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Short Communication

Effects of the Aqueous Extract of *Zingiber officinale* Rhizomes and a Combination of *Vernonia amygdalina* and *Ocimum gratissimum* leaves on the Fasting Blood Glucose and Lipid Profile Levels of Alloxan-Induced Diabetic Rats

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ABSTRACT

Vernonia amygdalina, Ocimum gratissimum, and Zingiber officinale are used ethnomedicinally to treat diabetes mellitus (DM) and hyperlipidaemia. However, there is no documented scientific justification. Thus, we evaluated the antidiabetic potentials of the aqueous extract of all 3 plants as well as their effect(s) on the lipid profile of diabetic rats. Alloxan-induced diabetic rats were treated with different doses of the aqueous extract of *Zingiber officinale(ZO)* and a combination of *Vernonia amygdalina(VA)* and *Ocimum gratissimum (OG),* and their fasting blood sugar (FBS) levels were compared with FBS levels of untreated diabetic rats and glibenclamide-treated rats. Normal control rats were given distilled water orally. Drugs and extracts were given daily (orally) for 14 days. FBS were monitored at various intervals over the 14 days. Lipid profile was assessed at the completion of the study. The aqueous extract of *ZO* significantly ($p<0.05$) reduced FSB levels in diabetic rats and showed a comparable effect to glibenclamide. The extract also significantly reduced total cholesterol and increased HDL levels ($p<0.05$). The combined use of *VA* and *OG* leaf extracts demonstrated significant ($p<0.05$) activity compared to the untreated diabetic rats. Additionally, extracts combination reduced significantly ($p<0.05$) the total cholesterol and increased the HDL levels at doses used in comparison with the untreated diabetic rats. In conclusion, our study suggests that combining *Vernonia amygdalina* and *Ocimum gratissimum* as done in folk medicine to manage DM could be beneficial. In addition, the aqueous extract of *Zingiber officinale* possesses promising antihyperglycaemic and lipid profile enhancing properties.

Keywords: Lipid profile, Fasting blood glucose, Scent leaf, Bitter leaf, Ginger rhizome.

Introduction

Diabetes mellitus (DM), is a metabolic illness often associated with elevated blood glucose due to total absence or insufficient insulin secretion from the pancreases with or without coexisting decline of insulin functioning. DM continues to remain a prominent source of death globally[1]. There is a need to identify newer and safer treatment regimens for its management, as current drugs available are marred by adverse effects, notably hypoglycemia. One of such new and safe alternatives to oral hypoglycemic agents is ethnomedcine.[2] Plants have been a source of healing for centuries, with their roots, leaves, flowers, and even bark used to manage a wide range of illnesses.[3] This traditional practice, known as herbal medicine or botanical medicine, is distinct from conventional medicine.[3] In recent years, herbal medicine has gained renewed interest as scientific research sheds light on its potential benefits.

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Advancements in quality control and analysis, alongside clinical trials, help to establish the effectiveness of several herbal remedies in preventing and treating various diseases. Interestingly, many modern pharmaceuticals have their origins in plants. Familiar drugs like aspirin, digitalis, and quinine were all once used as herbal remedies.[2] This highlights the long history and potential of plants in healthcare. Examples of such plants are *VA* (Bitter leaf), *OG* (Scent leaf), and *ZO* (Ginger). *Zingiber officinale* (*ZO*) is a flowering plant in the Zingiberaceae family renowned for its pungent, flavorful rhizome (underground stem). *ZO* boasts a long history of use in various cultures worldwide. Important for both culinary and medicinal purposes, this versatile plant transcends its role as a common spice and holds potential health benefits, making it a popular choice in alternative and complementary medicine. The use of *ZO* in traditional medicine practices around the world cannot be over emphasized. For centuries, it has been employed to treat various ailments, including having a positive impact on blood sugar regulation, potentially benefiting individuals with diabetes and lowering cholesterol levels.[3] The rhizomes of *ZO* are shown in Figure 1. On the other hand, *Vernonia amygdalina* (*VA*) generally identified as bitter leaf plant, belonging to the Asteraceae family is usually used in traditional medicine across Africa. Ethnomedicinal uses of *VA* leaves include its potential as an antimalarial, antidiabetic, anti-inflammatory, and antimicrobial agent.[4] Also, *Ocimum gratissimum* (*OG*), known as African basil or clove basil and locally as scent leaf in Nigeria, is another plant with extensive ethnomedicinal use.[5] It is of the Lamiaceae family, native to tropical regions, and is widely sought after in trado-medicine for its aromatic and therapeutic properties. In traditional medicine, *OG* is employed for its antimicrobial, anti-inflammatory, analgesic, and antidiabetic effects.[5]. However, until now, the therapeutic activity of the combined crude leaf extracts of *VA* and *OG* has not been scientifically

demonstrated, more so that both plants are combined traditionally to treat DM. In view of this, our aim in this study was to certify the use of these plants in folkloric and possibly establish a synergistic effect between *VA* and *OG* in the treatment of DM, as previous studies have established the positive effects of *VA* and *OG* administered separately in the treatment of DM. [6,7]

Materials and Methods

Collection, Identification, and extraction of Plant Material

In January 2024, mature rhizomes of *ZO* were collected from Isihor Community, while mature leaves of VA and *OG* were obtained from Iguosa Community, (GPS Cordinates of 5º 451 to 6º 151 E, 5º 151 to 6º 451 N) both in Ovia North East Local Government Area, Edo State, Nigeria. Voucher specimens of the plant samples were archived at the Department of Pharmacognosy, University of Benin. Additionally, all specimens were taken to the Herbarium unit, Department of Plant Biology and Biotechnology, Faculty of Life Sciences, University of Benin where they were identified by a seasoned plant taxonomist; Prof Henry Akinnibosun Adewale (FLS, MRSB; with voucher specimen number of UBH-Z384 for *ZO)*. The *ZO* rhizomes, leaves of *VA and OG* were air-dried for several days, pulverized into a fine powder, and 500 g of the ZO rhizome powder, 420 g of *VA,* and 380 g of *OG* of the powdered samples were separately macerated in 2 litres of distilled water for 72 hours. Each extract (ZO rhizome extract {ZORE, VA leaf extract {VALE} and OG leaf extract {OGLE}) was strained with a filter cloth, and the filtrate concentrated in an oven at a temperature of 40ºC. The percentage yield of the extract was calculated, and extracts were reconstituted with distilled water before administration.

Figure 1: Rhizomes of *Zingiber officinale*

Drugs and Chemicals

All the drugs and chemicals used in this study were of analytical grade and included the following: distilled water, alloxan (minimum assay 98.5%, Qualikens Lab reagent), glibenclamide (Daonil® Sanofi-aventis, France), normal saline (Bioflex Pharma LTD, India), and glucose (Bioflex Pharma LTD, India),).

Animals

Adult albino rats (either sex) weighing between 140 and 250 g were sourced from the animal facility at the Department of Anatomy, University of Benin, Nigeria. These animals were then conveyed to the animal house of the Department of Pharmacology and Toxicology, University of Benin and allowed 14 days to acclimatize under standard environmental conditions, with access to standard grower's mash and water as required. All animal experiments were done in accordance with the National Institutes of Health guide for care and use of laboratory animals (Pub No.85-23, revised 1985). Ethical approval was sourced from the Faculty of Pharmacy Ethics committee, University of Benin, with ethical approval number: EC/FP/024/11.

Experimental protocol

Induction of diabetes

DM was induced in the rats by single intraperitoneal injection of 150 mg/kg alloxan monohydrate following an overnight fasting period.[8] DM was confirmed three days after, and alloxan-treated rats with a fasting blood sugar (FBS) ≥ 200 mg/dl (11.1 mmol/L) were recruited as diabetic and designated as alloxan –induced diabetic rats (AIDR).[9] Monitoring of the blood sugar level was done using blood samples obtained from tail vein punctures and analyzed with a glucometer (Accucheck, Glaxosmithline, UK). Blood glucose levels exceeding 200 mg/dl were considered for the study.[10]

Experimental protocol

Aqueous *ZORE* was administered alone, while *VALE and OGLE* were administered together based on the traditional way these plants are used in folkloric medicine.[6,7]

Doses used were picked from preliminary studies, and acute toxicity had been previously carried out on all plants[11]).

A total of thirty-five albino rats were distributed into seven groups of five rats each. The animal grouping was as follows:

Group 1: normal control rats were given distilled water (0.2 ml/kgBW) daily.

Group 2: untreated AIDR (diabetic control) given distilled water (0.2 ml/kgBW) daily.

Group 3: AIDR administered glibenclamide (5 mg/kgBW) daily.

Group 4: AIDR administered 150 mg/kgBW of ZORE.

Group 5: AIDR administered 300 mg/kgBW of ZORE.

Group 6: AIDR administered 100 mg/kgBW of a combination of *VALE* and *OGLE*

Group 7: AIDR administered 200 mg/kgBW of a combination of *VALE* and *OGLE*

Different doses of the extracts, drug, and distilled water were administered once to the rats on a daily basis for 14 days orally.

Determination of extract yield

The percentage yield of the aqueous extract from all plants were computed by weighing the pulverized leaves and rhizome separately prior to extraction and the resulting concentrated extract after extraction. The yield was determined using the formula (equation 1):

Percentage yields for *VALE* and *OGLE* leaves were calculated separately using the formula:

$$\frac{\text{Weight of extract from leaves}}{\text{Weight of powdered leaves}}$$

While that of *ZORE* was calculated as follows (equation 2):

$$\frac{\text{Weight of extract from rhizomes}}{\text{Weight of powdered rhizomes}}$$

Measurement of Fasting blood glucose (FBG) levels

The FBG of alloxan- induced diabetic rats (AIDR) was checked using a glucometer by collecting blood from the tail vein. Blood glucose estimation was done on day 0 at 2nd, 6th, and 24th hour intervals and thereafter on the 7th and 14th day following drug and extracts administration1.[6] The results obtained were expressed as mg/dl.

Blood sample collection

On the day of euthanasia (day 14), food and water were withdrawn from the animals. They were then euthanized via chloroform anesthesia, and blood samples (2 ml) were collected via the abdominal aorta. The blood was placed in lithium heparinized tubes to prevent clotting and used for lipid profile analysis. [6]

Analysis of effects on the Lipids of AIDR

Blood samples were collected using 2 ml syringes from the abdominal aorta of the rats were collected in lithium heparinized bottles to avoid clotting. The samples were centrifuged at 3,000 g for 300 seconds and plasma obtained was thereafter used for the determination of triglycerides (TGL), total cholesterol (CROL), High density lipoproteins (HL) and Low density lipoproteins (LL).

Determination of TGL Concentration

The TGL concentration was determined using the Randox TGL kit GPO-PAP method. TGL levels were estimated following enzymatic hydrolysis with lipases. [12].

Calculation of TGL concentration

This was computed using;

Triglyceride concentration= Absorbance of sample/Absorbance of standard x 200 mg/dl

Determination of CROL
CROL concentration was evaluated using the Randox CROL kit and the enzymatic endpoint method. This was done following specimen saponification as described by Richmond (1973)[12] who provided the first step towards the enzymatic procedure. Although the full enzymatic procedure was first published in 1974 [13].

Calculation of CROL concentration:
This was calculated by using;
Absorbance of sample/ absorbance of standard x 200 mg/dl

Determination of HL
HL concentration was determined using the Randox HL Cholesterol kit[14].

Calculation of HDL-cholesterol concentration
This was calculated using;
HL concentration in the supernatant = Absorbance of sample/ Absorbance of standard x Concentration of standard
LL cholesterol in mg/dl
LL Cholesterol = Total CROL - TGL/5 + HL. [14]

Statistical analysis
All results obtained are expressed as mean ± standard error of mean (SEM). While statistical significance difference between the groups was determined by a two-way mixed analysis of variance (ANOVA) conducted on GraphPad Prism® (version 9.5.1) with Tukey post hoc. The significance level was set at $p< 0.05$.

Results and Discussion

The percentage yield of extracts
The extraction of each plant was done once and % yield calculated from the extract obtained relative to the powdered plant material. This is presented in Table 1.

The effect of treatments on fasting blood glucose of AIDR
The results are depicted in Table 2. There was no significant difference in the fasting blood glucose levels on the 2nd and 6th hours on the first day after treatment between the *ZORE* treated groups and the untreated AIDR group. This hourly interval check within the same day following treatment is important, especially in situations where a fast onset of reduction is needed, such as in hyperglycemic crisis, where waiting 24 hours to ascertain decline in levels of fasting blood glucose may prove detrimental to the patient.
However, in AIDR administered glibenclamide a substantial reduction in blood glucose levels ($p<0.05$) was noted compared to untreated AIDR from the 2nd hour on the first day following treatment up to the 14th day. AIDR treated with 150 and 300 mg/kg of aqueous ZORE showed a notable significant decrease in blood glucose concentration ($p<0.05$) compared to untreated diabetic rats from the 24th hour (day 1) up to the 14th day. This reduction from the 24th hour improved on days 7 and 14, with the most significant decrease observed on the 7th day by the 150 mg/kg *ZORE* and on the 14th day by the 300 mg/kg *ZORE*. The effect of *ZORE* is comparable to that of glibenclamide, from the 24th hour to the 14th day. *ZORE* exhibited a similar but less efficacious effect on AIDR compared to glibenclamide. The results for the combination of *VALE* and *OGLE* are also presented in Table 2. In AIDR treated with 100 and 200 mg/kg of the combination of VALE and OGLE, a significant reduction in the fasting blood glucose level ($p<0.05$) compared to the untreated AIDR was only observed from the 7th day up to the 14th day. This reduction was most significant on the 7th day. Therefore, it appears that an initial delayed effect was noticed.

Table 1: Percentage yield of extracts

Extract	Percentage yield (%)
ZORE	6.60
VALE	5.75
OGLE	4.47

Table 2: Effect of the aqueous extract of *Zingiber officinale* and a combination of *Vernonia amygdalina* and *Ocimum gratissimum* on the fasting blood glucose of AIDR

	Fasting blood glucose in mg/dl					
Groups (mg/kg)	0hr	2hr	6hr	24hr	7th day	14th day
NC	88.2±0.3	88.2±0.3[a]	86.1±0.3[a]	85.2±0.3[a]	86.2±0.51[a]	89.1±0.11[a]
DC	85.2±0.5	380.5±0.1	402.5±0.3	600.9±0.3	601.5±0.2	598.8±0.21
DZ (150)	77.7±0.6	320.5±0.2	450.6±0.2	210.5±0.3[a]	101.5±0.3[a]	150.9±0.22[a]
DZ (300)	80.5±0.2	280.5±0.3[a]	400.5±0.3	410.5±0.4[a]	280.5±0.4[a]	110.5±0.11[a]
DBS (100)	85.2±0.35	401.5±0.5	405.2±0.3	403.4±0.3[a]	190.5±0.6[a]	201.5±0.31[a]
DBS (200)	79.0±0.31	380.5±0.1	410.5±0.2	405.5±0.4[a]	89.5±0.8[a]	150.2±0.3[a]
DG (5)	78.5±0.22	150.5±0.3[a]	89.2±0.5[a]	330.5±0.3[b]	80.5±0.2[a]	85.5±0.51[a]

Values are mean blood glucose levels ±SEM (n=5 per group). [a]$p<0.05$, significantly different from the untreated diabetic rats. NC: Normal control, DC: Untreated AIDR, DZ: AIDR treated with ZO, DBS: AIDR treated with a combination of VALE and OGLE. DG: AIDR treated with Glibenclamide.

The 200 mg/kg dose of *VALE* and *OGLE* combination produced the most significant ($p<0.0001$) decline in the fasting blood glucose level on the 7th day, and by the 14th day significant reduction was still evident. This effect of both *VALE* and *OGLE* compares well with glibenclamide, where a significant reduction ($p<0.05$ and $p<0.0001$) in the fasting blood glucose level of the AIDR was noticed throughout the period of the study.

Effect on TGL, CROL, HL and LL of AIDR
The effect of the extracts on TGL, CROL, HL and LL are shown in Table 3. When AIDR were given *ZORE* (150 and 300 mg/kg doses), their CROL levels were considerably ($p<0.05$) lower compared to untreated AIDR. Meanwhile, the CROL level was not significantly different in normal and AIDR treated with glibenclamide. A comparable pattern was noticed in the HL, where the initial level was high in normal rats. However, treatment with alloxan decreased the HL values, as observed in the untreated AIDR. Interestingly, these values were significantly increased ($p<0.05$) upon treatment with *ZORE* and this effect also compares favorably with the reference drug-glibenclamide, yielding a better outcome than the standard medication. The extract had no significant effect on the LL ($p<0.05$) in the AIDR (Table 3), while TGL levels in the AIDR treated with the various doses of ZORE (150 and 300 mg/kg) decreased significantly compared with the untreated AIDR.
Table 3 also shows the effect on TGL, CROL, HL and LL of AIDR treated with a combination of *VALE* and *OGLE*, where a significant ($p<0.05$) decline in the CROL of AIDR in comparison to the untreated AIDR was observed. Similarly, HL level was originally high in normal rats; however, induction of diabetes reduced the HL values significantly ($p<0.05$) as seen in the untreated AIDR. These values were increased significantly ($p<0.05$) following treatment with a combination of both *VALE* and *OGLE*.
The LL of AIDR was not reduced ($p<0.05$) when treated with both doses of the extract combination in comparison with the untreated AIDR (Table 3). Similarly, there was no significant difference in the TGL level of the AIDR treated with a combination of *VALE* and *OGLE*

in comparison with the untreated AIDR rats. Despite this, the positive impact of increased HL and lowered CROL levels is an additional advantage especially in the obese diabetic patients.

Table 3: Effects of the aqueous extract of *Zingiber officinale* and a combination of *Vernonia amygdalina* and *Ocimum gratissimum* on the lipid profile of AIDR

Treatment (mg/kg)	CROL (mmol/l)	HL (mmol/l)	TGL (mmol/l)	LL (mmol/l)
NC	41.0 ±4.4	72.8±17.2	40.0±8.1	4.8±4.1
DC	51.3±6.5	40.8±7.4[b]	30.1±9.6	13.0±4.5
DZ (150)	44.0±8.7[a]	50.4±9.6[a]	22.1±2.5	15.2±4.5
DZ (300)	43.2±4.2[a]	57.0±5.3[a]	20.2±3.4	12.7±5.4
DBS (100)	34.0±4.6[a]	54.4±5.6[a]	32.1±5.9	22.2±8.3
DBS (200)	31.7±7.3[a]	42.1±8.2[a]	29.7±5.4	21.7±8.1
DG (5)	38.8±3.7[a]	47.1±2.8[a]	15.3±4.7[a]	11.0±5.7[b]

Values are mean levels ± SEM (n=5, per group), [a]p<0.05 significantly different from the untreated diabetic rats and [b]P<0.05 significantly different from the control rats. CROL: Total Cholesterol; HL: High Density Lipoprotein; TGL: Triglycerides; LL: Low Density Lipoprotein. NC: Normal control, DC: Untreated AIDR, DZ: AIDR treated with *ZO*, DBS: AIDR treated with a combination of VALE and OGLE. DG: AIDR treated with Glibenclamide.

The results from our study investigating the effect of *ZORE* on fasting blood glucose levels in rats suggest a potential effect on DM management in rats. The group that received the lower dose of the extract, however, showed better effect. Previous studies have reported that *ZORE* administration led to reduced blood glucose levels in rats with DM [11,15] which aligns with the observations from our study.

The probable mechanism is linked to the insulinomimetic action of natural plant extracts further clarified by Zhao *et al.,*[16] where it was discovered that these plant extracts enhance insulin release Li *et al.,*[17] confirming *ZORE*'s potential in modulating glucose-catabolizing and gluconeogenic enzymes involved in blood glucose regulation in another investigation that looked at these pathways. *ZORE*'s positive effect on DM management may also be by decreasing the rate at which carbohydrates is absorbed into portal hepatic circulation, thereby boosting glucose distribution and uptake, thus encouraging glycogen storage, and modifying insulin secretion. According to DeFronzo *et al*[18], decreasing the absorption rate of carbohydrates is similar to the mechanism of action of alpha-glucosidase inhibitors like acarbose and miglitol.

The decrease in fasting blood glucose levels in AIDR treated with the leaf extracts of *VALE* and *OGLE* show that these plants have activity against DM. Both extracts revealed varying levels of anti-hyperglycemic action at the different dose levels, similar to that used by Nammi *et al.*, [19] who revealed a dose related blood glucose reducing effect with fresh juices of leaves of *Cantharanthus roseus* Linn in both normal and alloxan-induced diabetic rabbits. The extract combination (*VALE* and *OGLE*) was found to lower fasting blood glucose levels, although not as effective as glibenclamide. Both extracts may exert their effect by acting as an insulinomimetic just like ZORE as previously explained which probably involves reduction in hepatic gluconeogenesis and increase skeletal muscle glucose uptake.[20] Additionally, the extracts combination may lower glucose levels in rats by enhancing glucose catabolizing enzymes and inhibiting potential gluconeogenic enzymes, a mode of action observed by Singh *et al*., [21] in *Cantharanthus roseus* in streptozotocin-induced rats. Therefore, based on the results obtained, both *VALE* and *OGLE* lowered the blood glucose level in diabetic rats in a dose-dependent manner.

Alloxan and dialuric acid, the byproduct of their reaction, create superoxide radicals, which initiate a redox cycle. These radicals dismutate into hydrogen peroxide while concurrently creating a significant increase in the concentration of calcium in the cytosol, which leads to a tremendous death of beta cells and decreased insulin synthesis and release.[10] Compared to normal rats given distilled water, the fasting blood glucose level of AIDR was considerably higher (p<0.0001) in the untreated group.

A sulfonylurea was used as standard in this study exemplified by glibenclamide, which are a class of oral hypoglycemic agents commonly used in the treatment of type 2 diabetes mellitus. They act by stimulating insulin secretion from pancreatic beta cells in patients with remaining beta cell function.[16] This mechanism indicates their effectiveness in mild alloxan-induced diabetes, while they are less effective in severe alloxan-induced diabetes.[22, 23] In the present study, AIDR treated with the *ZORE* singly and a combination of *VALE* and *OGLE* showed a normal fasting blood glucose levels compared to untreated AIDR. This suggests that these extracts may have stimulated the remaining intact beta cells to synthesize and release insulin. Additionally, these extracts may have lowered the fasting blood glucose levels by enhancing tissue glucose utilization. Hence, all extracts may be acting both an insulin sensitizer and secretagogue. Lipids such as triglycerides, phospholipids, and others; while they play many vital roles in the body, abnormal concentration can lead to cardiovascular disease. Insulin deficiency can result in metabolic modifications in animals, including elevated blood glucose levels and elevated cholesterol concentration.[23]

A major complication of diabetes mellitus is hyperlipidemia, which is a syndrome characterized by raised levels of CROL, TGL, and variations in lipoprotein composition of the blood. In severe cases of diabetic mellitus, the kidneys often lose the capability to eliminate waste products from the blood.[25] Research suggests that HL play more essential role than other lipoproteins in preventing atherosclerosis.[26] On the lipid profile, a decline in the levels of CROL, TGL, and LL in the groups receiving *ZORE* (150 and 300 mg/kg) compared to the untreated AIDR group was observed. These findings align with previous studies suggesting *ZORE*'s potential in improving lipids in diabetic conditions.[27, 28] The decrease in LL, often referred to as "bad cholesterol," is particularly significant. LL plays a major role in atherogenesis, the formation of plaque in arteries. Lower LL levels can potentially reduce the risk of cardiovascular complications in diabetic patients. The decrease in TGL levels observed with *ZORE* is another positive finding as it relates to diabetic management since high TGL levels are a possible risk factor for circulatory disease and pancreatitis.[27]

The exact mechanisms by which *ZORE* extract exerts these beneficial effects are not fully understood, but several possibilities exist. *ZORE* may increase the excretion of bile acids, which are cholesterol breakdown products eliminated through feces. This can lead to lower cholesterol levels in the body. *ZORE* may stimulate the breakdown and utilization of fats for energy, reducing their circulation in the bloodstream. The extract also possesses antioxidant potentials that can help ameliorate oxidative stress, a major contributor to diabetic complications. Reduced oxidative stress might improve overall cardiovascular health and lipid metabolism.[27]

The outcomes of this research are consistent with previously done research on the hypolipidemic effects of *ZORE* in diabetic models. For instance, a study by Eidi *et al*.,[27] found that *ZORE* reduced CROL, LL, and TGL levels in AIDR. While another study reported similar cholesterol-lowering effects of *ZORE* in diabetic rats, with a dose-dependent reduction in CROL levels.[28]

This study adds to the growing body of evidence suggesting that *ZORE* has potential benefits for improving the lipid profile in diabetic rats. *ZORE* appears to reduce CROL, LL, and TGL levels, potentially reducing the risk of vascular complications in diabetic patients. More research is warranted to explore the underlying mechanisms and translate these findings into effective therapeutic strategies for humans.

The results of the lipids in this study on animals given a combination of *VALE* and *OGLE* showed that both combinations reduced CROL and increased the HL, which are beneficial effects, especially in diabetes. AIDR administered 100 and 200 mg/kg of both extracts had a significant reduction (p<0.05) in CROL but no significant difference in

TGL concentrations compared to the controls and untreated AIDR. The HL levels in AIDR were significantly ($p<0.05$) increased by *VALE* and *OGLE*. This suggests that the extract may confer some cardiovascular protective effects by enhancing the level of HL, termed the good cholesterol, and reducing the CROL. The LL levels were observed to have been increased in rats treated with both *VALE* and *OGLE*; the reason for this is unclear. However, the reduction of CROL and subsequent increase in HL level negates the impact of this increase noticed in the LL. There are two main types of fat in the blood, TGL and CROL. Many laboratories measure the CROL, and commonly, the lower the better. This lowering was observed on treatment with both *VALE* and *OGLE*. Low CROL levels reduce diabetic complications; hence, the combination used in this study can be said to prevent diabetic complications.

Conclusion

The outcomes of this investigation suggest that combined use of the aqueous *VALE* and *OGLE* showed positive effects in DM management with a positive impact on the Lipids of AIDR. Similar positive impact on FBS and Lipids were observed in AIDR treated with only *ZORE*. This positive impact on CROL, LL, HL and TGL is an additional benefit for the obese diabetics. Additional investigation is encouraged to ascertain the exact mechanisms underlying these interesting and positive impacts on DM management and lipid-modulating effects of these plant extracts.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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