Antidiabetic and Antiradical Effects of *Garcinia kola* Seeds in Dexamethasone-Induced Hyperglycemic Rats

**Abstract**

**Background:** In traditional medicine, the maceration of seeds of *Garcinia kola* (GK) is used to treat various diseases including diabetes. In traditional pharmacopoeia, GK seeds are used to strengthen the immune system and as a stimulant and aphrodisiac. **Aims:** This study aimed to evaluate the antidiabetic and antiradical scavenging effects of the hydroalcoholic extract of GK seeds (HAEGS) in a dexamethasone-induced hyperglycemic (DexIH) rat model. **Settings and Design:** This study was an interventional study. **Subjects and Methods:** Here using *in vivo* model, we assessed some pharmacological properties of HAEGS in DexIH rat. Hypoglycemia, antihyperglycemia, spasmolytic and laxative activities were also evaluated in DexIH. **In vitro** study assessed antiradical activity. The HAEGS was obtained by decocation introducing 250 g with water–ethanol mixture (30:70). The plant extract was administered to the animals at doses of 50 (GK50) and 100 (GK100) mg/kg body weight. All animal experiments were in accordance with ARRIVE guidelines and were performed in accordance with the scientific procedures of UK Animals. Antiradical activity of GK was assessed *in vitro* by inhibition of the activity of 2,2-diphenyl-1-picrylhydrazyl. **Statistical Analysis Used:** Statistical analysis was performed using GraphPad Prism 5.03 software, and *P* values less than 0.05 were considered statistically significant. **Results:** At doses 50 and 100 mg/kg, GK significantly (*P* < 0.001) regulated DexIH after two weeks of treatment compared to the normoglycemic control and hyperglycemic rats. The extract at both doses significantly (*P* < 0.001) inhibited the spasmolytic activity in both normoglycemic and hyperglycemic rats compared to lomiodin®. In rats DexIH rats, only dose 100 mg/kg significantly (*P* < 0.05) increased laxative effects when compared to the negative control. **Conclusions:** This study justifies the traditional use of GK seeds as an antidiabetic.

**Keywords:** 2,2-diphenyl-1-picrylhydrazyl scavenging, dexamethasone, *Garcinia kola*, intestinal transit, oral glucose tolerance test, rat

**Introduction**

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia due to defect in insulin secretion, insulin action, or both.[1] Insufficient insulin secretion and insulin resistance are the basic pathologic characteristics of type 2 diabetes mellitus (T2DM).[2] In general, diabetes sets in following a metabolic disorder also called metabolic syndrome, which is manifested by frequent headaches, fatigue, dizziness, visual disturbances, frequent urges to urinate, and drowsiness among others. Oxidative stress is closely associated with diabetes mellitus, particularly T2DM, where it very often causes micro- and macroangiopathies. Oxidative stress has been known to cause damage to the cells, tissues, even to organs by impairing important biomolecules and cells.[3] Production of high levels of reactive oxygen species (ROS) causes a significant decrease in antioxidant defense mechanisms, leading to protein, lipid and DNA damage, and subsequent disruption of cellular functions and cell death, but at lower levels induce subtle changes in intracellular signaling pathways.[4]

Many plants are traditionally considered antidiabetic or are involved in treating the complications of diabetes. *Garcinia kola* (GK) seeds, stem bark, and roots are part of these plants heavily used in traditional pharmacopoeia in the treatment of diabetes mellitus.[5-7] The seeds of GK are bitter, they are used as a stimulant and aphrodisiac, and are generally chewed like kola nuts all day long and without moderation largely by the elderly. Other

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How to cite this article: Nkono Ya Nkono BL, Rouamba A, Kinyok MCJ, Omokolo JGS, Tcheudi BT, Tigui BA, et al. Antidiabetic and antiradical effects of *Garcinia kola* seeds in dexamethasone-induced hyperglycemic rats. Int J App Basic Med Res 2022;12:203-10.
medicinal use of *Garcinia kola* (GK) seeds intervene in cold symptoms, antimicrobial, diarrhea, dysentery, liver disorders, poison antidote, and sickle cell.\(^9\)

Recently, it was reported that the reduced glucose concentration could be due to the activity of bitter kola seed extract against inflammation and ROS of free radicals on the pancreatic beta cells.\(^9\) It has also been reported that GK seed ameliorates renal, hepatic, and testicular oxidative damage in streptozotocin-induced diabetic rats. GK seed administration significantly ameliorated hyperglycemia-mediated damage by decreasing the blood glucose level (72.8% and 84.6% on the 7th and 14th posttreatment days, respectively).\(^10\) It has been reported in many investigations that bioactive fractions of different medicinal plants having free radical scavenging and antioxidant are used in many diseases such as cancer, tissue inflammatory, and cardiovascular disease.\(^11\)-14

Therefore, this study aimed to evaluate the *in vivo* antidiabetic and *in vitro* free radical scavenging effects of hydroalcoholic extract of GK seeds (HAEGS) in a dexamethasone-induced hyperglycemic rat model.

### Subjects and Methods

#### Place and duration

This study was an interventional study; the *in vivo* experimental aspect of this study was conducted at the Laboratory of Animal Physiology between May and July 2020. The *in vitro* experimental study was carried out at the Applied Biochemistry and Chemistry Laboratory, during the same period.

#### Chemicals and drugs

Chemicals were from analytical grade: Dexamethasone sodium phosphate (Rotexmedica®, Panpharma, Germany), D- (+)-glucose (Sigma Aldrich, Germany), glibenclamide (Daonil®, Sanofi, Pari-France), loperamide hydrochloride (Imodium®, Jasen, street Camille Desmoulins-France), sodium picosulfate (Fructin®, DB Pharma, Château Neuf-France), methanol (Prolabo Paris, France). 2,2-diphenyl-1-picrylhydrazyl (DPPH), ascorbic acid (Vitamin C), aluminum trichloride (AlCl₃), quercetin, and dimethyl sulfoxide (DMSO) were purchased by Sigma–Aldrich (St. Louis-USA).

#### Plant materials

The decoction of the hydroalcoholic (30% water and 70% ethanol) extract of GK seeds was obtained by introducing 250 g of powder into an Erlenmayer flask by supplementing the total volume to 1 L with water–ethanol mixture (30:70) and then brought to boil at 80°C for 15 min. After cooling and filtration with Whatman paper No. 4, the filtrate was concentrated with Rotavapor. The extract was reconstituted in 100% DMSO solution for purification and filtered through a 0.45 µm diameter microporous filter and then prepared at 1% by dissolving in distilled water at concentrations of 5 mg/mL and 10 mg/mL for administration to animals at doses of 50 and 100 mg/kg.

### Study design and population

#### Animals

All animal experiments were in accordance with ARRIVE guidelines and were performed in accordance with the scientific procedures of UK Animals.\(^15\)

To evaluate antidiabetic properties, 30 rats of Wistar strain were used. The animals were divided into 5 groups of 6 rats each (the sixth animal was used for making histological sections). Glibenclamide 2.5 mg/kg was used as a positive control. To evaluate the effect of GK on intestinal transit in normoglycemic and hyperglycemic rats, we used 48 rats. Each group consisted of 3 normoglycemic rats and 3 hyperglycemic rats. Imodium® and Fructin® were used as positive controls, respectively, for the evaluation of the spasmylocytic and laxative effect of GK. All the animal experiments were carried out in accordance with the guidelines of Cameroon National Ethics committee (Ref. FWIRB 00001954).

#### In vivo study

##### Induction of hyperglycemia

Induction of hyperglycemia was done as previously reported.\(^16\) Briefly, hyperglycemia was induced in rats by repeated administration of dexamethasone sodium phosphate (Rotexmedica®, Germany) for 3 days at a dose of 4 mg/kg body weight intravenously once daily between 7 a.m. and 8 a.m. After administering the last dose of dexamethasone, the animals were subjected to a 12-hour food fast, then the fasting blood glucose levels were measured using a OneTouch Ultra brand glucometer. The animals which had a fasting blood glucose level greater than 120 mg/dl were selected for carrying out our experiments.

##### Grouping of experimental animals

The rats were divided into five groups of six animals each for blood glucose level tests as following:

- **Group 1**: Negative fasting control group (NFC), normoglycemic animals that did not receive oral glucose overload at any time during the entire duration of the test/negative normal control (NNC), normoglycemic animals having undergone oral glucose overload. The NFC and NNC animals did not receive any treatment but rather received orally a solution of 1% DMSO (10 mL/kg) which served as vehicle.
- **Group 2**: NDC: Negative dexamethasone-induced hyperglycemic rats control group (NDC). The animals of the NDC group were the hyperglycemic animals and received no treatment other than the vehicle solution of...
1% DMSO (10 ml/kg, p.o).
• Group 3: GK50: Dexamethasone-induced hyperglycemic rats treated with GK 50 mg/kg (p.o)
• Group 4: GK100: Dexamethasone-induced hyperglycemic rats treated with GK 100 mg/kg (p.o)
• Group 5: Glib2.5: Dexamethasone-induced hyperglycemic rats treated with glibenclamide at a dose of 2.5 mg/kg (p.o).

For the spasmolytic and laxative tests, the animals were divided as follows:
• Group 1: Negative control normoglycemic and negative control hyperglycemic animals given 9% NaCl solution, p.o (10 ml/kg)
• Group 2: Normoglycemic and DexIH animals as positive control group received Imodium® (2 mg/kg, p.o) or Fructine® (5 mg/kg, p.o).
• Group 3 and 4: Normoglycemic and hyperglycemic animals treated with respective doses of 50 and 100 mg/kg of GK (p.o).

*Treatment of animals with hydroalcoholic extract of* *Garcinia kola* *seeds*

The animals received HAEGS orally once daily for 14 days at doses of 50 and 100 mg/kg, which are minimal therapeutic doses. These doses were estimated after screening based on the therapeutic dose used in traditional medicine.

*Oral glucose tolerance test*

To carry out this test, the animals were fasted on food and not on water for a minimum of 12 hours, and then the fasting blood glucose level was measured. The OGTT was performed in normoglycemic animals on the first day before induction of hyperglycemia and on the fourteenth day in hyperglycemic-induced dexamethasone rats after a 14-day pretreatment with plant extract and different treatments. Blood glucose level was measured at minute zero using a OneTouch Ultra brand glucometer from the tail puncture of the rats, and the various treatments were immediately administered to the animals by gastric intubation. Thirty minutes after the administration of the various treatments, all groups of animals received D-glucose at a dose of 3 g/kg of body weight orally. Blood glucose level was then measured at 30, 60, 90, and 120 min after glucose load.

*Evaluation of gastrointestinal motility*

30 min after oral administration of fructose, Imodium and HAEGS at two test groups (50 and 100 mg/kg respectively), animals received 10% charcoal suspension (20 ml/kg, p.o). Twenty minutes after oral gavage of the 10% charcoal suspension, the animals were sacrificed after anesthesia with ketamine (50 mg/kg). The small intestine was then completely removed from each animal after performing a midline laparotomy by sectioning from the pylorus to the cecum when avoiding pulling it. The total length of the small intestine (TLSI), as well as the length travelled by the charcoal suspension (LTCS), was measured.

The determination of the spasmyloytic and laxative effects (%) was made by calculation as previously described\(^{[15]}\) using equations (1) and (2) as follows:

\[
\text{Spasmolytic effect} \( \% \) = 100 - \left( \frac{\text{LTCS}}{\text{TLSI}} \right) \times 100 \quad (1)
\]

\[
\text{Laxative effect} \( \% \) = \left( \frac{\text{LTCS}}{\text{TLSI}} \right) \times 100 \quad (2)
\]

*In vitro study*

2,2-diphenyl-1-picrylhydrazy radial scavenging activity

Antiradical activity of GK seeds was assessed in vitro by inhibition of the activity of DPPH. The DPPH radical scavenging assay was performed as previously described\(^{[18]}\) The DPPH radical is a stable purple-colored radical. It discolors in the presence of an antioxidant compound, which reduces it to a colorless nonradical molecule. The discoloration of the DPPH radical in the presence of the antioxidant compound is monitored using a spectrophotometer at 517 nm.

In a 96-well plate, 100 µL of solution of the DPPH radical dissolved in methanol (20 µg/mL) was mixed with 100 µL of plant extract dissolved in methanol at different concentrations (250 µg/mL – 3.90625 µg/mL). A well without plant extract served as a control and contained only 100 µL of methanol and 100 µL of the DPPH solution. The plate was incubated for 15 min protected from light, and the optical density (OD) was measured at 517 nm using an Epoch brand spectrophotometer. The experiment was carried out in triplicate and the percentage radical scavenging activity (RSA) was calculated according to the formula as follows.

\[
\text{RSA} \( \% \) = \left( \frac{\text{control} - \text{sample}}{\text{control}} \right) \times 100 \quad (3)
\]

Ascorbic acid was used as a positive control and the concentration of 25 µg/mL showed 86.74% radical scavenging activity.

*Total flavonoid content*

To determine total flavonoid content in the sample of HAEGS, the aluminum chloride colorimetric method was used\(^{[19]}\) A volume of 100 µL of 2% AlCl, dissolved in methanol was mixed with an equal volume of extract diluted in methanol (initial concentration 1 mg/mL). Absorbance was measured after 10 min incubation at 37°C away from light at a wavelength of 415 nm against a blank. The blank consisted of a mixture of 100 µL of 2% AlCl3 and 100 µL of methanol.

Quercetin was used as a reference compound for establishing the standard curve. Stock quercetin solution was prepared by dissolving 5.0 mg quercetin in 1.0 mL methanol, and
then the standard solutions of quercetin were prepared by serial dilutions using methanol (5–200 μg/mL). The experiment was repeated in triplicate and the results were expressed in mg quercetin equivalent (QE) per mass of dry extract (mg QE/mass of extract). The concentration of total flavonoid content in the test samples was calculated from the calibration plot (Y = 0.02X + 0.0116, R² = 0.9997).

**Statistical analysis**

All the tests were performed as individual triplicate experiment (for *in vitro* tests as well as for the evaluation of intestinal transit) and quintuple experiment (for *in vivo* evaluation of hypoglycemic and antihyperglycemic properties). The data were analyzed with the GraphPad Prism software version 5.0.3. All the data were expressed as mean ± standard error of mean (n = number of experiments). The statistical analyses were obtained by the analysis of variance, followed by the Bonferroni’s posttest where necessary. The confidence interval was set at 95% with a significance threshold of less than 5% (P < 0.05).

**Results**

**Effect of hydroalcoholic extract of *Garcinia kola* seeds on oral glucose tolerance test**

Figure 1 shows the effect of HAEGS on OGTT in normoglycemic and dexamethasone-induced hyperglycemic (DexIH) rats.

After two weeks of treatment, all groups of animals recovered a fasting blood sugar level (12 h) around normal values [Figure 1c] with the highest fasting blood level in the DexIH negative control group NDC (81.16 ± 2.72 mg/dL) who received exclusively dexamethasone, followed by the glycaemia of the normal negative control (NNC) group (73.00 ± 1.03 mg/dL). Compared to the NNC and NDC groups after two weeks of treatment, taking fasting blood glucose (12 h) revealed that HAEGS had a nonsignificant hypoglycemic effect (P > 0.05) at the two doses tested with a greater effect at the dose of 50 mg/kg (68.33 ± 1.58 mg/dL) compared to the dose of 100 mg/kg (72.66 ± 1.14 mg/dL).

To assess glucose intolerance on normoglycemic and DexIH rats, OGTT was performed. Figure 1a shows that different treatments of HAEGS non-significantly prevented postprandial glycemia peak in normoglycemic rats when compared to the NNC group. This result is similar to that of the positive control group (Glib2.5) that received glibenclamide at a dose of 2.5 mg/kg [Figure 1b].

In DexIH rats, only dose 100 mg/kg of HAEGS significantly prevented the postprandial glycemia peak when compared to NNC and NNC groups [Figure 1c]. In the positive control group, glibenclamide reduced postprandial glycemia highly significantly (P < 0.001) only at the 2nd h after oral glucose overload compared to the NNC and NDC groups [Figure 1d].

**Effect of HAEGS on intestinal transit**

The effects of HAEGS on intestinal transit are shown in Figure 2. In normoglycemic rats, the plant extract inhibited spasmolytic activity (P<0.001) in a dose-response manner (30.84 ± 8.19% and 23.88 ± 2.64% at 50 and 100 mg/kg, respectively) when compared to the positive control group that received the reference drug (Imodium). Compared to the...
negative control group that received the vehicle, it should be noted that only the 100 mg/kg dose of HAEGS induced a significant spasmolytic effect \( (P < 0.05) \) only in DexIH rats \( (37.82 \pm 2.22\% \) and \( 18.26 \pm 0.51\% \), respectively, for the group that received the vehicle and the group that received the HAEGS at the dose of 100 mg/kg). With regard to the evaluation of the laxative effect of HAEGS, no significant difference \( (P > 0.05) \) was observed in normoglycemic animals compared to the positive control groups that received Fructine® and the negative control that received the vehicle [Figure 2b]. On the other hand, in DexIH rats, only dose 100 mg/kg significantly \( (P < 0.05) \) increased laxative effects when compared to the negative control. The potentiation of this effect was dose related because no significant difference \( (P > 0.05) \) was observed in both normoglycemic and hyperglycemic rats in comparison to the reference laxative drug Fructin® [Figure 2b]. It should also be noted that only the 100 mg/kg dose of HAEGS induced in DexIH rats a significant increase \( (P < 0.05) \) in the laxative effect \( (81.74 \pm 0.51\%) \) compared to the negative control group \( (62.20 \pm 2.22\%) \) [Figure 2b].

**Effect of hydroalcoholic extract of *Garcinia kola* seeds on 2,2-diphenyl-1-picrylhydrazyl free radical scavenging**

*In vitro* antiradical activity of HAEGS revealed vitamin C-like antiradical activity [Figure 3]. The lowest concentration tested on DPPH radical scavenging had a percentage of \( 6.87 \pm 0.56\% \) for HAEGS \( (3.90625 \mu g/mL) \) and \( 17.96 \pm 3.06\% \) for Vitamin C \( (0.39062 \mu g/mL) \), which showed a highly significant difference \( (P < 0.001) \). On the other hand, six other concentrations were tested and the last two concentrations tested of HAEGS did not show any significant difference compared to Vitamin C \( (P > 0.05) \). It should be noted that the concentration of Vitamin C corresponds to one-tenth of that of the HAEGS. The highest concentration of HAEGS \( (250 \mu g/mL) \) had a percentage of DPPH radical scavenging similar to that of Vitamin C \( (25 \mu g/mL) \), notably \( 80.79 \pm 0.54\% \) and \( 86.74 \pm 0.71\% \), respectively, for the HAEGS and Vitamin C.

**Total flavonoid content**

Total flavonoid content of HAEGS was \( 2.94 \pm 0.33 \) mg QE/100 mg extract.

**Histopathological examination of the pancreatic tissues**

Figure 4 shows a photomicrograph of pancreatic tissue from normoglycemic and DexIH rats that received different treatments.

The histological analysis showed, in the normal control [Figure 4a], a normal structuring of the pancreatic parenchyma. Compared to the normal group, the animals of the negative control group [Figure 4b] showed several histopathological alterations, in particular hypertrophy of the islets of Langerhans. The batches treated with the reference drug [Figure 4c], just like those receiving the extract at different doses [Figure 4d and e], presented a restructuring of the pancreatic tissue close to that of the normal control. Indeed, it appears from the histopathological study of pancreas that extract restored the histological integrity of these organs initially altered by dexamethasone.

**Discussion**

Dexamethasone is a synthetic glucocorticoid, which has a high affinity for the glucocorticoid receptor. It has been used to rapidly generate insulin resistance in rodents in a relatively short period of time.\(^{[20]}\) It was reported that the acute high doses of dexamethasone \( (4, 8, \) and \( 16 \) mg/kg) for 6 days caused hepatic steatosis and showed mild-to-moderate arteriosclerosis in the aorta. These changes may be secondary consequences of insulin resistance.\(^{[21]}\) The present study reported that treatment with dexamethasone intravenously at a dose of \( 4 \) mg/kg for three consecutive days induced postprandial hyperglycemia in Wistar rats and induced pancreatic lesions in the pancreatic parenchyma of untreated rats. This study revealed that HAEGS had hypoglycemic activity after two weeks of treatment of DexIH rats. The OGTT also showed that HAEGS prevents the postprandial blood
glucose level spike in both normoglycemic rats (P > 0.05) and DexIH rats (P < 0.05). It was observed in the DexIH rats after fourteen days of treatment with HAEGS at a dose of 100 mg/kg of body weight that the plant extract has significantly prevented the postprandial peak in blood glucose level 30 min after oral glucose overload. Intuitively, health-care providers believe that the best metabolic status corresponds to persons who concomitantly exhibit low mean glucose concentrations (HbA1c approximately at 7% or below) and small glucose variability, i.e., the least exposures to chronic hyperglycemia and acute glucose swings from peaks.\[22\] Experimental studies have shown that dexamethasone produces fatty accumulation in the liver parenchyma, which results in fatty liver disease. Steatosis is the first stage of nonalcoholic fatty liver syndrome and is the hepatic manifestation of insulin resistance.\[21,23,24\]

A spasmyloytic substance partially inhibits intestinal peristalsis, while a laxative substance accelerates intestinal transit. Administered to rats, the spasmyloytic substance (Imodium® 2 mg/kg) opposes the progression of the food bolus, unlike the laxative substance (Fructine® 5 mg/kg), which acts in synergy with the sense of peristaltic movements of the small intestine. The extract at both doses significantly (P < 0.001) inhibited the spasmyloytic activity in both normoglycemic and hyperglycemic rats compared to Imodium®. In rats made hyperglycemic, only dose 100 mg/kg significantly (P < 0.05) increased laxative effects when compared to the negative control. This suggests that the extract may contain compounds that exert the same effects as acetylcholine. Acetylcholine increases gastrointestinal contraction by stimulating muscarinic receptors in a process mediated by G-protein, phospholipase C, and inositol triphosphate.\[25\] The increase in small intestine contractility might be due to the stimulatory influence of some phytochemical components of GK on intestinal muscarinic receptor.\[17\] The quantitative phytochemical screening of GK seeds (g/100 g) was reported and revealed phenols 0.147 ± 0.00, saponins 2.471 ± 0.00, alkaloids 0.647 ± 0.20, flavonoids 2.041 ± 0.30, and glycosides 3.421 ± 0.00.\[26\]

In vitro antiradical activity of GK revealed vitamin C-like antiradical activity.

Figure 3: Antiradical activity of *Garcinia kola* seeds. Values are means ± ESM, n = 3. a: (P < 0.01), b: (P < 0.001) significant from Vitamin C.

Figure 4: Microphotograph of pancreatic tissue (H and E, ×100) of dexamethasone-induced hyperglycemic rats treated with hydroalcoholic extract of *Garcinia kola* seeds (50 and 100 mg/kg b. w.) for 14 days. (a) NNC: Negative normal control (normoglycemic group): Histological analysis showed normal pancreatic structure in the normal control group with high number of β-cells (the blue arrows show the endocrine pancreas which contains the pancreatic islets of Langerhans including the beta cells, the red arrows show the exocrine pancreas (acinis), and the green arrow shows the pancreatic artery). (b) NDC: Negative dexamethasone control: Compared to normal control group, the animals in the negative control group showed hypertrophy of the islets of Langerhans. (c) Gilb2.5: Positive dexamethasone control; (d and e) GK50 & GK100: Experimental groups which received the extract at the respective doses of 50 and 100 mg/kg. The groups treated with the reference substance, like those receiving the extract at different doses, presented a restructuring of these organs, close to that of the normal control.
Free radical and reactive oxygen species (ROS) are basically the main cause of several disorders in humans that are generated as an imbalance between formation and neutralization of pro-oxidants, resulting in oxidative stress.[27] The results imply that the radical scavenging activity of the extracts may be attributed to their proton-donating abilities.[28] It has been established that the flavonoids of plant extracts are part of one of the most important hydrogen-donating groups.[29] The flavonoids present in HAEGS may be responsible for the anti-hyperglycemic, laxative, and the scavenging activity against DPPH effects observed in vivo and in vitro, respectively.[30-32] These pharmacological effects of GK seeds could be attributed to numerous flavonoids, as plant extract revealed a total flavonoid 2.94 ± 0.33 mgEq/100 mg extract. Several studies demonstrated the involvement of flavonoids in the regulation of blood sugar and diabetes complications.[6,33-36]

Histopathological examination of the pancreas of untreated DexIH rats revealed several histopathological alterations, in particular hypertrophy of the islets of Langerhans. This abnormality was less in the groups of animals treated with HAEGS at the two doses tested, which had a structuring of the pancreatic tissue close to that of the normal control. It has been reported that the treatment with higher doses of dexamethasone intraperitoneally produced fatty accumulation in liver parenchyma which resulted in hepatic steatosis.[23] The mechanism responsible for the development of steatosis might be due to break down of lipids into fatty acids (lipolysis), decreased sensitivity to insulin, and deposition of fat in liver tissue.[37,38] Recent studies have suggested that hyperinsulinemia, chronic inflammation, and hyperglycemia, all commonly seen in diabetics, can lead to increased tumor growth; the underlying molecular mechanisms of this association are not fully understood.[39]

Conclusions
From this study, we can conclude that these results suggest that the HAEGS regulates blood glucose levels, possesses laxative and anti-free radical properties, which justifies its traditional use in Sub-Saharan Africa. However, further pharmacological and biochemical investigations will clearly elucidate the mechanism of action and will be helpful in projecting this plant as a therapeutic target in diabetes research.

Ethical clearance
All the animals experiments were carried out in accordance with the guidelines of Cameroon National Ethics committe (Ref. FWIRB 00001954).

Financial support and sponsorship
Ministry of Higher Education, Cameroon and University Joseph Ki-Zerbo, Burkina Faso. The authors would like to thank the Ministry of Higher Education, which financed the in vivo experimentation of this study through the research modernization grant. The authors would also like to thank Laboratory of Biochemistry and Applied Chemistry, University Joseph Ki-Zerbo, Burkina Faso, for carrying out the in vitro experiments of this study.

Conflicts of interest
There are no conflicts of interest.

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