

Full Length Research Paper

## Anti-hyperglycemic effect of cocoyam (*Xanthosoma sagittifolium*) corm in alloxan-induced diabetic albino rats

Oluyemisi Folake FOLASIRE<sup>1,2\*</sup>, Olayinka Ayotunde ORIDUPA<sup>3</sup>, Adedotun Joshua OWOLABI<sup>1</sup>  
and Oladejo Thomas ADEPOJU<sup>1</sup>

<sup>1</sup>Department of Human Nutrition, College of Medicine, University of Ibadan, Ibadan, Oyo State, Nigeria.

<sup>2</sup>Department of Family Medicine, University College Hospital, Ibadan, Oyo State, Nigeria.

<sup>3</sup>Department of Veterinary Physiology, Biochemistry and Pharmacology, Faculty of Veterinary Medicine, University of Ibadan, Ibadan, Oyo State, Nigeria.

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Diabetes mellitus constitutes a global public health concern and dietary approach is key to the control and prevention of lethal complications. This study investigated the hypoglycemic and anti-hyperglycemic effects of *Xanthosoma sagittifolium*-incorporated diets in normoglycemic and alloxan-induced diabetic rats. Seventy normoglycemic male Wistar strain albino rats (120 to 200 g) were divided into two groups of thirty-five each. Group 1 was randomly distributed into seven subgroups and each subgroup assigned to 100% rat pellets, *X. sagittifolium*-incorporated rat pellet (25, 50 and 75%), 100% *X. sagittifolium*, 100% *X. sagittifolium* + Glibenclamide (oral hypoglycaemic agent for treatment of diabetes) or 100% rat pellets + Glibenclamide. Diabetes was induced in Group 2 rats fasted for 12 h by intraperitoneal injection of Alloxan (100 mg/kg body weight). Initial fasting blood glucose levels (BGL) were recorded, and alloxan-treated rats with BGL >200 mg/dl 48 h post-induction were considered diabetic and divided into seven subgroups. Dietary treatment was carried out, and blood glucose level (BGL) monitored for 14 days. Data obtained were analyzed using one way analysis of variance (ANOVA) and Tukey's post-hoc test at  $p < 0.05$ . *X. sagittifolium* caused a significant reduction in the BGL of alloxan-induced diabetic rats ( $p < 0.05$ ) but no hypoglycemic effect in normoglycemic rats. Rats fed 25% (BGL:  $165.2 \pm 16.9$  mg/dl), 50% (BGL:  $189.2 \pm 15.9$  mg/dl) and 75% (BGL:  $152.0 \pm 23.0$  mg/dl) *X. sagittifolium* showed better control of BGL by 24 h post-prandial compared with rats administered glibenclamide (BGL:  $195.0 \pm 18.6$  mg/dl) and 100% *X. sagittifolium* (BGL:  $221.0 \pm 17.0$  mg/dl). Rats fed 75% (BGL:  $118.4 \pm 11.0$  mg/dl) or 100% (BGL:  $97.0 \pm 17.1$  mg/dl) *X. sagittifolium* had better controlled BGL compared with rats fed pellets and pellets + glibenclamide (BGL:  $154.2 \pm 19.8$  mg/dl) on day 7. *X. sagittifolium* corm has an antihyperglycemic effect, and its consumption should be encouraged among diabetic patients as a good replacement for other high-calorie diets.

**Key words:** Antihyperglycemic effect, *Xanthosoma sagittifolium*, diabetes mellitus, albino rat.

### INTRODUCTION

Diabetes mellitus constitutes a global public health concern and dietary approach is key to the control and

prevention of lethal complications. More than 90% of all diabetics have type 2 Diabetes mellitus (T2DM), which

often goes undiagnosed. Less than 10% have type 1 Diabetes mellitus (T1DM). In the T1DM, insulin is no longer produced, because the  $\beta$ -islet cells of the pancreas are destroyed thus the insulin dependent state, while in T2DM there is still some amount of insulin produced because the islet cells are not destroyed; however there is ineffective or insufficient insulin production. The development of T2DM has been linked to environmental and lifestyle factors. (Tuomilehto et al., 2001). Thus, the prevalence of type 2 diabetes mellitus (T2DM) is increasing at an alarming rate throughout the world, due to people living longer, obesity and sedentary lifestyles (Tuomilehto et al., 2001; Bloomgarden, 2004). The sub-Saharan African region has close to 7 million diabetics; these estimated prevalence is expected to double to 15 million by 2025. (International Diabetic Federation (IDF), 2016). According to the IDF report, Nigeria has the highest number of people living with Diabetes mellitus and impaired glucose tolerance, with more than 1.56 million cases of diabetes. The prevalence of diabetes mellitus and impaired fasting glucose in a recent study from Southeastern part of Nigeria reported 3.0 and 1.1% (Ejike et al., 2015). Majority cannot afford the standard treatment and many more are not aware. Clinical and experimental evidence have shown that oxidative stress plays a major role in the pathogenesis and progression of diabetes mellitus, a metabolic disorder characterized by insulin hypersensitivity and hyperglycemia (Maritim et al., 2003). Complications such as oxidative DNA damage, cardiovascular disease, nerve damage, blindness, nephropathy and insulin resistance in diabetic patients can be related to increase oxidative stress as well as reduction in antioxidant capacity (Lodovicia et al., 2008; Styskal et al., 2012; Tiwari et al., 2013).

*Xanthosoma sagittifolium* (family Araceae), commonly known as Cocoyam, is one of the most important root and tuber crops world-wide (Jennings, 1987; Onwueme and Charles, 1994). The white or pink variant is nutritionally superior to cassava and yam with a content of 70 to 80% water, 20 to 25% starch and a significant amount of vitamins which are particularly in proportions compatible with the diet requirement of diabetic patients (Amusa et al., 2011).

A previous study reflected that other parts of *X. sagittifolium* also show high potential antioxidant effects (de Almeida et al., 2013). In the study, lyophilized *X. sagittifolium* leaf was fed to healthy rats for four weeks, and it was reported that the leaves had high total fiber content (predominantly insoluble dietary fiber), the rat showed increased fecal mass and fat excretion, with

improved bile acid profiles. The researchers suggested that consumption of *X. sagittifolium* leaf may have the property of lowering the risk of colon cancer, which is a sequel to increased oxidative stress (Ukpong et al., 2014). According to de Almeida et al. (2013) the inflorescence of *X. sagittifolium* contains high amounts of terpenoids, glycosides and tannins, moderate amounts of flavonoids and alkaloids, and trace amounts of saponins and steroids. Inflorescent *X. sagittifolium* was also reported to be a good source of micro and macro elements. These researchers concluded that presence of these elements and phytochemicals in appreciable quantities highlighted the nutritional and therapeutic value of *X. sagittifolium* inflorescence.

The management of diabetes mellitus, particularly type 2, involves lifestyle adjustment, physical activities and dietary changes to high fiber low-calorie diets. The use of food and medicinal plants in the traditional management of diabetes mellitus plays an important role in the lives of rural people in developing countries which are poorly served with health facilities (Karou et al., 2011; Bahmani et al., 2014; Ezurike and Prieto, 2014). One of the aims of dietary adjustment in the treatment of diabetes mellitus is the maintenance of normoglycemic levels. Currently, there is a dearth of information on the corm of *X. sagittifolium*, a dietary supplement recommended for diabetic patients. This study, therefore, was designed to assess the hypoglycemic and anti-hyperglycemic effects of consumption of various percentages of *X. sagittifolium* (cocoyam) corm-replacement diets on normoglycemic and alloxan-induced diabetic albino rats.

## MATERIALS AND METHODS

### Experimental animal

Seventy (70) apparently healthy (male) Albino rats of Wistar strain brand weighing between 120 to 200 g were purchased from and housed at the Experimental Animal House of the Department of Physiology, University of Ibadan, Nigeria. The rats were allowed to acclimatize for one week under a constant 12 h light: dark cycle and fed with rat pellets and water *ad libitum* at room temperature (27°C).

### Processing of cocoyam feed

*X. sagittifolium* corm was purchased from Bodija market, Ibadan, which is popular for foodstuffs purchase. They were washed, peeled and per-boiled for 10 min. The corms were mashed, air-dried, milled and moulded into the modified feed as: 25, 50, 75 and 100% *X. sagittifolium* mixed with commercial rat pellets. The study was performed over a 14 days period.

\*Corresponding author. E-mail: yemisifolasire2011@gmail.com. Tel: +234 803 400 2041.

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**Table 1.** Mean Fasting blood glucose levels (mg/dl) of normoglycemic rats, rats fed with *X. sagittifolium* feeds and rats administered with glibenclamide\*.

Group	FBG	1 h	2 h	6 h	12 h	24 h
Normoglycemic	71.0±7.1	96.8±4.9	122.8±17.6	112.6±14.8	81.4±4.9	79.6±4.3
CY 25%	71.0±3.8	108.8±7.6	121.2±13.0	126.8±8.5*	91.8±8.6	95.6±5.9
CY 50%	69.6±7.2	106.6±3.1	125.0±6.6*	117.8±6.1	98.2±5.1	88.8±7.8
CY 75%	58.2±2.9	88.8±5.6	123.0±5.3*	125.6±7.6*	83.0±4.5	82.8±4.9
CY 100%	65.6±5.9	127.2±6.6*	132.2±9.7*	125.2±11.2*	90.4±8.4	98.4±5.9
Glib+CY100%	75.4±4.4	132.2±7.9*	127.8±7.8*	108.8±6.3	124.4±6.7*	115.8±6.9
Glib	69.2±3.9	123.0±5.5*	97.2±4.5*	79.4±5.5	90.8±5.1*	85.0±8.6

\*Value is significantly ( $p < 0.05$ ) increased; **FBG** = fasting blood glucose; CY = Cocoyam (*X. sagittifolium* corm), Glib = Glibenclamide.

### Hypoglycemia study

Thirty-five normoglycemic rats were randomly and equally divided into seven groups with similar mean weight. Rats in group 1 served as the control for this experiment and were fed with standard rat pellets. Rats in groups 2, 3 and 4 were respectively fed with 25, 50 or 75% *X. sagittifolium* feed combined with the standard rat pellet while group 5 rats were fed with 100% *X. sagittifolium* feed alone. Rats in group 6 were fed with 100% *X. sagittifolium* with glibenclamide (5 mg/kg) while rats in group 7 served as the positive control and were fed 100% rat pellets with glibenclamide (5 mg/kg). The rate of feed consumption was monitored before the commencement of the experiment to determine the amount of feed provided to each group per day. Before commencement of the feeding regimens above, the rats were made to fast overnight and fasting blood glucose levels determined. The blood glucose levels (BGL) before and during the period of feeding were monitored using a glucometer (AccuChek active®) at 1, 2, 3, 6, 12 and 24 h post-feeding with *X. sagittifolium* corm or administration of glibenclamide to determine their hypoglycemic effect. Glibenclamide is an oral hypoglycemic agent used in the treatment of hyperglycemia in diabetes mellitus. A common and serious side effect of treatment with glibenclamide is hypoglycaemia, hence using it as a standard in this study.

### Hyperglycemia study

Diabetes mellitus was induced in normoglycemic rats by an intraperitoneal injection of a single dose of alloxan monohydrate (100 mg/kg). The same pattern of rats grouping adopted above was also used for this study, with control rats being diabetic but untreated through the course of this experiment. The 8<sup>th</sup> group of normoglycemic rats was also included in the hyperglycemia study. The study essentially had 3 controls: (1). Normoglycemic rats (to show the rats were non-diabetic before the study commenced); (2). Diabetic untreated rats (showed that diabetes was induced in the study); and (3). Diabetic rats treated with glibenclamide (showed standard management of diabetes). Marked increase in blood glucose levels post-administration of alloxan was indicative of induction of diabetes (Adeyi et al., 2012). Alloxan, a glucose analogue, selectively accumulates in the  $\beta$ -islet cells of pancreas and cause toxic necrosis and production of free radical eventually leading to selective destruction of the cell and failure of insulin production. Blood glucose levels of  $\geq 200$  mg/dl were considered diabetic 48 h post-administration of alloxan. Feeding with *X. sagittifolium* corm and administration of glibenclamide to the respective groups commenced at (0 h) and the post-prandial blood

glucose levels monitored at 1, 2, 3, 6, 12 and 24 h post-feeding with *X. sagittifolium* corm or administration of glibenclamide and also on days 1, 2, 3, 5, 7 and 10 of study.

The data obtained for each group was analyzed using one way analysis of variance (ANOVA), and differences between means were determined using Tukey's post-hoc test. The level of significance was set at  $p < 0.05$ .

## RESULTS

### Effect of *X. sagittifolium* feeds on normoglycemic rats

Fasting and post-prandial blood glucose of normoglycemic rats fed with the graded percentages of *X. sagittifolium*-incorporated feed showed a normal increase and subsequent decline within the initial 24 h period of *ad libitum* feeding compared to the control rats fed with commercial rat pellets (Table 1). Body weight progressively increased over the course of the 14 days observation period (Table 2).

In Table 3, diabetic rats fed with 25, 50, 75 and 100% *X. sagittifolium* feed showed significant reductions in blood glucose levels compared to the diabetic but untreated rats ( $p < 0.05$ ). In the initial 2 h post-prandial, BGL continued to increase in rats fed with the lower percentages (25 and 50%) of *X. sagittifolium*, but a non-significant decrease was observed for rats fed with 75 and 100% *X. sagittifolium* feed ( $p > 0.05$ ). By 12 h post-prandial, BGL in all rats fed with *X. sagittifolium* were significantly reduced compared to BGL at 0 h. Rats fed with 100% *X. sagittifolium* or commercial rat pellets alone and administered with glibenclamide also had lowered BGL by 12 h post-prandial, but not earlier.

Blood glucose level of rats fed with 25, 50 or 75% *X. sagittifolium* showed better control by 24 h post-prandial compared to rats administered with glibenclamide and also in combination with 100% *X. sagittifolium*. By day 7, BGL of rats fed with 75 or 100% *X. sagittifolium* was better controlled compared with rats fed with commercial rat pellets alone and administered with glibenclamide. This trend was consistently observed until the end of the

**Table 2.** Mean body weight change (grams) in normoglycemic rats\*.

Treatment	0 Week	2 Weeks
Normal control (100% Rat pellets)	153.2±17.3	211.16±17.3*
Normal + 25% CY	160.2±3.4	184.48±5.4*
Normal +50% CY + 50% Rat pellets	161.8±13.8	186.8± 5.2
Normal + 75% CY	163.8±4.6	162.04±11.2
Normal + 100% CY	161.4±16.5	153.8±5.0
Normal + 100 % CY + Glib	134.8±6.6	154.68±32.4
Normal + 100% Rat pellets + Glib	128.8±6.1	140.72±16.0

\* Weight is significantly increased; CY = Cocoyam (*X. sagittifolium* corm); Glib = Glibenclamide.

**Table 3.** Fasting blood glucose levels (mg/dl) of alloxan-induced diabetic rats fed with *X. sagittifolium* incorporated feeds. Diet

Group	Diab. Ctr	CY 25%	CY 50%	CY 75%	CY 100%	Glib+CY100%	Glib	Normal Ctr
FBG	89.4±9.7	78.8±7.6	83.0±9.7	78.8±7.4	85.2±4.7	96.4±4.3	74.2±9.3	71.0±9.3
24 h Post-Ind	308.6±17.9	243.6±12.9	185.8±13.3	403.4±18.2	237.2±13.8	237.4±10.9	214.6±8.2	108.8±8.1
0 h*	477.4±16.5	285.4±19.9	216.6±13.8	405.0±22.8	345.2±17.9	364.4±16.8	359.8±13.4	121.2±12.1
1 h	325.6±19.8	344.4±22.3	279.0±15.2	370.8±16.6	363.8±18.3	377.0±21.6	362.2±18.4	99.6±13.7
2 h.	374.4±16.5	410.0±24.5	328.6±13.7	341.4±17.3	336.4±24.3	442.2±22.3	407.2±24.3	116.6±4.83
6 h.	406.2±19.5	296±17.5	243.6±19.1	213.4±19.9	309.6±25.9	442.2±24.2	466.2±15.1	112.4±7.73
12 h	343.8±15.5	276.8±17.9	222.0±17.0	142.4±4.3	317.0±20.6	292.0±16.4	313.0±6.8	85.6±5.3
Day 1	236.8±11.6	165.2±16.9	189.2±15.9	152.0±23.0	272.4±18.7	221.0±17.0	195.0±18.6	103.6±11.5
Day 2	247.4±18.7	124.6±7.7	171.0±15.3	183.4±8.5	279.8±15.7	247.6±11.4	221±18.1	101.8±5.7
Day 3	238.6±18.2	124.6±7.6	169.4±20.0	188.8±16.0	230.2±8.7	232.8±12.6	183.0±6.71	103.4±5.9
Day 5	258.0±14.6	148.4±15.1	197.6±20.0	165.6±19.0	124.8±19.0 <sup>a</sup>	298.6±17.6	174.6±13.9	106.2±4.4
Day7	292.0±13.4	122.2±13.9 <sup>a</sup>	181.2±14.1	118.4±11.0	97.0±17.1 <sup>a</sup>	292±13.4	154.2±19.8	101.0±3.7
Day 10	329.0±22.4	148.2±15.1	155.4±11.6	121.2±9.84 <sup>a</sup>	125.4±11.1 <sup>a</sup>	245.4±19.7	171.2±14.5	109.8±8.3
Day 14	349.0±23.2	135.2±26.1	166.0±16.2	125.0±11.3 <sup>a</sup>	124.0±15.3 <sup>a</sup>	131.1±19.0	127.3±18.2	112.0±7.3

\*0 h reading was taken 48 h post-induction of diabetes. All blood glucose level values were significantly ( $p < 0.05$ ) increased except values with superscript <sup>a</sup> which were statistically unchanged compared to control normoglycemic rats.

14 – day observation period, and by day 14, the mean BGL of the diabetic rats had returned to about the pre-induction levels. BGL of diabetic but untreated rats remained persistently high throughout the course of the study (Table 3).

In Table 4, weight gain in all diabetic rats fed with *X. sagittifolium* and or administered with glibenclamide were comparable to the weight gain in the normoglycemic control rats. The untreated diabetic rats on the other hand significantly lost weight at the termination of the study ( $p < 0.05$ ).

## DISCUSSION

This study demonstrated that *X. sagittifolium* corm possesses anti-hyperglycemic effect, and its consumption did not reduce blood glucose levels in normoglycemic

conditions. Adeyi et al. (2012) reported that alloxan destroys the  $\beta$ -cells of the Islet of Langerhans which secrete insulin, a hormone required for glucose metabolism in the body, leading to the development of insulin-dependent diabetes mellitus (DM) in rats within a few hours post-exposure (Szkudelski, 2001; Kikumoto et al., 2010). The mechanism of action of alloxan induced DM is through selective destruction of  $\beta$ -islet cells of the pancreas. This action leads to the generation of reactive oxygen species (free radical, superoxides radicals and hydrogen peroxide) ultimately causing complete destruction of the  $\beta$ -cells of pancreas (Lenzen, 2008; Rohilla and Ali, 2012).

Post-prandial BGL of the diabetic rats fed with graded percentages of *X. sagittifolium* corm showed a profound decline through the hourly monitoring, followed up by daily monitoring records. Rats, fed with 75% *X. sagittifolium* showed the most consistent glycaemic

**Table 4.** Mean body weight change (grams) in diabetic rats.

Group	Day 1	Day 3	Day 14
Diabetic rat + 100% Rat pellets	169.6±15.4	162.0±28.9	154.6±41.8
Diabetic rat + 25% CY	132.4±5.08	141.4±9.9	151.4±18.6*
Diabetic rat + 50% CY	141.4±13.8	144.4±16.7	150.4±19.9
Diabetic rat + 75 CY	130.6±32.7	141.0±28.6	152.3±23.5*
Diabetic rat + 100% CY	140.6±10.9	143.4±15.4*	162.2±23.7
Diabetic rat + Glib	144.4±10.2	145.8±15.2	154.0±18.1
Diabetic rat + 100% CY + Glib	139.0±23.5	142.4±27.8	148.6±29.5
Non-diabetic rat + 100% Rat pellets	139.0±25.7	143.0±21.4	154.8±20.5

\*Value is significantly ( $p < 0.05$ ) changed compared to the weight on Day 1; CY = Cocoyam (*X. sagittifolium* corm), Glib = Glibenclamide.

control through the course of the study, indicating the maximum effective dose of *X. sagittifolium*. Levels of inclusion beyond this will not produce further significant effect in the blood glucose level. This was comparable to the antihyperglycemic effect of glibenclamide, a known antidiabetic agent, as shown in Table 3. It can be inferred from this study that the blood glucose level reduced to about the pre-induction levels by the fourteenth day, and this significant reduction can be linked to the level of inclusion of *X. sagittifolium* corm. No previous study reported the anti-hyperglycemic properties of this plant corm to compare our findings with. However, some other plants in this environment have been shown to have antihyperglycemic effects which may be comparable with *X. sagittifolium*. In a previous study, the effect of kolaviron (200 mg/kg) a compound isolated from *Garcinia kola* was investigated in alloxan-induced diabetic male rats and compared to an anti-diabetic drug; metformin hydrochloride (MET) (30 mg/kg). The results showed that KV and MET significantly ( $p < 0.05$ ) decreased the fasting blood glucose of the diabetic rats. Also, treatment with KV restored the relative weights of testes, activities of antioxidant enzymes, sperm and hormonal indices of the diabetic animals. The antioxidant parameters assessed were reduced glutathione, catalase, superoxide dismutase, glutathione-S-transferase and glutathione peroxidase (Adaramoye and Lawal, 2014).

Another study by Herbert et al. (2011) reported the hypoglycemic potential of the aqueous leaf extract of *Phyllanthus amarus* (260 mg/kg) in alloxan-induced Type 1 diabetes rat model. The blood glucose level was significantly ( $p < 0.05$ ) and dose-dependently reduced by 112, 61 and 31% at 24 hours, 7 days, and 14 days post-administration, respectively (Herbert et al., 2011).

A report on total phenolics, flavonoid content and *in-vitro* antioxidant activity of methanol extract of *X. sagittifolium* corm showed that the corm had 0.32 g/100 g total phenolics, 0.26 g/100 g flavonoid and remarkably higher antioxidant activity in the 1, 1-diphenyl-2picrylhydrazyl (DPPH;  $78.22 \pm 0.56\%$ ), hydroxyl radical ( $69.11 \pm 0.21\%$ ), superoxide radical ( $83.27 \pm 0.08\%$ ) scavenging

and ABTS radical cations ( $76.11 \pm 0.07\%$ ) assays. The activity of these reactive oxygen species (superoxide, hydrogen peroxide, free radicals) has been reported in the mechanism of induction of diabetes by alloxan (Lenzen, 2008; Rohilla and Ali, 2012). These mechanisms has also been reported in human development of diabetes and its complication (Styskal et al., 2012; Tiwari et al., 2013). Hence, availability of food items with high anti-oxidant activity against these reactive species is to be promoted. The Phenolic and flavonoid compounds have generally attracted much attention as potent antioxidant agents, and *X. sagittifolium* corm is reported to have a high content of these phytochemicals (Nishanthini and Mohan, 2012). The study by Arruda et al. (2004) also reported that *X. sagittifolium* leaf and the leaf extract showed high antioxidant properties in vitamin D deficient rats. The aerial part of *X. violaceum*, a close relative of *X. sagittifolium* was also reported to have antihyperglycemic activity (Faisal et al., 2014). Alloxan induces diabetes through oxidative stress, the *X. sagittifolium* corm has been reported to have high antioxidant activity, in this study, the corm was able to produce antihyperglycemic effect on the BGL in alloxan-induced diabetic rats, thus, reversing the effect of oxidative stress.

## Conclusion

*X. sagittifolium* corm had a profound effect on reducing the post-prandial blood glucose level of alloxan-induced diabetic rats at various levels of its inclusion in rats' diets. Rats fed with 75% *X. sagittifolium* showed the best control of the blood glucose level in the rats. The blood glucose control ability of *X. sagittifolium* was comparable to the antihyperglycemic effect of glibenclamide, a known antidiabetic agent. Blood glucose level reduced to about the pre-induction levels by the fourteenth day, and this significant reduction can be linked to the level of inclusion of *X. sagittifolium* corm, thereby confirming its antihyperglycemic effect. Based on the findings of this

study, there is a need to conduct further trials and randomized controlled trials on *X. sagittifolium* corm to fully establish its beneficial effect in enhancing smooth glycemic control when used as a replacement diet to other high-calorie diets in diabetic patients. Also, the glycemic index of *X. sagittifolium* corm would need to be determined as well as further studies to assess the response of diabetic patients to *X. sagittifolium* diet and acceptability of the diets by the patients.

## Conflict of Interests

The authors have not declared any conflict of interests.

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