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Article

In Vitro Glucose Uptake, α-Amylase, Antioxidant and Cytotoxic Evaluation of Dalbergiella Welwitschii as a Potential Glucose-Lowering Agent for Type 2 Diabetes

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Abstract: Hyperglycemia is a major complication of type 2 diabetes. Medicinal plants could mitigate this complication due to their bioactive phytochemicals. *Dalbergiella welwitschii* is a plant used traditionally to manage hyperglycemia in Nigeria. This study explores the glucose-lowering potential of different parts of *Dalbergiella welwitschii* through *in vitro* glucose uptake and α-amylase inhibitory assays alongside antioxidant and phytochemical screening. The glucose uptake activity was evaluated using yeast cells (*Saccharomyces cerevisiae*) at glucose concentrations of 25, 10 and 5 mM, and extract concentrations of 1000, 500 and 250 µg/mL, respectively. α-Amylase inhibitory activity was determined using the 3,5-dinitosalicyclic acid (DNSA) method. Antioxidant activity was assessed using the DPPH radical scavenging assay and cytotoxicity was evaluated using the brine shrimp lethality assay. Stem extract of *Dalbergiella welwitschii* exhibited percentage glucose uptake of 92.20 ± 0.16, 96.70 ± 0.00, 85.40 ± 0.17 comparable to the standard Glimepiride-metformin-HCl (92.23 ± 0.06, 91.30 ± 0.10, 88.47 ± 0.42) at 10 mM glucose concentration. The leaf, stem and root had moderate α-amylase inhibitory activity (289.8 ± 0.03, 150.6 ± 0.03, 263.1 ± 0.03 µg/mL) compared with acarbose (33.2 ± 0.00 µg/mL). Phytochemical screening revealed the presence of alkaloids, flavonoids and phenols across all plant parts with higher concentrations in the leaves. The stem extract (0.403 µg/mL) exhibited strong antioxidant activity comparable to ascorbic acid (0.474 µg/mL) and butylated hydroxyanisole (0.315 µg/mL). Brine shrimp lethality assay indicated relatively low cytotoxicity for the extracts compared with the standard cyclophosphamide. These findings indicate that *Dalbergiella welwitschii* possesses promising glucose-lowering properties through a mechanism involving enhanced glucose utilization, moderate carbohydrate digestion and antioxidant activity supporting its potential for further pharmacological investigation.

Keywords: *Dalbergiella welwitschii*; diabetes; antioxidant; herbal medicine

1. Introduction

Type 2 diabetes mellitus is a chronic condition that affects how the body processes blood glucose. Individuals with type 2 diabetes either do not produce sufficient insulin or have insulin resistance. The International Diabetes Foundation estimates that of the about 96 million adults living in Nigeria, 3.6 million suffer from diabetes. This figure though alarming does not adequately portray the reality of the situation, given that majority go undiagnosed due to lack of access to modern healthcare facilities or proper health education. These factors have contributed to making type 2 diabetes a major public health challenge in Nigeria [1,2].

For years people in rural areas have utilized herbal remedies to manage type 2 diabetes and its related symptom of hyperglycemia [3]. The continued use of medicinal plants has stimulated interest in the identification of plant-derived compounds with glucose-lowering properties. These medicinal plants contain active phytochemicals that may contribute to diabetes control. There is documented evidence of the antidiabetic activity of some popular plants such as *Vernonia amygdalina* (Bitter leaf) and *Moringa oleifera* [4,5] providing examples of successful scientific validation of traditional medicinal plants. In recent years underutilized plants have been studied to establish their antidiabetic potential. To effectively reduce the burden of type 2 diabetes there is a need

to integrate medicinal plants into modern diabetes care. This integration would help reduce the cost of diabetes management especially in rural communities with limited access to standard healthcare. To facilitate this integration there is a need to provide scientific evidence and studies supporting the efficacy of local herbal remedies and understand their mechanism of blood glucose control.

Dalbergiella welwitschii (Baker) Baker f., locally known as West African Blackwood, a wooden shrub in the *Fabaceae* (*Papilionaceae*) family is used traditionally in the management of diabetes and hormonal disorders in Nigeria [6,7]. A wide variety of Phytocompounds comprising mainly of flavonoids, phenolic compounds and alkaloids have been discovered in the leaves [8–10]. *Dalbergiella welwitschii* is an invasive shrub that colonizes abandoned farmland, hence is widely available for integration into herbal practice [11].

Although report on the phytochemical composition of *Dalbergiella welwitschii* leaf is available [12]. Limited information exist regarding its glucose-lowering mechanisms particularly its influence on glucose uptake and carbohydrate digesting enzymes. Therefore this study investigated the glucose uptake activity, α-amylase inhibitory activity, antioxidant activity, phytochemical composition and preliminary cytotoxicity of leaf, stem and root extracts of Dalbergiella welwitschii.to provide preliminary evidence supporting its traditional use. Since plant parts differ in phytochemical content and this variation can influence bioactivity

2. Materials and Methods

2.1. Plant Collection and Extraction

Dalbergiella welwitschii (Baker) Baker f. plant was collected in an abandoned farmland at Jericho, Ibadan southwest Local Government, Ibadan Oyo State Nigeria. The plant was identified and authenticated at the University of Ibadan Herbarium, where a voucher specimen was deposited (UIH-23199). Various parts of the plant was used for extraction, because secondary metabolites are accumulated and distributed differently within plant parts. To prepare for extraction, the plant was divided into its components, allowed to dry at ambient temperature, and then ground into a coarse powder. Approximately 6 kg of the stem and 3 kg of the root were extracted with ethanol for 72 h using a modified Soxhlet extraction system. The leaf material (2 kg) was extracted with ethanol at room temperature by cold maceration for 72 h with intermittent stirring. All extracts were filtered, concentrated with a rotatory evaporator and dried in the oven at 40 °C.

2.2. Phytochemical Studies

Quantitative phytochemical content of saponins (%), alkaloid (%), flavonoid (mg/g QE) phenol (mg/g GAE) and tannin (mg/g GAE) were estimated Using established procedures [13].

To estimate percentage alkaloid, 5 g of sample was mixed with 20% acetic acid in ethanol and allowed to stand for four hours at room temperature. The mixture was filtered and concentrated on water bath then concentrated ammonium hydroxide was added dropwise until precipitation was complete. The precipitate was collected washed with 1% ammonia solution filtered and dried at 80 °C. The alkaloid content was calculated using the equation.

$$\%\ \text{alkaloid} = \frac{\text{weight of precipitate}}{\text{weight of sample}} \times 100$$

Total saponins content was determined by gravimetric method [14]. Exactly 5 g of extract was added to 100 mL of 20% ethanol, the mixture was then heated on a water bath at 100 °C for 4 h. The mixture was filtered and the residue re-extracted using another 100 mL ethanol. The filtrates were combined and concentrated, and the concentrate was mixed with 20 mL diethyl ether in a separatory funnel and shaken vigorously. The aqueous layer was partitioned again with 20 mL diethyl ether and 60 mL n-butanol was added. The purified concentrate was washed with 10 mL 5% sodium chloride and dried to a constant weight at 105 °C. The saponins content was expressed as mg/g dry weight of sample

$$\text{Saponins (mg/g)} = \frac{\text{weight of precipitate}}{\text{weight of sample}} \times 100$$

Total phenolic content (TPC) was estimated using Folin-Ciocalteu reagent, 0.1 mL of extract was mixed with 1 mL of the diluted reagent. The mixture was allowed to stand for 5 min, then 1 mL 7.5% *w*/*v* sodium carbonate was added. The mixture was incubated at 25 °C for 90 min until the appearance of a blue colour. The absorbance of the mixture was measured on a UV spectrophotometer at 765 nm. The TPC was expressed as Gallic acid equivalent (mg/g/GAE) using the Gallic acid calibration curve [15].

The total tannin content (TTC) was determined by adding 0.1 mL of extract to 0.5 mL Folin-Ciocalteu reagent, then 1 mL 35% Na_2CO_3 was added and the mixture was diluted to 10 mL with distilled water. The sample

was incubated in the dark for 30 min then absorbance was measured at 725 nm using distilled water as blank. The TTC was expressed as mg/g Gallic acid equivalent (mg/g/GAE) using the regression equation obtained from the Gallic acid calibration curve [16]. The total phenolic content and total tannin content was calculated using gallic acid concentration using the equation:

$$\text{TTC} = \frac{\text{gallic acid concentration } \times \text{volume of extract in mL}}{\text{weight of plant extract in g}}$$

To determine Total Flavonoid Content (TFC) 2 mL of 2% Aluminium chloride was added to 2 mL of 1 mg/mL extract. The mixture was incubated for 1 h and the sample absorbance was measure at 415 nm. A blank solution was prepared using 2 mL of sample in 2 mL of ethanol without $AlCl_3$. The TFC was calculated as quercetin equivalent (mg/g/QE) from the quercetin calibration curve.

$$\text{TFC} = \frac{\text{Quercetin concentration } \times \text{volume of extract in mL}}{\text{weight of plant extract in g}}$$

Qualitative phytochemical test was performed using standard laboratory procedures [17] as follows. A mixture of glacial acetic acid and concentrated H_2SO_4 was added to each of the plant extract to test for the presence of triterpenes and steroid. Formation of a pink/purple or violet blue colour indicated terpenes or steroids, respectively. Chloroform then 10% ammonia was added to the extract appearance of a pink colour indicated the presence of glycoside. A 10% ammonia solution was added to the extract, a pink Colouration was a positive indication of antraquinones. Five drops of concentrated HCl was added to the extract, red colour indicated presence of anthocyannins.

2.3. In Vitro Antidiabetic Studies

In vitro α-amylase studies on *Dalbergiella welwitschii* were done using the 3,5-dinitrosalicyclic acid (DNSA) method [18]. A stock solution of plant extract and positive control acabose was prepared by dissolving 1 mg in 1 mL of a mixture of 10% DMSO and a buffer solution comprising of of 0.02 M Na_2HPO_4/NaH_2PO_4 and 0.06 M NaCl at a pH of 6.9 to give a 1000 µg/mL concentration respectively. The stock solution was then diluted to give concentrations of 500, 250, 125, 62.5 and 31.25 µg/mL to allow for evaluation of bioactivity across a broad concentration range. A solution of 200 µL of α-amylase and 200 µL of each extracts and standard was incubated at 30 °C for 10 min, respectively. Thereafter 200 µL of 1% starch solution was added to each concentration the entire mixture was further incubated for 3 min. The DNSA solution was prepared by dissolving 12 g sodium potassium tartrate tetrahydrate in 8 mL of 2 M NaOH and 20 mL 96 mM of 3,5-dinitrosalicyclic acid. The prepared DNSA solution was added to the extract mixture and boiled at 85–90 °C to terminate the reaction. The mixture was cooled to room temperature diluted with 5 mL distilled water and the absorbance was measured at 540 nm on a UV-Vis spectrophotometer. Absorbance of a blank solution without the plant extract was measured representing 100% enzyme activity. The percentage α-amylase inhibitory activity was expressed as percentage inhibition and calculated using the equation:

$$\%\ \alpha - \text{amylase inhibition} \frac{\text{Absorbance}_{\text{control}} - \text{Absorbance}_{\text{sample}}}{\text{Absorbance}_{\text{control}}} \times 100$$

The percentage α-amylase inhibition was plotted against the extract concentration and the IC_{50} values were extrapolated from the graph.

The *in vitro* glucose uptake in yeast cells (*Saccharomyces cerevisiae*) studies were performed using the method as described by Nair et al. and Sankar et al. [19,20] with some modifications. Three concentrations of the test samples were prepared by dissolving 2 mg of extracts in 2 mL of distilled deionized water to give 1000 µg/mL concentration. This was further diluted to give rise to 500 and 250 µg/mL concentrations. These concentrations were selected to give an estimate of low, intermediate and high concentrations commonly employed in preliminary in-vitro screening.

A shaker bath was used to incubate a mixture of 1 mL glucose solution and 1 mL of the test material for 10 min at 37 °C. One hundred microliters of 10% (*V*/*V*) yeast solution was added to initiate the uptake reaction. The entire combination was incubated in a shaker bath for 60 min after which it was centrifuged at 2500 rpm for 5 min and decanted. The mixture was placed on warm water to kill the yeast cells and terminate the reaction. A control solution was prepared using glucose and yeast solution only. Glimepiride (1 mg) + Metformin HCl (500 mg) a commonly prescribed antidiabetic formulation in Nigeria served as a practical reference. The absorbance values of the decanted solution were measured on a UV spectrophotometer at 485 nm. The percentage increase in glucose-uptake was determined using the equation below:

$$\text{Increase in glucose-uptake (\%)} = (\text{ABS Sample} - \text{ABS Control}/\text{ABS Sample}) \times 100.$$

2.4. In Vitro Antioxidant Assay

The *in vitro* antioxidant activity of *Dalbergiella welwitschii* extract was tested Using the DPPH (2,2-dipheny-1-picryl hydrazine) radical scavenging assay [21]. The antioxidant power of plant extracts was assessed against 1 mM of DPPH radical. Samples were prepared in five concentrations of 1.0, 0.5, 0.25, 0.125 and 0.625 mg/mL, respectively. A spectrum lab S22PC visible spectrometer with model number 721S was used to detect the absorbance at 517 nm. Butylated hydroxyl anisole and ascorbic acid were used as reference standards. A solution of DPPH in ethanol without any test sample was used to measure the maximum absorbance of DPPH, and served as the control. The IC_{50} values were obtained from the equation of regression generated from a plot of concentration versus percentage inhibition.

$$\% \text{ inhibition} = \frac{\text{Absorbance}_{\text{control}} - \text{Absorbance}_{\text{sample}}}{\text{Absorbance}_{\text{control}}} \times 100$$

2.5. Brine Shrimp Cytotoxicity Assay

The preliminary toxicity levels of the plant extracts were tested using the Brine shrimp lethality assay [22]. A 1000 µg/mL stock solution of the solvent extracts and standard compound cyclophosphamide was prepared by dissolving 6 mg of the test samples in 6 mL of 1% DMSO. Serial dilution of the stock solution gave rise to concentrations of 500 µg/mL and 250 µg/mL. Using a Pasteur pipette, 10 brine shrimps were added to the entire solution, and the volume was made up to 5 mL with sea water. The experiment was left for a full day, and the number of shrimps that were alive in each concentration was counted. Using probit Finney analysis the lethal concentration at 50% (LC_{50}) was extrapolated from a plot of percentage mortality transformed to probit values and logarithm of concentration. [23].

2.6. Statistical Analysis

All reported values represent mean of triplicate measurements (n = 3). Statistical analysis of the glucose uptake activity was performed using one-way analysis of variance (ANOVA) and Turkey's Post Hoc test using Graphpad prism 10. Data were analyzed at 95% confidence level and $p < 0.05$. Descriptive statistical analysis was carried out for the antioxidant and brine shrimp lethality assay, values were expressed as mean ± standard deviation. The brine shrimp lethality assay was also subjected to a dose response analysis usin Probit Finely analysis.

3. Results

The extraction yield varied among the plant parts. The leaf gave the highest extraction yield (10.69%), followed by the root extract (3.39%). The stem extract had the lowest yield of 3.32%. The high yield of the leaf indicates that it contains more solvent extractable material based on the extraction technique used. The various percentage yields does not translate to improved biological activity, because bioactivity is influenced by the nature of phytochemicals and not the quantity of extractable material.

3.1. In Vitro Glucose Uptake Activity

The Glucose Uptake activities of *Dalbergiella welwitschii* solvent extract in yeast cells are presented in Table 1. All extracts produced an increase in percentage glucose-uptake comparable to the standard. Significant difference were observed among the different concentrations, although some group showed no statistically significant difference ($p < 0.05$). The stem showed relatively consistent Glucose uptake across all tested concentrations with minimal variation similar to the reference drug Glimepiride + Metformin HCl. In contrast, the leaf and root extract showed concentration dependent variation in glucose uptake. An increase in extract concentration was associated with an increase in glucose uptake, while higher glucose uptake resulted in reduced uptake activity.

Table 1. *In vitro* Glucose uptake in yeast cells of *Dalbergiella welwitschii* extracts.

25 mM Glucose Concentration			
	1000 µg/mL	500 µg/mL	250 µg/mL
Leaf	95.27 ± 0.06 ^{ab}	92.70 ± 0.10 ^{ed}	45.67 ± 0.25 ^{h}
Stem	95.13 ± 0.15 ^{d}	74.47 ± 1.70 ^{g}	83.23 ± 0.60 ^{f}
Root	97.57 ± 1.85 ^{a}	95.77 ± 0.06 ^{bc}	36.63 ± 0.15 ^{j}
Glimepiride + Metformin HCl	95.23 ± 0.06 ^{ab}	90.93 ± 0.06 ^{e}	92.93 ± 0.12 ^{cd}

Table 1. *Cont.*

10 mM Glucose Concentration			
Leaf	73.37 ± 1.60 ^{g}	74.47 ± 1.70 ^{g}	83.23 ± 0.60 ^{f}
Stem	92.20 ± 0.16 ^{cd}	96.70 ± 0.00 ^{a}	85.40 ± 0.17 ^{ab}
Root	93.40 ± 0.10 ^{bc}	75.23 ± 0.61 ^{g}	87.47 ± 0.23 ^{e}
Glimepiride + Metformin HCl	92.23 ± 0.06 ^{cd}	91.30 ± 0.10 ^{d}	88.47 ± 0.42 ^{f}
5 mM Glucose Concentration			
Leaf	91.23 ± 0.42 ^{de}	88.33 ± 0.23 ^{f}	83.27 ± 0.46 ^{h}
Stem	95.20 ± 0.20 ^{a}	94.70 ± 0.10 ^{ab}	91.10 ± 0.10 ^{f}
Root	87.60 ± 0.20 ^{g}	92.40 ± 0.10 ^{cd}	88.27 ± 0.50 ^{i}
Glimepiride + Metformin HCl	87.13 ± 0.06 ^{g}	93.30 ± 0.17 ^{bc}	88.53 ± 0.38 ^{f}

Values with same letters are not significantly different at $p < 0.05$.

3.2. In Vitro α-Amylase Inhibitory

α-Amylase inhibition increased generally with increasing extract concentration (Table 2). The calculated IC_{50} values were 289.8, 150.6 and 263.1 µg/mL for the leaf, stem and root extracts, respectively. These IC_{50} values were low in comparison to the standard acarbose (33.2 ± 0.00 µg/mL).

Table 2. α-Amylase inhibitory activity of *Dalbergiella welwitschii.*

Conc µg/mL	Leaf	Stem	Root
1000	58.43 ± 0.00	92.01 ± 0.02	75.25 ± 0.01
500	52.09 ± 0.01	90.031 ± 0.01	52.11 ± 0.02
250	40.43 ± 0.04	74.94 ± 0.04	32.76 ± 0.04
125	33.43 ± 0.02	32.19 ± 0.03	19.72 ± 0.01
62.5	32.27 ± 0.02	11.68 ± 0.03	11.13 ± 0.02
31.25	27.35 ± 0.01	0.00 ± 0.00	3.82 ± 0.001

3.3. Quantitative and Qualitative Phytochemical Screening

The qualitative and quantitative phytochemical composition of *Dalbergiella welwitschii* is presented in Table 3. Alkaloids, flavonoids, phenol, tannins and saponins were detected in varying amounts across the leaf, stem and root. The leaf extract showed higher concentration of alkaloids (5.73 ± 0.09 mg/g), phenol (3.11 ± 0.003 mg/g/GAE) and saponins (2.92 ± 0.02 mg/g) compared with the stem and root extracts. Qualitative screening showed the presence of steroids in the leaf and root, while anthraquinones and anthocyannins were detected in the stem. Glycosides were present only in the leaf extract.

Table 3. Quantitative and Qualitative Phytochemical Test on *Dalbergiella welwithschii.*

Secondary Metabolites	Leaf	Stem	Root
Saponin (mg/g)	2.92 ± 0.02	1.89 ± 0.02	2.18 ± 0.0123
Alkaloid (mg/g)	5.73 ± 0.09	3.91 ± 0.008	3.04 ± 0.0163
mg/g Flavonoid (QE)	0.17 ± 0.05	0.029 ± 0.03	0.084 ± 0.002
mg/g phenol (GAE)	3.11 ± 0.003	1.031 ± 0.012	2.40 ± 0.0023
mg/g tannin (GAE)	0.135 ± 0.002	0.065 ± 0.001	0.100 ± 0.001
Steroids	Present	Absent	Present
Triterpenes	Absent	Absent	Present
Glycosides	Present	Absent	Absent
Anthraquinones	Absent	Present	Absent
Anthocyanins	Absent	Present	present

3.4. In-Vitro Antioxidant Studies

The concentration-response relationship of the leaf, stem and root extracts and the reference antioxidants against DPPH radical is presented in Figure 1. DPPH radical scavenging activity varied with extract concentration with increasing inhibition observed for the leaf and root. A non-linear inhibition was observed for the stem extract. The stem extract exhibited the highest scavenging activity while the root extract exhibited the lowest activity. The reference standards BHA and ascorbic acid demonstrated increasing inhibition across the tested concentration. The calculated IC_{50} values were 0.953, 0.403 and 1.022 µg/mL for the leaf, stem and root extracts, respectively compared with 0.315 and 0.474 µg/mL for BHA and ascorbic acid.

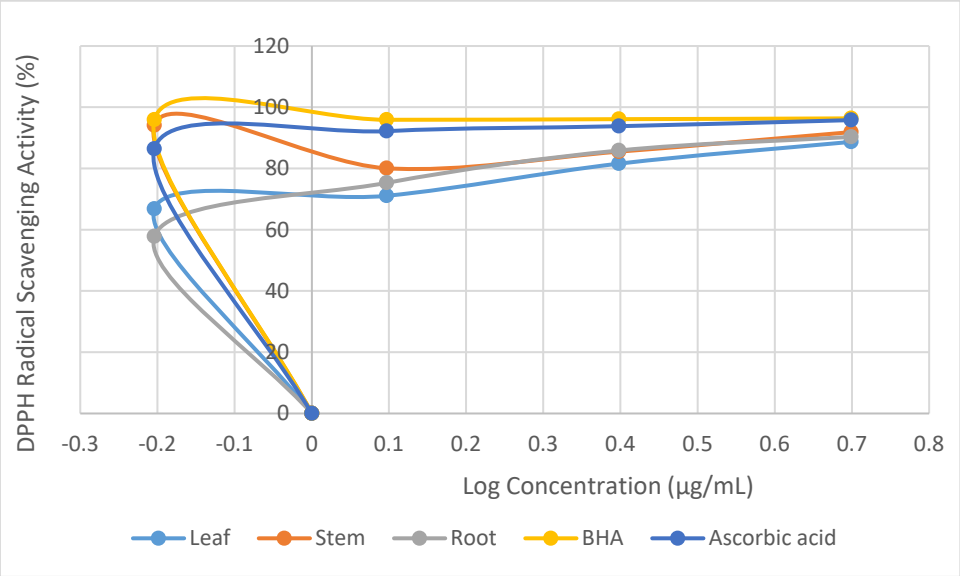

Figure 1. Concentration-percentage inhibition curve of DPPH radical scavenging activity for *Dalbergiella welwitschii.*

3.5. Brine Shrimp Lethality Assay

The brine shrimp lethality assay results for the solvent *extracts* of *Dalbergiella welwitschii* are presented in Table 4. The LC_{50} values for the leaf, stem and root extract were 251.2 µg/mL, 638.95 µg/mL and 295.1 µg/mL, respectively. All plant extracts showed higher LC_{50} values compared with cyclophosphamide (177.82 µg/mL).

Table 4. Brine Shrimp Cytotoxicity of *Dalbergiella welwithschii* Solvent Extracts.

Plant Extract	Percentage Mortality			LC_{50} µg/mL
	250 µg/mL	500 µg/mL	1000 µg/mL	
Leaf	50	63	90	251.2
Stem	13	47	70	638.95
Root	40	80	80	295.1
Cyclophosphamide	13	80	100	177.82

4. Discussion

The yeast cell assay provides a cost efficient and reproducible assay for preliminary antidiabetic screening. Increased glucose uptake in yeast cell suggest that the plant extracts may have the ability to improve cellular glucose utilization and help reduce post-prandial blood glucose which is a desired target in type 2 diabetes management [24]. The enhanced glucose uptake observed for the stem could imply that extracellular glucose is cleared more effectively mimicking improved glycemic control. Lack of uptake at higher glucose concentrations observed for the leaves and roots may suggest saturation of the transport system or metabolic stress in the yeast cells [25]. This could also explain why glucose uptake activity was not dose dependent on plant extract concentration. Since the glucose uptake assay is an insulin independent assay, it suggests that the plant extracts may contribute to lowering glucose concentration by potentially improving membrane permeability, glucose utilization and clearance which is important for insulin resistance and late stage type 2 diabetes [26]. This assay provides preliminary information on the use of *Dalbergiella welwitschii* extract as an alternative remedy for the management of Diabetes mellitus especially in preventing hyperglycemia. Cellular glucose-uptake is not only advantageous in diabetic management, but it can also provide fuel for energy and metabolism especially for important cells with high metabolic rate such as the brain neurons [27].

Alpha-amylase is a key digestive enzyme involved in the hydrolysis of carbohydrate into glucose. Rapid digestion of carbohydrate contributes to a sharp increase in blood glucose levels. Inhibition of the α-amylase enzyme delays carbohydrate breakdown, thereby slowing glucose release and absorption in the intestine [28]. Plant samples with α-amylase inhibitory potential reduce the rate of glucose appearance in circulation, thereby improving post-prandial glycemic control. They also may possess the ability to reduce insulin demand therefore minimize glucose fluctuations. Though the α-amylase inhibition in this study is low compared to that of acarbose, this is desirable because complete enzyme inhibition can lead to gastrointestinal issues due to undigested

carbohydrate [29]. Moderate α-amylase activity is of therapeutic advantage since it slows carbohydrate digestion without complete suppression which may improve tolerability. Nano-formulations of Nickel ferrites, zinc-doped nickel ferrites and manganese using extracts of *Dalbergiella welwitschii* showed good α-glucosidase inhibitory activities further validating the findings of this current research [30,31].

Oxidative stress plays a central role in the onset and progression of diabetes mellitus and its complication. Chronic hyperglycemia leads to excessive production of reactive oxygen species through glucose autoxidation, protein glycation and mitochondrial dysfunction. This eventually results in vascular and tissue damage [32]. Hence it is essential that any herbal remedies proposed for use in diabetes control should also have antioxidant properties [33]. Significant radical scavenging activities of *Dalbergiella welwitschii* stem extract indicate the presence of redox active constituents capable of donating electrons or hydrogen atoms, thereby stabilizing and terminating radical chains [34]. Antioxidant effects arise from cumulative and sustained activity. Antioxidant activity improves insulin sensitivity, protects β-cell function, and reduces inflammation and endothelial damage. Antioxidant activity complements α-amylase inhibition by reducing oxidative stress associated with post-prandial hyperglycemia. It also complements glucose uptake enhancement by preserving cellular function and metabolic efficiency [35].

Cytotoxicity assays are very important since some plants produce toxins for self-preservation. Cytotoxicity helps provide preliminary information on the starting dose for in-vivo experiments, and proposed potential use of a plant extract. The brine shrimp cytotoxicity is a rapid, cheap preliminary toxicity screening used to evaluate general cytotoxic potential of bioactive extracts and compounds [36]. It can help to distinguish pharmacologically active samples from those with known toxicity. The low cytotoxicity observed is an important consideration in the preliminary evaluation of biological activity of the extracts, particulary where prolonged exposure is anticipated [37]. The low cytotoxicity levels of the extracts together with their demonstrated biological activities, supports further investigation of their phytochemical constituents as potential sources of bioactive compounds.

Phytochemical screening provides insight into the bioactive constituents responsible for observed pharmacological activities. Qualitative screening helps identify classes of secondary metabolites while quantitative screening helps estimate their relative abundance. The quantitative phytochemical screening of the different parts of *Dalbergiella welwitschii* revealed that the extracts are chemically diverse and this may have an effect on the biological activity of the various plant parts. Phytochemical screening of *Dalbergiella welwitschii* leaves has identified a cross section of volatile and non-volatile compounds belonging to a variety of chemical classes validating this present research [38]. The qualitative phytochemical classes identified in the extracts suggest a synergistic interaction contributing to the observed biological activities [39]. Quantitative variation in phytochemical content explains the dose-dependent effect observed for some of the bioactivities. The presence of phenol and flavonoids in the extracts could contribute to neutralizing free radicals via hydrogen atom or electron donation. Tannins chelate pro-oxidant metal ions such as Fe^{2+}, Fe^{3+}, Cu^{2+}, Zn^{2+} thereby reducing reactive oxygen species formation [40]. Moderate levels of alkaloids and saponins contribute to enzyme inhibition such as α-amylase and modulation of glucose transport. The absence of highly toxic secondary metabolites could explain the low general cytotoxicity observed in the Brine Shrimp lethality assay.

Although the leaves exhibited higher phytochemical content. The stem extract demonstrated higher antioxidant and glucose uptake activities. Biological activities in most cases depend on molecular structure, reactivity, bioavailability and synergistic interaction rather than total abundance [41]. The stem extract may contain more potent or functionally active compounds. This provides the basis for further bioactivity-guided fractionation.

Despite the promising results obtained in this study, the findings are limited to *in vitro* assays. Yeast cells lack mammalian insulin signaling pathways and therefore cannot fully replicate human glucose metabolism. Investigations using mammalian cell lines, in-vivo animal models are necessary to further characterize the biological activities and potential therapeutic relevance of *Dalbergiella welwitschii*.

5. Conclusions

The glucose uptake activity observed in yeast cells highlights the potential of *Dalbergiella welwitschii* extracts to act as a glucose lowering agent. The insulin independent nature of the assay suggest its usefulness in insulin resistant states. The enhanced glucose uptake activity complements the moderate α-amylase activity because α-amylase inhibition limits glucose entry into the blood while glucose uptake enhances glucose clearance from the blood. Antioxidant activity suggests that the plant may help mitigate oxidative stress, a key contributor to diabetes and its complications. The Brine Shrimp cytotoxicity suggest that the extracts possesses a favourable preliminary cytotoxicity which could be exploited for further pharmacological development. The qualitative and quantitative phytochemical profiles of the various parts of *Darbergiella welwitschii* provides a chemical basis for the observed biological activities. This could lead to sustainable harvesting of more bioactive parts for future

research. These findings also support the traditional use of *Dalbergiella welwitschii* in the management of hyperglycemia and highlight its potential as a source of bioactive compounds. Further studies involving bioactivity-guided fractionation, and further related biological testing are required to fully elucidate its pharmacological mechanisms.

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