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COMPARATIVE INVESTIGATION OF THE ALPHA AMYLASE INHIBITORY AND ANTIOXIDANT POTENTIAL OF THE LEAF EXTRACTS OF *Vernonia amygdalina* AND *Dacryodes edulis*

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ABSTRACT
The antioxidant and alpha amylase inhibitory potential of plants have been linked to the abundance of secondary metabolites in them. Vernonia amygdalina and Dcryodes edulis plants are rich in antidiabetic and antioxidant activities and other known medicinal values. The overall aim of the study was to ascertain the antioxidant properties and in vitro antidiabetic efficacies of the aqueous leaf extracts of Dacryodes edulis and Vernonia amygdalina. Total phenol and flavonoid contents, 1,1-diphenyl-2-picrylhydrazyl (DPPH), total reducing power, ferric reducing power, and total antioxidant capacity antioxidant assays were performed on the aqueous leaf extract of V. amygdalina and D. edulis to determine the antioxidant capacity of the leaves. The in vitro alpha amylase inhibitory activity was conducted using DNSA method to explore the antidiabetic potential of the leaf extracts. The result revealed high concentrations of total phenol, total flavonoid content, ferric reducing antioxidant potential (FRAP), 1,1-diphenyl-2-picrylhydrazyl (DPPH) and total antioxidant capacity (TAC) in both extracts with V. amygdalina demonstrating the highest potential. The IC_{50} value for DPPH was shown to be 5.77 (V. amygdalina) and 16.46 (D. edulis). The study further revealed high alpha amylase inhibitory activity of the leaf extracts with IC_{50} of 16.02 (V. amygdalina) and 18.12 (D. edulis). Based on the findings of this study, D. edulis and V. amygdalina may be useful in the treatment of diabetes mellitus and other oxidative stress-related diseases.

KEYWORDS: *Vernonia amygdalina, Dacryodes edulis, Antioxidants, DPPH, Total antioxidant capacity, Alpha amylase*

INTRODUCTION

Blood glucose levels that consistently rise are a hallmark of a group of metabolic diseases known as diabetes mellitus. Defects in insulin action, manufacturing, or both can be the cause of this illness. Proteins, fats, and carbs are metabolically processed abnormally when insulin is insufficient and resistant to the tissues it is supposed to reach (Dineshkumar *et al.,* 2018). Diabetes is associated with a number of immediate and long-term health consequences. Diabetic ketoacidosis, malignant hyperthermia-like syndrome with rhabdomyolysis, and hyperosmolar hyperglycemia are examples of acute health issues that represent a high risk of morbidity and

death in the short term (Kazeem *et al.,* 2013). Long-term consequences could include cardiovascular and atherosclerotic issues, neurological disorders, lipid abnormalities, retinopathy, renal failure, non-alcoholic fatty liver disease, and hypertension.

According to data from 2013, there were 382 million diabetics worldwide (International Diabetes Federation, 2017). Comparably, data from 2017 showed that the number had increased to 425 million worldwide (International Diabetes Federation, 2017). According to Mitra *et al*. (2017), there will be a 39 percent increase in this number by 2035. About 16 million Africans had been diagnosed with diabetes as of 2017, with Nigeria accounting for 11% of cases (International Diabetes Federation IDF, 2017). According to projections made by the International Diabetes Federation (IDF) (2017), 41 million people in Africa will have diabetes mellitus by 2045.

By inhibiting digestive enzymes like α-amylase and α-glucosidase from hydrolyzing glucose from carbohydrates, one method of managing diabetes mellitus is by dampening this process (Liu *et al.,* 2016). First in the gut, the α-amylase splits further dietary carbohydrates like starch into simpler units. The α-glucosidase then breaks these down further to produce glucose, which is easily absorbed and enters the bloodstream (Alqahtani *et al.,* 2020). A significant biological target for the therapy of type 2 diabetes is α-amylase inhibition (Ganesan *et al.,* 2020). One medication for diabetes mellitus that functions as α-glucosidase inhibitor is acarbose (Wyne and Bakris, 2007). Combining α-amylase and α-glucosidase may be a viable treatment strategy for diabetes mellitus. However, it has not been observed that any DM medications inhibit α-amylase.

Reactive oxygen species (ROS) have been implicated in the pathophysiology of various disease states, including diabetes mellitus (DM) and long-term development of associated late complications (Agbor *et al.,* 2017; Koudou *et al*., 2018). Oxidative-induced tissue damage is mediated via activation of a number of cellular stress-sensitive pathways, which include nuclear factor-kB (NF- kB), p38 mitogen-activated protein kinase, NH_2- terminal

Jun kinases/stress-activated protein kinases and hexosamines (Koudou *et al*., 2018). Oxidative stress in diabetes mellitus could be through enzymatic or non-enzymatic processes. Oxidation of glucose, lipid peroxidation and non-enzymatic glycation of proteins result in damage to enzymes, cellular machinery and also increased insulin resistance due to oxidative stress (Dineshkumar *et al*., 2018).

The common bitter leaf plant, *Vernonia amygdalina*, often referred to as insulin leaves is a shrub widely grown and consumed in tropical Africa. It has demonstrated significant antidiabetic potential (Akinola *et al*., 2010). Studies have confirmed the hypoglycemic effects of *V. amygdalina* leaves in diabetic rats induced by streptozotocin and alloxan (Okugbo and Killian, 2022; Osinubi, 2010; Akah and Okafor, 2017). When compared to the conventional medication chlorpropamide, *V. amygdalina* effectively reduced blood glucose levels in both normal and diabetic rats (Osinubi, 2010; Tona *et al.,* 2018). Drinking tea made from its leaves has been found to significantly lower blood sugar levels (Halim *et al.,* 2020). Beyond diabetes, the plant is reputed to treat various other illnesses due

to its rich bioactive compounds, such as flavonoids, saponins, and alkaloids. Key constituents like dicaffeoyl-quinic acid and its isomers, potent polyphenols, may be responsible for its antidiabetic effects (Okugbo and Killian, 2022). Additionally, *V. amygdalina* exhibits strong antioxidant activity, as demonstrated by assays like DPPH and ABTS. This suggests its potential to mitigate oxidative stress and related damage, which are critical factors in diabetic conditions (Egharevba *et al.,* 2019; Ong *et al.,* 2011; Alara *et al*., 2019).

Similarly, *Dacryodes edulis* has shown promising therapeutic properties. Rich in phenolic compounds, it exhibits notable antioxidant activity, which helps neutralize reactive oxygen species. Its antidiabetic potential is evidenced by its ability to modulate glucose uptake and inhibit enzymes like α-amylase and α-glucosidase. The ethanol and aqueous extracts of *D. edulis* have demonstrated significant hypoglycemic effects in in vivo and in vitro models, further validating its use in traditional medicine for diabetes management (Erukainure *et al.,* 2020; Babayemi *et al.,* 2024).

This investigation is aimed at highlighting the medicinal value of *V. amygdalina* and *D. edulis* while emphasizing the need to compliment and integrate ethnobotanical practices with scientific research to develop innovative solutions for managing diabetes and oxidative stress.

MATERIALS AND METHODS

Collection and Preparation of the Leaf Samples

Fresh leaf of *V. amygdalina* and *D. edulis* were collected from the main campus of University of Benin, Benin City, Edo State on April 30th 2019. Before being ground into a powder for aqueous extraction, fresh *V. amygdalina* and *D. edulis* leaves were immediately rinsed with distilled water and allowed to dry in the shade. To ensure the best extraction, the macerated leaves were continuously stirred for a full day. Two layers of muslin cloth were then used to filter the mixture. After that, the clear filtrate was concentrated using rotary evaporation and paced over a water bath at 40°C. The resulting 78g of semi-solid residue was kept in an airtight container and kept cold at -4ºC until it was reconstituted.

Estimation of Antioxidant Capacity

Folin-Ciocalteu method was used to estimate the total phenolic content according to the method described by Patel *et al.* (2010). Colorimetric measurements of the total flavonoid content were made using the methodology outlined by Patel *et al.* (2010), Pallab *et al.* (2013), and Patel *et al.* (2012). The DPPH inhibition potential of the leaf extracts was tested using the methodology outlined by Brand Williams *et al*. (1995). Colorimetric method as described by Jayanthi and Lalitha, (2011) was used to estimate total reducing power. Molybdenum reagent solution was employed in the analysis of total antioxidant capacity.

Determination of the percentage DPPH Inhibition

The radical scavenging activity was calculated as follows;

$$DPPH\% = \frac{(Ao - A1)}{(Ao)} \times 100$$

Alpha Amylase Inhibitory Assay

Alpha amylase inhibitory activity of the plant extracts was done using spectrophotometric method. The test was carried out in triplicate and absorbance was read at 540nm.

$$\%\ inhibition\ = \frac{A\ (control) - A(extract)}{A(control)} \times 100$$

Data Analysis

All analyses were carried out in triplicate and results expressed as Mean ± SEM. Data analysis was done using Excel 2013. One-way analysis of variance (ANOVA) was used for comparison of means. The IC_{50} values were calculated using linear regression graph.

RESULTS

Total Flavonoid and Total Phenolic Contents

Figures 1 and 2 show that *Vernonia amygdalina* contains high concentrations of total flavonoids (120±0.06) and total phenol (228.23±39.53) when compared to *D. edulis* with total phenol (205±28.27) and total flavonoids (80±0.05) ($p < 0.05$).

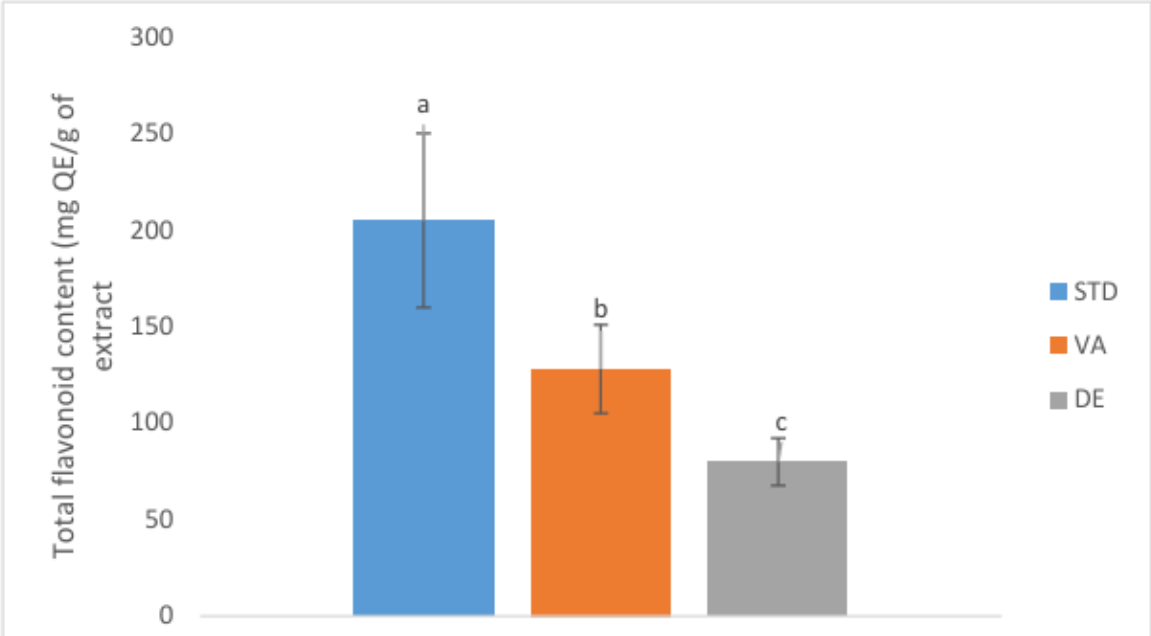

Fig. 1: Total flavonoid content of aqueous leaf extracts of *V. amygdalina* and *D. edulis*. Total flavonoid was expressed as mg Quercetin Equivalent /g extract. Values were expressed as mean ± SEM, n=3/group. Different lower case letters represent significant differences between means. ($P < 0.05$).

Key: STD = Standard, VA = *Vernonia amygdalina,* DE = *Dacryodes edulis*

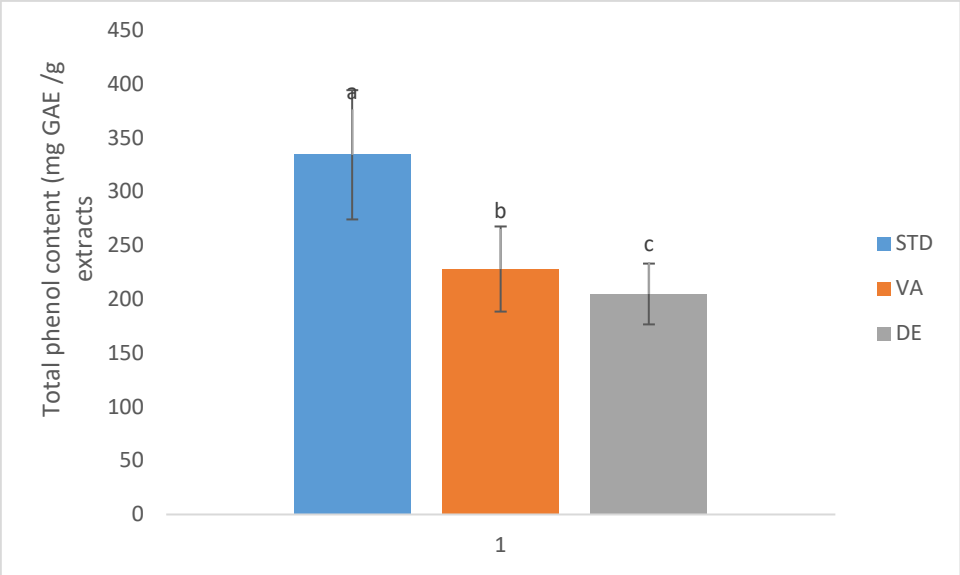

Fig. 2: Total phenolic content of aqueous leaf extracts of *Vernonia amygdalina* and *Dacroyedes edulis.* Total phenolic content is expressed as mg Gallic acid Equivalent /g extract. Values were expressed as mean ± SEM, n=3/group. Different lower case letters represent significant differences between means ($P < 0.05$). STD = Standard, VA = *Vernonia amygdalina, DE* = *Dacryodes edulis.*

Reducing Power, Ferric Reducing Antioxidant Potential (Frap) and DPHH Inhibitory Activity and Total Antioxidant Activity of the Aqueous Leaf Extracts of V. Amygdalina and D. Edulis

Figs. 3, 4, 5 and 6 show that aqueous leaf extract of *V. amygdalina* and *D. edulis.* Possess high reducing power, ferric reducing antioxidant potential, DPPH inhibitory activity and total antioxidant activity of the aqueous extract of *V. amygdalina*

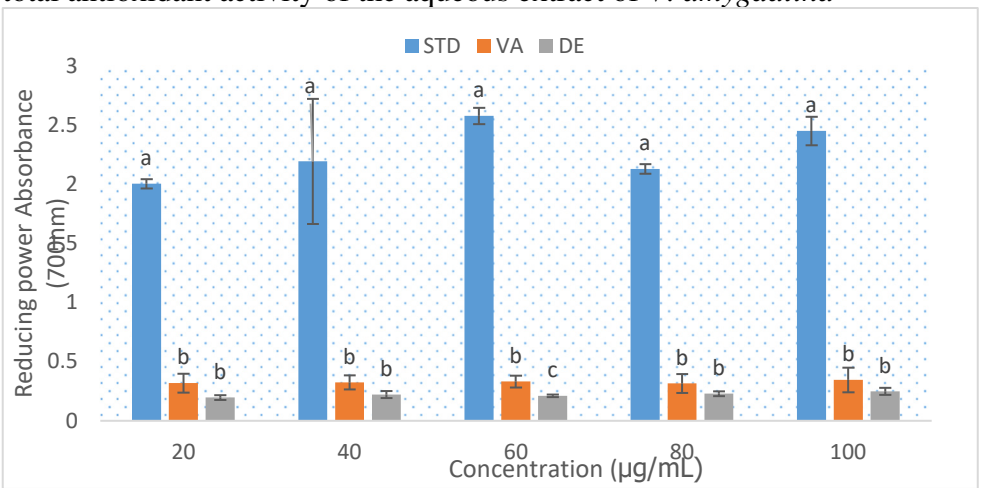

Fig. 3: Reducing power of aqueous extracts of *V. amygdalina* and *Dacryodes edulis* leaf at different concentrations. Values are expressed as mean ± SEM, n=3/group. Different lower case letters represent significant differences between means ($P < 0.05$). Ascorbic acid was used as standard.

Key: STD = Standard, VA = *Vernonia amygdalina,* DE = *Dacryodes edulis*

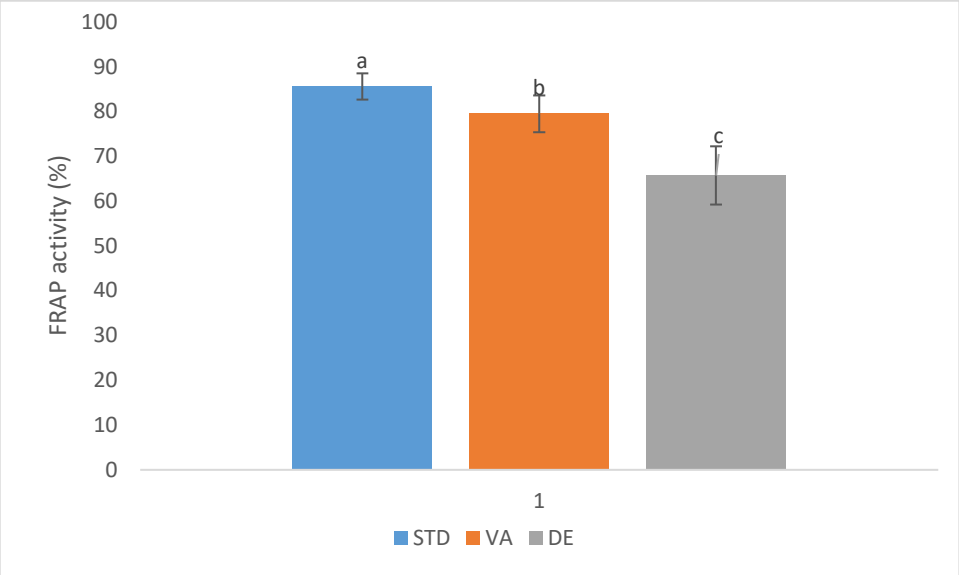

Fig. 4: Ferric reducing antioxidant potential (FRAP) of aqueous extracts of *V. amygdalina* and *D. edulis* leaf at different concentrations. Values are expressed as mean ± SEM, n=3/group. Different lower case letters represent significant differences between means ($p < 0.05$).
Key: STD = Standard, VA = *Vernonia amygdalina,* DE = *Dacryodes edulis*

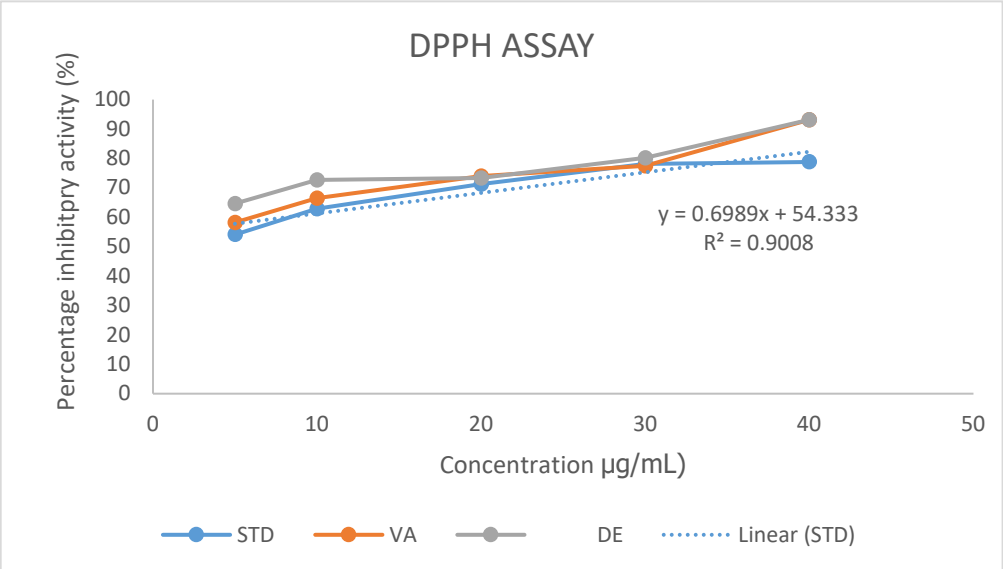

Fig. 5: DPPH inhibitory activity of the aqueous leaf extracts of *V. amygdalina* and *D. edulis.* The result is presented as mean ± SEM. Mean values were considered significantly different ($P < 0.05$). Ascorbic acid was used as standard.
Key: STD = standard, VA = *Vernonia amygdalina,* DE = *Dacryodes edulis*

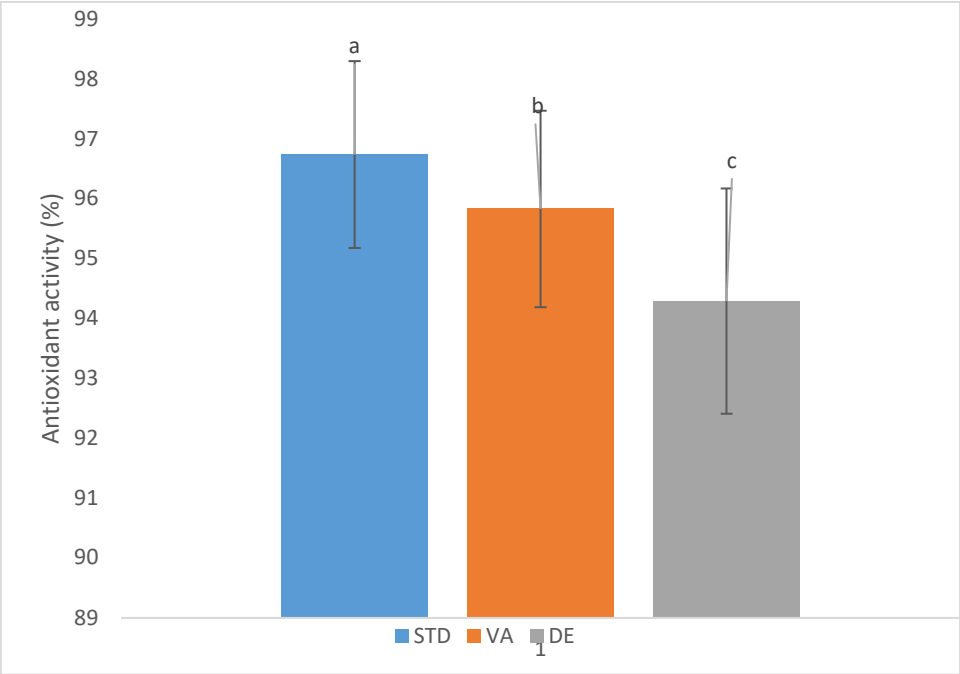

Fig. 4: Total antioxidant capacity (TAC) of aqueous extracts of *Vernonia amygdalina* and *Dacryodes edulis* leaf at different concentration. Values are expressed as mean± SD, n=3/group. Different lower case letters represent significant differences between means ($P < 0.05$).
Key: STD = Standard, VA = *Vernonia amygdalina, DE = Dacryodes edulis*

Figure 7 shows the alpha amylase inhibitory activity of *V. amygdalina*

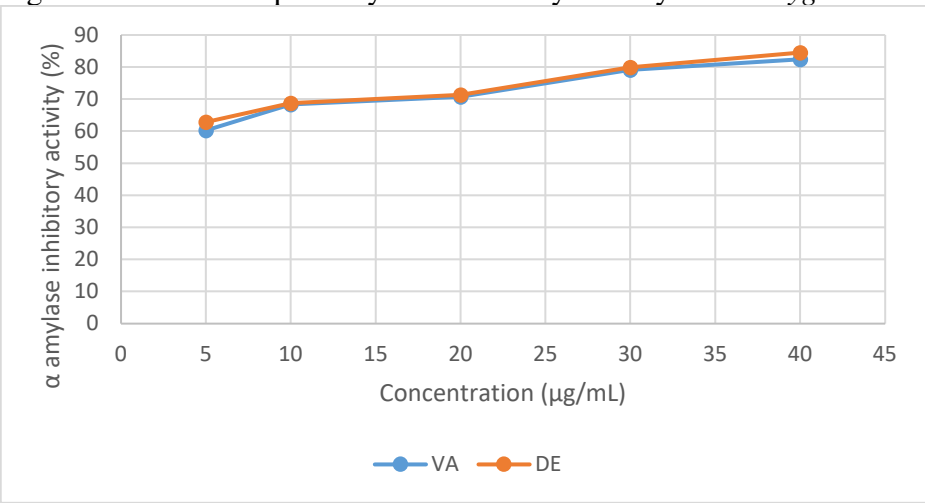

Fig. 7: α amylase inhibitory activity of *Vernonia amygdalina* and *Dacryodes edulis*
The results are presented as mean ± SEM. Mean values were considered significantly different at $p < 0.05$.
Key: VA = *Vernonia amygdalina* and DE = *Dacryodes edulis.*

Table 2: IC_{50} values of *Vernonia amygdalina* and *Dacryodes edulis*

Assay	Sample	
	V. amygdalina	***D. edulis***
DPPH	5.77	16.46
Alpha amylase inhibitory activity	16.02	18.12

DISCUSSION

Oxidative stress is a possible crucial regulator of various pathologies, including type 2 diabetes and neurodegenerative diseases. ROS affects multiple signalling pathways, leading to compromised insulin secretion, insulin resistance, and β-cell dysfunction in diabetes. Antioxidants are vital components of our body that fight disease by reducing oxidative stress or nullifying the excess toxic free radicals produced under various pathological conditions (Kiokias *et al*., 2020). Overconsumption of radicals leads to oxidative stress, which is bad for human health. One of the main classes of free radicals in the human body are reactive oxygen species (ROS), which can damage DNA and cells oxidatively and cause diseases like cancer (Kirtonia *et al.,* 2020). Antioxidants can directly reduce oxidative stress damage by functioning as ROS or free radical scavengers. As a result, it's critical to promote antioxidant activity and regulate inflammation appropriately.

In the present study, as shown in Figures 1-6, the antioxidant properties of the aqueous leaf extracts of V. amygdalina and D. edulis were determined. The study shows significant concentrations of total phenol content, total flavonoid content, total antioxidant activity, DPPH and FRAP. This is in consonance with the studies conducted by Wang *et al*. (2020). Their findings revealed that *V. amygdalina*, leaf extracts have antioxidant, DNA protection and anti-inflammation effects.

Numerous studies have suggested that *V. amygdalina* and *D. edulis* may have some therapeutic uses, such as antibiotic, antioxidant, or anti-cancer agent (Temneanu, *et al.,* 2011; Yao *et al.,* 2016). Research on *Vernonia amygdalina* antioxidant properties have employed both alcoholic and aqueous extracts. Only a small number of studies have compared the two extracts, and the findings of those studies are debatable (Temneanu, *et al.,* 2011). Plants that possess antioxidant and anti-inflammatory properties have a strong correlation with polyphenols and flavonoids. Luteolin has also been shown to inhibit the synthesis of pro-inflammatory cytokines (Lv *et al.,* 2011). The levels of polyphenols and flavonoids are strongly correlated with the antioxidant activity of *Vernonia amygdalin* leaves (Wang *et al.,* 2020). Similarly, flavonoids have been identified as the main bioactive substance in *D. edulis* that is responsible for the antioxidant activity (Yao *et al.,* 2016). Another finding revealed the ability of the methanol extract of *D. edulis* leaves to ameliorate oxidative stress induced in STZ- rats (Ononamadu *et al.,* 2019).

Hyperglycemia and uncontrolled α-amylase activity have been linked (Tiwari and Rao, 2020). Thus, in order to control the post-prandial rise in blood glucose in diabetic patients, inhibiting α amylase constitutes a crucial therapeutic target (Tiwari and Rao, 2020). The alpha amylase inhibitory activity of *V. amygdalina* leaf and *D. edulis* extracts was found to be high in this study. This is

in consonance with the studies conducted by Norainny *et al.* (2022) to investigate and identify the alpha amylase inhibitors in the various extracts of *V. amygdalina*. The study showed that leaf extracts of *V. amygdalina* showed greater potency compared to acarbose. The study further identified the following alpha amylase inhibitors in the leaf extract of *V. amygdalina*; 2Z)-3,7-dimethylocta-2,6-dien-1-yl]-2,4-dihydroxy-6-(2-phenylethyl)benzoid acid, 2-hexylpentanedioic acid , ,4E)-5-[1-hydroxy-2,6-dimethyl-4-oxo-6-({3,4,5-trihydroxy-6-(hydroxymethyl) oxan-2-yl] oxy} methyl) cyclohex-2-en-1-yl]-3-methylpenta-2,4-dienoic acid, ,5-trimethyl-4-(3-{[3,4,5-trihydroxy-6-(hydroxymethyl) oxan-1yl) oxy} butyl), [(6E)-2,10-dihydroxy-2,6,10-trimethyldodeca-6,11-dien-3-yl] oxy} and -6-(hydroxymethyl) oxane-3,4,5-triol cyclohex-2-en-1-one (Norainny *et al.,* 2022). Analyses on Molecular mechanism of the alpha amylase inhibitory activity of the leaf extracts of *V. amygdalina* proved positive against the enzyme alpha amylase (Norainny *et al.,* 2022). The five compounds identified to possess alpha amylase inhibitory activity were docked and they were found to possess varying inhibitory efficacies on the active sites of the beta pancreatic (Norainny *et al.,* 2022).

Using DNSA analytical method, the present result also indicated the high alpha amylase inhibitory activity of the aqueous leaf extract of *D. edulis* as shown in fig. 7. This result is in consonance with the finding so of (Chimaobi *et al*., 2019 who demonstrated the Percentage of inhibition of α-amylase by 800 µg/ml of the tested *D. edulis* extract/fractions and compounds using the same method. The result showed that the aqueous methanol fraction demonstrated the highest inhibitory potential. Previously, Chimaobi *et al*. (2019), proved that *D. edulis* possess strong alpha amylase inhibitory activities. Similarly, in *vitro* studies conducted by Okugbo and Killian, (2022) showed that the aqueous leaf extract of *D. edulis* possess high antihyperglycemic N

CONCLUSION

Based on the findings of this study, *V. amygdalina* and *D. edulis* may be regarded as potent and efficacious in the management of diabetes mellitus and oxidative stress related diseases. The bioactive compounds of the leaf extracts of *V. amygdalina* and *D. edulis* can be characterized and optimized for antidiabetic drug development.

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