Pharmacogn. Res., 2026; 18(1):191-199.
https://www.phcogres.com

Original Article

Pharmacodynamic Interaction between *Cyamopsis tetragonoloba* (Cluster Beans) and Acarbose: An *in vitro* and *in vivo* Study

Ruchika Mourya[1,*], Manivannan Elangovan[1], Hamendra Singh Parmar[2], Rajesh Sharma[1]

[1]School of Pharmacy, Devi Ahilya Vishwavidyalaya, Takshashila Parisar, Khandwa Road (Ring Road), Indore, Madhya Pradesh, INDIA.
[2]School of Biotechnology, Devi Ahilya Vishwavidyalaya, Takshashila Parisar, Khandwa Road, Indore, Madhya Pradesh, INDIA.

ABSTRACT

Aim: To investigate pharmacodynamic interaction of *Cyamopsis tetragonoloba* (Cluster beans or guar beans) with acarbose on type-2 antidiabetic targets α-glucosidase and α-amylase. **Background:** The simultaneous use of herbal and ayurvedic medicines along with allopathic medicines is a common practice in India, without knowing their interactions. In particular, diabetic patients often use a combination of herbal, ayurvedic, and allopathic medications to achieve better results. *Cyamopsis tetragonoloba* (also known as cluster beans or guar beans), a popular vegetable in India, is thought to provide potential advantages for diabetes patients. Therefore, it was thought worthwhile to investigate pharmacodynamic interaction of *Cyamopsis tetragonoloba* (Cluster beans or guar beans) with a type-2 antidiabetic drug acarbose. **Materials and Methods:** In the current study, an aqueous and ethanol extract of *Cyamopsis tetragonoloba* was prepared and tested for antidiabetic activity *in vitro* and *in vivo* in combination with acarbose. At first, the *Cyamopsis tetragonoloba* extracts have been tested for their ability to adsorb glucose and inhibit α-amylase and α-glucosidase. Then, an oral glucose tolerance test, acute and subacute study for *Cyamopsis tetragonoloba* extracts and acarbose was conducted on male albino Wister rats. **Results:** The present results demonstrate the co-administration of aqueous extract and ethanol extract with acarbose have shown statistically significant reduction in blood glucose level in streptozotocin induced male diabetic rats. The aqueous extract with acarbose was more effective for postprandial hyperglycemia compares to ethanol extract with acarbose and acarbose. The additive pharmacological effect on blood glucose level has been observed after the co administration of extract of *C. tetragonoloba* with acarbose in streptozotocin induced male diabetic rats. **Conclusion:** To summarise, the interaction of herbal and pharmaceutical medicines is a critical to both patients and health care practitioners. It is necessary to continue research on potential risks and benefits associated with the combination of *C. tetragonoloba* and Acarbose on pharmacokinetic aspects. Such data is crucial for the formulation of future clinical guidelines to improve health-care outcomes in diabetes.

Keywords: Diabetes mellitus, *Cyamopsis tetragonoloba*, Anti-diabetic activity, Acarbose, Ethanol extract, Aqueous extract.

Correspondence:
Mrs. Ruchika Mourya
School of Pharmacy, Devi Ahilya Vishwavidyalaya, Takshashila Parisar, Khandwa Road (Ring Road), Indore-452001, Madhya Pradesh, INDIA.
Email: mouryaruchika98@gmail.com

Received: 13-06-2025;
Revised: 27-08-2025;
Accepted: 09-10-2025.

INTRODUCTION

Diabetes Mellitus (DM) is a chronic metabolic disorder characterised by hyperglycemia due to the failure of pancreatic cells to produce sufficient or efficient insulin.[1] The raise in blood glucose level resulted by DM causes physical harm as well as multiple organ damage and tissue failure.[2] Pancreatic beta cell malfunction is a significant cause of type 2 diabetes, and it is linked to insulin resistance and insufficiency. The insulin-regulated glucose transporter GLUT-4 receptor, present in muscle and adipose tissue, may lead to insulin resistance by increasing glucose uptake to these tissues.[3] Endoplasmic reticulum stress reduces insulin sensitivity in DM, and enhanced glucose metabolism can cause an increase in mitochondrial Reactive Oxygen Species (ROS) generation.[4] Overproduction of ROS destroys beta cells, impairing cellular activity and resulting in cell death in numerous organs and blood vessels, eventually leading to insulin deficit.[5] Furthermore, elevated levels of ROS activate inflammatory pathways, with catastrophic effects.[6] The complications of DM are divided into two categories: microvascular complications, which affect the microvascular network of blood vessels in the kidney, eyes, and nerves, diabetic retinopathy, which causes retinal rupture due to high blood

DOI: 10.5530/pres.20262368

glucose, and diabetic neuropathy, which damages peripheral nerves associated with lower limbs and leads to diabetic foot ulceration.[7-9] The Macrovascular complications involve high blood glucose levels affecting arteries and large blood vessels, leading to the development of cardiovascular disease in diabetic patients.[8]

Currently available treatment for type 2 DM includes insulin secretagogues, biguanides, insulin sensitizers, alpha glucosidase inhibitors, incretin mimetics, amylin antagonists, and SGLT2 inhibitors.[10-12] Among these treatments, Acarbose is an α-glucosidase inhibitor that declines the enzymatic activity of α-glucosidase.[13] The α-glucosidase enzyme presents in the brush border of the small intestine, and acarbose binds reversibly or competitively to the oligosaccharide binding of the α-glucosidase enzyme.[14] The acarbose inhibits the α-glucosidase enzyme, delays the digestion of carbohydrates in the small intestine, and inhibits the absorption of glucose from the brush border of the small intestine. This results in a low level of glucose reaching the blood. The diabetic patients living in India often use a combination of herbal, ayurvedic, and allopathic medications to achieve better results. The simultaneous use of herbal and ayurvedic medicines along with allopathic medicines is a common practice in India, without knowing their interactions. Furthermore, many people assume that herbal remedies are natural and thus safe to use.[15] *Cyamopsis tetragonoloba* (also known as cluster beans or guar beans), a popular vegetable in India, is thought to provide potential advantages for diabetes patients.[16,17] Cluster bean is gaining attention as functional food due to its high nutritional profile, including high levels of protein, fiber, carbohydrates, oil, moisture, polyphenols, tannins, and phytic acid.[18-20] Cluster bean seeds, rich in fatty acids like linoleic, palmitic, and oleic acids, are used by diabetes patients due to their tannins, flavonoids, and coumarins.[20] Cluster beans have been shown to have antioxidant, antidiabetic, antibacterial, and cytotoxic properties.[18-21] Antioxidant molecules in *C. tetragonoloba* can help diabetics improve their insulin sensitivity and glucose homeostasis.[22] Therefore, it was thought worthwhile to investigate the pharmacodynamic interaction of *C. tetragonoloba* with an α-glucosidase inhibitor-based antidiabetic drug known as Acarbose.

MATERIALS AND METHODS

Collection of *Cyamopsis tetragonoloba* (cluster beans) beans

Ten kilogrammes of cluster beans were bought from the local market in Indore, Madhya Pradesh, India and their identity was verified by Dr. G.P. Choudhary, Associate Professor of Pharmacognosy, School of Pharmacy, Devi Ahilya Vishwavidyalaya, Indore-452001, M.P., India. *C. tetragonoloba* beans were dried in a shed and ground into a fine powder with an electric grinder.

Animals and experimental approval

Thirty-five male Wistar rats weighing between 260–300 g were obtained from the Central Animal House, Devi Ahilya Vishwavidyalaya, Indore. The animals were segregated into different groups and kept in separate cages with natural light and dark cycles in an air-conditioned room (25±1°C) with consistent humidity levels of 55±5%. The experimental protocol was approved by the Institutional Animal Ethical Committee (IAEC approval No. 779/CPCSEA/IACE/2022/005).

Chemical and reagents

Acarbose Extra Pure 95% was purchased from Sisco Research Laboratories Pvt. Ltd., D-88/2, TTC Industrial Area, Navi Mumbai, Maharashtra, India. α-glucosidase, 4-nitrophenyl-β-D-Glucopyranoside (pNPG), and α-amylase were purchased from Sigma-Aldrich and Titans Biotech Limited, Bhiwadi, Rajasthan, respectively. The glucose test kit (GOD-POD method) was obtained from Robonik (India) Pvt. Ltd., Plot No. 3 and 4, MIDC, Morivali, Ambernath (W), India. Streptozotocin (Sigma-Aldrich) was received as a gift sample from the School of Biotechnology, Devi Ahilya Vishwavidyalaya, Indore.

Extraction of crude plant extract

The Soxhlet equipment was utilised to prepare the ethanol extract by a hot continuous extraction procedure.[23] The dried *C. tetragonoloba* beans were kept in the extractor and ethanol was used as solvent. The extraction was done at 78°C for 3 hr. To remove moisture from the extract, the liquid was filtered through anhydrous sodium sulphate. The ethanol extract of *C. tetragonoloba* was dried and concentrated with a rotatory vacuum evaporator.[24] However, the aqueous extract was prepared by maceration method (24 hr) followed by decoction method.[25]

Determination of glucose adsorption capacity

Separately, 0.25 g of ethanol and 0.25 g of aqueous extracts of C. *tetragonoloba* were added to 25 ml of glucose solutions of different concentrations (5, 10, 20, 50, and 100 mMol). The individual mixture was stirred well, then incubated in a shaker water bath at 37°C for 6 hr, then centrifuged for 15 mins at 3000 rpm. The GOD-POD kit was used to measure the final glucose level in the supernatant in order to calculate the glucose adsorption capacity (mMol g^{-1}).[26,27] All measurements were taken in triplicate, and the results are shown in Table 1. Glucose bound was calculated as follows:

$$\text{Bound glucose (mMol g}^{-1}) = \frac{G1 - G6}{W} \times V$$

G1: glucose concentration of original solution, G6: glucose concentration after 6 hr (mMol L^{-1}), V: volume of sample (L), W: weight of sample (g).

α-amylase inhibitory activity

The solutions of different concentrations (ranging from 100 μg mL^{-1} to 1,000 μg mL^{-1}) of acarbose, ethanol and aqueous extracts were prepared in distilled water. Then, 50 μl solution of acarbose and extracts of different strengths were added to 50 μL of α-amylase solution, separately. The phosphate buffer was used as a blank and acarbose as control. The mixture was incubated at 37°C for 10 min, followed by the addition of 50 μL of soluble starch (1%, W/V), and again incubated at 37°C for 15 min. Then, 1 M HCl (2 μL) was added to the above mixture to stop the enzymatic reaction. At last, 10 μL of iodine reagent was added. The color change was noted, and the absorbance was recorded at 630 nm with the help of a microplate reader.[28]

$$\% \text{ Inhibitory effect} = \frac{\text{Abs control} - \text{Abs test}}{\text{Abs control}} \times 100$$

α-glucosidase inhibitory activity

The solutions of different concentrations (ranging from 100 μg mL^{-1} to 1,000 μg mL^{-1}) of ethanol and aqueous extracts were prepared in distilled water. Then 2U/mL of α-glucosidase enzyme was added to 20 μL of extract solutions. The mixtures were incubated at 37°C for 5 min. followed by addition of 20 μL of 1 mM p-nitrophenyl glucopyranoside prepared in 50 mM of phosphate buffer (pH 6.8). These mixtures were incubated at 37°C for 20 min. Tat last, 50 μL of 1 mM sodium carbonate was added. The α-glucosidase activity was determined by recording absorbance at 405 nm.[29] The α-glucosidase inhibitory activity was calculated using the formula:

$$\alpha - \text{glucosidase inhibitory activity} = \frac{(AC+) - (AC-) - (AS - AB)}{(AC+) - (AC-)} \times 100$$

Where AC +: Absorbance of enzyme in solvent, AC -, absorbance of solvent only, AS: absorbance of test sample enzyme a, AB: absorbance of test sample only.

Oral glucose tolerance test

Oral glucose tolerance tests for non-diabetic normal rats were performed.[30] Twenty normal rats were randomly divided into four groups and each group contained five male rats. The rats were allowed to fast overnight. Group-1 (control) was treated with normal saline; Group-2 was treated with acarbose at a dose of 5 mg kg^{-1}; Group-3 was treated with an ethanol extract of *C. tetragonoloba* at a dose of 250 mg kg^{-1} and Group-4 was treated with an ethanol extract (250 mg kg^{-1}) with acarbose (5 mg kg^{-1}). After 30 min of extract administration, all the groups were administered glucose orally at 2 mg kg^{-1} of body weight of rats. The blood glucose level was measured at 0 (just prior to glucose administration), 30, 60, 90, and 120 min. after glucose loading by glucometer.

Induction of diabetes in rats

Type 2 diabetes was induced in male Wistar rats by a single intraperitoneal (i.p.) injection of Streptozotocin (STZ) dissolved in a citrate buffer; pH 4.5 (60 mg kg^{-1} of body weight) and nicotinamide in normal saline was administered (110 mg kg^{-1} of body weight) after 15 min. The control group was given a vehicle citrate buffer and normal saline. Hyperglycemia was confirmed by higher fasting glucose levels measured 72 hr following STZ or vehicle injections. Rats with fasting glucose levels of more than 126 mg dL^{-1} were considered diabetic.[31]

Effect of extract on blood glucose level (acute and sub-acute study)

The thirty-five male rats were randomly divided into seven groups, each consisting of five male rats. The treatment for all animal groups is described in Table 2. The blood glucose level was measured at 0, 1, 2 and 3 hr after the treatment for the acute test, and at 0, 1, 7, 14, and 21 days after the treatment for the subacute test.

RESULTS

Effect of extracts of *C. tetragonoloba* on glucose adsorption

The adsorptive capacity of the aqueous extract was found to be the maximum at 2.692 mMol/g at 100 mM glucose, while the lowest was 0.092 mMol/g at 5 mM glucose. The ethanol extract results demonstrated that the adsorptive capacity was highest at 1.2 mMol/g at 100 mM glucose and lowest at 0.066 mMol/g

Table 1: Experimental design for acute and sub-acute study.

Group	Treatment
Group 1: Control	Water and feed ad libitum.
Group 2: Diabetic control	Water and feed ad libitum,
Group 3: Acarbose treated diabetic rats	5 mg/kg body weight per day of acarbose for 21 days.
Group 4: Indian cluster bean treated diabetic rats	250 mg/Kg body weight per day of aqueous extract of Indian cluster bean for 21 days.
Group 5: Indian cluster bean treated diabetic rats	250 mg/Kg body weight per day of ethanol extract of Indian cluster bean for 21 days.
Group 6: Indian cluster bean and acarbose treated diabetic rats	5 mg/kg and 250 mg/kg body weight per day of acarbose and aqueous extract of Indian cluster bean respectively for 21 days.
Group 7: Indian cluster bean and acarbose treated diabetic rats	5 mg/kg and 250 mg/kg body weight per day of acarbose and ethanol extract of Indian cluster bean respectively for 21 days.

Table 2: Glucose adsorptive capacity of ethanol extract of *C. tetragonoloba*.

Concentration (mM)	Glucose adsorptive capacity of ethanol extract (mM g^{-1})	Glucose adsorptive capacity of aqueous extract (mM g^{-1})
5	0.092	0.066
10	0.145	0.101
20	0.264	0.211
50	1.30	0.623
100	2.692	1.200

(Mean, n=3, p<0.05)

at 5 mM glucose. The results of the ethanol extract and aqueous extract mean are significantly different (p<0.05).

Effect of *C. tetragonoloba* on α- amylase and α-glucosidase enzymatic activity

The α-amylase enzyme has been found to be inhibited by aqueous extract (Table 3). At lower concentrations of the aqueous extract, 5.9±0.20% inhibition was observed, but at higher concentrations, 44.09±0.05% inhibition was recorded. Similarly, the percentage inhibition of lower and higher concentrations of ethanol extract were found to be 3.68±0.08% and 22.98±0.11%, respectively (Table 4). The percent inhibition of alpha-glucosidase enzyme was highest (35.8±0.06%) and lowest (7.4±0.01%) at concentrations of ethanol extract of 1000 μg mL^{-1} and 100 μg mL^{-1}, respectively. The concentrations of aqueous extract at 1000 μg mL^{-1} and 100 μg mL^{-1} showed the highest (40.3±0.13%) and lowest (8.2±0.15%) percent inhibition of the alpha-glucosidase enzyme. Aqueous extract has inhibited the α-amylase enzyme and the α-glucosidase enzyme with 5.3 mg/mL and 5.81 mg/mL IC_{50} values, respectively.

On contrast, the IC_{50} value 110 mg/mL and 6.5 mg/mL has been observed by ethanol extract for inhibition of α-amylase and α-glucosidase enzymes, respectively. We have investigated the *in vitro* amylase and glucosidase inhibitory activity for the aqueous and ethanol extracts of *C. tetragonoloba*. The aqueous extract of *C. tetragonoloba* has inhibited the α-amylase enzyme and the α-glucosidase enzyme with IC_{50} values of 5.3 mg/mL and 5.81 mg/mL, respectively. A higher concentration will be required for potent inhibitory activity of the α-amylase enzyme and the α-glucosidase enzyme. On contrast, the IC_{50} values of 110 mg/mL and 6.5 mg/mL have been observed by ethanol extract for inhibition of α-amylase and α-glucosidase enzymes, respectively.

Oral glucose tolerance test

A normal rat model was chosen for the oral glucose tolerance test. The glucose level observed were 120.20±1.77 mg/dL and 104.80±2.72 mg/dL after 180 min of glucose loading by aqueous extract and aqueous extract with acarbose, respectively.

Table 3: Inhibition of α-amylase enzyme by ethanol extract and aqueous extract of *C. tetragonoloba*.

Concentration (μg mL^{-1})	% Inhibition by ethanol extract	% Inhibition by aqueous extract
100	3.6±0.08	5.9±0.20
300	08.06±0.12	11.96±0.1
500	11.81±0.07	21.1±0.26
700	16.96±0.09	35.514±0.18
1000	22.98±0.11	44.09±0.05

(Mean±SE, n=3, p<0.05)

The glucose levels measured with ethanol extract and ethanol extract with acarbose after 180 min of glucose loading were 143.40±1.91 mg/dL and 123.80±1.82 mg/dL, respectively. The blood glucose level declined by 2.76% after 90 min and 16.36% after 120 min in the aqueous extract with the acarbose-treated group with respect to the acarbose-treated group. The aqueous extract has a lower 4.09% blood glucose level than the acarbose. The acarbose has a lower blood glucose level than ethanol extract with acarbose. The results of the OGTT are listed in Tables 5 and 6. The results of the oral glucose tolerance test have revealed that the aqueous extract with acarbose had a greater blood glucose lowering effect, shown in Figures 1 and 2. The effect of acarbose and aqueous extract with acarbose was found to be similar in normal rats after 2 hr of glucose loading. The ethanol extract with acarbose has a significantly lower blood glucose-lowering effect as compared to the aqueous extract with acarbose. The ethanol extract lowers the blood glucose level because of the phenolic contents that are soluble in ethanol.

Acute and sub-acute study

The glucose levels of 214.60±7.99 mg/dL and 199.20±4.70 mg/dL were observed after 3 hr of the administration of ethanol extract and ethanol extract with acarbose in streptozotocin-induced diabetic rats. The reduction of glucose by ethanol extract and aqueous extract was significantly different (p<0.05) between the diabetic control group and the normal control group. The glucose levels of 169.60±5.53 mg/dL and 126.00±3.78 mg/dL were measured after 3 hr of the administration of aqueous extract and aqueous extract with acarbose in streptozotocin-induced diabetic rats, illustrated in Figure 3. The reduction of glucose by ethanol extract and aqueous extract with acarbose was significantly different (p<0.05) between the diabetic control group and the normal control group. The blood glucose level of diabetic male rats is listed in Table 7. The 14^{th} day of administration has shown the glucose effect of *C. tetragonoloba* extract, and the 7^{th} day has shown a decrease in blood glucose due to the co-delivery of acarbose with both extracts. On the 14^{th} day of concurrent administration of an aqueous extract with acarbose and an ethanol extract with acarbose, the blood glucose levels were measured at

179.60±17.22 mg/dL and 214.20±21.20 mg/dL, respectively. The blood glucose levels of diabetic control group 501±34.92 mg/dL were lowered to 240.8±9.1 mg/dL and 179.60±17.22 mg/dL by the administration of the ethanol and aqueous extracts of *C. tetragonoloba*, respectively (Table 8). The difference in mean was found to be significant (p<0.05) and shown in the Figure 4.

DISCUSSION

This study comprehensively evaluates the efficacy of aqueous and ethanol extracts of *C. tetragonoloba* (guar) in adsorbing glucose, inhibiting key carbohydrate-digesting enzymes, and managing blood glucose levels in both normal and diabetic rat models. The findings underscore the superior performance of the aqueous extract across multiple parameters, attributed largely to its high fiber content and the presence of bioactive compounds. The glucose adsorptive capacity of the extracts indicates their potential to reduce glucose absorption in the small intestine, thus mitigating postprandial hyperglycemia. The study found that the aqueous extract of *C. tetragonoloba* exhibited a maximum adsorptive capacity of 2.692 mMol/g at 100 mM glucose, significantly higher than the ethanol extract's capacity of 1.2 mMol/g at the same concentration.

Even at lower glucose concentrations (5 mM), the aqueous extract maintained a higher adsorptive capacity (0.092 mMol/g) compared to the ethanol extract (0.066 mMol/g). This superior adsorptive capacity of the aqueous extract is primarily due to its rich content of water-soluble fibers, such as galactomannan. These fibers form a viscous gel in the digestive tract, which can trap glucose molecules and slow their absorption. This mechanism reduces the postprandial spike in blood glucose levels, making the aqueous extract particularly effective for managing diabetes.[32] The significant difference in adsorptive capacity (p<0.05) between the aqueous and ethanol extracts underscores the importance of fiber content and solubility in determining the efficacy of glucose adsorption. Inhibiting α-amylase and α-glucosidase enzymes is crucial for managing postprandial hyperglycemia, as these enzymes break down complex carbohydrates into glucose. The study revealed that the aqueous extract demonstrated a higher inhibition of α-amylase, with a maximum inhibition of 44.09±0.05% at higher concentrations, compared to 22.98±0.11% by the ethanol extract. Similarly, for α-glucosidase inhibition, the aqueous extract showed higher efficacy, with 40.3±0.13% inhibition at 1000 µg/mL compared to 35.8±0.06% by the ethanol extract. The IC_{50} values, which represent the concentration required to inhibit 50% of enzyme activity, further support these findings. The aqueous extract had lower IC_{50} values for both α-amylase (5.3 mg/mL) and α-glucosidase (5.81 mg/mL), compared to the ethanol extract (110 mg/mL for α-amylase and 6.5 mg/mL for α-glucosidase). These results suggest that the aqueous extract is more potent in inhibiting these enzymes, likely due to its higher content of water-soluble fibers and bioactive compounds such as phenolic acids and flavonoids. Phenolic compounds, including p-coumaric acid, gallic acid,

Table 4: Percent inhibition of α- glucosidase enzyme by ethanol extract and aqueous extract of *C. tetragonoloba*.

Concentration (µg mL^{-1})	% Inhibition by ethanol extract	% Inhibition by aqueous extract
100	7.4±0.11	8.2±0.15
300	19.77±0.06	20.6±0.05
500	28.73±0.09	32.9±0.11
700	33.95±0.14	36.04±0.01
1000	35.8±0.06	40.3±0.13

(Mean±SE, n=3, p<0.05)

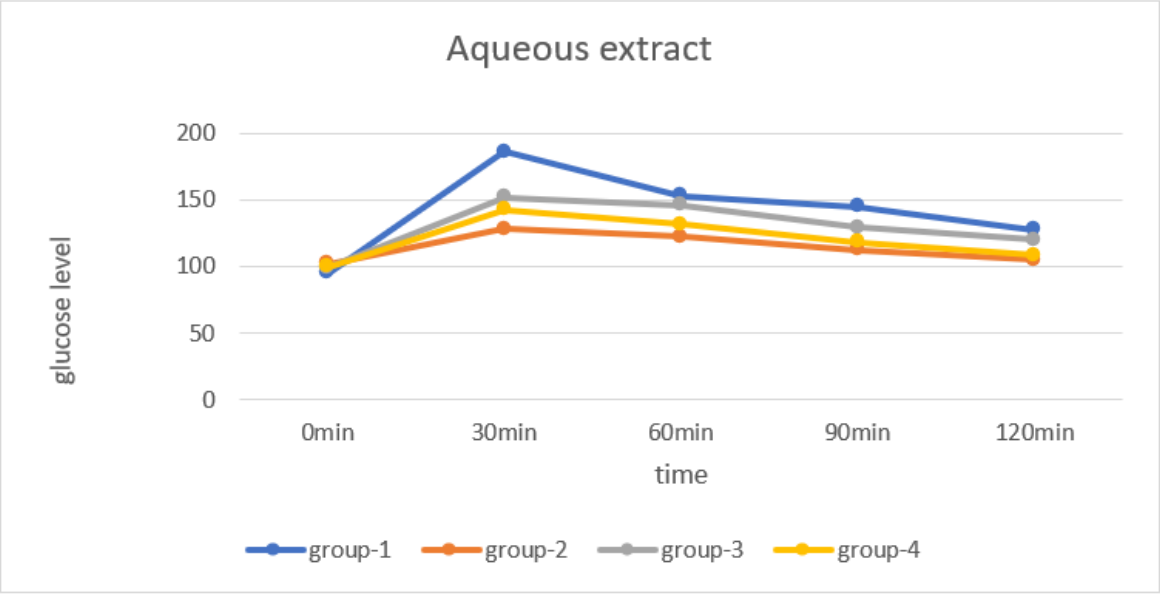

Figure 1: Effect of aqueous extract of *C. tetragonoloba* on oral glucose tolerance in normal rats.

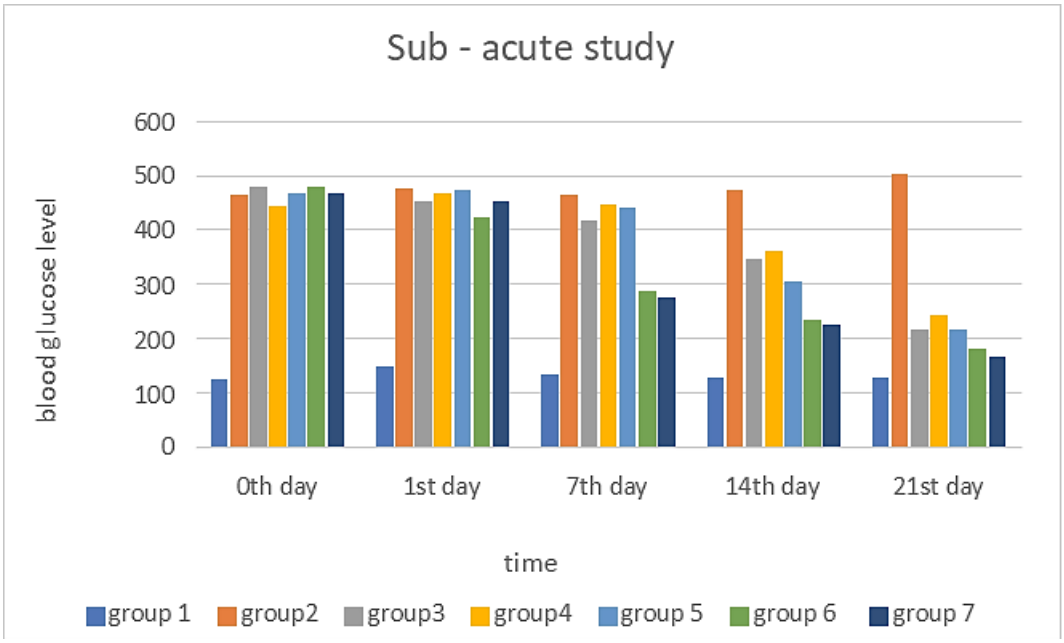

Figure 2: Effect of ethanolic extract of *C. tetragonoloba* on oral glucose tolerance in normal rats.

Table 5: Effect of aqueous extract of *C. tetragonoloba* on oral glucose tolerance in normal rats.

Group	0 min	30 min	60 min	90 min	180 min
Group-1 (Control)	99±1.94	136±1.98	183±1.45	165±1.70	147±2.034
Group-2 (Acarbose)	99.6±2.21	128.20±2.24	142.40±2.01	132.80±1.98	125.20±1.65
Group-3 (Aqueous extract)	99.80±3.59	141.40±4.36	166.20±4.78	149.20±3.05	120.20±1.77
Group-4 (Aqueous extract+acarbose)	99.56±3.24	133±3.39	152±3.44	128.80±2.03	104.80±2.72

(Mean±SEM, n=5, p<0.05)

Table 6: Effect of ethanol extract of *C. tetragonoloba* on oral glucose tolerance in normal rats.

Group	0 min	30 min	60 min	90 min	120 min
Group-1 (Control)	99±1.94	146±1.98	183±1.45	165±1.70	137±2.034
Group-2(Acarbose)	99.6±2.21	128.20±2.235	142.40±2.01	132.80±1.98	125.20±1.65
Group-3 (Ethanol extract)	99±3.01	165.4±1.46	185.8±1.39	157.2±0.96	143.40±1.91
Group-4 (Ethanol extract+acarbose)	101.60±3.54	158.20±2.39	176.60±1.12	143.00±1.30	123.80±1.82

(Mean±SEM, n=5, p<0.05)

kaempferol, quercetin, and ferulic acid, present in the extracts, are known to inhibit carbohydrate metabolism enzymes. Gallic acid, in particular, is a strong inhibitor of disaccharidases such as maltase, trehalase, and lactase, but its main inhibitory action is on α-amylase.[33,34] The higher efficacy of the aqueous extract in enzyme inhibition may be due to the higher solubility and bioavailability of these phenolic compounds in an aqueous medium. The OGTT results in normal rats demonstrated that the aqueous extract, both alone and in combination with acarbose, significantly lowered blood glucose levels more effectively than the ethanol extract. After 180 min of glucose loading, the aqueous extract with acarbose resulted in a blood glucose level of 104.80±2.72 mg/dL, compared to 123.80±1.82 mg/dL for the ethanol extract with acarbose. This indicates a synergistic effect between the aqueous extract and acarbose, enhancing the glucose-lowering effect. The aqueous extract alone also showed a greater reduction in blood glucose levels (120.20±1.77 mg/dL) compared to the ethanol extract (143.40±1.91 mg/dL) after 180 min. These findings suggest that the aqueous extract has a more potent postprandial glucose-lowering effect, likely due to its higher fiber content and the presence of bioactive compounds that inhibit carbohydrate-digesting enzymes. In

streptozotocin-induced diabetic rats, both extracts significantly reduced blood glucose levels, but the aqueous extract was more effective. After 3 hr of administration, the aqueous extract with acarbose reduced glucose levels to 126.00±3.78 mg/dL, compared to 199.20±4.70 mg/dL for the ethanol extract with acarbose. Aqueous extract with acarbose had a potent postprandial glucose-lowering effect and was observed in acute treatment. The aqueous extract with acarbose reduced blood glucose levels after 2 and 3 hr in a diabetic rat model. The ethanol extract of *C. tetragonoloba* has also shown a blood glucose-lowering effect. That effect was less compared to the acarbose and aqueous extracts with acarbose. The results of acute treatment have shown that the aqueous extract of *C. tetragonoloba* with acarbose may be used to treat postprandial hyperglycemia. The sub-acute study has shown that the after the administration of aqueous extract and ethanol extract reduces the blood glucose level after the 14th day. The co-administration of acarbose with aqueous and ethanol extract had reduced the blood glucose level from 7th day. The highest lowering effect of blood glucose level was observed at 21th day of treatment by aqueous extract with acarbose. The co-administration of aqueous extract with acarbose have shown additive effect against the hyperglycemia may be because of Gaur gum. It is a viscous galactomannan extract from the endosperm of *C. tetragonoloba* seeds. Guar gum has demonstrated hypoglycemic activity. Guar gum is a polysaccharide, that forms gel when mixed with water. It increases the viscosity of the stomach and small intestine, which reduces the movement and absorption of glucose. This effect delays the gastric emptying.[35,36] The 20% gaur gum reduced 52% of the glucose level in rats after 28 days of treatment; the effect was significantly higher than that of the control drug, glibenclamide (2 mg/kg). The gaur gum reduces the cholesterol, triglycerides, and LDL-C levels in diabetic rats.[37] Guar gum increases the effect of insulin in diabetic patients. Guar gum increases insulin sensitivity and decreases lipid content in the blood via a delay in gastric emptying and a slow absorption of glucose. The glucose utilization in adipose tissue was observed after the treatment of guar gum.[38]

Table 7: **Effect of aqueous and ethanol extracts of *C. tetragonoloba* on acute study in diabetic rats.**

Blood Glucose Level				
	Blood Sample Time (h)			
	0	1	2	3
Group 1	106.00±2.85	134.00±5.93	127.60±1.32	114.80±1.24
Group 2	531.20±39.47	537.20±38.23	528.00±37.22	522.00±42.92
Group 3	342.40±9.54	294.80±12.75	238.40±13.44	184.00±7.77
Group 4	366.20±8.15	308.20±6.12	233.00±8.82	214.60±7.99
Group 5	361.60±9.26	285.40±8.30	223.80±6.71	199.20±4.70
Group 6	358.80±5.77	275.00±9.44	224.80±8.25	169.60±5.53
Group 7	349.60±15.62	243.00±12.66	173.20±22.23	126.00±3.78

(Mean±SEM, n=5, p<0.05 compare to diabetic control group)

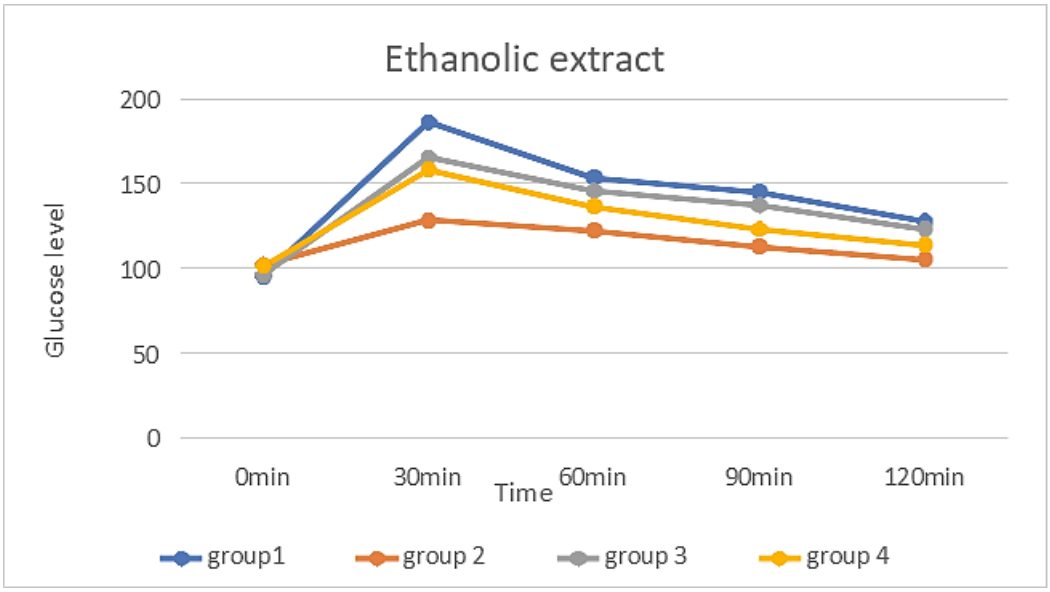

Figure 3: Effect of aqueous and ethanolic extracts of *C. tetragonoloba* on sub-acute study in diabetic rats.

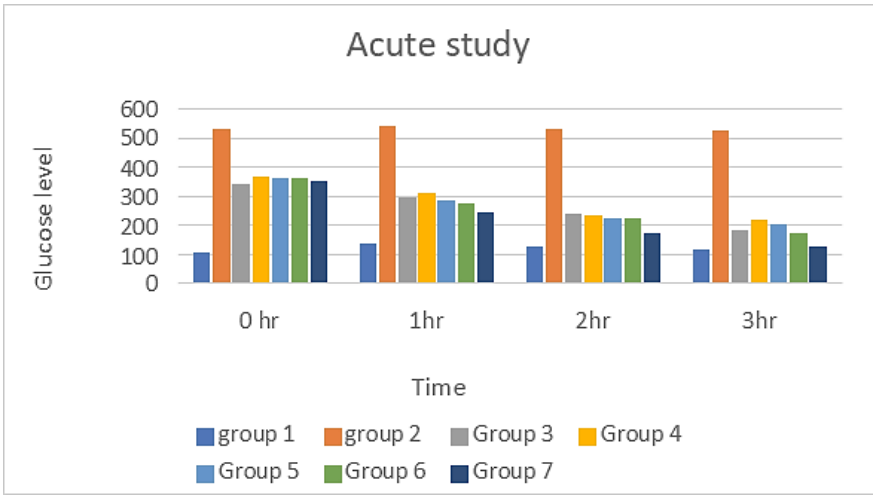

Figure 4: Results of acute study after treatment of extracts of *C. Tetragonoloba*.

Table 8: Effect of aqueous and ethanol extracts of *C. tetragonoloba* on sub-acute study in diabetic rats.

	Sample time (days)				
	Day 0	Day 1	Day 7	Day 14	Day 21
Group-1	124.60±2.27	146±3.91	131.8±9.41	124.80±1.24	125.8±0.66
Group-2	462.60±33.82	475±39.22	464.20±44.75	471.20±27.28	501±34.92
Group-3	479±36.91	451.60±41.1	415.80±47.89	345.60±34.30	215.60±15.91
Group-4	442±10.53	467±9.92	444.2±3.76	360±10.0	240.8±9.1
Group-5	467.60±40.58	471.20±60.54	439.60±59.77	304.40±48.49	214.20±21.20
Group-6	479.60±29.09	422.2±28.70	284.60±32.35	232±21.49	179.60±17.22
Group-7	466±46.67	452±45.03	273.40±45.88	224.80±27.9	165±128.76

The *in vivo* study results suggest that the co-administration of aqueous extract with acarbose may be used to reduce postprandial hyperglycemia. The results of the *in vitro* study corroborate those of the *in vivo* study. The results of glucose adsorption capacity of aqueous extract support the additive effect of aqueous extract with acarbose on streptozotocin-induced diabetic rats.

CONCLUSION

The present results demonstrate the co-administration of aqueous extract and ethanol extract with acarbose have shown statistically significant reduction in blood glucose level in streptozotocin induced male diabetic rats. The aqueous extract with acarbose was more effective for postprandial hyperglycemia compares to ethanol extract with acarbose and acarbose. The additive pharmacological effect on blood glucose level has been observed after the co administration of extract of *C. tetragonoloba* with acarbose in streptozotocin induced male diabetic rats. However, it is vital to understand the pharmacodynamic interactions yielding therapeutic benefits as a result of synergistic action. To summarise, the interaction of herbal and pharmaceutical medicines is a critical to both patients and health care practitioners. It is necessary to continue research on potential risks and benefits associated with the combination of *C. tetragonoloba* and Acarbose on pharmacokinetic aspects. Such data is crucial for the formulation of future clinical guidelines to improve health-care outcomes in diabetes.

ACKNOWLEDGEMENT

The authors are grateful to the School of Pharmacy, Devi Ahilya Vishwavidyalaya, Indore for providing necessary research facilities. RM is grateful to the All-India Council of Technical Education (AICTE), New Delhi, for PG scholarship.

ABBREVIATIONS

GLUT-4: Glucose Transporter Type 4; **OGTT:** Oral Glucose Tolerance Test; **SGLT2:** Sodium-Glucose Co-Transporter 2; **STZ:** Streptozotocin.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

IAEC approval No. 779/CPCSEA/IACE/2022/005.

SUMMARY

The study highlights the superior efficacy of the aqueous extract of *C. tetragonoloba* in managing glucose metabolism and reducing blood glucose levels. The higher adsorptive capacity, stronger enzyme inhibitory effects, and more pronounced glucose-lowering outcomes suggest that the aqueous extract, particularly when combined with acarbose, holds promise as a natural therapeutic agent for managing diabetes. The presence of water-soluble fibers and bioactive compounds in the aqueous extract likely contributes to its enhanced performance. Further research should focus on identifying the specific active compounds and their mechanisms of action to fully harness the therapeutic potential of *C. tetragonoloba* extracts in diabetes management.

REFERENCES

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2009;32 Suppl 1 (Suppl 1):S62-7:S62-7. doi: 10.2337/dc09-S062.
2. Banday MZ, Sameer AS, Nissar S. Pathophysiology of diabetes: an overview. Avicenna J Med. 2020;10(4):174-88. doi: 10.4103/ajm.ajm_53_20, PMID 33437689.
3. Stöckli J, Fazakerley DJ, James DE. GLUT4 exocytosis. J Cell Sci. 2011;124(24):4147-59. doi: 10.1242/jcs.097063, PMID 22247191.
4. Burgos-Morón E, Abad-Jiménez Z, Marañón AM, Iannantuoni F, Escribano-López I, López-Domènech S, *et al.* Relationship between oxidative stress, ER stress, and inflammation in type 2 diabetes: the battle continues. J Clin Med. 2019;8(9):1385. doi: 10.3390/jcm8091385, PMID 31487953.
5. Masenga SK, Kabwe LS, Chakulya M, Kirabo A. Mechanisms of oxidative stress in metabolic syndrome. Int J Mol Sci. 2023;24(9):7898. doi: 10.3390/ijms24097898, PMID 37175603.
6. Mittal M, Siddiqui MR, Tran K, Reddy SP, Malik AB. Reactive oxygen species in inflammation and tissue injury. Antioxid Redox Signal. 2014;20(7):1126-67. doi: 10.1089/ars.2012.5149, PMID 23991888.
7. Cade WT. Diabetes-related microvascular and macrovascular diseases in the physical therapy setting. Phys Ther. 2008;88(11):1322-35. doi: 10.2522/ptj.20080008, PMID 18801863.
8. Rahman S, Rahman T, Ismail AA, Rashid AR. Diabetes-associated macrovasculopathy: pathophysiology and pathogenesis. Diabetes Obes Metab. 2007;9(6):767-80. doi: 10.1111/j.1463-1326.2006.00655.x, PMID 17924861.
9. Feldman EL, Callaghan BC, Pop-Busui R, Zochodne DW, Wright DE, Bennett DL, *et al.* Diabetic neuropathy. Nat Rev Dis Primers. 2019;5(1):41. doi: 10.1038/s41572-019-0092-1, PMID 31197153.
10. Padhi S, Nayak AK, Behera A. Type II diabetes mellitus: a review on recent drug based therapeutics. Biomed Pharmacother. 2020;131:110708. doi: 10.1016/j.biopha.2020.110708, PMID 32927252.
11. Vieira R, Souto SB, Sánchez-López E, Machado AL, Severino P, Jose S, *et al.* Sugar-lowering drugs for type 2 diabetes mellitus and metabolic syndrome – Review of classical and new compounds. Part-I Pharm (Basel). 2019;12(4).
12. Haddad F, Dokmak G, Bader M, Karaman R. A comprehensive review on weight loss associated with anti-diabetic medications. Life (Basel). 2023;13(4):1012. doi: 10.3390/life13041012, PMID 37109541.
13. Khoo CM. Diabetes mellitus treatment. In: Quah SR, editor. International encyclopedia of public health. 2nd ed. Oxford: Academic Press; 2017. p. 288-93. doi: 10.1016/B978-0-12-803678-5.00108-9.
14. Hossain U, Das AK, Ghosh S, Sil PC. An overview on the role of bioactive α-glucosidase inhibitors in ameliorating diabetic complications. Food Chem Toxicol. 2020;145:111738. doi: 10.1016/j.fct.2020.111738, PMID 32916220.
15. Galib R, Dang P, Kumar V, Rana R, Yadav P, Prajapati PK. Patterns of concomitant use of Ayurveda and conventional anti-diabetic formulations – experiences at a tertiary care Ayurveda hospital, India. Ayu. 2020;41(2):72-8. doi: 10.4103/ayu.AYU_81_20, PMID 34908791.
16. Tran N, Pham B, Le L. Bioactive compounds in anti-diabetic plants: from herbal medicine to modern drug discovery. Biology (Basel). 2020;9(9):252. doi: 10.3390/biology9090252, PMID 32872226.
17. Riaz S, Hussain I, Ibrahim M, Ishtiaq M, Ali Q, Muazzam Ali M, *et al.* Extraction and optimization of active metabolites from cluster bean: an *in vitro* biological and phytochemical investigation. Dose Response. 2022;20(2):15593258221098992. doi: 10.1177/15593258221098992, PMID 35558873.
18. Mukhtar HM, Ansari SH, Bhat ZA, Naved T. Antihyperglycemic activity of *Cyamopsis tetragonoloba* beans on blood glucose levels in alloxan-induced diabetic rats. Pharm Biol. 2006;44(1):10-3. doi: 10.1080/13880200500509025.
19. Pathak R, Singh M, Henry A. Genetic diversity and interrelationship among clusterbean (*Cyamopsis tetragonoloba*) genotypes for qualitative traits. Indian J Agric Sci. 2011;81(5):402.
20. Bouchenak M, Lamri-Senhadji M. Nutritional quality of legumes and their role in cardiometabolic risk prevention: a review. J Med Food. 2013;16(3):185-98. doi: 10.1089/jmf.2011.0238, PMID 23398387.
21. Majeed Y, Shaukat MB, Abbasi KY, Ahmad MA. Indigenous plants of Pakistan for the treatment of diabetes: a review. Agrobiol rec. 2021;4:44-63.
22. Joshi T, Mandal SK, Puri S, Asati V, Deepa PR, Sharma PK. Investigating the antioxidant activity enhancer effect of *Cyamopsis tetragonoloba* seed extract on phenolic phytochemicals. Front Plant Sci. 2023;14:1131173. doi: 10.3389/fpls.2023.1131173, PMID 36968395.
23. Redfern J, Kinninmonth M, Burdass D, Verran J. Using Soxhlet ethanol extraction to produce and test plant material (essential oils) for their antimicrobial properties. J Microbiol Biol Educ. 2014;15(1):45-6. doi: 10.1128/jmbe.v15i1.656, PMID 24839520.
24. El-Lethy SR, Talaat IM, Tarraf SA, El Moursi A. Impacts of some biostimulants on guar (*Cyamopsis tetragonoloba* L.) plants. Bull Natl Res Cent. 2019;43(1):169. doi: 10.1186/s42269-019-0196-5.
25. Jiang H, Lin Y, Ren W, Fang Z, Liu Y, Tan X, *et al.* Adverse drug reactions and correlations with drug–drug interactions: A retrospective study of reports from 2011 to 2020. Front Pharmacol. 2022;13:923939. doi: 10.3389/fphar.2022.923939, PMID 36133826.
26. Paul S, Majumdar M. In vitro antidiabetic propensities, phytochemical analysis, and mechanism of action of commercial antidiabetic polyherbal formulation "Mehon". Proceedings. 2021;79(1):7.
27. Ahmed F, Sairam S, Urooj A. *In vitro* hypoglycemic effects of selected dietary fiber sources. J Food Sci Technol. 2011;48(3):285-9. doi: 10.1007/s13197-010-0153-7, PMID 23572748.
28. Sagbo IJ, van de Venter M, Koekemoer T, Bradley G. *In vitro* antidiabetic activity and mechanism of action of *Brachylaena elliptica* (Thunb.) DC. Evid Based Complement Alternat Med. 2018; 2018:4170372. doi: 10.1155/2018/4170372, PMID 30108655.
29. Etsassala NG, Badmus JA, Marnewick JL, Egieyeh S, Iwuoha EI, Nchu F, *et al.* Alpha-glucosidase and alpha-amylase inhibitory activities, molecular docking, and antioxidant capacities of Plectranthus ecklonii constituents. Antioxidants (Basel). 2022;11(2):378. doi: 10.3390/antiox11020378, PMID 35204260.
30. Kuo FY, Cheng KC, Li Y, Cheng JT. Oral glucose tolerance test in diabetes, the old method revisited. World J Diabetes. 2021;12(6):786-93. doi: 10.4239/wjd.v12.i6.786, PMID 34168728.
31. Ghasemi A, Khalifi S, Jedi S. Streptozotocin-nicotinamide-induced rat model of type 2 diabetes (review) [review]. Acta Physiol Hung. 2014;101(4):408-20. doi: 10.1556/APhysiol.101.2014.4.2, PMID 25532953.
32. Mudgil D, Barak S, Khatkar BS. Guar gum: processing, properties and food applications – a review. J Food Sci Technol. 2014;51(3):409-18. doi: 10.1007/s13197-011-0522-x, PMID 24587515.
33. Abdel-Moneim A, Abd El-Twab SM, Yousef AI, Ashour MB, Reheim ES, Hamed MA. New insights into the *in vitro, in situ* and *in vivo* antihyperglycemic mechanisms of gallic acid and p-coumaric acid. Arch Physiol Biochem. 2022;128(5):1188-94. doi: 10.1080/13813455.2020.1762659, PMID 32401050.
34. Ombra MN, d'Acierno A, Nazzaro F, Spigno P, Riccardi R, Zaccardelli M, *et al.* Alpha-amylase, α-glucosidase and lipase inhibiting activities of polyphenol-rich extracts from six common bean cultivars of Southern Italy, before and after cooking. Int J Food Sci Nutr. 2018;69(7):824-34. doi: 10.1080/09637486.2017.1418845, PMID 29336184.
35. Cameron-Smith D, Habito R, Barnett M, Collier GR. Dietary guar gum improves insulin sensitivity in streptozotocin-induced diabetic rats. J Nutr. 1997;127(2):359-64. doi: 10.1093/jn/127.2.359, PMID 9039840.
36. Lebovitz HE. Oral antidiabetic agents: the emergence of alpha-glucosidase inhibitors. Drugs. 1992; 44 Suppl 3:21-8. doi: 10.2165/00003495-199200443-00004, PMID 1280574.
37. Samarghandian S, Hadjzadeh MA, Amin Nya F, Davoodi S. Antihyperglycemic and antihyperlipidemic effects of guar gum on streptozotocin-induced diabetes in male rats. Pharmacogn Mag. 2012;8(29):65-72. doi: 10.4103/0973-1296.93328, PMID 22438666.
38. Landin K, Holm G, Tengborn L, Smith U. Guar gum improves insulin sensitivity, blood lipids, blood pressure, and fibrinolysis in healthy men. Am J Clin Nutr. 1992;56(6):1061-5. doi: 10.1093/ajcn/56.6.1061, PMID 1442658.

Cite this article: Mourya R, Elangovan M, Parmar HS, Sharma R. Pharmacodynamic Interaction between *Cyamopsis tetragonoloba* (Cluster Beans) and Acarbose: An *in vitro* and *in vivo* Study. Pharmacog Res. 2026;18(1):191-9.