Hypoglycaemic and Antioxidative Properties of Freeze-Dried *Garcinia Kola* Seeds in Type 2 Diabetics and Non-Diabetics with Chronic Foot/Leg Ulcer in Ibadan, Nigeria: A case-control clinical study

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Summary

INTRODUCTION

The antidiabetic and antioxidative properties of *Garcinia kola* (GK) seed extracts have been well documented in animal studies; however, data on freeze-dried powder of GK seeds (FDGK) in humans are scarce. This study investigated the effect of 8-weeks supplementation of FDGK on glycaemic control and oxidative stress levels in Type 2 diabetics with or without foot/leg ulcer and compared with non-diabetics with or without chronic foot/leg ulcer in Ibadan, Nigeria.

MATERIALS AND METHODS

Thirty diabetics with foot/leg ulcer (DFU), 30 diabetics without ulcer (T2DM), 30 non-diabetics with chronic foot/leg ulcer (NDCU) and 30 non-diabetics without ulcer (NDC) were divided into: subgroup-1 (250mgGK); subgroup-2 (500mgGK); subgroup-3 (No-supplementation). Plasma glucose (FPG), glycated haemoglobin-A1c (HbA1c), total plasma peroxides (TPP), total antioxidant status (TAS), oxidative stress index (OSI), antioxidant-micronutrients were determined in fasting blood samples. Wounds were clinically assessed and rated using modified ABDEFS.

RESULTS

All participants supplemented with 250mgGK or 500mgGK for 8 weeks showed decreases in TPP and OSI with improvement in wound healing, increases in TAS and antioxidant-micronutrients ($p<0.05$).

In addition, significant decreases in FPG were observed in DFU and T2DM supplemented with 250mgGK, and also in NDC supplemented with 500mgGK. In non-supplemented subgroups, increases in TPP and OSI with decreases in TAS and antioxidant-micronutrients ($p<0.05$) were observed.

CONCLUSION

Supplementation with *Garcinia kola* could be used as an adjunct for prevention and treatment of diabetes mellitus complicated with or without foot/leg ulcer

RECOMMENDATIONS

Caution must be taken when used as prophylactic in non-diabetics to prevent occurrence of hypoglycaemia.

***Keywords**: Freeze-Dried Garcinia Kola Seeds, Hypoglycaemic Agent, Antioxidant Agent, Chronic Ulcer, Type 2 Diabetes Mellitus*

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Introduction

The incidence of diabetes mellitus (DM) is increasing exponentially across the globe including Africa, and especially in the sub-Saharan Africa populations [1]. This increase in DM is accompanied with a corresponding increase in the prevalence of foot complications and lower extremity amputations [2]. Nigeria, a country in the sub-Saharan Africa, has been reported to bear a greater burden of DM [3] and diabetic foot/leg ulcer (DFU) [4, 5].

In Nigeria, the average costs of successfully treating a patient with DFU is 1,200.00 US dollars or 1,000.00 EUR, which is equivalent to 181,581.00 NGN [4, 6]. This treatment cost was at the time of the publication; however at present day, where the official exchange rate is about 500 NGN to 1 USD, the equivalent cost is 600,000 NGN. This amount is unaffordable by most hospital patients with DM as half of Nigerian populations (50.1%) live below the poverty line in 2019 according to the World Development Indicator, WDI [7]. This number is even projected to increase due to the dual effects of the world pandemic COVID-19 and unstable oil prices. Besides the direct high economic cost and human resources involved in the management of DFU, the psychological costs of amputations are even higher and when the amputation involves the 'bread winner', the family is crippled [6,8]. There are also indirect costs relating to loss of productivity, individual patients' and family costs and loss of health related quality of life [6]. In general, DFU patients suffer the societal stigma of losing a limb and face difficulties of seeking or maintaining employment. The psychological trauma in some cases may lead to severe depression and eventually suicide [4]. In order to avert or reduce these psychological traumas, the question of how best to manage DFU with minimal cost that can be affordable by the populace then becomes imperative.

There have been exponential growth in the fields of herbal medicine and these herbs are gaining recognition both in the developing and developed countries because of their natural

origin, effectiveness and less side effects [9]. The growing public interest and awareness of natural medicines have led the pharmaceutical industry and academic researchers to pay more attention to medicinal plants [10]. Similarly, because the World Health Organization (WHO) has authenticated the use of herbal remedies for the treatment of DM [11], a resurgent interest in herbal medicines continues to play an important role in diabetic therapy; particularly in the developing countries where most people have limited resources and do not have adequate access to quality healthcare [12]. Consequently, the World Health Assembly (WHA) resolution on Traditional Medicine Strategy '2002-2005' was adopted in 2009 and updated in 2013 to support Member States for the decade (2014–2023). These strategic goals were "Harnessing the potential contribution of traditional medicine to health, wellness and people-centred health-care"; and "Promoting the safe and effective use of traditional medicine by regulating, researching and integrating traditional medicine products, practitioners and practice into health systems where appropriate" [13]. In line with these two goals, this study makes use of freeze-dried *Garcinia kola* (GK) seeds powder in the management of Type 2 diabetics and non-diabetics with or without foot/leg ulcers.

Garcinia kola (GK) is the botanical name for bitter kola, which is derived from the bitter astringent and resinous taste of the kola [14]. It is popular in Southern Nigeria, where it is extensively used as food and in herbal medicine [15]. The fruit, seeds, nuts and plant bark have been used for centuries in traditional medicine to treat ailments such as bronchitis, cirrhosis, hepatitis, throat infections, prevent or relieve colic disorders, cure head or chest colds and suppressed coughs [16]. Also, GK has been scientifically proven to possess purgative, antiparasitic, antimicrobial, anti-viral and anti-inflammatory properties [16,17]. The latex or gum of GK plant is used internally against gonorrhoea [18], and externally applied on fresh wounds to prevent sepsis, thus assisting in wound healing [18].

Furthermore, experimental studies using STZ-induced diabetic rats have reported that GK possesses some hypoglycaemic/antidiabetic [19,20], hypolipidemic/antilipidemic [20] and antioxidant [19,21] properties. In addition, it has been shown to possess hepatoprotective activities [22] and anti-atherogenic properties with great potential to protect against coronary heart disease [20]. Similarly, the administration of GK seed significantly improves the architecture of the kidney, liver and testes [19], enhance sperm characteristics and sexual drive (libido) [23], as well as restore the plasma levels of Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH), testosterone, Triiodothyronine (T_3), and Thyroxine (T_4) to normal [24]. Similarly, GK seed has been shown to possess significant anti-pyretic activity [25], significantly reduces intraocular pressure (IOP) when used as an eye drop [26] and be a potent anti-ulcer agent [27]. Premised on these biochemical and medicinal properties, GK may be useful in controlling glucose and reducing oxidative stress as well as help in the wound healing in people with chronic ulcer such as DFU.

Rationale of the study

From time immemorial, DM and its complications have been managed conventionally through the pharmacological means, including the use of insulin and/or oral hypoglycaemic agents, and/or the non-pharmacological therapy such as diet and exercise [28]. The pharmacological management protocol may not be affordable to all, especially the indigent populations, thus leading to lack of

or low compliance by this group of people [29]. Likewise, the pharmacological therapy may be associated with serious adverse effects, which include lactic acidosis, diarrhoea, and liver diseases among others [29,30]. Thus, there is need for scientific research to explore alternative and less expensive natural resources with effective therapy, which is relatively less toxic and easily available. These natural resources such as medicinal plants may either be used as substitute or act in synergy to other hypoglycaemic drugs [31].

Several medicinal plants, among which is GK, have been scientifically reported in rat experimental studies to lower plasma glucose [32,33] and enhance antioxidant system by inhibiting lipid peroxidation as well as scavenging free radicals [15,19,21,32]. Furthermore, the medicinal uses of the extracts (aqueous and ethanol among others) of GK have been well established in these rat studies; however, there is paucity of data on the use of freeze-dried powder samples of GK seeds in human studies. In addition, GK seeds are abundantly available and affordable in Nigeria. The freeze-dried powder sample is necessary because high moisture content in any organic compound or material can cause microbial contamination and growth and this may have negative impact on the long term storage of the aqueous form of the medicinal plants [34].

This study investigated the effect of 8-week supplementation with freeze-dried powder samples of GK seeds on glycaemic control and oxidative stress levels in Type 2 diabetics with or without foot/leg ulcer and compared with non-diabetics with or without chronic foot/leg ulcer in Ibadan, Nigeria.

Materials and Methodology

Study design, setting, population and intervention

This interventional case-control study with 8-week supplementation was conducted at the Metabolic Research Ward, Medical-Out-Patient (MOP) and Surgical Out-Patient (SOP) Clinics of the University College Hospital (UCH), Ibadan, Nigeria, West Africa, from January 2016 to September 2018. The study was designed as a single-blind study, which was blinded to all the participants, physicians and laboratory scientists except the researchers. The sample size was determined using the case-control formula: $[n = r+1(p^*)(1-p^*)[(Z_\beta + Z_{\alpha/2})^2/(p_1 - p_2)^2]$ as described by Charan and Biswas [35] giving a minimum of 30 participants per group.

A total of 120 male and female participants between the ages of 40 and 80 years were consecutively recruited and divided into 4 main groups namely: 30 Type 2 diabetics with foot/leg ulcer (DFU), 30 Type 2 diabetics without foot/leg ulcer (T2DM), 30 apparently healthy non-diabetics with chronic ulcer (NDCU) and 30 apparently healthy non-diabetics without ulcer (NDC). Each of the main group was further divided randomly into 3 subgroups: subgroup-1 received 250 mg/kg body weight/day of encapsulated GK (250 mg GK); subgroup-2 received 500 mg/kg body weight/day of encapsulated GK (500 mg GK) and subgroup-3 received no supplementation (NS). The random division was done using consecutive numbering system: first three numbers representing 250 mg GK, 500 mg GK and NS respectively and so on.

Ethical consideration and recruitment criteria

The study protocol was performed in accordance with the declaration of Helsinki and was approved by the joint University of Ibadan/University College Hospital Institutional Research Ethics Committee. Informed consent was obtained from each participant before enrolment into the study. All participants were briefed about the study and the option to quit the study at any time was given. Participants below 40 years or above 80 years, pregnant or lactating females, DFU and non-diabetics with chronic ulcer less than 6 weeks, diabetics with other complications such as retinopathy, nephropathy, autonomic neuropathy, and other comorbidities were excluded from the study. Also, excluded from the study are non-diabetics with fasting plasma glucose (FPG) in pre-diabetes level (5.6-6.9 mmo/L), non-diabetics with post-trauma ulcer, haematological ulcer and vasculitis, current smokers (cigarette or tobacco) and alcohol users.

The foot ulcers in DFU group were clinically graded using 'Wagner's Grades 1 and 2 ulcer' grading system [36]. All the DFU and T2DM participants were previously diagnosed according to the criteria of American Diabetes Association [37] and were continued on the medications prescribed by the attending physician, which include the use of single doses of metformin, glibenclamide or insulin only or combined doses of metformin with glibenclamide or metformin with insulin. All participants in DFU and T2DM groups received the herbal treatment as a supplement to the medications prescribed by the attending physician (conventional treatment), while the NS subgroups of DFU andT2DM groups were only on conventional treatment with no supplementation. The NS subgroups were not given placebo because of their diabetic conditions. During the study period, all participants were advised to adhere to the medications prescribed only by the attending physicians; adhere to the modified dietary instructions given by the dietician, stop self-prescription of any multivitamins or mineral supplements and abstain from eating bitter kola (GK) seeds.

Preparation and encapsulation of the freeze-dried GK seed powder

The grated seeds of GK were freeze-dried using a pressure freeze-drying machine at temperature of –65ºC and –40ºC (machine and sample temperature respectively) to a constant weight. The dried pulps were then blended into powder using a blender, sieved with laboratory sieve with a mesh size of 0.5 mm and the resulting sieved powdery samples were stored in air-tight containers at –20ºC until required. Two hundred and fifty (250) mg of freeze-dried GK seeds powder were measured into size 2 capsules using a manual mini homemade capsule filler CN–20 CL (CapsulCN International Co., Ltd, Zhejiang, China). The participants in the 250 mg GK subgroup were administered a capsule per day, while participants in the 500 mg GK subgroup were administered 2 capsules per day (1 capsule in the morning and 1 capsule at night). The dosage used was based on the extrapolated age and weight from the acute toxicity test carried out on rat model [38].

Physical Examination Procedure: Clinical assessment of ulcer

In this study, the modified ABDEFS tool of evaluating chronic ulcers by Oluwatosin *et al* [39] was adopted and used in clinical assessment of the wound healing progress. This evaluating tool is described below:

Aetiology: 1) Local, e.g. trauma, infection
2) Controlled systemic disease
3)Uncontrolled systemic disease
4) Malignancy

Size: 1) Less than or equal to 2.5 cm in one dimension
2) Greater than 2.5 cm in one dimension

Depth 1) Superficial partial thickness
2) Deep dermal
3) Full thickness

Re-epithelisation: 1) >75% of the wound
2) 50 – 75 of the wound
3) 25 – 49 of the wound
4) <25% of the wound

Granulation tissue:1) >75% of the surface area
2) 50 – 75 of the surface area
3) 25 – 49 of the surface area
4) <25% of the surface area

Slough 1) <25% of the surface area
2) 25 – 49 of the surface area
3) 50 – 75 of the surface area
4) >75% of the surface area

Necrotic tissue: 1) <25% of the surface area
2) 25 – 49 of the surface area
3) 50 – 75 of the surface area
4) >75% of the surface area

Odour 1) No odour
2) Faint odour at close range
3) Moderate odour in the room
4) Strong odour in the room

Exudates quantity: 1) No exudates
2) Scanty exudates
3) Moderate exudates
4) Large exudates

Edge: 1) Flat, shelving, punched out
2) Undermined, raised

Points corresponding to appropriate description were allocated to each feature on the ulcer. The minimum possible score of 10 corresponds to the best healing ulcers while the maximum score of 35 corresponds to the worst healing ulcers. The attending physicians did the wound assessment and recorded the grading.

Follow-up details

All participants were followed up for 8 weeks.

1. At the fixed date and time, participants were requested to undergo an overnight fast of about 10 to 12 hours until when blood samples were collected at 8.00 am the following morning.
2. Participants with wounds were assessed by the attending physician and these were documented.
3. All supplemented participants were given the encapsulated freeze-dried GK seed that was enough for use for two weeks. Each participant was asked to come back to the hospital fortnightly (if were out–patients) with the unused encapsulated herbs until the 8 weeks were completed. This was to check their level of compliance.
4. Participants in the NS subgroup were also asked to come back fortnightly for general health and wound assessments.
5. At each visit to the hospital, all participants were asked to list the multivitamins and mineral supplements as well as herbal supplements taken during the last 2 weeks. This was done to double check on the compliance with the instructions given at the very beginning of the study.
6. At 4 and 8 weeks of treatment, blood samples were collected from each participant respectively for the second and last determinations of biochemical parameters, to compare with the baseline measures. The attending physician to the participants again assessed the wounds and these were recorded.

Body Mass Index (BMI) classification and age stratification

The BMI is a ratio between weights to the squared height (kg/m^2) of a participant. The general population is classified into five categories based on BMI: low body weight or underweight (BMI<18.5 kg/m^2), normal-weight (BMI: 18.5-24.9 kg/m^2), overweight/class I obesity (BMI 25.0-29.9 kg/m^2), obese/class II obesity (BMI: 30.0-39.9 kg/m^2) and extremely obese/class III obesity (BMI > 40 kg/m^2) [40]. Similarly, according to Wen-Bing *et al*. [41], age was stratified into young adults (18-39 years), middle-aged adults (40-59 years) and senior adults (>60 years).

Blood samples collection, storage and variables

Ten millilitres of blood samples were collected after a 10 hour overnight fast from each participant at baseline, 4 and 8 weeks of supplementation with 250 mg GK, 500 mg GK or NS. The blood samples were collected and dispensed into appropriate tubes. Plasma samples were obtained by centrifuging at 3000 rpm for 10 minutes. All plasma samples and whole blood samples for micronutrient metals were stored in small aliquots at –80ºC until the day of analysis while samples for fasting plasma glucose (FPG) and glycated haemoglobin A1c (HbA1c) were analysed the same day of collection. Levels of glycaemic indexes including FPG and HbA1c; oxidative stress biomarkers such as total plasma peroxides (TPP), total antioxidant status (TAS), vitamin A, vitamin C, vitamin E, manganese (Mn), zinc (Zn), and selenium (Se) were determined while oxidative stress index (OSI) was calculated.

Laboratory determination of biochemical parameters

All tests were carried out using standard procedures. Fasting glucose, from fluoride oxalate plasma, was determined in-house using a commercial kit obtained from DIALAB (Austria). The technique as described by the manufacturer uses glucose oxidase method and was based on Trinder's reaction [42]. In this method, glucose was oxidized to gluconic acid and hydrogen peroxide in the presence of glucose oxidase. The formed hydrogen peroxide then reacts, in the presence of peroxidase, with phenol and 4-aminoantipyrine to form a quinonimine dye. The intensity of the pink colour formed was proportional to the glucose concentration and was measured using spectrophotometric method at wavelength of 500 nm (Spectro SC spectrophotometer, Labomed Inc. USA).

The levels of HbA1c were determined using Clover A1c test cartridge on the Clover A1c analyser (Infopia Co., Ltd, Korea). The method was based on automated boronate affinity assay. In this method, 4 μL of EDTA whole blood samples were collected at the sample collecting area of the reagent packs, then the reagent packs were inverted into the cartridges, where the blood samples were instantly lysed releasing the haemoglobin and the boronate resin binding the glycated haemoglobin. Thereafter, each cartridge was inserted into the Clover A1c Analyser. The blood sample mixture was automatically rotated, placing the blood sample in the measuring zone. The total haemoglobin was photometrically measured by the diffused reflectance of the optical sensor composed of both a Light Emitting Diode (LED) and a Photo Diode (PD).

Total plasma peroxide concentrations were determined in heparinised plasma samples

using FOX-2 assay according to the method described by Miyazawa [43] with minor modifications by Harma *et al*. [44]. This method is based on the oxidation of ferrous ion to ferric ion by various types of peroxides contained within the plasma samples to produce a coloured ferric-xylenol orange complex, which were measured spectrophotometrically at 560 nm (spectro SC spectrophotometer, Labomed inc. USA).

Plasma levels of TAS from heparin tubes were determined by a Fenton-type reaction described by Koracevic *et al*. [45]. In this method, standardization solution of Fe-EDTA complex reacts with hydrogen peroxide leading to the formation of hydroxyl radicals ($HO^{\cdot}$). These reactive oxygen species degrade benzoate resulting in the release of thiobarbituric acid reactive substance (TBARS). The antioxidants from the added samples of human blood or standards result in suppression of the production of TBARS and were measured spectrophotometrically at 532 nm using spectro SC spectrophotometer (Labomed Inc. USA). The rates of inhibition of colour were proportional to the concentrations of antioxidant status present in the samples.

The oxidative stress index (OSI) is an indicator of the degree of oxidative stress. It was calculated from the values of TPP and TAS using the formula (TPP/TAS x 100) [44].

Plasma vitamin A, vitamin C, and vitamin E from heparin tubes were determined by High Performance Liquid Chromatography (HPLC) system using HPLC Waters 616/6261c machine. Precipitating reagents were added to precipitate the higher molecular components, which were removed by centrifugation and supernatants were then injected into the HPLC system. The separation via HPLC follows an isocratic method at 30°C using a reversed phase column. Vitamin A were determined at 325 nm as described by Talwar *et al*. [46], vitamin C were determined at 270 nm using the method of Sanderson and Schorah [47] and vitamin E were determined at 290 nm [46].

Manganese, Zn and Se were determined in EDTA whole blood samples using Atomic Absorption spectrophotometry (AAS) technique. In this technique, the atoms of the element aspirated into the AAS vaporize and absorb light of the same wavelength as that emitted by the element when in the excited state. The procedures include thawing of frozen plasma samples and diluting with 0.1N hydrochloric acid (1:20) to release bound trace metals in order to enhance accurate measurement. The digested samples were aspirated directly into the AAS for analyses. Working standard solutions were prepared in part per million (ppm) and used for the standardization of the corresponding elements. Manganese, Zn and Se were determined by the technique respectively described by Casey *et al*. [48], Kaneko *et al*. [49], and Pleban *et al*. [50] using a 210/211 VGP atomic absorption spectrophotometer (Buck Scientific, USA).

Data analysis

All data were presented as frequency, percentages, and non-normally distributed variables as median with interquartile range (IQR). The data were subjected to statistical analysis using Statistical Package for Social Sciences (SPSS) version 20 (IBM Corp., Armonk, NY, USA). The descriptive analyses were performed using the Chi-square test for categorical variables. Wilcoxon signed rank tests were used for non-normally distributed continuous variables. A value of $p<0.05$ was taken as being statistically significant.

Results

The results for baseline and 8 weeks of GK supplementation were presented. A total of 120 participants were enrolled into the study, out of which, 110 participants completed the study with 10 participants lost to follow-up (Figure 1).

The data for the socio-demographic characteristics of the study population are shown in Table (1). In this table, DFU participants were mostly overweight/obese females between 50-59 years and were all married (70%, 56.7%, 60% and 100%, respectively), with one-third having secondary school education. T2DM participants, 53.3% were females ranging in age between 60-79 years (60-69 years, 30%; 70-79 years, 30%), and 60% were overweight/obese, 80% were married and 60% had secondary school education. The NDCU and NDC participants were mostly married (86.7% and 93.3%), normal-weight (70% and 83.3%), females (53.3% and 66.7%) and between 50-59 years (53.3% and 46.7%), respectively. Half (50%) of the participants in NDCU and 86.7% in NDC had tertiary education. The medical history of the study participants showed the durations of DM in DFU (50%) and T2DM (60%) were mostly less than 10 years (50% and 60%, respectively), with DFU (50%) and T2DM (73.3%) on single dosage of hypoglycaemic therapy. Most of the participants, in DFU (63.3% and 50%, respectively) and NDCU (80% and 67.7%, respectively), had non-healing wounds between 9-12 weeks, which were mostly managed with normal saline with iodine and dressing powder.

Tables (2 – 5) reveal the comparison of the mean values of glycaemic indexes, wounds, oxidative stress biomarkers and antioxidant micronutrients at baseline and 8-weeks of supplementation with 250 mg GK, 500 mg GK or NS in all the study participants.

In Table (2), significant decreases in FPG were found in DFU and T2DM participants supplemented with 250 mg GK while significant decrease was observed in NDC participants supplemented with 500 mg GK when baseline data were compared with 8 weeks of GK supplementation. Levels of HbA1c were observed to decrease significantly in DFU supplemented with 500 mg GK. Similarly, improvement in wound healing, as depicted by decreases in the wound assessment tool, were observed in DFU and NDCU participants supplemented with 250 mg GK or 500 mg GK. However, in NS subgroup, FPG significantly increased in T2DM and HbA1c decreases significantly in NDCU participants.

Table (3) revealed significant decreases in TPP and OSI levels across all the groups supplemented with 250 mg GK or 500 mg GK. Significant increases were observed in TAS of DFU and NDC supplemented with 250 mg GK or 500 mg GK; however, significant increases were found in T2DM and NDCU supplemented with 500 mg GK. In NS subgroups, increases in TPP and depletion of TAS were found across all the groups; while OSI increases in T2DM, NDCU and NDC groups ($p<0.05$).

In Table (4), significant increases were observed in vitamin A, vitamin C and vitamin E of all the groups supplemented with 250 mg or 500 mg GK, however in the NS subgroups, significant decreases were found across all the groups.

Lastly, in Table (5), significant increases in Mn and Zn were observed across all the groups supplemented with 250 mg or 500 mg GK while decreases in these parameters were found in the NS subgroups ($p<0.05$). However, the values of Se were observed to increase in T2DM supplemented with 500 mg GK and NDC supplemented with 250 mg or 500 mg GK ($p<0.05$).

Discussion

In the past decades, researchers have developed considerable interests in medicinal plants with more focus on dietary and medicinal phytochemicals that can inhibit, reverse or retard diseases resulting from oxidative and inflammatory processes [32]. *Garcinia kola* (GK), one of the several plants reported to possess medicinal properties, have been reported to elicit a number of pharmacological activities including anti-inflammatory, anti-atherogenic, anti-diabetic, analgesic, anti-oxidant, anti-genotoxic and hepatoprotective properties [21,32,51].

Premised on these properties, GK seeds have been reported to serve as raw material for pharmaceutical industries [52].

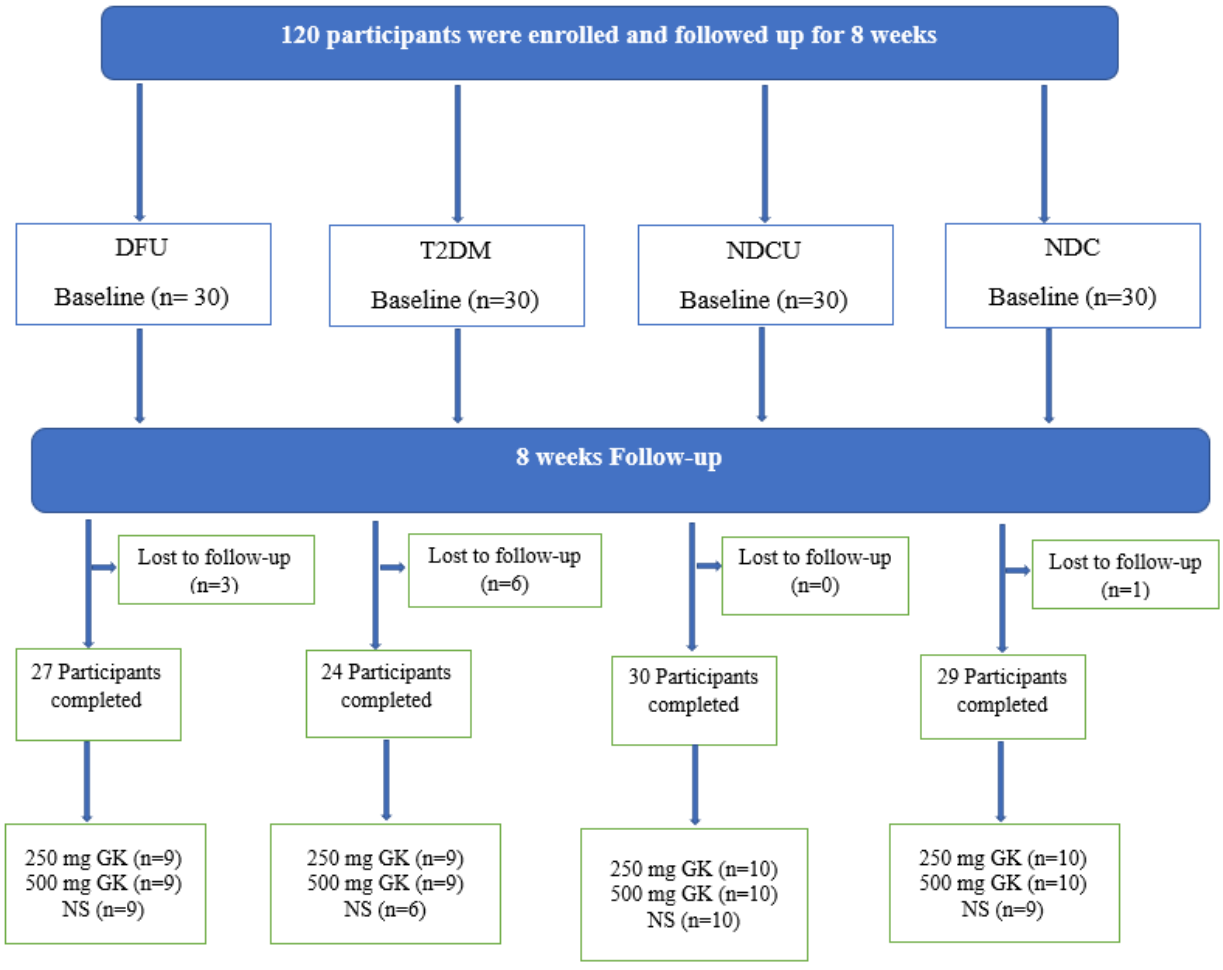

Figure 1: Flow Diagram of Study Population

Table 1: Socio-Demographic and Medical Characteristics of the Study Participants

Parameters	DFU n (%)	T2DM n (%)	NDCU n (%)	NDC n (%)	Chi-Square	p-values
Gender					**1.466**	**0.690**
Male	13 (43.3)	14 (46.7)	14 (46.7)	10 (33.3)		
Female	17 (56.7)	16 (53.3)	16 (53.3)	20 (66.7)		
Age Group					**37.052***	**0.000**
40-49	4 (13.3)	5 (16.7)	8 (26.7)	14 (46.7)		
50-59	18 (60)	7 (23.3)	16 (53.3)	14 (46.7)		
60-69	6 (20)	9 (30.0)	6 (20.0)	2 (6.7)		
70-79	2 (6.7)	9 (30.0)	0	0		
BMI					**22.810***	**0.000**
Underweight	0	0	0	0		
Normal weight	9 (30)	12 (40)	21 (70.0)	25 (83.3)		
Overweight/Obese	21 (70)	18 (60)	9 (30.0)	5 (16.7)		
Marital Status					**12.969***	**0.044**
Married	30 (100)	24 (80)	26 (86.7)	28 (93.3)		
Divorced	0	1 (3.3)	3 (10.0)	1 (3.3)		
Widow/Widower	0	5 (16.7)	1 (3.3)	1 (3.3)		
Education Level					**43.103***	**0.000**
No Formal Education	5 (16.7)	2 (6.7)	1 (3.3)	0		
Basic Education	6 (20.0)	3 (10.0)	8 (26.7)	0		
Secondary Education	10 (33.3)	18 (60.0)	6 (20.0)	4 (13.3)		
College and Above	9 (30.0)	7 (23.3)	15 (50.0)	26 (86.7)		
T2DM Duration (Years)					**3.257**	**0.354**
< 10	15 (50)	18 (60)	-	-		
10-20	13 (43.3)	7 (23.3)	-	-		
21-30	2 (6.7)	3 (10)	-	-		
>30	0	1 (3.3)	-	-		
Diabetes Mellitus Medication					**3.455**	**0.063**
Single Therapy	15 (50)	22 (73.3)	0	-		
Combined Therapy	15 (50)	8 (26.7)	0	-		
Wound duration					**3.359**	**0.186**
6-8 weeks	7 (23.3)	-	2 (6.7)	-		
9-12 weeks	19 (63.3)	-	24 (80.0)	-		
13-16 weeks	4 (13.3)	-	4 (13.3)	-		
Wound Dressing					**5.985**	**0.050**
Normal saline with iodine and dressing powder	15 (50.0)	-	21 (67.7)	-		
Compression bandage with nano crystallised silver	10 (33.3)	-	10 (32.3)	-		
Normal saline and honey	5 (16.7)	-	0	-		

*Significant at $p<0.05$

Table 2: Comparison of Baseline and 8 Weeks Post-Supplementation Glycaemic Index and Wound Assessment in All Sub-Groups

	250 mg GK				500 mg GK				NS		
Parameters	**Baseline Med(IQR)**	**8 weeks Med(IQR)**	**p-value**		**Baseline Med(IQR)**	**8 weeks Med(IQR)**	**p-value**		**Baseline Med(IQR)**	**8 weeks Med(IQR)**	**p-value**
DFU	**n=10**	**n=9**			**n = 10**	**n = 9**			**n = 10**	**n = 9**	
FPG(mmol/dL)	6.77 (6.48, 7.18)	6.12 (5.77, 6.50)	0.038*		6.07 (5.79, 6.47)	5.78 (5.66, 6.07)	0.109		7.11 (6.79, 7.29)	7.15 (6.69, 7.19)	0.153
HbA1c (%)	6.00 (6.00, 9.00)	6.00 (6.00, 8.00)	0.083		‡6.00 (5.75, 7.25)	‡6.00 (5.00, 6.50)	0.046*		7.00 (6.00, 11.00)	7.00 (6.00, 10.00)	0.317
WA	22.00 (20.00, 24.25)	18.00 (16.50, 20.50)	0.007*		21.50 (20.00, 24.25)	18.00 (16.50, 21.50)	0.007*		24.00 (21.75, 25.25)	24.00 (20.00, 24.50)	0.230
T2DM	**n = 10**	**n = 9**			**n = 10**	**n = 9**			**n = 10**	**n = 9**	
FPG(mmol/dL)	6.58 (5.64, 8.28)	5.63 (4.70, 5.85)	0.015*		6.23 (5.26, 7.87)	5.57 (4.50, 6.08)	0.066		5.72 (5.20, 6.83)	6.16 (6.09, 6.36)	0.046*
HbA1c (%)	6.00 (5.75, 8.25)	6.00 (5.50, 6.50)	0.157		6.00 (5.00, 9.00)	6.00 (5.00, 7.00)	0.317		5.50 (5.00, 6.00)	6.00 (4.75, 6.00)	1.000
WA	-	-	-		-	-	-		-	-	
NDCU	**n = 10**	**n = 10**			**n = 10**	**n = 10**			**n = 10**	**n = 10**	
FPG(mmol/dL)	4.43 (3.46, 5.39)	4.68 (3.83, 4.99)	0.575		4.37 (3.79, 5.56)	4.43 (3.99, 5.08)	0.646		4.60 (4.23, 6.10)	4.95 (4.61, 5.46)	0.575
HbA1c (%)	4.00 (4.00, 5.25)	4.00 (4.00, 4.25)	0.157		5.00 (4.00, 6.00)	5.00 (4.00, 5.25)	0.157		5.50 (5.00, 6.00)	5.00 (5.00, 5.00)	0.046*
WA	19.00 (17.00, 20.00)	15.00 (12.25, 17.00)	0.004*		17.00 (15.00, 18.25)	12.50 (10.75, 14.25)	0.005*		17.50 (17.00, 20.00)	18.50 (17.50, 20.00)	0.762
NDC	**n = 10**	**n = 10**			**n = 10**	**n = 10**			**n = 10**	**n = 9**	
FPG(mmol/dL)	4.86 (4.48, 5.23)	4.63 (4.31, 5.04)	0.514		4.97 (4.38, 5.42)	4.15 (3.88, 4.86)	0.005*		4.92 (4.29, 5.31)	4.97 (4.42, 5.25)	0.859
HbA1c (%)	4.50 (4.00, 5.00)	4.00 (4.00, 5.00)	0.317		5.00 (4.00, 5.00)	4.00 (4.00, 5.00)	0.083		4.50 (4.00, 5.00)	5.00 (4.00, 5.00)	0.317
WA	-	-	-		-	-	-		-	-	-

n=sample size for each group; p-value=Baseline compared with 8 weeks; Med(IQR)=median(interquartile range); FPG=Fasting plasma glucose; HbA1c=Glycated haemoglobin A1c; WA=wound assessment tool; ‡Mean values at baseline (6.40 %) and 8 week (5.78 %).

Table 3: Comparison of Baseline and 8-Weeks Post-Supplementation of Oxidative Stress Biomarkers in All Sub-Groups

	250 mg GK			500 mg GK			NS		
Parameters	**Baseline Med(IQR)**	**8 weeks Med(IQR)**	**p-value**	**Baseline Med(IQR)**	**8 weeks Med(IQR)**	**p-value**	**Baseline Med(IQR)**	**8 weeks Med(IQR)**	**p-value**
DFU	**n = 10**	**n=9**		**n = 10**	**n=9**		**n = 10**	**n=9**	
TPP (µmol/L)	87.56 (78.93, 95.18)	79.19 (76.65, 90.36)	0.007*	77.92 (59.52, 85.28)	74.62 (45.18, 78.69)	0.008*	81.98 (78.68, 90.86)	87.82 (81.73, 97.46)	0.037*
TAS (µmol/L)	1800.00(1300.00, 3400.00)	2000.00(1700.00, 3250.00)	0.007*	4250.00(2475.00, 5000.00)	4900.00(2900.00, 6050.00)	0.007*	1650.00(1125.00, 9800.00)	1500.00(950.00, 9100.00)	0.020*
OSI (%)	4.96 (2.73, 7.26)	3.96 (2.79, 5.32)	0.008*	1.74 (1.01, 2.86)	1.49 (0.82, 2.52)	0.008*	4.54 (0.93, 6.19)	3.84 (1.07, 9.50)	0.037*
T2DM	**n = 10**	**n = 9**		**n = 10**	**n = 9**		**n = 10**	**n = 9**	
TPP (µmol/L)	51.52 (36.42, 88.58)	40.61 (29.44, 80.46)	0.008*	33.76 (29.19, 63.07)	26.40 (23.10, 64.22)	0.011*	78.43 (48.60, 84.64)	84.78 (70.56, 92.77)	0.043*
TAS (µmol/L)	†2800.00(575.00, 5675.00)	†2800.00(850.00, 4550.00)	0.007*	3900.00(3025.00, 4725.00)	4100.00(3800.00, 5150.00)	0.008*	3500.00(2300.00, 5525.00)	3150.00(1725.00, 3650.00)	0.027*
OSI (%)	2.73 (1.15, 5.72)	2.13 (1.01, 4.43)	0.008*	0.98 (0.73, 1.88)	0.66 (0.52, 1.26)	0.008*	2.33 (1.16, 2.92)	2.93 (1.55, 5.02)	0.028*
NDCU	**n = 10**	**n = 10**		**n = 10**	**n = 10**		**n = 10**	**n=**	
TPP (µmol/L)	49.24 (37.44, 60.66)	47.72 (33.88, 58.38)	0.036*	54.82 (35.40, 63.96)	51.27 (31.98, 63.70)	0.014*	51.78 (40.99, 68.53)	53.81 (48.73, 69.04)	0.014*
TAS (µmol/L)	5500.00(2725.00, 11750.00)	6000.00(3025.00, 12225.00)	0.383	4300.00(1550.00, 15275.00)	4850.00(1850.00, 15725.00)	0.004*	6200.00(1950.00, 14225.00)	6100.00(1700.00, 14175.00)	0.273
OSI (%)	1.08 (0.40, 2.33)	0.82 (0.33, 3.16)	0.385	1.41 (0.22, 3.86)	1.17 (0.20, 3.14)	0.005*	0.84 (0.23, 2.91)	0.88 (0.28, 4.08)	0.013*
NDC	**n = 10**	**n = 10**		**n = 10**	**n = 10**		**n = 10**	**n = 9**	
TPP (µmol/L)	53.81 (37.56, 72.21)	48.43 (32.11, 66.63)	0.005*	53.30 (35.40, 71.45)	49.75 (31.98, 66.37)	0.005*	46.96 (23.86, 85.41)	51.27 (28.17, 90.61)	0.058
TAS (µmol/L)	11550.00(5050.00, 13850.00)	12200.00(5425.00, 14250.00)	0.005*	14450.00(9500.00, 16700.00)	14800.00(9975.00, 17025.00)	0.005*	14200.00(11375.00, 23375.00)	14100.00(11500.00, 25200.00)	0.287
OSI (%)	0.47 (0.33, 1.55)	0.41 (0.26, 1.32)	0.005*	0.42 (0.20, 0.85)	0.36 (0.19, 0.69)	0.005*	0.34 (0.14, 0.57)	0.40 (0.16, 0.60)	0.047*

n=sample size for each group; p-value=Baseline compared with 8 weeks; Med(IQR)=median(interquartile range); TPP: Total plasma peroxides; TAS: Total antioxidant status; OSI: Oxidative stress index; †Mean values at baseline (3130.0 µmol/L) and 8 week (3000.0 µmol/L).

Table 4: Comparison of Baseline and 8-Weeks Supplementation of Antioxidant Vitamins in All Subgroups

	250 mg GK			500 mg GK			NS		
Parameters	**Baseline Med(IQR)**	**8 weeks Med(IQR)**	**p-value**	**Baseline Med(IQR)**	**8 weeks Med(IQR)**	**p-value**	**Baseline Med(IQR)**	**8 weeks Med(IQR)**	**p-value**
DFU	**n = 10**	**n=**		**n = 10**	**n=**		**n = 10**	**n=**	
Vit. A (µmol/L)	3.01 (2.50, 3.14)	3.21 (2.53, 3.28)	0.007*	3.13 (2.47, 3.38)	3.32 (2.62, 3.52)	0.008*	2.75 (2.68, 3.15)	2.51 (2.38, 2.90)	0.010*
Vit. C (µmol/L)	17.58 (13.18, 19.18)	21.26 (15.67, 22.39)	0.008*	15.81 (11.56, 18.30)	20.74 (13.16, 22.48)	0.008*	13.30 (12.80, 18.68)	11.31 (10.45, 16.60)	0.108
Vit.E*10^6 (µmol/L)	†10.87 (10.35, 13.38)	†10.67 (10.39, 13.52)	0.007*	††11.39 (10.57, 12.12)	††11.35 (10.35, 12.39)	0.007*	9.10 (8.12, 10.91)	8.86 (8.06, 10.65)	0.010*
T2DM	**n = 10**	**n = 9**		**n = 10**	**n = 9**		**n = 10**	**n = 9**	
Vit. A (µmol/L)	3.03 (2.91, 3.18)	3.21 (3.09, 3.30)	0.008*	3.19 (3.03, 3.27)	3.32 (3.15, 3.43)	0.007*	3.06 (2.90, 3.24)	2.74 (2.62, 3.04)	0.028*
Vit. C (µmol/L)	19.35 (18.55, 20.05)	22.42 (21.72, 23.90)	0.008*	19.96 (17.48, 20.42)	22.43 (21.53, 24.25)	0.008*	20.12 (19.22, 20.78)	16.83 (16.46, 19.02)	0.028*
Vit.E*10^6 (µmol/L)	13.19 (12.08, 13.56)	13.24 (12.11, 13.65)	0.006*	‡12.22 (11.79, 12.99)	‡11.93 (11.78, 13.22)	0.007*	‡‡12.29 (11.99, 12.94)	‡‡12.58 (11.86, 12.87)	0.027*
NDCU	**n = 10**	**n = 10**		**n = 10**	**n = 10**		**n = 10**	**n = 10**	
Vit. A (µmol/L)	3.91 (3.54, 4.58)	4.04 (3.71, 4.74)	0.005*	4.11 (3.70, 4.68)	4.26 (3.85, 4.86)	0.005*	3.56 (3.38, 4.08)	3.32 (3.17, 3.85)	0.005*
Vit. C (µmol/L)	30.90 (28.13, 51.46)	33.57 (32.18, 54.54)	0.005*	32.57 (29.87, 54.57)	36.47 (32.85, 58.39)	0.005*	31.26 (28.38, 56.11)	27.77 (25.68, 56.17)	0.012*
Vit.E*10^6 (µmol/L)	14.93 (13.20, 17.80)	14.96 (13.24, 17.83)	0.004*	15.16 (12.93, 20.71)	15.21 (12.97, 20.75)	0.004*	16.15 (13.28, 17.61)	16.13 (13.25, 17.59)	0.007*
NDC	**n = 10**	**n = 10**		**n = 10**	**n = 10**		**n = 10**	**n = 9**	
Vit. A (µmol/L)	4.68 (4.37, 4.93)	4.81 (4.54, 5.08)	0.005*	4.34 (4.28, 4.54)	4.54 (4.43, 4.74)	0.005*	4.22 (3.94, 4.55)	4.05 (3.71, 4.39)	0.008*
Vit. C (µmol/L)	56.02 (51.08, 56.82)	59.18 (55.50, 61.53)	0.005*	56.07 (52.46, 58.22)	59.33 (56.46, 62.60)	0.005*	57.28 (56.21, 59.46)	57.28 (55.99, 59.69)	0.314
Vit.E*10^6 (µmol/L)	18.33 (17.50, 26.69)	18.36 (17.54, 26.73)	0.005*	19.11 (17.85, 25.90)	19.15 (17.90, 25.94)	0.003*	17.59 (16.93, 18.76)	17.45 (16.88, 18.77)	0.027*

n=sample size for each group; p-value=Baseline compared with 8 weeks; Med(IQR)=median(interquartile range); Vit. A: vitamin A; Vit. C: vitamin C; Vit. E: vitamin E; †Mean values at baseline (11.22 µmol/L) and 8 week (11.23 µmol/L); ††Mean values at baseline (11.32 µmol/L) and 8 week (11.35 µmol/L); ‡Mean values at baseline (12.42 µmol/L) and 8 week (12.45 µmol/L); ‡‡Mean values at baseline (12.51 µmol/L) and 8 week (12.47 µmol/L).

Table 5: Comparison of Baseline and 8-Weeks Supplementation of Antioxidant Metals in All Subgroups

	250 mg GK				500 mg GK				NS		
Parameters	**Baseline Med(IQR)**	**8 weeks Med(IQR)**	**p-value**		**Baseline Med(IQR)**	**8 weeks Med(IQR)**	**p-value**		**Baseline Med(IQR)**	**8 weeks Med(IQR)**	**p-value**
DFU	**n = 10**	**n=**			**n = 10**	**n=**			**n = 10**	**n=**	
Mn (nmol/L)	133.08(111.15, 145.91)	147.41(112.55, 150.00)	0.008*		127.23(108.10, 155.19)	130.85(120.72, 163.77)	0.008*		117.89(112.26, 120.48)	115.88(111.21, 120.79)	0.015*
Zn (µmol/L)	12.01 (9.61, 15.16)	12.78 (10.29, 16.03)	0.008*		12.78 (9.82, 15.35)	13.86 (10.97, 16.62)	0.008*		10.74 (8.91, 11.08)	9.94 (7.73, 10.67)	0.011*
Se (µmol/L)	0.02 (0.01, 0.02)	0.02 (0.01, 0.03)	0.157		0.02 (0.02, 0.02)	0.02 (0.02, 0.03)	0.317		0.02 (0.01, 0.02)	0.02 (0.01, 0.02)	0.083
T2DM	**n = 10**	**n = 9**			**n = 10**	**n = 9**			**n = 10**	**n = 9**	
Mn (nmol/L)	144.77(139.37, 152.31)	147.41 (141.29, 158.65)	0.008*		164.04 (144.14, 174.67)	172.61 (152.36, 177.95)	0.008*		160.10 (136.16, 167.43)	157.39 (149.98, 165.28)	0.028*
Zn (µmol/L)	15.17 (14.55, 15.42)	16.10 (15.40, 16.66)	0.008*		15.28 (15.11, 15.58)	16.12 (16.04, 16.44)	0.008*		15.37 (15.17, 15.45)	14.59 (14.27, 14.62)	0.028*
Se (µmol/L)	0.03 (0.03, 0.03)	0.03 (0.03, 0.04)	0.083		†0.03 (0.02, 0.03)	†0.03 (0.03, 0.04)	0.046*		0.03 (0.03, 0.03)	0.03 (0.02, 0.03)	0.083
NDCU	**n = 10**	**n = 10**			**n = 10**	**n = 10**			**n = 10**	**n = 10**	
Mn (nmol/L)	191.93 (153.38, 224.96)	194.02 (155.53, 228.38)	0.005*		195.66 (176.33, 235.50)	197.96 (179.30, 238.12)	0.005*		187.23 (164.14, 205.02)	185.92 (161.82, 203.03)	0.005*
Zn (µmol/L)	12.80 (11.66, 16.39)	13.64 (12.45, 17.68)	0.005*		14.42 (11.13, 17.87)	15.26 (11.94, 19.27)	0.005*		13.33 (11.02, 14.69)	12.44 (9.92, 14.24)	0.007*
Se (µmol/L)	0.03 (0.03, 0.04)	0.03 (0.03, 0.04)	0.157		0.04 (0.03, 0.05)	0.04 (0.03, 0.05)	0.317		0.04 (0.03, 0.04)	0.03 (0.03, 0.04)	0.317
NDC	**n = 10**	**n = 10**			**n = 10**	**n = 10**			**n = 10**	**n = 9**	
Mn (nmol/L)	279.82 (258.82, 291.91)	282.35 (261.61, 295.07)	0.005*		215.18 (204.13, 276.70)	217.26 (207.13, 279.77)	0.005*		243.58 (210.57, 277.24)	268.91 (207.00, 278.68)	0.008*
Zn (µmol/L)	15.82 (15.06, 17.85)	17.08 (16.10, 18.52)	0.005*		17.67 (15.60, 18.66)	18.91 (17.27, 19.66)	0.005*		15.89 (14.85, 19.37)	15.37 (14.47, 19.92)	0.021*
Se (µmol/L)	0.04 (0.04, 0.04)	0.05 (0.04, 0.05)	0.025*		0.04 (0.04, 0.05)	0.05 (0.04, 0.06)	0.025*		0.04 (0.04, 0.04)	0.04 (0.04, 0.05)	1.000

n=sample size for each group; p-value=Baseline compared with 8 weeks; Med(IQR)=median(interquartile range); Mn: Manganese; Zn: Zinc; Se: Selenium; †Mean values at baseline (0.028 µmol/L) and 8 week (0.032 µmol/L).

In this study, the socio-demographic data revealed a non-significant increase in the number of female participants than males across all groups. This finding can be supported by the research studies by Hilawe *et al*. [53] where DM was reported to be more prevalent in women than in men in Cameroon, South Africa, Uganda and sub-Saharan Africa. However, it contradicted the findings in Ghana and Sierra Leone where DM was more in men than women [53]. This study also disagrees with the study by Li *et al*. [54], where more men were reported to have DM than women. Similarly in this study, foot/leg ulcers were more common in females with or without T2DM than in males. This finding agreed with the study of Akaa *et al*. [55] and contradicted the study of Danmusa *et al*. [56].

The higher number of females with T2DM and foot/leg ulcer observed in this study may be due to the fact that women generally are more conscious of their health and the health of their families, thus attend hospital more than men.

Secondly, higher numbers of females with chronic foot/leg ulcers may be due to their greater involvement in outdoor activities, especially when trying to complement their spousal efforts in raising money for the families. Gone are the days when women were mostly "house wives" and financial responsibilities lied solely on their husbands' shoulders.

Finally, the occurrence of DM, especially DFU, in more females than males implied that many home maintenances/upkeeps would be affected as women are traditionally 'caretakers of homes', thus affecting families' well-being.

Similarly in this study, the socio-demographic results revealed that T2DM occurred more from age 50 years and above, especially at the senior adults age grouping (≥60 years), while foot/leg ulceration was observed to be more frequent in middle-aged adults (50-59 years). This finding is consistent with the previous report where older age was implicated in the development and progression of T2DM and DFU [57]. Overweight or obesity is another risk factor associated with T2DM and its associated complication [58]. In this study, most participants in DFU and T2DM were either overweight or obese (Class I obesity) [40]. This finding further support earlier studies where overweight/obesity were implicated in aetiology of T2DM and its complication including DFU [58,59]. Therefore, there is need to continually educate people with T2DM, during the health talks, to reduce their weight as obesity can also contribute to impaired glucose homeostasis.

This study also revealed that most of the participants were married and educated with at least secondary education. This level of education may have contributed to the understanding displayed by the participants to the importance of the research study, hence their willingness to participate in the study and complied with the instructions of the study. The onset of foot ulcer in most of the study participants with DM of less than 10 years duration suggested poor control of glycemia and therefore a strong indication for tighter control regime in diabetic patients. This is to prevent occurrence of diabetic complications in these patients.

In this study, supplementations with 250 mg GK were shown to reduce FPG in DFU and T2DM; while supplementation with 500 mg GK reduces FPG in NDC participants. However, in the NS subgroups, FPG levels were found to be elevated. These findings supported the previous studies in animals, where GK was reported to lower hyperglycaemia and thus possessed antidiabetic properties [32,33,60]. Consequent to the reduction of FPG in NDC participants

supplemented with 500 mg GK, there is need to monitor the glucose levels when using this supplement, especially at higher dosage, as prophylactics in non-diabetics.

Similarly, GK has been reported as a beneficial therapy in managing wounds in diabetes mellitus [61]. Therefore in this present study, the GK attributed decrease in plasma glucose may have contributed to the improvement in wound healing observed in the DFU and NDCU participants supplemented with 250 mg GK or 500 mg GK; while non-supplementation may have worsen hyperglycaemia, especially in DFU, and consequently the no change in wound healing observed in the DFU and NDCU participants. The improvement in wound healing of DFU and NDCU supplemented with 250 mg GK or 500 mg GK can be supported by the study of Nwaehujor *et al*. [61].

Similarly in this study, supplementation with either 250 mg GK or 500 mg GK significantly lower the levels of oxidative stress biomarkers, as depicted by the significant decreases in TPP and OSI levels as well as enhanced total antioxidant defence system, depicted by the substantial increases in levels of vitamin A, vitamin C, vitamin E, Mn, Zn and TAS. These findings corroborated the previous studies by Farombi and Owoeye [32], Mazi *et al*. [15] and Joshua *et al*. [21]. These researchers reported the antioxidative properties of GK in animal studies.

Limitations

The main limitation of this study is the use of relatively small sample size. Further study involving a large sample size is therefore recommended to validate the antidiabetic and antioxidative properties of the freeze-dried powder samples of *Garcinia kola* seeds in humans.

Conclusion

Garcinia kola seeds possess hypoglycaemic properties, effectively enhanced wound healing, reduced oxidative stress and improved antioxidant defence system in Type 2 diabetics with or without foot/leg ulcer as well as non-diabetics with or without chronic foot/leg ulcer in Ibadan, Nigeria. Therefore, Garcinia kola as either therapeutic or prophylactic measure can be used as a potential source of natural antioxidant and hypoglycaemic agents. However, as an hypoglycaemic agent, especially at higher dosage, caution must be taken when using it for prophylactic purposes in non-diabetics in order to prevent occurrence of hypoglycaemia in these people.

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Authors' Contributions

The contributions of the authors are stated as follows: EBB, OMA and AAK conceived the idea and designed the study; AAO, JOM, AOI and AAF added intellectual input to the proposal; EBB wrote the proposal and prepared the manuscript; EBB, OJA and ATA acquired and analysed the data; AAO, AFA, OMA, JOM and AAK contributed to the drafting of the manuscript, performed manuscript editing and review. All Authors approved the final version

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