each plate (100 ul of the sample was loaded onto each well). The inhibition zone shown in the table 5. for all the samples. Darshan Dharajiya suggested that the T. foenum-graecum leaves was able to give a maximum zone of inhibition against T. viridae (ZOI = 14.5±0.5 mm and AI = 0.649) followed by ethyl acetate extract (ZOI = 12.0±1.0 mm and AI = 0.537). Extraction of fenugreek and black cumin seeds by infusion method has some inhibitory effect on the growth of St. Aureus bacteria and candida fungi in disc diffusion method and agar well diffusion method with a zone inhibition of diameters of 24mm and 20mm respectively.

Pilot study of the antidiabetic effect of herbs (Fenugreek, Aavaram poo, Black cumin seed)

Table 6: Patient details.

Patient details	Patient 1	Patient 2
Age	Uma Maheshwar R	Palaniyammal A
Name	46	65

Sex	Female	Female
Blood sugar level	250mg/dl	230mg/dl
Other disease	Kidney Stone pain, and Hernia	Cholesterol
Sample Name	Fenugreek & Black cumin	Avaram Poo

We conducted a 30-day study with our family members. Prior to beginning the trial, patients' data such as blood sugar level, cholesterol level, age, and other diseases were recorded. For 30 days, patient 1 drank fbc tea on an empty stomach, while patient 2 drank aavarm flower tea tea on an empty stomach. The patient has adhered to a particular diet, which is listed in Table 7. The blood sugar level was measured once every seven days, and figure 11. shows the data that was evaluated. According to the findings, both have anti-diabetic qualities.

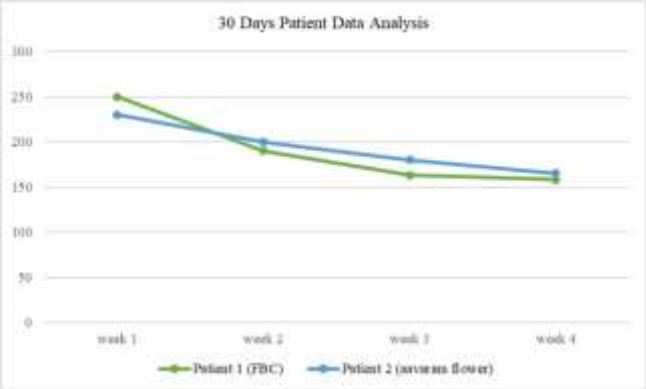

Figure 11: 30 days Patient Data Analysis for FBC & aavaram tea.

Table 7: Diet chart followed by the patients.

Timings	6:30 am	8: 30 am (Breakfast)	11:00 am	1.30 pm (Lunch)	4:30 pm	7:30 pm (Dinner)	10:00 pm
Day 1	FBC herbal tea/ Avaram flower herbal tea	Millet Dosa	Buttermilk 1 glass, Fruits (apple/amla/ grapes)	Mixed vegetable salad (Broccoli, spinach, green beans), brown rice, fish	Roasted Chana	Whole wheat chapati,	Milk without sugar
Day 2	FBC herbal tea/ Avaram flower herbal tea	Oat meal	Buttermilk 1 glass, Fruits (apple/amla/ grapes)	Paneer curry, whole wheat chapati, egg	Kidney beans	Mixed vegetable, ragi kozh	Turmeric milk
Day 3	FBC herbal tea/ Avaram flower herbal tea	Ragi dosa	Buttermilk 1 glass, Fruits (apple/amla/ grapes)	Pea's pulao, bitter gourd	Cucumber, carrot, green tea	Vegetable chapati	Milk without sugar
Day 4	FBC herbal tea/ Avaram flower herbal tea	Ragi kozh	Buttermilk 1 glass, Fruits (apple/amla/ grapes)	Brown rice, fish, green vegetables	Sprouts salad	Green gram dosa	Turmeric milk
Day 5	FBC herbal tea/ Avaram flower herbal tea	Wheat upma	Buttermilk 1 glass, Fruits (apple/amla/ grapes)	White rice, green vegetables, egg	Green tea with honey, chick peas	Whole wheat chapati, ridge gourd chutney	Milk without sugar
Day 6	FBC herbal tea/ Avaram flower herbal tea	Dosa	Buttermilk 1 glass, Fruits (apple/amla/ grapes)	Whole wheat chapati, paneer/ Palak gravy	Roasted chana	Whole wheat chapati, Palak gravy	Turmeric milk
Day 7	FBC herbal tea/ Avaram flower herbal tea	Whole wheat chapati	Buttermilk 1 glass, Fruits (apple/amla/ grapes)	Multigrain chapati, paneer gravy	Black beans	Green gram dosa	Milk without sugar

However, FBC tea performed better than aavarm flower tea. (Wilai, et al., 2013) suggested bitter melon showed a significant decline of total advanced glycation endproducts (AGEs) in serum after 16 weeks of the intervention. (Bemplidakis, et al., 2023) says that dietary supplement from Portulaca oleracea and titrated Cistus creticus extract, along with vitamins and minerals, may improve the metabolic profile of people with prediabetes. There are also some reports suggesting that the hypoglycaemic properties of *Trigonella foenum-graecum* result from its high content of dietary fiber (up to as much as 30%), especially its insoluble fraction

(Przeor, et al., 2022). Because of their antidiabetic properties, fenugreek & black cumin seed may be used as medicinal agents.

CONCLUSION

Diabetes type 2 is a chronic metabolic condition characterised by high blood sugar levels as a result of insulin resistance and decreased insulin production. It affects the body in a variety of ways, including cardiovascular illness, neuropathy, and nephropathy. Herbal-based medicines have been studied as a supplemental strategy for treating type 2 diabetes. Some herbal remedies have shown promise in terms of glucose control and lowering diabetes-related problems. So, we conducted a study to determine which herbal tea effectively reduces diabetes among the combination of fenugreek and black cumin seed herbal tea (FBC) or aavaram flower herbal tea, and the results show that consuming FBC herbal tea for 30 days will reduce the blood sugar level up to 40-70 mg/dl. As a result, we conclude that adding FBC herbal tea to our daily diet is a simple and effective method to lower the risk of type 2 diabetes.

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