

Bridelia ferruginea Tea Consumption Improves Antioxidant Status in Individuals Living with Type 2 Diabetes

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Abstract: Background: It is well-known that persistent hyperglycaemia predisposes individuals with diabetes to oxidative stress. *Bridelia ferruginea* Benth., a tropical African plant, is known for its antioxidant activity. Methods: This comparative cross-sectional study assessed the oxidative status and associated parameters in 70 individuals living with type 2 diabetes (ILWT2D) who were receiving standard diabetes treatment and consistently drank *Bridelia* tea (*Bridelia* group) compared to 92 ILWT2D receiving standard diabetes treatment only (comparator group). Lipid peroxidation assessed using thiobarbituric acid reactive substances (TBARS) served as an indicator of oxidative stress. In addition, the total antioxidant capacity (TAC), glycated haemoglobin (HbA1c), and dietary intake of antioxidant-rich foods were assessed. Results: The comparator group had significantly better glycaemic control [median HbA1c—7.7% (IQR 6.7–9.4)] than the *Bridelia* group [9.2% (7.6–11.4)], $p = 0.001$. The comparator group had been on metformin treatment for a significantly longer period than the *Bridelia* group ($p < 0.0001$). Participants in the comparator group consumed antioxidant-rich fruits more frequently (monthly basis) than those in the *Bridelia* group who ate fruits seldomly ($p < 0.0001$). There was no significant difference ($p = 0.11$) observed in oxidative stress levels between the *Bridelia* group and the comparator group [TBARS: 323.0 ng/L (287.5–374.0) and 317.0 ng/L (272.5–342.0), respectively]. Nonetheless, the *Bridelia* group had significantly higher antioxidant capacity ($p = 0.001$) compared to the comparator group [TAC: 1.01 mmol/L (0.93–1.10) versus 0.92 mmol/L (0.84–1.03), respectively]. Participants in the comparator group, who did not drink *Bridelia* tea, had been on longer metformin treatment with better glycaemic control. However, those who drank the *Bridelia* tea showed comparable levels of oxidative stress and exhibited elevated antioxidant levels compared to those who did not. Conclusion: *Bridelia* tea consumption may serve as a sustainable source of antioxidants; however, its effect on mitigating oxidative stress in ILWT2D requires further investigation, particularly given that no significant improvement in TBARS was observed. Future studies are needed to clarify the potential role of *Bridelia* tea in oxidative stress management in resource-limited settings like Ghana.

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1. Introduction

Diabetes is a major global public health threat that contributed to the 41 million non-communicable disease (NCD)-related deaths globally in 2017 [1]. Additionally, the WHO [1] reported that in 2017, 78% of global NCD-related deaths occurred in low- and middle-income countries (LMICs). The number of people with diabetes has nearly quadrupled from about 151 million at the start of this millennium to over half a billion people in 2021 [2,3]. Type 2 diabetes accounts for a huge proportion (96%) of the number of people with diabetes in recent times [3]. Diabetes presents significant health and socioeconomic costs to individuals, households, and governments in LMICs [2,3].

Diabetes is a condition characterised by chronic elevation in blood glucose levels resulting from diminished insulin sensitivity of peripheral tissues or pancreatic insulin insufficiency. Persistent hyperglycaemia is known as a major driver of the excessive production of reactive oxygen species (ROS) in diabetes [4–7]. When the antioxidant defence system has limited capacity to counteract increasing ROS levels, oxidative stress results [8–10]. Several studies have reported high oxidative stress in individuals living with type 2 diabetes (ILWT2D) [4,11,12].

Oxidative stress has been implicated in the progression of type 2 diabetes to type-1-like diabetes and, ultimately, the development of cardiovascular complications with health [13] and socioeconomic [14–17] consequences. These adverse implications are more pronounced in low-resourced settings [16–18], especially in the aftermath of the COVID-19 pandemic [19,20]. A cardinal goal of diabetes management, especially type 2 diabetes, is the prevention of disease progression. Consistently achieving and maintaining normal glucose status is expected to limit hyperglycaemia-induced oxidative stress and associated complications. However, studies have shown that a significant proportion of individuals with diabetes do not achieve good glycaemic control [21,22], especially in developing countries, where more than half of patients with diabetes have poor glycaemic control [21,23]. The poor glycaemic status in these individuals could increase the risk of reactive oxygen species and subsequent cardiometabolic derangement.

In light of this, effective diabetes management should encompass measures to enhance antioxidant capacity to protect against oxidative damage. Thus, sustainable antioxidant interventions are needed to ensure redox homeostasis [24] and limit the deleterious health effects of oxidative stress in persons with diabetes [13]. In recent times, antioxidants from natural sources, particularly plant sources, have received significant attention in diabetes research and health care in the quest for sustainable antioxidant therapy [25–27]. Interest in natural plant antioxidants is largely driven by the potential for low toxicity, unwanted side effects from synthetic products, and improved sustainability [28,29].

The antioxidant potential of *Bridelia ferruginea* Benth., a tropical African plant widely available in Ghana, is well-documented [30–32]. It is also known to possess glucose-lowering properties [31,33], and it has been used for generations in some tropical African communities to treat symptoms of diabetes [32–34]. Bakoma et al. [30] identified significant bioactive compounds, including polyphenol and flavonoids, in the leaves of *B. ferruginea*, which may contribute to its antioxidant and glucose-lowering properties [35–38]. In Ghana, Bridelia tea, produced from *B. ferruginea*, is used in herbal medicine for its glucose-lowering effects. However, there is limited information on the effect of the tea consumption on oxidative status. Therefore, the objective of this study was to assess the impact of Bridelia tea on oxidative stress and antioxidant status in ILWT2D consuming the tea.

2. Materials and Methods

2.1. Study Design and Participants

This study comprised an observational study. It applied a comparative cross-sectional design, as used in previous studies [39–41]. The study participants included male and female ILWT2D attending an outpatient diabetes management clinic at the Centre for Plant Medicine Research (CPMR), Mampong-Akuapem, Ghana and two general hospitals (Owen government hospital and Kumasi South Government Hospital) in Ghana. The study was conducted from 22 February 2023 to 31 July 2023. The study was approved by the Health Sciences Research Ethics Committee (HSREC) at the University of the Free State, South Africa (ethics approval number: UFS-HSD2022/0953/2911-0003; final approval date: 31 July 2023) and the Committee on Human Research Publication and Ethics (CHRPE), School of Medical Sciences, KNUST, Ghana (ethics approval reference: CHRPE/AP/087/22; approval date: 16 March 2022).

This comparative cross-sectional study assessed and compared dietary intake, oxidative stress status, antioxidant status, and glycaemic status between two groups of ILWT2D. One group (the *Bridelia* group) comprised 70 outpatient ILWT2D who consistently drank *Bridelia* tea prescribed by the medical herbalists at the CPMR clinic, in addition to standard metformin treatment for at least 4 weeks. Previous studies have shown improvement in antioxidant status and oxidative stress levels after 3–6 weeks of intake of plant polyphenols, including an African tea product, rooibos (*Aspalathus linearis*) tea, an indigenous African herbal tea product, which showed improvement in antioxidant and oxidative stress markers after consumption in individuals susceptible to oxidative stress [42,43]. Participants brewed two tablespoons of the tea in 300 mL of boiling water for 5 min twice daily for consumption. In this observational study, the authors did not have control of the prescription of *Bridelia* tea. Participants had already been prescribed the tea as part of their routine treatment before enrolment in the study. Because the tea was prescribed by medical herbalists for its glucose-lowering effect, it was ethically inappropriate [44,45] to have a no-*Bridelia* treatment control group at the CPMR. Consequently, the second group comprised an external comparator group [46] that included 92 ILWT2D who had also been taking metformin (or another biguanide) treatment only for at least 4 weeks prescribed by physicians at the diabetes clinic of the two general hospitals. Individuals who were taking antioxidant supplements were excluded from the study. Patients who had co-morbid conditions characterised by high oxidative stress, like HIV/AIDS, liver disease, and cancer, were also excluded from the study. Additionally, those who had smoked within the past year and those who consumed more than 2 units of alcohol per week were also excluded. Patients who had been exposed to *Bridelia* tea were excluded from the comparator group. Convenience sampling was used to select participants who gave voluntary informed consent for the two groups.

2.2. Measurements

2.2.1. Sociodemographic, Health, and Lifestyle Assessment

A structured questionnaire was used to collect information on participants' socio-demographic, health, and lifestyle characteristics. Information was also collected on dietary/herbal supplement intake, tea consumption practices (excluding *Bridelia* tea), and awareness of antioxidants.

2.2.2. Anthropometric Assessment

Weight, height, and weight circumference were measured in line with the International Society for the Advancement of Kinanthropometry (ISAK) standard techniques [47]. A portable stadiometer (Seca 213, Hamburg, Germany) and weighing scale (Kinlee®,

Zhongshan, China) were used for the height and weight measurements, respectively. An inelastic tape measure was used for the waist circumference measurement. Body mass index was classified using the WHO guidelines [48] and the WHO [49] criteria to categorise waist circumference measurements.

2.2.3. Dietary Intake Assessment

Participants' usual dietary intake of antioxidant-rich foods and food products over the past six months was assessed using a food frequency questionnaire (FFQ) adapted from the Food and Agricultural Organisation (FAO) for use in low-resource settings like Ghana [50]. The FFQ was modified to reflect commonly consumed antioxidant-rich food sources in Ghana, grouped as follows: fruits, vegetables, roots, and tubers (mainly potatoes and beetroots), natural spices, oils, beverages, and chocolate products. Each food group consists of a list of antioxidant-rich Ghanaian foods. Participants were asked to indicate how often they consumed any of the foods on the list across daily, weekly, monthly, or seldom/never categories. The average frequency of intake of foods in each food group was computed for each participant. The overall intake (OI) across the six food groups was determined by summing the average frequencies of intake (AFI) of each of the six food groups divided by the total number of food groups (six) as follows:

$$\text{OI} = [\text{AFI (fruits)} + \text{AFI (vegetables)} + \text{AFI (roots and tubers)} + \text{AFI (natural spices)} + \text{AFI (oils)} + \text{AFI (beverages and chocolate products)}] \div \text{total number of food groups (six)}.$$

2.2.4. Biochemistry

Venous blood samples (5 mL) were collected from each participant after a 12 h overnight fast to measure glycated haemoglobin (HbA1c), lipid peroxidation using the thiobarbituric acid reactive substances (TBARS) assay, and total antioxidant capacity (TAC) using the enzyme-linked immunosorbent assay (ELISA). The blood sampling was performed by a qualified phlebotomist following the WHO standard procedure [51]. The TBARS and TAC measurements were performed using standard laboratory techniques at the Clinical Analysis Laboratory, Department of Biochemistry, KNUST, Ghana. The SD Biosensor standard F200 (Cheongju, Republic of Korea) point-of-care autoanalyzer, provided by Codix Ghana Limited, was used to determine HbA1c concentrations. The plasma lipid peroxidation assay was performed using human lipid peroxidation (TBARS) ELISA test kits from Melson Shangai Chemical Limited, China. The plasma TAC assay was also performed using a human total antioxidant capacity assay ELISA test kit (Melson Shangai Chemical Limited, Shangai, China). Fasting blood glucose (FBG) and random blood glucose levels were determined on-site using the Onetouch Select (Guangzhou, China) point-of-care glucometer. Blood glucose status was classified based on the WHO [52] criteria.

2.3. Statistical Analysis

Statistical analysis of the dataset was performed using SAS statistical analysis software, version 9.4 of the SAS System for Unix. Copyright © 2016, SAS Institute Inc. SAS, and all other SAS Institute Inc. product or service names, are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA. Statistical analysis of the data was performed by the Biostatistician at the Department of Biostatistics, Faculty of Health Sciences, University of the Free State, South Africa. The test of normality showed a non-normal distribution of the data on all of the study variables. Participants' background sociodemographic information was presented using descriptive statistics expressed as medians with interquartile ranges (median (IQR)) for numerical data. Categorical sociodemographic data were presented as frequencies and percentages. Inferential statistics was

performed using the Chi-square test. However, where there were cells with a count of less than five for categorical variables, Fisher's exact test was performed. Food frequency data on intake of antioxidant-rich foods were transformed into continuous variables for analysis. The most frequent category was assigned the highest value, and the least frequent category was assigned the lowest value, as follows: daily intake (4), weekly intake (3), monthly (2), and seldom/never (1). Median (IQR) frequencies of intake of each of the six food groups were determined. Additionally, the median (IQR) overall intake of antioxidant-rich foods across the six food groups was also determined. Comparisons of the numerical outcome variables between the Bridelia and comparator groups were performed using the Mann–Whitney or the Kruskal–Wallis non-parametric tests. Multiple regression analysis was performed to assess the potential confounding effects of participants' characteristics on the study outcomes. The level of statistical significance was set at $p < 0.05$.

3. Results

3.1. Background Characteristics of the Bridelia and Comparator Groups

3.1.1. Sociodemographic Characteristics

Table 1 presents the sociodemographic characteristics of participants in the two groups. Compared to the comparator group, there were significantly more females than males in the Bridelia group ($p = 0.0003$). The median age of the participants in the comparator and Bridelia groups was not significantly different (55.5 years (50.5–64.0) versus 55.0 years (50.0–63.0), respectively, $p = 0.77$), with both groups having a similar distribution of young/middle adults and older adults ($p = 0.80$). The Bridelia group had a higher proportion of participants with a high educational status than the comparator group ($p = 0.02$). The control group had a higher proportion of farmers (15.3%) compared to the treatment group (0.0%), while the treatment group had a higher percentage of artisans (17.7%) compared to the control group (6.8%) ($p = 0.01$).

Table 1. Sociodemographic characteristics of participants in Bridelia and comparator groups.

Variable	Comparator	Bridelia	Total	95% CI	p-Value
	n (%)	n (%)	n (%)		
Gender					0.0003
Male	9 (9.8)	23 (32.9)	32 (19.8)		0.0003
Female	83 (90.2)	47 (67.1)	130 (80.2)		0.0003
Total	92 (100.0)	70 (100.0)	162 (100.0)		
† Age					0.80
Young/middle adults	60 (65.2)	47 (67.1)	107 (66.0)		0.87
Older adults	32 (34.8)	23 (32.9)	55 (34.0)		0.87
* Median age (years)	55.5 (50.5–64.0)	55.0 (50.0–63.0)		–3.0, 3.0	0.77
Total n (%)	92 (100.0)	70 (100.0)	162 (100.0)		
‡ Level of education					0.002
Low	31 (33.7)	9 (12.9)	40 (24.7)		0.003
Middle	53 (57.6)	46 (65.7)	99 (61.1)		0.33
High	8 (8.7)	15 (21.4)	23 (14.2)		0.02
Total	92 (100.0)	70 (100.0)	101 (100.0)		
Employed					0.40
Yes	60 (65.2)	50 (71.4)	110 (67.9)		0.50
No	32 (34.8)	20 (28.6)	52 (32.1)		0.50
Total	92 (100)	70 (100)	162 (100)		
Occupation					0.01
Professional	7 (11.9)	5 (9.8)	12 (10.9)		0.77
^ Trader	32 (54.2)	27 (52.9)	59 (53.6)		1.00

Farmer	9 (15.3)	0 (0.0)	9 (8.2)	
Artisan	4 (6.8)	9 (17.7)	13 (11.8)	0.14
Others	7 (11.9)	10 (19.6)	17 (15.5)	0.30
Total	59 (100.0)	51 (100.0)	110 (100)	

* Medians (interquartile ranges) are presented for continuous variables. CI: confidence interval of the median difference. † Young adults: 18–34 years; middle adults: 35–59 years; old adults: ≥60 years [53,54]. GSS: Ghana Statistical Service. ‡ Low: never attended school/primary education; middle: middle school/secondary/pre-tertiary vocational education; high: tertiary education. ^ Trader: persons involved in smallholder purchase and sale business.

3.1.2. Health History

Table 2 summarises participants' health history. Family history of diabetes was similar in the Bridelia and comparator groups ($p = 0.10$). There was no difference in the frequency of clinic visits between the two groups, although the majority (90.1% versus 82.8%) of participants in both groups visited the clinic on a combined weekly and monthly basis ($p = 0.19$).

The two study groups had a comparable proportion of participants with other health conditions ($p = 0.46$). However, the Bridelia group had a significantly higher proportion of persons with dyslipidaemia as one of the comorbid conditions (22.9% vs. 7.4%, $p = 0.02$), while the comparator group also had significantly more persons with hypertension comorbidity (92.7% vs. 77.1%) ($p = 0.03$). The comparator group also had a significantly higher proportion of participants with long-standing diabetes than the Bridelia group ($p = 0.0017$) and, consequently, a significantly higher percentage of participants had been on metformin treatment for a longer period than those in the Bridelia group ($p < 0.0001$).

Table 2. Health characteristics of participants.

Variable	Comparator	Bridelia	Total	95% CI	p-Value
	n (%)	n (%)	n (%)		
Family history of diabetes					0.10
Yes	63 (68.5)	39 (55.7)	102(63.0)		0.10
No	29 (31.5)	31 (44.3)	60 (37.0)		0.10
Total	92(100)	70 (100)	162 (100)		
Family member with diabetes					0.04
First-degree relative	45 (71.4)	34 (87.2)	79 (77.5)		0.09
Second-degree relative	11 (17.5)	1 (2.6)	12 (11.8)		0.03
Both first- and second-degree relatives	4 (6.4)	4 (10.3)	8 (7.8)		0.48
Do not know	3 (4.8)	0 (0.0)	3 (2.9)		0.28
Total	63 (100)	39 (100)	102 (100)		
Frequency of hospital visits					0.19
Weekly/monthly	82 (90.1)	48 (82.8)	130(87.2)		0.21
>Monthly	9 (9.9)	10 (17.2)	19 (12.8)		0.21
Total	91 (100)	58 (100)	149 (100)		
Has other health conditions					0.46
Yes	68 (73.9)	48 (68.6)	116(71.6)		0.49
No	24 (26.1)	22 (31.4)	46 (28.4)		0.49
Total	92 (100)	70 (100)	162 (100)		
* Other health conditions					
Hypertension, dyslipidaemia, and others	5 (7.4)	11 (22.9)	16 (13.8)		0.02
Hypertension and others	63 (92.7)	37 (77.1)	100(86.2)		0.03
Total	68 (100)	48 (100)	116 (100)		
† Duration of diabetes (months)	60.0 (24.0–132.0)	36.0 (12.0–72.0)		–46.0, –11.0	0.0017

‡ Duration of metformin use (weeks)	312.0(117.0–624.0)	8.0 (5.0–10.0)	–409.0, –247.0	<0.0001
^ Blood pressure medication and others (weeks)	312.0(130.0–520.0)	260.0 (20.0–520.0)	–156.0, 64.0	0.40

‡,^ Medians (interquartile ranges) are presented for continuous variables. CI: confidence interval of the median difference. † n: 91 (comparator), 69 (Bridelia). ‡ n: 92 (comparator), 69 (Bridelia). ^ n: 63 (comparator), 33 (Bridelia). * Hypertension only comprised 91.9% and 87.3% of the Bridelia and comparator groups, respectively, with hypertension and other conditions. In total, 45.5% (n = 5) of participants in the Bridelia group had comorbid dyslipidaemia, while 40% (n = 2) of the comparator group had dyslipidaemia.

3.1.3. Supplement Intake Practices

As shown in Table 3, dietary/herbal supplement intake behaviour was not significantly different between the Bridelia and comparator groups ($p = 0.66$). In both groups, most participants (85.7% vs. 88.0%) were not taking supplements. Among the few who took supplements (n: 10 and 11), there were similarities in the type of supplement, the duration of supplement intake, and the frequency of supplement intake between the comparator and Bridelia groups ($p > 0.05$). None of the participants who took supplements obtained a prescription or a recommendation from a dietitian or a nutritionist.

Table 3. Supplement intake practices.

Variable	Comparator	Bridelia	Total	p-Value
	n (%)	n (%)	n (%)	
Dietary/herbal supplement intake				0.66
Yes	11 (12.0)	10 (14.3)	21 (13.0)	0.81
No	81 (88.0)	60 (85.7)	141 (87.0)	0.81
Total	92 (100)	70 (100)	162 (100)	
Type of supplement				0.87
Food supplement	2 (18.2)	2 (20.0)	4 (19.0)	1.00
Multivitamin micronutrients	6 (54.6)	4 (40.0)	10 (47.6)	0.67
Herbal supplements	2 (18.2)	3 (30.0)	5 (23.8)	0.64
Others/Do not know	1 (9.0)	1 (10.0)	2 (9.5)	1.00
Total	11 (100)	10 (100)	21 (100)	
Duration of supplement intake				0.73
<1 week	3 (27.3)	1 (10.0)	4 (19.0)	0.59
1 week to <1 month	2 (18.2)	4 (40.0)	6 (28.6)	0.36
1 month to <6 months	1 (9.0)	2 (20.0)	3 (14.3)	0.59
6 months to <1 year	2 (18.2)	1 (10.0)	3 (14.3)	1.00
>1 year	3 (27.3)	2 (20.0)	5 (23.8)	1.00
Total	11 (100)	10 (100)	21 (100)	
Frequency of supplement intake				0.58
Daily	7 (70.0)	9 (90)	16 (80.0)	0.58
2–6 times weekly	2 (20.0)	0 (0)	2 (10.0)	0.47
Once monthly	0 (0.0)	1 (10.0)	1 (5.0)	1.00
Seldomly	1 (10.0)	0 (0.0)	1 (5.0)	1.00
Total	10 (100)	10 (100)	20 (100)	
Reasons for taking supplement				0.89
Control blood glucose	2 (18.1)	4 (40.0)	6 (28.6)	0.36
Enhance performance	1 (9.1)	0 (0.0)	1 (4.8)	1.00
Prescribed by physician	0 (0.0)	1 (10.0)	1 (4.8)	0.48
Prescribed by dietitian/nutritionist	0 (0.0)	0 (0.0)	0 (0.0)	1.00
Promote health	1 (9.1)	1 (10.0)	2 (9.5)	1.00
For weight loss	1 (9.1)	0 (0.0)	1 (4.8)	1.00
Boost nutrition status	3 (27.3)	2 (20.0)	5 (23.8)	1.00

Do not know	3 (27.3)	2 (20.0)	5 (23.8)	1.00
Total	11 (100)	10 (100)	21 (100)	
Source of information on supplement				1.00
Physician/nurse	6 (54.5)	6 (60.0)	12 (57.1)	1.00
Dietitian/nutritionist	0 (0.0)	0 (0.0)	0 (0.0)	1.00
Pharmacist	1 (9.1)	0 (0.0)	1 (4.8)	1.00
Internet	1 (9.1)	0 (0.0)	1 (4.8)	1.00
Family and friends	3 (27.3)	2 (0.0)	5 (23.8)	1.00
Television	0 (0.0)	1 (10.0)	1 (4.8)	0.48
Others	0 (0.0)	1 (10.0)	1 (4.8)	0.48
Total	11 (100)	10 (100)	21 (100)	

3.1.4. Tea Intake Practices

Compared to the comparator group, a significantly higher proportion of participants in the Bridelia group reported tea consumption other than Bridelia tea, ($p = 0.02$) (Table 4). However, the type of tea consumed, the reasons for taking tea, and the frequency of tea intake were not significantly different between the two groups ($p > 0.05$).

Table 4. Tea intake practices.

Variable	Comparator	Bridelia	Total	<i>p</i> -Value
	n (%)	n (%)	n (%)	
Takes tea				0.01
Yes	18 (19.6)	26 (37.1)	44 (27.2)	0.02
No	74 (80.4)	44 (62.9)	118 (72.8)	0.02
Total	92 (100)	70 (100)	162 (100)	
Type of tea				0.86
Regular tea	12 (66.7)	18 (69.2)	30 (68.2)	1.0
Green tea/herbal tea/do not know	6 (33.3)	8 (30.8)	14 (31.8)	1.0
Total	18 (100)	26 (100)	44 (100)	
Reasons for taking tea				0.20
As food/meal	9 (50.0)	18 (69.2)	27 (61.4)	0.23
As medicine/supplement/other	9 (50.0)	8 (30.8)	17 (38.6)	0.23
Total	18 (100.0)	26 (100.0)	44 (100.0)	
Frequency of tea intake				0.48
Daily	7 (50.0)	16 (61.5)	23 (57.5)	0.52
Weekly	7 (50.0)	10 (38.5)	17 (42.5)	0.52
Total	14 (100.0)	26 (100.0)	40 (100.0)	
Who introduced to tea				0.71
Self/family/friends	14 (82.4)	19 (73.1)	33 (76.7)	0.71
Physician/dietitian/nurse/others	3 (17.7)	7 (26.9)	10 (23.3)	0.71
Total	17 (100)	26 (100)	43 (100)	

3.1.5. Lifestyle Practices

Table 5 presents the lifestyle practices of participants. Smoking behaviour was similar between the two study groups ($p > 0.05$), with almost all participants in both groups (97.1% vs. 98.9%) having no smoking history. Alcohol consumption ($p = 0.05$) and the type of alcohol consumed ($p = 0.33$) were also not significantly different between the few participants in the Bridelia ($n = 10$) and comparator ($n = 5$) groups who reported alcohol use. The proportion of participants with or without exposure to dietary advice within the two study groups was not significantly different ($p = 0.84$). However, among those who had received dietary advice, a significantly higher proportion in the Bridelia group compared

with the comparator group received advice from a dietitian or a nutritionist ($p < 0.0001$). The *Bridelia* group had a significantly higher proportion of participants with low compliance to dietary advice compared to those in the comparator group ($p = 0.04$).

Table 5. Lifestyle practices.

Variable	Comparator	Bridelia	Total	95% CI	p-Value
	n (%)	n (%)	n (%)		
Smoked in the past					0.58
Yes	1 (1.1)	2 (2.9)	3 (1.9)		0.58
No	91 (98.9)	68 (97.1)	159 (98.1)		0.58
Total	92 (100)	70 (100)	162 (100)		
* How long since smoking stopped (weeks)	52 (52–52)	2.5 (2–3)		49.0, 50.0	0.54
Consumed alcohol					0.05
Yes	5 (5.4)	10 (14.3)	15 (9.3)		0.06
No	87 (94.6)	60 (85.7)	147 (90.7)		0.06
Total	92 (100)	70 (100)	162 (100)		
Type of alcohol					0.33
Beer	4 (80.0)	10 (100.0)	14 (93.3)		0.33
Other	1 (20.0)	0 (0.0)	1 (6.7)		0.33
Total	5 (100)	10 (100)	15 (100)		
Received dietary advice					0.84
Yes	50 (55.6)	40 (57.1)	90 (56.3)		0.87
No	40 (44.4)	30 (42.9)	70 (43.8)		0.87
Total	90 (100)	70 (100)	98 (100)		
Who recommended diet					<0.0001
Self/family/friends/others	2 (4.0)	1 (2.5)	3 (3.3)		1.00
Nurse/doctor	24 (48.0)	2 (5.0)	26 (28.9)		<0.0001
Dietitian/nutritionist	24 (48.0)	37 (92.5)	61 (67.8)		<0.0001
Total	50 (100)	40 (100)	90 (100.0)		
Follow dietary advice					0.03
Yes	43 (87.8)	27 (69.2)	70 (79.5)		0.04
No	6 (12.2)	12 (30.8)	18 (20.5)		0.04
Total	49 (100)	39 (100)	88 (100)		

* Medians (interquartile ranges) are presented for continuous variables. CI: confidence interval of the median difference.

3.1.6. Awareness of Antioxidants

Table 6 shows information on participants' awareness of antioxidants. There was no significant difference in the proportion of participants who reported familiarity with antioxidants in the two study groups ($p = 0.40$). Almost all of the participants in both groups were not familiar with antioxidants.

Table 6. Awareness of antioxidants.

Variable	Comparator	Bridelia	Total	p-Value
	n (%)	n (%)	n (%)	
Familiar with antioxidants				0.40
Yes	2 (2.2)	4 (5.7)	6 (3.7)	0.40
No	90 (97.8)	66 (94.3)	156 (96.3)	0.40
Total	92 (100)	70 (100)	162 (100)	

3.2. Anthropometric Indices

There was a significantly higher proportion of overweight participants in the comparator group than in the Bridelia group ($p = 0.049$) (Table 7). The proportion of participants in the waist circumference categories was not significantly different between the Bridelia and comparator groups ($p = 0.16$). Additionally, there was no significant difference ($p = 0.57$) in the median BMI between the Bidelia [27.3 kg/m² (24.4–30.2)] and comparator [28.7 kg/m² (22.6–32.7)] groups.

Table 7. Anthropometric indices.

Variable	Comparator	Bridelia	Total	95% CI	p-Value
	n (%)	n (%)	n (%)		
Body mass index					0.09
Underweight/normal	28 (30.8)	22 (31.9)	50 (31.3)		1.00
Overweight	39 (42.9)	19 (27.5)	58 (36.3)		0.049
Obese	24 (26.4)	28 (40.6)	52 (32.4)		0.06
Median (kg/m ²)	27.3 (24.4–30.2)	28.7 (22.6–32.7)		−1.4, 2.6	0.57
Total n (%)	91 (100)	69 (100)	160 (100)		
Waist circumference					0.14
Central obesity	69 (75.8)	43 (65.2)	112 (71.3)		0.16
Normal	22 (24.2)	23 (34.9)	45 (28.7)		0.16
Median (cm)	98.6 (93.1–106.1)	96.6 (84.2–110.0)		−7.1, 3.1	0.50
Total n (%)	91 (100)	66 (100)	157 (100)		

Medians (interquartile ranges) are presented for continuous variables. CI: confidence interval of the median difference.

3.3. Frequency of Dietary Intake of Antioxidant-Rich Food

Results regarding the frequency of dietary intake of antioxidant-rich foods are shown in Table 8. Participants in the comparator group had significantly more frequent intake of antioxidant-rich fruits than those in the Bridelia group ($p < 0.0001$). Participants in the two groups had a similar frequency of intake of antioxidant-rich vegetables, natural spices, oils, roots and tubers, and beverages and chocolate products. Additionally, both groups consumed antioxidant-rich foods at a monthly frequency.

Table 8. Frequency of intake of antioxidant-rich foods.

Variables	Comparator		Bridelia		95% CI	p-Value
	n	Median (IQR)	n	Median (IQR)		
Fruits	92	1.6 (1.4–1.9)	70	1.3 (1.1–1.6)	−0.3, −0.1	<0.0001
Vegetables	92	2.2 (1.9–2.4)	70	2.1 (1.8–2.5)	−0.2, 0.1	0.44
Natural spices	92	1.8 (1.5–2.0)	70	1.7 (1.4–2.1)	−0.2, 0.2	0.92
Oils	91	3.0 (3.0–4.0)	70	3.0 (2.0–3.0)	−1.0, 0.0	0.0019
Roots and tubers	91	1.0 (1.0–1.5)	70	1.0 (1.0–1.5)	0.0, 0.0	0.92
Beverages and chocolate products	92	1.2 (1.0–1.6)	70	1.2 (1.0–1.6)	0.0, 0.0	0.70
Overall intake of antioxidant-rich food	92	1.9 (1.6–2.1)	70	1.7 (1.6–1.9)	−0.2, −0.0	0.03

Medians (interquartile ranges) are presented. CI: confidence interval of the median difference. The median values represent the frequency of intake as follows: daily intake (4), weekly intake (3), monthly (2), and seldom/never (1).

3.4. Biochemical Indices

Table 9 presents the biochemical indices of participants in the two groups. The distribution of blood glucose status of participants was similar between the two groups ($p = 0.72$), with most of the participants in each group having high blood glucose levels (82.9% and 87.6%). However, the comparator group had a significantly higher proportion of participants with good glucose control compared to the Bridelia group (35.9% vs. 17.7%, $p = 0.01$), which was also evidenced by the fact that more participants in the Bridelia group had higher HbA1c levels compared to the comparators [9.2% (7.6–11.4) vs. 7.7 (6.7–9.4), $p = 0.0004$].

The difference in lipid peroxidation levels between the participants in the Bridelia and comparator groups was not statistically significant ($p = 0.11$). However, the participants in the Bridelia group had significantly ($p = 0.0004$) higher total antioxidant capacity than those in the comparator group.

Table 9. Biochemical indices of participants.

Variable	Comparator n (%)	Bridelia n (%)	Total n (%)	95% CI	p-Value
† Blood glucose status					0.72
Normal	3 (3.4)	3 (4.3)	6 (3.8)		1.00
Impaired	8 (9.0)	9 (12.9)	17 (10.7)		0.45
High	78 (87.6)	58 (82.9)	136 (85.5)		0.50
Median FBG (mmol/L)	9.3 (7.9–12.3)	10.7 (8.4–13.0)		−0.44, 2.01	0.23
Median RBG (mmol/L)	13.8 (11.4–17.1)	15.4 (10.9–22.6)		−8.60, 2.90	0.34
Total n (%)	89 (100)	70 (100)	159 (100)		
* Glycated haemoglobin					0.0113
Good control	33 (35.9)	12 (17.7)	45 (28.1)		0.01
Poor control	59 (64.1)	56 (82.4)	115 (71.9)		0.01
Median HbA1c (%)	7.7 (6.7–9.4)	9.2 (7.6–11.4)		0.60, 2.00	0.0004
Total n (%)	92 (100)	68 (100)	160 (100)		
Oxidative status					
Lipid peroxidation (TBARS) (ng/L)	317.0 (272.5–342.0)	323.0 (287.5–374.0)		−3.50, 30.50	0.11
Total antioxidant capacity (mmol/L)	0.92 (0.8–1.0)	1.01 (0.9–1.1)		0.04, 0.14	0.0004

Medians (interquartile ranges) are presented for continuous variables. CI: confidence interval. † Blood glucose level defined as normal—FBG 3.5–6.0 mmol/L and RBG < 7.8 mmol/L; impaired—FBG 6.1–6.9 mmol/L and RBG 7.8–11.1; high—FBG ≥ 7.0 mmol/L and RBG > 11.1 mmol/L. * Good control: HbA1c < 7.0%. Poor control: HbA1c > 7.0%.

3.5. Predictors of Oxidative Stress and Antioxidant Status

Table 10 presents the results of the multiple regression analysis of the relationship between the main outcome variables (oxidative stress and antioxidant status) and the background characteristics of the participants, which showed significant differences between the comparator and Bridelia groups. Only oil intake significantly predicted oxidative stress (TBARS) levels in the comparator group. A unit increase in oil intake was predicted to increase TBARS levels by 0.39 ng/L in the comparator group (β -coefficient = 0.39, (95% CI: 0.11, 0.66), $p = 0.007$). The combined effect of the predictor variables accounted for 12% and 11% of the proportion of variance in oxidative stress and antioxidant status, respectively, in the comparator group (adjusted $R^2 = 0.12$). However, all of the predictor variables combined did not seem to influence oxidative stress levels in the Bridelia group (adjusted $R^2 = -0.15$). In the Bridelia group, the predictor variables accounted for 24% of the proportion of variance in antioxidant status (adjusted $R^2 = 0.24$) (Table 10).

Table 10. Multiple regression analysis showing the relationship between participant characteristics with oxidative stress and antioxidant status.

Variable *	Comparator			Bridelia		
	β (95% CI)	<i>p</i> -Value	Adjusted R ²	β (95% CI)	<i>p</i> -Value	Adjusted R ²
Oxidative stress (TBARS)						
Duration of metformin intake	0.22 (0.13, 0.57)	0.21	0.12	1.91 (−4.38, 8.19)	0.54	−0.15
Glycated haemoglobin	−0.25 (−0.54, 0.02)	0.07		0.01 (−0.43, 0.45)	0.97	
Antioxidant status (TAC)	0.10 (−0.22, 0.41)	0.54		0.08 (−0.25, 0.42)	0.62	
Follow dietary advice	0.12 (−0.21, 0.45)	0.46		−0.13 (−0.52, 0.25)	0.48	
Oil intake	0.39 (0.11, 0.66)	0.007		−0.10 (−0.54, 0.33)	0.62	
Total antioxidant food intake	−0.02 (−0.34, 0.30)	0.91		0.06 (−0.41, 0.53)	0.79	
Antioxidant status (TAC)						
First-degree relative with diabetes	−0.21 (−0.60, 0.17)	0.27	0.11	0.43 (0.03, 0.82)	0.0374	0.24
Duration of metformin intake	0.02 (−0.56, 0.59)	0.95		2.26 (−4.04, 8.56)	0.44	
Glycated haemoglobin	0.18 (−0.30, 0.65)	0.45		−0.23 (−0.71, 0.24)	0.30	
Oxidative stress (TBARS)	0.39 (−0.10, 0.88)	0.11		0.27 (−0.20, 0.75)	0.24	
Dietitian/nutritionist-recommended diet	−0.34 (−0.77, 0.10)	0.12		0.06 (−0.42, 0.53)	0.80	
Oil intake	−0.47 (−0.95, 0.01)	0.057		−0.07 (−0.61, 0.47)	0.78	

β : coefficient of regression; adjusted R²: the proportion of variance in the dependent variable (oxidative stress and antioxidant status) that is accounted for by the independent variables; CI: confidence interval. * Sex, education, occupation, duration of diagnosis, other health conditions, fruit intake, and tea intake behaviour were excluded from the regression model due to severe multicollinearity (beta variance inflation factors were greater than 10).

4. Discussion

This observational study examined the effect of the consumption of an antioxidant-rich tea on oxidative stress and the antioxidant status of ILWT2D. Although there was no significant difference in oxidative stress levels between the participants in the Bridelia group and their comparator counterparts, participants who drank Bridelia tea had significantly higher antioxidant status than those who did not. Because this study applied a cross-sectional design, which inherently cannot control for potential confounding variables [44,45,55], it is important to highlight any differences and similarities in the background characteristics of the participants to provide context for the observed effects of Bridelia tea in the study participants consuming the tea.

It is well-known that age is a potential confounder of oxidative status, as oxidative stress increases with ageing [56–58]. In the present study, most participants in both groups fell into a middle-age group (median age of 55 years), which could contribute to age-related oxidative stress [59]. Participants who drank Bridelia tea and their comparator counterparts had comparable ages, thus decreasing the likelihood that age was a potential confounder of oxidative status in one group over the other. The median age of the study groups is comparable to the 57–58 years reported in a study on correlates of oxidative stress in a healthy population in New York [60] but lower than the 42.5 years reported by Black et al. [61] in a study that investigated oxidative status among individuals with and without psychiatric conditions.

The distribution of gender, education, and type of occupation was significantly different between the Bridelia and comparator groups. There was a higher proportion of females in the comparator group than in the Bridelia group. Several previous studies have documented gender differences in levels of oxidative stress [60–63]. Kander et al. [63] suggested that pre-menopausal women tend to have lower levels of oxidative stress due to the antioxidant effects of oestrogen. This protective effect seems to diminish during the post-menopausal stage [60,63]. Trevisan et al. [60] found a high level of oxidative stress

among post-menopausal women, while another study by Elvira et al. [62] reported a higher level of oxidative stress in women than in men, irrespective of the menopausal stage of the women. In the present study, the gender differences did not seem to have had an impact on oxidative stress levels as there was no significant difference in lipid peroxidation (TBARS) status between the comparator group, which had a higher proportion of females, and the Bridelia group with more males.

The significant differences in educational status and type of occupation did not seem to impact oxidative stress status between the two groups. There are limited reports on the relationship between educational status and oxidative stress and antioxidant status. One study associated lower oxidative status with more years of education, a proxy for higher socioeconomic status [61]. However, in a developing country like Ghana, with a high unemployment rate among individuals with high education status [64,65], more years of education may not necessarily translate into higher socioeconomic status. This is supported by the findings of the present study, where there was no significant difference in employment status between the Bridelia group, with a higher proportion of participants with middle to high education status, and the comparator group. Furthermore, educational achievement did not seem to impact the oxidative stress status between the two groups, as both groups had comparable lipid peroxidation status.

Furthermore, even though the Bridelia group, with a higher proportion of participants with middle to high educational status, had higher total antioxidant capacity, it is less likely that the observed difference in antioxidant status is influenced by their level of education. This is because the participants who drank Bridelia tea did not significantly exhibit antioxidant-enhancing behaviours. For instance, they had comparable lifestyles, dietary/herbal supplement intake, and tea intake practices to their counterparts who did not consume the tea. They also had similar levels of awareness of antioxidants, suggesting that the level of education did not influence the two groups differently. In addition, it would be expected that the Bridelia group with higher education status would be better informed regarding the intake of antioxidant-rich foods, but this was not observed.

Although the Bridelia group had a significantly higher proportion of participants who reported consuming tea products, other than Bridelia tea, the two groups had comparable reported intake of antioxidant-rich tea products like green tea and herbal tea. The reported frequency of other tea intake was also not significantly different between the two groups.

Excess body weight has been linked to oxidative stress in many previous studies [66–71]. However, others [61] did not find an association between oxidative status and BMI, although it was correlated with waist circumference, which is regarded as a better indicator of obesity than BMI [49]. The waist circumference status of participants in the two groups in the present study did not seem to influence their oxidative and antioxidant status, as there were no significant differences in the distribution of waist circumference indices between the two groups. Additionally, both groups had comparable median BMIs representing overweight status.

The participants in the comparator group had had diabetes for a longer duration of time, and they had also been on metformin treatment for a longer period than their Bridelia group counterparts. Long-standing hyperglycaemia in diabetes is widely known to stimulate oxidative stress [4–7]. Gunawardena et al. [72] reported high lipid peroxidation status in ILWT2D compared with individuals with normoglycaemia. Thus, successfully controlling hyperglycaemia would limit hyperglycaemia-induced oxidative stress. In the present study, a larger proportion of the Bridelia group had poor glycaemia control than the comparators, thus predisposing them to higher oxidative stress and potentially lower antioxidant status. Interestingly, however, the participants who consumed Bridelia tea had comparable oxidative status to and higher antioxidant status than their counterparts in the comparator group.

Several studies have reported that metformin treatment in type 2 diabetes directly confers an oxidative-stress-lowering effect by suppressing reactive-oxygen-generating oxidative phosphorylation in the mitochondria [73–75]. In addition, metformin has been suggested to confer antioxidant benefits by enhancing the activity of antioxidant enzymes [76]. It would be expected that the comparator group, who had diabetes for a longer duration, would have significantly higher oxidative stress than the Bridelia group. However, the prolonged exposure to metformin treatment with its associated oxidative-stress-lowering effects [73–75] could have mitigated hyperglycaemia-induced oxidative stress in the comparator group [76]. It has also been reported that metformin treatment for at least three months (~12 weeks) improves oxidative stress in ILWT2D [77]. In that regard, it is noteworthy that the participants who drank Bridelia tea had been on metformin treatment for about eight weeks, with potentially limited exposure to the benefits of metformin on their oxidative and antioxidant indices. Thus, it is reasonable to infer that although more participants in the Bridelia group had poor glycaemia control, the higher antioxidant capacity they exhibited is more likely to be related to the antioxidant effects of the tea.

The antioxidant effect of Bridelia tea consumption seems to have also mitigated the oxidative-stress-inducing effect of the poor glycaemic status among those who consumed the tea. Given this, coupled with the finding that the Bridelia group had comparable overall antioxidant-rich food intake, it is plausible to suggest that without tea consumption, participants in the Bridelia group may have had higher oxidative stress and lower antioxidant capacity than their counterparts.

Although the findings of this observational study suggest Bridelia tea consumption improved antioxidant capacity in individuals living with type 2 diabetes, it is important to indicate that the cross-sectional design of the study limits the generalisability of the study findings due to inherently limited ability to control potential confounders, including some participant characteristics that were significantly different between the comparator and Bridelia groups. However, results of the multiple regression model suggest that the background characteristics of the participants had little confounding influence on the oxidative stress level and antioxidant status of the participants in the two groups. Furthermore, while TAC measures the body's ability to enhance endogenous antioxidant defences, TBARS assesses lipid peroxidation, which indicates oxidative damage to cell membranes. The lack of a significant difference in TBARS suggests that although Bridelia tea consumption increased antioxidant levels, this may not have been sufficient to reduce existing oxidative damage. This could be due to the short duration of the study or the prevailing oxidative stress conditions experienced by the participants. However, we would like to highlight that the Bridelia tea product was not administered by the researchers, as it was self-consumed by participants as part of their routine treatment at the clinic, as stated in Section 2.1 This further underscores the observational nature of our study, as we relied on participants' regular consumption patterns rather than controlled intake. Notably, previous studies have demonstrated that improvements in antioxidant status and reductions in oxidative stress can occur within relatively short periods. A study by Marnewick et al. [43] found significant changes in markers of oxidative stress and antioxidant capacity after six-week consumption of rooibos tea, an indigenous African herbal tea product, among individuals with cardiovascular diseases. This suggests that even short-term consumption of antioxidant-rich beverages can yield beneficial effects. In light of this context, we believe that our findings contribute valuable insights despite the relatively short duration of the study. Nevertheless, further studies using a randomised controlled design [45,55] would better demonstrate the impact of Bridelia tea consumption in ILWT2D.

Despite the study's limitations, the findings of the current study offer insights for diabetes healthcare practitioners who are interested in strategies to mitigate oxidative stress in patients with type 2 diabetes, especially in settings like Ghana, where the *B. ferruginea* plant

thrives. It could potentially serve as a readily accessible and sustainable source of natural antioxidants against oxidative stress in diabetes and other oxidative conditions.

5. Conclusions

In this study, individuals living with type 2 diabetes who did not drink *Bridelia* tea had better glycaemia control but showed comparable anthropometric indices, overall antioxidant-rich food intake, lifestyle practices, and oxidative stress levels to those who drank the tea. However, those who drank the tea exhibited significantly higher antioxidant status than those who did not. This suggests that *Bridelia* tea consumption likely enhanced endogenous antioxidant defences, as indicated by the increase in total antioxidant capacity, without directly reducing lipid peroxidation. Thus, *Bridelia* tea consumption could potentially serve as a sustainable source of antioxidants to mitigate oxidative stress in ILWT2D in resource-limited settings like Ghana.

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References

1. WHO. *Noncommunicable Diseases Country Profiles*; WHO: Geneva, Switzerland, 2018.
2. IDF. *IDF Diabetes Atlas 2021*, 10th ed.; IDF: Brussels, Belgium, 2021.

3. Global Burden of Disease Study Collaborators. Global, Regional, and National Burden of Diabetes from 1990 to 2021, with Projections of Prevalence to 2050: A Systematic Analysis for the Global Burden of Disease Study 2021. *Lancet* **2023**, *402*, 203–234. [https://doi.org/10.1016/S0140-6736\(23\)01301-6](https://doi.org/10.1016/S0140-6736(23)01301-6).
4. Rains, J.L.; Jain, S.K. Oxidative Stress, Insulin Signaling, and Diabetes. *Free Radic. Biol. Med.* **2011**, *50*, 567–575. <https://doi.org/10.1016/j.freeradbiomed.2010.12.006>.
5. Hurrle, S.; Hsu, W.H. The Etiology of Oxidative Stress in Insulin Resistance. *Biomed. J.* **2017**, *40*, 257–262. <https://doi.org/10.1016/j.bj.2017.06.007>.
6. Tabatabaei-Malazy, O.; Khodaeian, M.; Bitarafan, F.; Larijani, B.; Amoli, M.M. Polymorphisms of Antioxidant Genes as a Target for Diabetes Management. *Int. J. Mol. Cell Med.* **2017**, *6*, 135–147.
7. Newsholme, P.; Keane, K.N.; Carlessi, R.; Cruzat, V. Oxidative Stress Pathways in Pancreatic β -Cells and Insulin-Sensitive Cells and Tissues: Importance to Cell Metabolism, Function, and Dysfunction. *Am. J. Physiol. Cell Physiol.* **2019**, *317*, C420–C433. <https://doi.org/10.1152/ajpcell.00141.2019>.
8. Yoshikawa, T.; Naito, Y. What Is Oxidative Stress? *J. Jpn. Med. Assoc.* **2002**, *124*, 271–276.
9. Tauler Riera, P. Redox Status. In *Encyclopedia of Exercise Medicine in Health and Disease*; Mooren, F.C., Ed.; Springer: Berlin/Heidelberg, Germany, 2012; pp. 751–753, ISBN 978-3-540-29807-6.
10. Hussain, T.; Tan, B.; Yin, Y.; Blachier, F.; Tossou, M.C.B.; Rahu, N. Oxidative Stress and Inflammation: What Polyphenols Can Do for Us? *Oxidative Med. Cell. Longev.* **2016**, *2016*, 7432797. <https://doi.org/10.1155/2016/7432797>.
11. Newsholme, P.; Cruzat, V.F.; Keane, K.N.; Carlessi, R.; de Bittencourt, P.I.H., Jr. Molecular Mechanisms of ROS Production and Oxidative Stress in Diabetes. *Biochem. J.* **2016**, *473*, 4527–4550. <https://doi.org/10.1042/BCJ20160503C>.
12. Singh, A.; Kukreti, R.; Saso, L.; Kukreti, S. Mechanistic Insight into Oxidative Stress-Triggered Signaling Pathways and Type 2 Diabetes. *Molecules* **2022**, *27*, 950.
13. Świątkiewicz, I.; Wróblewski, M.; Nuskiewicz, J.; Sutkowy, P.; Wróblewska, J.; Woźniak, A. The Role of Oxidative Stress Enhanced by Adiposity in Cardiometabolic Diseases. *Int. J. Mol. Sci.* **2023**, *24*, 6382. <https://doi.org/10.3390/ijms24076382>.
14. Fu, A.Z.; Qiu, Y.; Radican, L.; Wells, B.J. Health Care and Productivity Costs Associated with Diabetic Patients with Macrovascular Comorbid Conditions. *Diabetes Care* **2009**, *32*, 2187–2192. <https://doi.org/10.2337/dc09-1128>.
15. Yang, W.; Dall, T.M.; Beronjia, K.; Lin, J.; Semilla, A.P.; Chakrabarti, R.; Hogan, P.F.; Petersen, M.P. Economic Costs of Diabetes in the U.S. in 2017. *Diabetes Care* **2018**, *41*, 917–928. <https://doi.org/10.2337/dci18-0007>.
16. Banker, K.K.; Liew, D.; Ademi, Z.; Owen, A.J.; Afroz, A.; Magliano, D.J.; Zomer, E. The Impact of Diabetes on Productivity in India. *Diabetes Care* **2021**, *44*, 2714–2722. <https://doi.org/10.2337/DC21-0922>.
17. Palmer, K.N.B.; Crocker, R.M.; Marrero, D.G.; Tan, T.W. A Vicious Cycle: Employment Challenges Associated with Diabetes Foot Ulcers in an Economically Marginalized Southwest US Sample. *Front. Clin. Diabetes Healthc.* **2023**, *4*, 1027578. <https://doi.org/10.3389/fcdhc.2023.1027578>.
18. Mapa-Tassou, C.; Katte, J.-C.; Mba Maadjhou, C.; Mbanya, J.C. Economic Impact of Diabetes in Africa. *Curr. Diabetes Rep.* **2019**, *19*, 5. <https://doi.org/10.1007/s11892-019-1124-7>.
19. Devi, R.; Goodyear-smith, F.; Subramaniam, K.; McCormack, J.; Calder, A.; Parag, V.; Huang, P. The Impact of COVID-19 on the Care of Patients with Noncommunicable Diseases in Low- and Middle-Income Countries: An Online Survey of Patient Perspectives. *J. Patient Exp.* **2021**, *8*, 23743735211034091. <https://doi.org/10.1177/23743735211034091>.
20. Sureshkumar, S.; Mwangi, K.J.; Mustapha, F.; Quint, J.; Tabrizi, R.; Palafox, B.; Etchebehere, M.; Kengne, A.P.; Madhu, P.P.; Peer, N.; et al. Exploring Key-Stakeholder Perceptions on Non-Communicable Disease Care during the COVID-19 Pandemic in Kenya. *Pan Afr. Med. J.* **2023**, *44*, 1–15.
21. Aschner, P.; Gagliardino, J.J.; Ilkova, H.; Lavalle, F.; Ramachandran, A.; Mbanya, J.C.; Shestakova, M.; Chantelot, J.; Chan, J.C.N. Persistent Poor Glycaemic Control in Individuals with Type 2 Diabetes in Developing Countries: 12 Years of Real-World Evidence of the International Diabetes Management Practices Study (IDMPS). *Diabetologia* **2020**, *63*, 711–721.
22. Alduwayhis, N.M.; Aleid, N.; Albarrak, A.N.; Aloraini, A.A. Glycemic Control for Type 2 Diabetes Mellitus Patients: A Systematic Review. *Cureus* **2022**, *14*, 6–13. <https://doi.org/10.7759/cureus.26180>.
23. Camara, A.; Baldé, N.M.; Sobngwi-Tambekou, J.; Kengne, A.P.; Diallo, M.M.; Tchatchoua, A.P.K.; Kaké, A.; Sylvie, N.; Balkau, B.; Bonnet, F.; et al. Poor Glycemic Control in Type 2 Diabetes in the South of the Sahara: The Issue of Limited Access to an HbA1c Test. *Diabetes Res. Clin. Pract.* **2015**, *108*, 187–192. <https://doi.org/10.1016/j.diabres.2014.08.025>.
24. Yan, Z.; Zhong, Y.; Duan, Y.; Chen, Q.; Li, F. Antioxidant Mechanism of Tea Polyphenols and Its Impact on Health Bene Fi Ts. *Anim. Nutr.* **2020**, *6*, 115–123. <https://doi.org/10.1016/j.aninu.2020.01.001>.
25. Akpoveso, O.O.P.; Ubah, E.E.; Obasanmi, G. Antioxidant Phytochemicals as Potential Therapy for Diabetic Complications. *Antioxidants* **2023**, *12*, 123. <https://doi.org/10.3390/antiox12010123>.
26. Naz, R.; Saqib, F.; Awadallah, S.; Wahid, M.; Latif, M.F.; Iqbal, I.; Mubarak, M.S. Food Polyphenols and Type II Diabetes Mellitus: Pharmacology and Mechanisms. *Molecules* **2023**, *28*, 3996. <https://doi.org/10.3390/molecules28103996>.
27. Liu, Y.; Luo, J.; Peng, L.; Zhang, Q.; Rong, X.; Luo, Y.; Li, J. Flavonoids: Potential Therapeutic Agents for Cardiovascular Disease. *Heliyon* **2024**, *10*, e32563. <https://doi.org/10.1016/j.heliyon.2024.e32563>.
28. Fresán, U.; Sabaté, J. Vegetarian Diets: Planetary Health and Its Alignment with Human Health. *Adv. Nutr.* **2019**, *10*, S380–S388. <https://doi.org/10.1093/advances/nmz019>.
29. Rahaman, M.; Hossain, R.; Torequl, M.; Olubunmi, I.; Oluyomi, A.; Adeyemi, S.; Abibat, O.; Learnmore, O.; Sevgi, K.; Daştan, D.; et al. Natural Antioxidants from Some Fruits, Seeds, Foods, Natural Products, and Associated Health Benefits: An Update. *Food Sci. Nutr.* **2023**, *11*, 1657–1670. <https://doi.org/10.1002/fsn3.3217>.

30. Bakoma, B.; Sanvee, S.; Metowogo, K.; Potchoo, Y.; Gadegbeku, K.E.; Aklikokou, K.; Gbeassor, M. Phytochemical Study and Biological Activities of Hydro-Alcoholic Extract of the Leaves of *Bridelia Ferruginea* Benth and Its Fractions. *Pharmacogn. J.* **2019**, *11*, 141–145. <https://doi.org/10.5530/pj.2019.1.23>.
31. Oyeboode, O.; Erukainure, O.L.; Zuma, L.; Ibeji, C.U.; Koorbanally, N.A.; Islam, M.S. In Vitro and Computational Studies of the Antioxidant and Anti-Diabetic Properties of *Bridelia Ferruginea*. *J. Biomol. Struct. Dyn.* **2020**, *40*, 3989–4003. <https://doi.org/10.1080/07391102.2020.1852961>.
32. Yeboah, G.N.; Owusu, F.W.A.; Archer, M.A.; Kyene, M.O.; Kumadoh, D.; Ayertey, F.; Mintah, S.O.; Atta-Adjei Junior, P.; Appiah, A.A. *Bridelia Ferruginea* Benth.; An Ethnomedicinal, Phytochemical, Pharmacological and Toxicological Review. *Heliyon* **2022**, *8*, e10366. <https://doi.org/10.1016/j.heliyon.2022.e10366>.
33. Thomford, K.P.; Yeboah, R.; Thomford, A.K.; Edoh, D.A.; Mensah, K.M.; Appiah, A.A. A Retrospective Clinical Study on the Effectiveness of the Aqueous Leaf Extract of *Bredelia ferrugenia* (Benth) in the Management of Diabetes Mellitus. *Int. J. Herb. Med.* **2015**, *2*, 43–45.
34. Mahomoodally, F.M.; Jugreet, S.; Ibrahime Sinan, K.; Zengin, G.; Ak, G.; Ceylan, R.; Jek, J.; Cziáky, Z.; Angelini, P.; Angeles Flores, G.; et al. Pharmacological Potential and Chemical Characterization of *Bridelia ferruginea* Benth. — A Native Tropical African Medicinal Plant. *Antibiotics* **2021**, *10*, 223. <https://doi.org/10.3390/antibiotics10020223>.
35. Costabile, G.; Vitale, M.; Luongo, D.; Naviglio, D.; Vetrani, C.; Ciciola, P.; Tura, A.; Castello, F.; Mena, P.; Del Rio, D.; et al. Grape Pomace Polyphenols Improve Insulin Response to a Standard Meal in Healthy Individuals: A Pilot Study. *Clin. Nutr.* **2019**, *38*, 2727–2734. <https://doi.org/10.1016/j.clnu.2018.11.028>.
36. Wang, Y.; Alkhalidy, H.; Liu, D. The Emerging Role of Polyphenols in the Management of Type 2 Diabetes. *Molecules* **2021**, *26*, 703. <https://doi.org/10.3390/molecules26030703>.
37. Fujii, Y.; Osaki, N.; Hase, T.; Shimotoyodome, A. Ingestion of Coffee Polyphenols Increases Postprandial Release of the Active Glucagon-like Peptide-1 (GLP-1(7-36)) Amide in C57BL/6J Mice. *J. Nutr. Sci.* **2015**, *4*, e9. <https://doi.org/10.1017/jns.2014.71>.
38. Bozzetto, L.; Annuzzi, G.; Pacini, G.; Costabile, G.; Vetrani, C.; Vitale, M.; Griffo, E.; Giacco, A.; De Natale, C.; Cocozza, S.; et al. Polyphenol-Rich Diets Improve Glucose Metabolism in People at High Cardiometabolic Risk: A Controlled Randomised Intervention Trial. *Diabetologia* **2015**, *58*, 1551–1560. <https://doi.org/10.1007/s00125-015-3592-x>.
39. Jadhav, A.V. Comparative Cross-Sectional Study for Understanding the Burden of Low Back Pain among Public Bus Transport Drivers. *Indian J. Occup. Environ. Med.* **2016**, *20*, 26–30. <https://doi.org/10.4103/0019-5278.183833>.
40. Woyesa, S.; Mamo, A.; Mekonnen, Z.; Abebe, G.; Gudina, E.K.; Milkesa, T. Lipid and Lipoprotein Profile in HIV-Infected and Non-Infected Diabetic Patients: A Comparative Cross-Sectional Study Design, Southwest Ethiopia. *HIV/AIDS-Res. Palliat. Care* **2021**, *13*, 1119–1126. <https://doi.org/10.2147/HIV.S339539>.
41. Zhang, T.; He, F.; Lin, S.; Wang, X.; Li, F.; Zhai, Y.; Gu, X.; Wu, M.; Lin, J. Does Aluminum Exposure Affect Cognitive Function? A Comparative Cross-Sectional Study. *PLoS ONE* **2021**, *16*, e0246560. <https://doi.org/10.1371/journal.pone.0246560>.
42. Devaraj, S.; Vega-López, S.; Kaul, N.; Schönlaue, F.; Rohdewald, P.; Jialal, I. Supplementation with a Pine Bark Extract Rich in Polyphenols Increases Plasma Antioxidant Capacity and Alters the Plasma Lipoprotein Profile. *Lipids* **2002**, *37*, 931–934. <https://doi.org/10.1007/s11745-006-0982-3>.
43. Marnewick, J.L.; Rautenbach, F.; Venter, I.; Neethling, H.; Blackhurst, D.M.; Wolmarans, P.; MacHaria, M. Effects of Rooibos (*Aspalathus linearis*) on Oxidative Stress and Biochemical Parameters in Adults at Risk for Cardiovascular Disease. *J. Ethnopharmacol.* **2011**, *133*, 46–52. <https://doi.org/10.1016/j.jep.2010.08.061>.
44. Mann, C.J. Observational Research Methods. Research Design II: Cohort, Cross Sectional, and Case-Control Studies. *Emerg. Med. J.* **2003**, *20*, 54–60. <https://doi.org/10.1136/emj.20.1.54>.
45. Noordzij, M.; Dekker, F.W.; Zoccali, C.; Jager, K.J. Study Designs in Clinical Research. *Nephron-Clin. Pract.* **2009**, *113*, 9–12. <https://doi.org/10.1159/000235610>.
46. Rippin, G.; Largent, J.; Hoogendoorn, W.E.; Sanz, H.; Bosco, J.; Mack, C. External Comparator Cohort Studies—Clarification of Terminology. *Front. Drug Saf. Regul.* **2024**, *3*, 1321894. <https://doi.org/10.3389/fdsfr.2023.1321894>.
47. ISAK. *International Standards for Anthropometric Assessment*, 1st ed.; ISAK: Underdale, South Australia, Australia, 2001; ISBN 978-84-16045-27-3.
48. WHO. A Healthy Lifestyle—WHO Recommendations. Available online: <https://www.who.int/europe/news-room/fact-sheets/item/a-healthy-lifestyle---who-recommendations> (accessed on 7 June 2024).
49. WHO. *Waist Circumference and Waist–Hip Ratio*; Report of a WHO Expert Consultation; WHO: Geneva, Switzerland, 2008.
50. FAO. *Dietary Assessment: A Resource Guide to Method Selection and Application in Low Resource Settings*; Food and Agriculture Organization of the United Nations: Rome, Italy, 2018; ISBN 9789251306352.
51. WHO. *WHO Guidelines on Drawing Blood: Best Practices in Phlebotomy*; World Health Organisation: Geneva, Switzerland, 2010; ISBN 978 92 4 159922 1.
52. WHO. *Classification of Diabetes Mellitus*; WHO: Geneva, Switzerland, 2019.
53. Ghana Statistical Service. *2010 Population & Housing Census Report: The Elderly in Ghana*; Ghana Statistical Service: Accra, Ghana, 2013.
54. Ghana Statistical Service. *Ghana 2021 Population and Housing Census: General Report Highlights*; Ghana Statistical Service: Accra, Ghana, 2022; Volume 3.
55. Spieth, P.M.; Kubasch, A.S.; Penzlin, A.I.; Illigens, B.M.W.; Barlinn, K.; Siepmann, T. Randomized Controlled Trials—A Matter of Design. *Neuropsychiatr. Dis. Treat.* **2016**, *12*, 1341–1349. <https://doi.org/10.2147/NDT.S101938>.
56. Wonisch, W.; Falk, A.; Sundl, I.; Winklhofer-Roob, B.M.; Lindschinger, M. Oxidative Stress Increases Continuously with BMI and Age with Unfavourable Profiles in Males. *Aging Male* **2012**, *15*, 159–165. <https://doi.org/10.3109/13685538.2012.669436>.

57. Luo, J.; Mills, K.; le Cessie, S.; Noordam, R.; van Heemst, D. Ageing, Age-Related Diseases and Oxidative Stress: What to Do Next? *Ageing Res. Rev.* **2020**, *57*, 100982. <https://doi.org/10.1016/j.arr.2019.100982>.
58. Hajam, Y.A.; Rani, R.; Ganie, S.Y.; Sheikh, T.A.; Javaid, D.; Qadri, S.S.; Pramodh, S.; Alsulimani, A.; Alkhanani, M.F.; Harakeh, S.; et al. Oxidative Stress in Human Pathology and Aging: Molecular Mechanisms and Perspectives. *Cells* **2022**, *11*, 552. <https://doi.org/10.3390/cells11030552>.
59. Liguori, I.; Russo, G.; Curcio, F.; Bulli, G.; Aran, L.; Della-Morte, D.; Gargiulo, G.; Testa, G.; Cacciatore, F.; Bonaduce, D.; et al. Oxidative Stress, Aging, and Diseases. *Clin. Interv. Aging* **2018**, *13*, 757–772. <https://doi.org/10.2147/CIA.S158513>.
60. Trevisan, M.; Browne, R.; Ram, M.; Muti, P.; Freudenheim, J.; Carosella, A.M.; Armstrong, D. Correlates of Markers of Oxidative Status in the General Population. *Am. J. Epidemiol.* **2001**, *154*, 348–356. <https://doi.org/10.1093/aje/154.4.348>.
61. Black, C.N.; Bot, M.; Scheffer, P.G.; Penninx, B.W.J.H. Sociodemographic and Lifestyle Determinants of Plasma Oxidative Stress Markers 8-OHdG and F2-Isoprostanes and Associations with Metabolic Syndrome. *Oxidative Med. Cell. Longev.* **2016**, *2016*, 7530820. <https://doi.org/10.1155/2016/7530820>.
62. Elvira, B.; Francesco, D.; La Daniele, R.; Daniela, P. Sex Differences in Oxidative Stress Biomarkers. *Curr. Drug Targets* **2014**, *15*, 811–815.
63. Kander, M.C.; Cui, Y.; Liu, Z. Gender Difference in Oxidative Stress: A New Look at the Mechanisms for Cardiovascular Diseases. *J. Cell. Mol. Med.* **2017**, *21*, 1024–1032. <https://doi.org/10.1111/jcmm.13038>.
64. Essuman, A. Perceptions of National Service Personnel and Youth Unemployment: Could Entrepreneurship Education and Curricula Rationalization Be the Solution? *J. Educ. Pract.* **2019**, *10*, 63–71. <https://doi.org/10.7176/jep/10-30-07>.
65. Yirenyki, E.G.; Debrah, G.; Adanu, K.; Atitsogbui, E. Education, Skills, and Duration of Unemployment in Ghana. *Cogent Econ. Financ.* **2023**, *11*, 2258680. <https://doi.org/10.1080/23322039.2023.2258680>.
66. Furukawa, S.; Fujita, T.; Shimabukuro, M.; Iwaki, M.; Yamada, Y.; Nakajima, Y.; Nakayama, O.; Makishima, M.; Matsuda, M.; Shimomura, I. Increased Oxidative Stress in Obesity and Its Impact on Metabolic Syndrome. *J. Clin. Investig.* **2004**, *114*, 1752–1761. <https://doi.org/10.1172/JCI21625>.
67. Vincent, H.K.; Taylor, A.G. Biomarkers and Potential Mechanisms of Obesity-Induced Oxidant Stress in Humans. *Int. J. Obes.* **2006**, *30*, 400–418. <https://doi.org/10.1038/sj.ijo.0803177>.
68. Warolin, J.; Coenen, K.R.; Kantor, J.L.; Whitaker, L.E.; Wang, L.; Acra, S.A.; Roberts, L.J.; Buchowski, M.S. The Relationship of Oxidative Stress, Adiposity and Metabolic Risk Factors in Healthy Black and White American Youth. *Pediatr. Obes.* **2014**, *9*, 43–52. <https://doi.org/10.1111/j.2047-6310.2012.00135.x>.
69. Huang, C.J.; McAllister, M.J.; Slusher, A.L.; Webb, H.E.; Mock, J.T.; Acevedo, E.O. Obesity-Related Oxidative Stress: The Impact of Physical Activity and Diet Manipulation. *Sports Med. Open* **2015**, *1*, 32. <https://doi.org/10.1186/s40798-015-0031-y>.
70. Marseglia, L.; Manti, S.; D'Angelo, G.; Nicotera, A.; Parisi, E.; Di Rosa, G.; Gitto, E.; Arrigo, T. Oxidative Stress in Obesity: A Critical Component in Human Diseases. *Int. J. Mol. Sci.* **2015**, *16*, 378–400. <https://doi.org/10.3390/ijms16010378>.
71. Estuti, W.; Marliyati, S.A.; Damanik, R.; Setiawan, B. Relation of Body Mass Index, Waist Circumference, and Body Fat Percentage to Lipid Profile and Oxidative Stress Markers in Menopausal Women. *J. Nutr. Sci. Vitaminol.* **2020**, *66*, S486–S493. <https://doi.org/10.3177/jnsv.66.S486>.
72. Gunawardena, H.P.; Silva, R.; Sivakanesan, R.; Ranasinghe, P.; Katulanda, P. Poor Glycaemic Control Is Associated with Increased Lipid Peroxidation and Glutathione Peroxidase Activity in Type 2 Diabetes Patients. *Oxidative Med. Cell. Longev.* **2019**, *2019*, 9471697. <https://doi.org/10.1155/2019/9471697>.
73. Anedda, A.; Rial, E.; González-Barroso, M.M. Metformin Induces Oxidative Stress in White Adipocytes and Raises Uncoupling Protein 2 Levels. *J. Endocrinol.* **2008**, *199*, 33–40. <https://doi.org/10.1677/JOE-08-0278>.
74. Fontaine, E. Metformin-Induced Mitochondrial Complex I Inhibition: Facts, Uncertainties, and Consequences. *Front Endocrinol.* **2018**, *9*, 23–28. <https://doi.org/10.3389/fendo.2018.00753>.
75. Feng, J.; Wang, X.; Ye, X.; Ares, I.; Lopez-Torres, B.; Martínez, M.; Martínez-Larrañaga, M.-R.; Wang, X.; Anadón, A.; Martínez, M.-A. Mitochondria as an Important Target of Metformin: The Mechanism of Action, Toxic and Side Effects, and New Therapeutic Applications. *Pharmacol. Res.* **2022**, *177*, 106114. <https://doi.org/10.1016/j.phrs.2022.106114>.
76. Cahova, M.; Palenickova, E.; Dankova, H.; Sticova, E.; Burian, M.; Drahotka, Z.; Cervinkova, Z.; Kucera, O.; Gladkova, C.; Stopka, P.; et al. Metformin Prevents Ischemia Reperfusion-Induced Oxidative Stress in the Fatty Liver by Attenuation of Reactive Oxygen Species Formation. *Am. J. Physiol. Gastrointest. Liver Physiol.* **2015**, *309*, G100–G111. <https://doi.org/10.1152/ajpgi.00329.2014>.
77. Esteghamati, A.; Eskandari, D.; Mirmiranpour, H.; Noshad, S.; Mousavizadeh, M.; Hedayati, M.; Nakhjavani, M. Effects of Metformin on Markers of Oxidative Stress and Antioxidant Reserve in Patients with Newly Diagnosed Type 2 Diabetes: A Randomized Clinical Trial. *Clin. Nutr.* **2013**, *32*, 179–185. <https://doi.org/10.1016/j.clnu.2012.08.006>.
78. WHO. *World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects Adopted*; WHO: Geneva, Switzerland, 2001; Volume 79.

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