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Effect of hot water infusion of roasted date palm seeds on improving insulin sensitivity and alleviating high-carbohydrate diet-induced hyperglycaemia in rats

***Chukwuma Raphael Ekeanyanwu Njoku-Henry, Doris Obiageri**

[*]Department of Biochemistry, Imo State University, Owerri, Imo State, Nigeria

[*]Corresponding author: ekeanyanwu.chukwuma@imsuonline.edu.ng

Abstract

The antihyperglycaemic potential of hot water infusion of roasted *Phoenix dactylifera* (date palm) seeds (HAERD) was evaluated in high-carbohydrate diet (HCD)-induced hyperglycaemic male Wistar rats. Doses of 200 and 500 mg/kg body weight were selected based on previous studies on date seed infusions and to establish a clear dose-response relationship. After 8 weeks of HCD feeding to induce hyperglycaemia, rats were treated orally with HAERD (200 and 500 mg/kg), metformin (150 mg/kg), or vehicle for 21 days.HAERD produced significant dose-dependent reductions in fasting blood glucose ($p < 0.05$), with the 500 mg/kg dose returning values to near normal by Week 6. The infusion also significantly improved serum insulin concentrations and HOMA-IR index in a dose-dependent manner ($p < 0.05$), approaching the effects of metformin. Furthermore, HAERD normalized the serum lipid profile by significantly lowering total cholesterol, triglycerides, LDL-C, and VLDL-C ($p < 0.0001$). It restored antioxidant enzyme activities (SOD, CAT, GPx) and markedly reduced malondialdehyde (MDA) levels ($p < 0.0001$). Treatment with HAERD also significantly decreased liver enzymes (ALT, AST, ALP) and bilirubin levels ($p < 0.0001$), accompanied by recovery of total protein and albumin. Histopathological examination revealed dose-dependent regenerative changes and near-normal tissue architecture in the liver, kidney, and heart at the 500 mg/kg dose, comparable to the metformin-treated group.These results demonstrate that HAERD exerts robust multi-target metabolic benefits antihyperglycaemic, hypolipidaemic, antioxidant, and multi-organ protective effects in HCD-induced hyperglycaemia. The 500 mg/kg dose showed efficacy approaching that of metformin ($p < 0.05$). The findings support the traditional use of roasted date palm seed infusion and its potential as a sustainable, affordable nutraceutical for managing hyperglycaemia and associated complications.

Keywords: *Phoenix dactylifera*, date palm seeds, hot water infusion, high-carbohydrate diet, hyperglycaemia, antihyperglycaemic, metformin.

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Introduction

Type 2 diabetes mellitus has emerged as one of the most pressing public health challenges worldwide. According to the International Diabetes Federation, approximately 537 million adults were living with diabetes in 2021, with projections estimating a rise to 783 million by 2045 (Aebi *et al*., 1984). The burden is particularly severe in low- and middle-income countries, where over 80% of cases occur. In Nigeria, the prevalence has risen dramatically in recent decades due to rapid urbanization, dietary shifts toward high-carbohydrate diets, and sedentary lifestyles. Current estimates indicate that Nigeria has one of the highest diabetes burdens in sub-Saharan Africa, with approximately 3 – 5 million adults affected and urban prevalence rates ranging from 5% to 10% (Uloko *et al*., 2018; IDF, 2021). Conventional antidiabetic agents remain the cornerstone of therapy but have notable limitations. Metformin, the first-line drug, primarily acts by suppressing hepatic gluconeogenesis and improving peripheral insulin sensitivity through activation of AMP-activated protein kinase (AMPK). Sulfonylureas stimulate insulin secretion from pancreatic β-cells by closing ATP-sensitive potassium channels, leading to membrane depolarization and calcium influx. Insulin therapy directly replaces or supplements endogenous insulin to promote glucose uptake and inhibit hepatic glucose production. While effective, these agents are frequently associated with adverse effects including gastrointestinal intolerance (metformin), hypoglycaemia and weight gain (sulfonylureas and insulin), and high treatment costs, which compromise long-term adherence, especially in resource-limited settings (Maruthur *et al*., 2016). These challenges have intensified interest in natural products from traditionally used medicinal plants, particularly those derived from underutilised agro-industrial waste. The seeds of the date palm (*Phoenix dactylifera L*.), which constitute 10–15% of the fruit and are frequently discarded as waste, have a long history of use in Middle Eastern and North African ethnomedicine for the management of diabetes and metabolic disorders (Vayalil, 2012; Shah *et al*., 2023). Recent research has highlighted the rich phytochemical profile of date palm seeds, including polysaccharides, phenolic acids, flavonoids, and unsaturated fatty acid esters (Alkhoori *et al*., 2022; Mrabet *et al*., 2020; Salomón-Torres *et al*., 2019; Manai *et al*., 2024). Several studies have reported hypoglycaemic, hypolipidaemic, and antioxidant activities of date seed extracts in streptozotocin- or high-fat diet-induced diabetic models (Hasan and Mohieldei, 2016; Khan *et al*., 2018). Similar investigations on Nigerian medicinal plants such as *Vernonia* amygdalina and *Gongronema latifolium* have demonstrated significant antihyperglycaemic and antioxidant effects

in high-carbohydrate diet models (Atangwho *et al*., 2012; Okon *et al*., 2022). Building on preliminary phytochemical and in silico findings showing a methyl oleate-rich profile with strong binding to pancreatic α-amylase, the present study evaluated the in vivo efficacy of the hot water infusion of roasted Phoenix dactylifera seeds (HAERD) in a high-carbohydrate diet (HCD)-induced hyperglycaemia model. High-carbohydrate diet (HCD)-induced hyperglycaemia in Wistar rats closely recapitulates key metabolic features of human type 2 diabetes, including glucose intolerance, insulin resistance, dyslipidaemia, and oxidative stress (Skovsø, 2014). The present study investigated the antihyperglycaemic, hypolipidaemic, antioxidant, and multi-organ protective effects of HAERD (200 and 500 mg/kg) in HCD-induced hyperglycaemic male Wistar rats, using Metformin (150 mg/kg) as a positive control. By evaluating glycaemic control, insulin sensitivity, lipid profile, oxidative stress markers, liver function parameters, and histopathological changes in liver, kidney, and heart over 21 days of treatment, this work aims to provide comprehensive preclinical validation of the traditional use of roasted date palm seed infusion and to explore its potential as a sustainable, affordable nutraceutical for managing hyperglycaemia and associated metabolic complications.

Materials and Methods

Materials

Equipment

All experimental procedures, including animal housing, diet preparation, treatment administration, biochemical assays, and histopathological evaluation, were performed using standard laboratory equipment available at the Department of Biochemistry Laboratory, Imo State University, Owerri, Nigeria, and the Multi-User Science Laboratory, Ahmadu Bello University, Zaria, Nigeria. The major equipment included a Memmert oven (Germany), Kenwood electric grinder Model BL335 (UK), Endecotts 1 mm sieve (UK), Haier refrigerator (China), Tecniplast standard plastic cages with stainless steel wire lids (Italy), a locally fabricated hand-operated pelleting machine, Roche handheld glucometer (Switzerland), Thermo Fisher Scientific spectrophotometer (USA), Eppendorf refrigerated centrifuge (Germany), Leica Microsystems rotary microtome (Germany), Olympus Corporation light microscope with digital photomicrographic system (Japan), and Whatman No. 1 filter paper (UK).

Reagents/chemicals

Reagents and chemicals were sourced from verified reputable suppliers and used strictly according to the manufacturers' instructions and within their expiry periods. The major reagents included glucose assay kits (GOD-POD method) from Randox Laboratories Ltd. (UK), lipid profile kits (total cholesterol, triglycerides, HDL-C, LDL-C) from Fortress Diagnostics Ltd. (UK), liver function assay kits (ALT, AST, ALP) from Agappe Diagnostics (Switzerland), insulin ELISA kits from Elabscience Biotechnology Inc. (USA), thiobarbituric acid reactive substances (TBARS) reagents for malondialdehyde (MDA) assay, Ellman's reagent (DTNB) for glutathione determination, catalase and superoxide dismutase assay reagents from Sigma-Aldrich (Germany), 10% neutral-buffered formalin and phosphate-buffered saline from Merck (Germany), and analytical-grade ethanol, methanol, sulfuric acid, trichloroacetic acid, and n-butanol from Merck (Germany).

Plant Material

Source and Identification of *Phoenix dactylifera* Seeds: Dry fruits of *Phoenix dactylifera* (date palm) were purchased from a reputable local market in Kano State, Nigeria. The seeds were manually separated from the fruit pulp, thoroughly washed with distilled water to remove any adhering fruit residues, and air-dried at room temperature. Botanical identification and authentication were carried out by Dr C.I.N Unamba, a plant taxonomist at the Department of Plant Science and Biotechnology (Botany), Imo State University, Owerri, Nigeria. A voucher specimen (Voucher No.: IMSU/PSB/PHOENIX/024) was deposited in the university herbarium for future reference.

Experimental Animals

Healthy adult male Wistar albino rats (*Rattus norvegicus*), weighing 106 – 163 g at the start of the study, were procured from the Animal House Unit, Department of Anatomy, Imo State University, Owerri, Nigeria. Upon arrival, the animals were housed in clean, well-ventilated standard plastic cages with stainless steel wire lids and wood shavings as bedding. They were maintained under controlled environmental conditions: temperature 22 ± 2 °C, relative humidity 55 ± 10%, and a 12-h light/12-h dark cycle. The rats were allowed two weeks of acclimatization to laboratory conditions with free access to standard rat chow (Vital Feed, Nigeria) and clean drinking water *ad libitum* before the commencement of the experiment. All procedures involving animals were conducted in accordance with internationally accepted principles for the use and

care of laboratory animals and were approved by the Institutional Animal Ethics Committee (IAEC).

Methods

Ethical approval

The National Institute of Health Care's Guide for the Care and Use of Laboratory Animals (NRC, 2011) was followed in this investigation. The study will comply with IACUC, NIH, and ARRIVE 2.0 guidelines (Percie du Sert *et al*., 2020).

Preparation of Hot Water Infusion of Roasted Date Seeds

Dry fruits of Phoenix dactylifera were purchased from a local market in Kano State, Nigeria. Seeds were manually separated from the pulp, thoroughly washed with distilled water to remove residual sugars and adhering matter, and air-dried under shade at ambient temperature (25–28 °C) for 10–14 days until constant weight was attained. The dried seeds were roasted in a controlled electric oven at 180 °C for 25 min to reduce antinutritional factors, enhance palatability, and improve the release of bound phenolics while preserving thermolabile bioactives (Al Juhaimi *et al*., 2018; Halabi *et al*., 2024). After cooling, the seeds were milled into fine powder and sieved to uniform particle size. The hot water infusion was prepared using a modified traditional decoction method. Briefly, 100 g of roasted seed powder was added to 1 L of boiling distilled water and maintained at gentle boiling for 60 min with occasional stirring. The mixture was cooled, filtered through Whatman No. 1 filter paper, concentrated under reduced pressure at 40 °C using a rotary evaporator, and lyophilized to obtain a dry powder. The infusion (HAERD) was stored in amber-coloured airtight containers at 4 °C until use. The detailed phytochemical composition and chemical characterization of the hot water infusion of roasted *Phoenix dactylifera* seeds (HAERD), including GC–MS analysis, were performed and are reported in a separate companion manuscript submitted to the *Basrah Journal of Date Palm Research* (Ekeanyanwu and Njoku-Henry, submitted).

Formulation of High-Carbohydrate Diet

A high-carbohydrate diet (HCD) was formulated to induce hyperglycaemia and insulin resistance in Wistar rats. The basal rodent chow (Vital Feed, Nigeria) was supplemented with refined sucrose and maize starch as primary carbohydrate sources, partially replacing protein- and fat-

rich ingredients. Based on a study by Ble-Castillo *et al*., (2012) the final diet composition was adjusted such that carbohydrates contributed about 65% of the total caloric content, while maintaining adequate protein (19%), lipids (6%), total caloric energy (3,900 kcal/kg), and micronutrient levels suitable for long-term feeding. All ingredients were accurately weighed, thoroughly mixed in a mechanical blender to ensure homogeneity, moistened with warm distilled water, and pelletized using a hand-operated pelleting machine to produce uniform cylindrical pellets (approximately 10–12 mm diameter). The pellets were air-dried at room temperature for 12 h and then oven-dried at 50 °C for 24 h to reduce moisture content below 10%, thereby preventing microbial growth and ensuring stability. Hyperglycaemia was induced by feeding the HCD ad libitum for 8 consecutive weeks. Fresh diet was provided daily, and drinking water was available ad libitum. Body weight and general health were monitored weekly. This prolonged high-carbohydrate regimen has been shown to progressively impair glucose tolerance, reduce insulin sensitivity, and produce sustained fasting hyperglycaemia that closely mimics early-stage type 2 diabetes (Skovsø. 2014; Komiyama *et al*., 2002; Dupas *et al*., 2016).

Experimental design

Thirty-six adult male Wistar albino rats (106 – 163 g) were used in this study. After one week of acclimatization, the animals were randomly assigned to six experimental groups (n = 6 per group) using a computer-generated random number sequence to ensure unbiased allocation. The groups were as follows:

- Group 1 (Normal control): Fed standard laboratory chow and received vehicle (distilled water) orally.
- Group 2 (HCD control): Fed high-carbohydrate diet (HCD) and received vehicle orally.
- Group 3 (HCD + Low-dose HAERD): Fed HCD and treated orally with hot water infusion of roasted date palm seeds (HAERD) at 200 mg/kg body weight.
- Group 4 (HCD + High-dose HAERD): Fed HCD and treated orally with HAERD at 500 mg/kg body weight.
- Group 5 (HCD + Positive control): Fed HCD and treated orally with metformin (150 mg/kg body weight).

- Group 6 (Normal + HAERD): Fed standard laboratory chow and treated orally with HAERD at 500 mg/kg body weight (safety/toxicity control group).

Hyperglycaemia was induced in Groups 2 – 5 by exclusive ad libitum feeding of the formulated HCD for eight consecutive weeks as previously described (Ble-Castillo et al., 2012; Skovsø, 2014). Successful induction was confirmed at the end of week 8 by measuring fasting blood glucose levels (≥150–180 mg/dL) using tail-vein sampling and a calibrated handheld glucometer. The treatment phase lasted 21 days and commenced immediately after confirmation of hyperglycaemia. During this period, Groups 3 – 5 continued receiving the HCD while being administered their respective treatments once daily by oral gavage between 08:00 and 10:00 h. The hot water infusion was freshly reconstituted in sterile distilled water immediately before administration. The gavage volume did not exceed 10 mL/kg body weight and was adjusted daily based on the most recent body weight. Groups 1 and 2 received the vehicle only. Group 6 continued on standard chow and received the infusion at 500 mg/kg to evaluate its effects in normoglycaemic animals. Body weight, food intake, and fasting blood glucose levels were monitored weekly throughout the study. Humane endpoints were predefined and included sustained body weight loss ≥20% within 7 days, severe lethargy, persistent diarrhoea, impaired mobility, or any signs of acute distress. Animals reaching these endpoints were immediately humanely euthanized. Personnel involved in biochemical assays and histopathological evaluation were blinded to treatment allocation wherever feasible to minimise observer bias. At the study endpoint (day 22), animals were fasted overnight, anaesthetised with ketamine/xylazine, and euthanised by cardiac exsanguination. Blood and major organs (liver, kidneys, and heart) were collected for biochemical and histopathological analyses.

Induction of Hyperglycaemia

Hyperglycaemia was induced in Groups 2–5 by exclusive ad libitum feeding of the formulated high-carbohydrate diet (HCD) for eight consecutive weeks, with free access to drinking water. This prolonged high-carbohydrate regimen has been shown to progressively impair glucose tolerance, reduce insulin sensitivity, and produce sustained fasting hyperglycaemia that closely mimics early-stage type 2 diabetes (Skovsø, 2014; Dupas *et al*., 2016). Body weight and food intake were monitored weekly to assess nutritional status and detect any feeding abnormalities.

Fasting blood glucose levels were measured at baseline and at the end of week 8 using tail-vein blood sampling and a calibrated handheld glucometer after overnight fasting (12 h, water ad libitum). Successful induction was confirmed when fasting blood glucose reached ≥150–180 mg/dL. Animals that did not meet this criterion after eight weeks were excluded from the treatment phase.

Sample Collection

At the study endpoint (day 22), animals were fasted overnight (12 h), deeply anaesthetised with ketamine/xylazine administered intraperitoneally, and humanely euthanised by cardiac exsanguination. Terminal blood samples were collected via cardiac puncture and immediately transferred into appropriate tubes. Serum was obtained by allowing blood to clot at room temperature for 30–45 min, followed by centrifugation at 3000 × g for 10–15 min at 4 °C. The resulting serum was aliquoted and stored at −80 °C until analysis for glucose, insulin, lipid profile, liver enzymes, and oxidative stress markers. Multiple aliquots were prepared to avoid repeated freeze–thaw cycles. Immediately after blood collection, a midline abdominal incision was made, and the liver, kidneys, and heart were carefully excised. Organs were rinsed briefly in ice-cold physiological saline (0.9% NaCl), blotted dry on sterile filter paper, and weighed to determine absolute and relative organ weights. Representative sections (approximately 1 cm^3) from each organ were fixed in 10% neutral-buffered formalin (fixative volume ≥10× tissue volume) for 48 h. Fixed tissues were processed using standard histological techniques (graded ethanol dehydration, xylene clearing, paraffin embedding), sectioned at 5 µm thickness, and stained with haematoxylin and eosin (H&E) for microscopic evaluation (Suvarna *et al*., 2019). All samples were labelled with a unique animal identifier, group, sample type, and collection date to ensure full traceability and reproducibility.

Biochemical Analysis

Biochemical analyses were performed on serum and 10% (w/v) tissue homogenates prepared in ice-cold phosphate-buffered saline (PBS, pH 7.4) containing protease inhibitors. All assays were conducted in duplicate using validated commercial enzymatic colorimetric or immunoassay kits according to the manufacturers' protocols. Each run included multi-point calibration curves, reagent blanks, and quality control samples to ensure accuracy and precision (intra-assay CV < 10%, inter-assay CV < 15%).

Fasting Blood Glucose

Fasting blood glucose was measured at baseline, weekly during the 8-week induction phase, and at the end of the 21-day treatment using tail-vein blood sampling after overnight fasting (12 h). Glucose levels were determined immediately with a calibrated handheld glucometer (Accu-Chek or equivalent). For endpoint confirmation, serum glucose was quantified using the glucose oxidase–peroxidase (GOD-POD) enzymatic colorimetric method with a commercial kit (Randox Laboratories Ltd., UK) and measured spectrophotometrically at 505 nm (Tietz, 1995).

Serum Insulin and HOMA-IR

Serum insulin concentrations were quantified using a rat-specific sandwich ELISA kit (Mercodia or Elabscience). The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was calculated as:

HOMA-IR = [fasting insulin (µIU/mL) × fasting glucose (mg/dL)] / 405 (Kang *et al*., 2005).

Lipid Profile

Serum total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) were measured using enzymatic colorimetric kits (Randox or Fortress Diagnostics). Low-density lipoprotein cholesterol (LDL-C) and very-low-density lipoprotein cholesterol (VLDL-C) were calculated using the Friedewald equation when TG < 400 mg/dL:

LDL-C = TC – HDL-C – (TG/5)

VLDL-C = TG/5 (Friedewald *et al*., 1972).

2.2.7.4 Oxidative Stress Markers

Malondialdehyde (MDA) was determined as thiobarbituric acid reactive substances (TBARS) using the method of Ohkawa *et al*. (1979). Superoxide dismutase (SOD) activity was assayed by the pyrogallol auto-oxidation method (Marklund and Marklund, 1974), catalase (CAT) activity by the Aebi method (Aebi, 1984), and reduced glutathione (GSH) using Ellman’s reagent (DTNB) (Ellman, 1959). All results were expressed per mg protein or per mL serum after protein quantification by the Bradford method.

Histological Examination

Immediately after sacrifice, the liver, kidneys, and heart were harvested, gently rinsed in ice-cold normal saline to remove residual blood, and fixed in 10% neutral-buffered formalin for 24 – 48 h. Fixed tissues were dehydrated through a graded ethanol series (70–100%), cleared in xylene, infiltrated with molten paraffin wax at 56 – 60 °C, and embedded in paraffin blocks. Sections were cut at 5 µm thickness using a rotary microtome, floated on a warm water bath, mounted on glass slides, and stained with haematoxylin and eosin (H&E). Stained slides were examined under a light microscope at ×40, ×100, ×200, and ×400 magnifications. Histopathological evaluation focused on tissue architecture, cellular morphology, necrosis, steatosis, inflammation, sinusoidal changes, tubular integrity, and myocardial fibre organisation. Representative photomicrographs were captured using a digital imaging system for documentation and qualitative comparison (Suvarna *et al*., 2019).

Statistical Analysis

All quantitative data were expressed as mean ± standard deviation (SD). Normality of distribution was assessed using the Shapiro–Wilk test, supplemented by visual inspection of histograms. Statistical analyses were performed using GraphPad Prism software (GraphPad Software, San Diego, CA, USA). Comparisons among the six experimental groups were conducted using one-way analysis of variance (ANOVA) followed by Tukey's honestly significant difference (HSD) post-hoc test when the overall F-test was significant ($p < 0.05$). Repeated-measures data (body weight and fasting blood glucose over time) were analysed using two-way repeated-measures ANOVA with Sidak's or Tukey's post-hoc tests. A two-tailed p-value < 0.05 was considered statistically significant. Levels of significance were denoted as *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, and ****$p < 0.0001$ versus the respective control group.

Results

Effects of Roasted Date Seed Infusion on Body Weight in Hyperglycaemic Wistar Rats

The body weight progression of Wistar rats during the six-week experimental period is presented in Table 1. Data are expressed as mean ± standard deviation. Sample size was n = 6 rats per group during the pre-induction and induction phases (Weeks 1–3). One-way repeated-measures ANOVA was performed separately for each group to evaluate the effect of time on body weight. Significant time-dependent increases were observed in the normal control group (Group 1; $F = 3.97$, $p = 0.0070$) and especially in the HAERD-only group (Group 6; $F = 7.82$, $p = 0.0001$). No

significant overall time effects were detected in the HCD control (Group 2; F = 0.39, p = 0.8504), low-dose HAERD (Group 3; F = 2.02, p = 0.1084), high-dose HAERD (Group 4; F = 1.73, p = 0.1582), or metformin (Group 5; F = 0.82, p = 0.5478) groups. During the pre-induction (Week 1) and induction phases (Weeks 2–3), body weights remained relatively stable across all groups with only minor fluctuations. Following initiation of treatment in Week 4, progressive increases became evident in several groups. The normal control (Group 1) showed a moderate but consistent rise, reaching statistical significance by Week 6. Group 6 (HAERD-only, 500 mg/kg) exhibited the most pronounced and statistically distinct stepwise weight gain (p = 0.0001), increasing from 122.8 ± 11.1 g (Week 1) to 163.4 ± 18.4 g (Week 6). Group 5 (metformin) displayed a numerical increase from Week 4 onward with high variability, though the overall time effect was not statistically significant. Groups 3 and 4 showed modest upward trends during the treatment phase, while the HCD control group (Group 2) remained largely stable throughout the experiment (p = 0.8504).

Effects of Roasted Date Seed Infusion on Blood Glucose Levels in Wistar Rats

Blood glucose levels during the six-week experimental period are presented in Table 2. During the pre-induction (Week 1) and induction phases (Weeks 2–3), most HCD-fed groups exhibited a significant rise in fasting blood glucose, consistent with the metabolic stress of sustained high-carbohydrate intake. Group 5 showed the highest variability and peak value in Week 3 (180.3 ± 115.4 mg/dL), largely due to an extreme individual reading. In contrast, the normal control (Group 1) and HAERD-only (Group 6) groups maintained stable glucose levels throughout induction. Following treatment initiation in Week 4, blood glucose levels stabilized or declined in the HCD-fed groups, with statistically significant time effects observed in Group 2 (F = 5.26, p = 0.0014), Group 3 (F = 5.85, p = 0.0009), and Group 4 (F = 2.80, p = 0.0343). The HCD control group (Group 2) peaked at 121.7 ± 5.6 mg/dL in Week 4 before returning toward baseline by Week 6. Both low-dose (Group 3) and high-dose (Group 4) HAERD groups showed progressive reductions, with Group 4 achieving the most consistent decline. Group 5 also exhibited a numerical decrease, though high variability limited statistical significance. Groups 1 and 6 remained stable throughout the treatment phase.

Effect of Roasted Date Seed Infusion on Serum Insulin and HOMA-IR in Diet-Induced Hyperglycaemic Wistar Rats

Serum insulin concentration and the homeostatic model assessment of insulin resistance (HOMA-IR) index are presented in Figure 1. The high-carbohydrate diet (HCD) control group showed markedly reduced serum insulin levels (0.95 ± 0.10 ng/mL) compared with the normal control group (3.29 ± 0.14 ng/mL, $p < 0.05$). Treatment with hot water infusion of roasted *Phoenix dactylifera* seeds (HAERD) produced a dose-dependent increase in serum insulin. The 200 mg/kg dose raised insulin to 1.61 ± 0.15 ng/mL, while the 500 mg/kg dose further increased it to 1.93 ± 0.04 ng/mL, a value comparable to the metformin-treated group (1.78 ± 0.08 ng/mL). The HAERD-only group (500 mg/kg) recorded the highest insulin level (3.81 ± 0.12 ng/mL). A parallel pattern was observed for the HOMA-IR index. The HCD control group exhibited a significantly lower index (0.24 ± 0.02) than the normal control (0.80 ± 0.04, $p < 0.05$). HAERD treatment improved HOMA-IR in a dose-dependent manner, reaching 0.43 ± 0.04 at 200 mg/kg and 0.49 ± 0.01 at 500 mg/kg, values similar to metformin (0.48 ± 0.02). The HAERD-only group showed the highest HOMA-IR index (0.99 ± 0.03).

Serum Lipid Profile in Hyperglycaemic Wistar Rats Treated with Roasted Date Seed Infusion

Serum lipid profile results are presented in Table 3. The high-carbohydrate diet (HCD) control group developed significant dyslipidaemia, characterised by elevated total cholesterol (81.31 ± 3.07 mg/dL), triglycerides (103.76 ± 4.68 mg/dL), LDL-C (8.97 ± 3.10 mg/dL), and VLDL-C (20.75 ± 0.94 mg/dL) compared with the normal control group ($p < 0.05$). Treatment with hot water infusion of roasted *Phoenix dactylifera* seeds (HAERD) for 21 days produced dose-dependent improvements in the lipid profile. Both 200 mg/kg and 500 mg/kg doses significantly reduced total cholesterol, triglycerides, LDL-C, and VLDL-C relative to the HCD control group. The high-dose HAERD (500 mg/kg) achieved reductions comparable to the metformin-treated group (150 mg/kg), particularly in triglycerides. The HAERD-only group (500 mg/kg) maintained a lipid profile similar to the normal control. One-way ANOVA revealed highly significant differences among groups for total cholesterol ($F = 38.92$, $p < 0.0001$), triglycerides ($F = 118.45$, $p < 0.0001$), LDL-C ($F = 6.78$, $p = 0.0009$), and VLDL-C ($F = 118.45$, $p < 0.0001$), with significant differences also observed for HDL-C ($F = 7.84$, $p = 0.0004$). Post-hoc Tukey's test confirmed that means with different superscript letters within the same parameter differ significantly ($p < 0.05$).

Serum Antioxidant Enzyme Activities and Lipid Peroxidation in Hyperglycaemic Wistar Rats Treated with Roasted Date Seed Infusion

Serum antioxidant enzyme activities (GPx, SOD, and catalase) and the lipid peroxidation marker malondialdehyde (MDA) are presented in Table 4. The high-carbohydrate diet (HCD) control group exhibited significantly reduced GPx (32.25 ± 1.71 U/L), SOD (27.75 ± 1.89 U/L), and catalase (21.75 ± 0.50 U/L) activities, accompanied by elevated MDA levels (4.91 ± 0.08 mg/dL) compared with the normal control group ($p < 0.0001$). Treatment with hot water infusion of roasted *Phoenix dactylifera* seeds (HAERD) for 21 days restored antioxidant enzyme activities in a dose-dependent manner. The 200 mg/kg dose increased GPx to 39.00 ± 1.41 U/L, SOD to 31.50 ± 1.29 U/L, and catalase to 21.00 ± 1.41 U/L, while reducing MDA to 4.23 ± 0.07 mg/dL. The 500 mg/kg dose further improved these parameters (GPx 39.25 ± 2.50 U/L, SOD 31.25 ± 2.87 U/L, catalase 22.00 ± 0.82 U/L) and lowered MDA to 4.14 ± 0.05 mg/dL, values comparable to the metformin-treated group (150 mg/kg). The HAERD-only group (500 mg/kg) showed the highest antioxidant enzyme activities and the lowest MDA level (3.00 ± 0.17 mg/dL). One-way ANOVA revealed highly significant differences among the experimental groups for all parameters ($p < 0.0001$).

Serum Liver Function and Protein Profile in Hyperglycaemic Wistar Rats Treated with Roasted Date Seed Infusion

Serum liver function enzymes (ALT, AST, and ALP) and protein profile are presented in Table 5. The high-carbohydrate diet (HCD) control group showed significantly elevated liver enzyme activities (ALT 92.50 ± 3.70 U/L, AST 107.75 ± 3.86 U/L, ALP 147.00 ± 10.20 U/L) and total bilirubin (1.19 ± 0.05 mg/dL) compared with the normal control group ($p < 0.0001$). Total protein and albumin levels were also lower in the HCD control.

Treatment with hot water infusion of roasted *Phoenix dactylifera* seeds (HAERD) for 21 days produced dose-dependent reductions in liver enzyme activities and bilirubin, accompanied by recovery of total protein and albumin. The 500 mg/kg dose reduced ALT to 81.50 ± 4.73 U/L, AST to 83.75 ± 3.59 U/L, and ALP to 117.50 ± 2.08 U/L, with values comparable to the metformin-treated group (150 mg/kg). The HAERD-only group (500 mg/kg) maintained liver enzyme activities and protein levels similar to the normal control. One-way ANOVA revealed highly significant differences among the experimental groups for all parameters ($p < 0.0001$).

Histopathological changes

Histopathological examination of the liver, kidney, and heart (H&E staining, ×400 magnification) is presented in Figure 2. The normal control group (Group 1) showed typical tissue architecture across all organs. In contrast, the HCD control group (Group 2) exhibited clear degenerative changes, including hepatic necrosis and fat deposition around central veins, disruption of renal corpuscles with glomerular distortion and tubular damage, and myocardial fibre disorganization with widened interfibrillar spaces. Treatment with hot water infusion of roasted *Phoenix dactylifera* seeds (HAERD) produced dose-dependent regenerative effects. At 200 mg/kg (Group 3), partial recovery was observed with reduced necrotic areas in the liver, improved glomerular and tubular integrity in the kidney, and decreased myocardial disarray. At 500 mg/kg (Group 4), regeneration was more advanced and near-complete, with restoration of normal lobular architecture in the liver, intact renal corpuscles and tubules in the kidney, and well-arranged myocardial fibres in the heart. The metformin-treated group (Group 5) showed substantial recovery comparable to the high-dose HAERD group. The HAERD-only group (Group 6) displayed normal histological features across all organs with no pathological changes, confirming the safety of the infusion at the therapeutic dose.

Table 1: Body weight progression (g) in Wistar rats with high-carbohydrate diet-induced hyperglycaemia treated with hot water infusion of roasted *Phoenix dactylifera* seeds (mean ± SD, n = 6 per group)

Week	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Week 1 (Pre)	120.8 ± 10.2^{a}	118.2 ± 22.0^{a}	121.7 ± 22.1^{a}	117.8 ± 14.1^{a}	130.0 ± 27.0^{a}	122.8 ± 11.1^{a}
Week 2 (Induction)	122.7 ± 9.2^{a}	125.7 ± 9.5^{a}	125.3 ± 19.2^{a}	117.5 ± 14.4^{a}	126.2 ± 28.6^{a}	117.5 ± 13.3^{a}
Week 3 (2nd Induction)	128.7 ± 7.5^{ab}	118.7 ± 22.8^{a}	130.0 ± 14.8^{a}	125.0 ± 7.1^{ab}	137.5 ± 29.8^{a}	131.7 ± 12.5^{b}
Week 4 (Treatment Week 1)	138.3 ± 10.8^{bc}	106.3 ± 25.8^{a}	137.4 ± 9.0^{ab}	126.7 ± 9.8^{ab}	148.3 ± 34.7^{b}	141.4 ± 13.8^{bc}
Week 5 (Treatment Week 2)	140.0 ± 14.1^{bc}	125.0 ± 26.5^{a}	143.0 ± 9.7^{b}	130.8 ± 18.6^{b}	154.2 ± 35.6^{bc}	149.4 ± 16.8^{c}
Week 6 (Treatment Week 3)	141.2 ± 13.6^{c}	133.3 ± 20.7^{a}	145.0 ± 12.2^{b}	139.2 ± 22.5^{b}	153.3 ± 39.2^{c}	163.4 ± 18.4^{d}
F value (within group)	3.97	0.39	2.02	1.73	0.82	7.82
P value	0.0070	0.8504	0.1084	0.1582	0.5478	0.0001

Values are mean ± SD of body weight across six time points (n = 6 initially; reduced to n = 5 in selected groups due to missing data). Different superscripts indicate significant differences over time ($p < 0.05$, repeated-measures ANOVA with Tukey's test).

Table 2: Blood glucose levels (mg /dL) in Wistar rats during high-carbohydrate diet induction and 21-day treatment with hot water infusion of roasted *Phoenix dactylifera* seeds

Week	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Week 1 (Pre)	103.7 ± 7.4^{a}	107.0 ± 7.6^{a}	110.7 ± 7.3^{a}	116.5 ± 9.0^{a}	116.3 ± 11.6^{a}	105.0 ± 10.3^{a}
Week 2 (Induction)	96.2 ± 8.8^{a}	99.0 ± 9.5^{b}	103.7 ± 12.7^{b}	107.7 ± 15.0^{b}	105.7 ± 12.6^{a}	102.5 ± 10.8^{a}
Week 3 (2nd Induction)	104.3 ± 6.8^{a}	116.8 ± 6.0^{c}	122.8 ± 4.8^{c}	126.0 ± 5.8^{c}	180.3 ± 115.4^{b}	110.8 ± 7.6^{a}
Week 4 (Treatment Week 1)	101.2 ± 7.1^{a}	121.7 ± 5.6^{c}	121.4 ± 4.1^{c}	119.0 ± 8.4^{ac}	156.3 ± 75.4^{b}	110.0 ± 7.9^{a}
Week 5 (Treatment Week 2)	97.2 ± 4.3^{a}	112.0 ± 10.8^{ac}	119.2 ± 4.0^{c}	114.8 ± 12.6^{abc}	129.7 ± 37.3^{ab}	109.0 ± 7.9^{a}
Week 6 (Treatment Week 3)	98.8 ± 2.4^{a}	104.0 ± 12.3^{ab}	108.8 ± 8.2^{a}	105.3 ± 12.9^{b}	110.5 ± 17.8^{a}	105.8 ± 8.4^{a}
F value (within group)	1.63	5.26	5.85	2.80	1.48	0.76
P value	0.1821	0.0014	0.0009	0.0343	0.2248	0.5893

Values are mean ± SD of blood glucose (mg/dL) (n = 6/group). Different superscripts across weeks indicate significant differences over time ($p < 0.05$, repeated-measures ANOVA with Tukey's test).

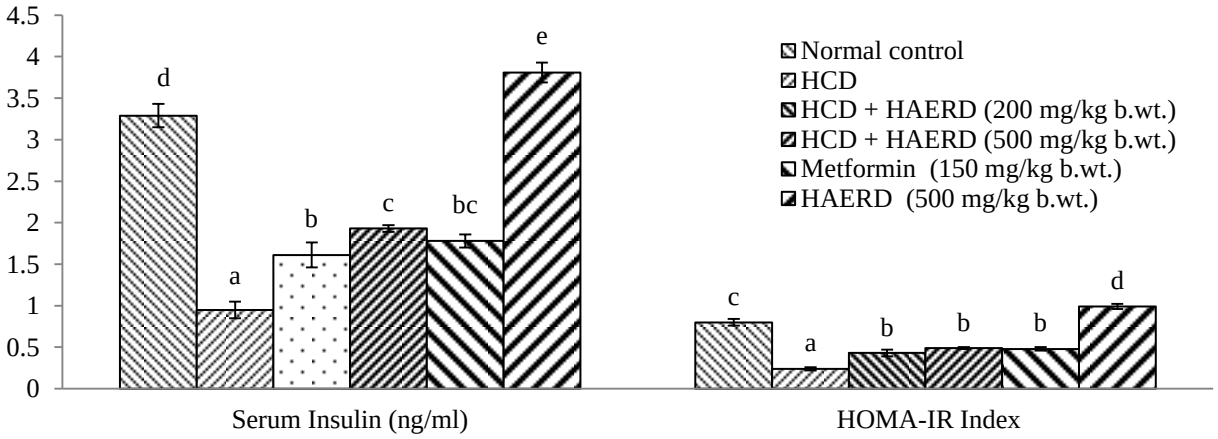

Figure 1: Effect of hot water infusion of roasted *Phoenix dactylifera* seeds on serum insulin concentration and HOMA-IR index in high-carbohydrate diet–induced hyperglycaemic Wistar rats.

Bars represent mean ± standard deviation (SD) (n = 3)**.** Different superscript letters above the bars indicate statistically significant differences between groups at $p < 0.05$, as determined by one-way analysis of variance (ANOVA) followed by Tukey's post-hoc multiple comparison test**.** The experimental groups include normal control, high-carbohydrate diet (HCD) control, HCD + hot water infusion of roasted *Phoenix dactylifera* seeds (HAERD) at 200 mg/kg and 500 mg/kg body weight, HCD + metformin (150 mg/kg body weight), and HAERD only (500 mg/kg body weight)**.**

Table 3: Serum lipid profile (mg/dL) in Wistar rats following high-carbohydrate diet induction and 21-day treatment with hot water infusion of roasted *Phoenix dactylifera* seeds (HAERD)

Group	Total Cholesterol (mg/dL)	HDL-C (mg/dL)	Triglycerides (mg/dL)	LDL-C (mg/dL)	VLDL-C (mg/dL)
Group 1 (Normal Control)	59.18 ± 2.35^{a}	43.39 ± 4.07^{a}	69.54 ± 2.64^{a}	4.13 ± 1.81^{a}	13.91 ± 0.53^{a}
Group 2 (HCD)	81.31 ± 3.07^{b}	51.59 ± 0.64^{b}	103.76 ± 4.68^{b}	8.97 ± 3.10^{b}	20.75 ± 0.94^{b}
Group 3 [HCD + HAERD] (200 mg/kg b.wt.)	71.78 ± 2.66^{c}	53.00 ± 2.90^{b}	83.59 ± 2.84^{c}	2.07 ± 1.60^{a}	16.72 ± 0.57^{c}
Group 4 [HCD + HAERD] (500 mg/kg b.wt.)	72.04 ± 3.55^{c}	49.56 ± 1.09^{ab}	82.60 ± 1.38^{c}	6.00 ± 3.30^{ab}	16.52 ± 0.28^{c}
Group 5 [Metformin] (150 mg/kg b.wt.)	72.15 ± 0.81^{c}	51.09 ± 1.68^{b}	73.20 ± 1.70^{a}	6.42 ± 1.97^{ab}	14.64 ± 0.34^{a}
Group 6 [HAERD 500 mg/kg b.wt.] (Toxicity/Safety Control)	73.60 ± 3.44^{c}	50.63 ± 2.05^{b}	67.68 ± 2.38^{a}	9.36 ± 1.50^{b}	13.54 ± 0.48^{a}
F-value (within group)	38.92	7.84	118.45	6.78	118.45
p-value	< 0.0001	0.0004	< 0.0001	0.0009	< 0.0001

Values are mean ± SD (mg/dL) (n = 3/group). Different superscripts within column indicate significant differences ($p < 0.05$, ANOVA with Tukey's test); same letters indicate no significance.

Table 4: Serum Antioxidant Enzyme Activities and Lipid Peroxidation (MDA) in Wistar Rats Following High-Carbohydrate Diet Induction and 21-Day Treatment with Hot Water Infusion of Roasted *Phoenix dactylifera* Seeds (HAERD)

Group	GPx (U/L)	SOD (U/L)	Catalase (U/L)	MDA (mg/dL)
Group 1 (Normal Control)	49.75± 2.50^{a}	36.00± 2.45^{a}	25.00± 0.82^{a}	3.46 ± 0.10^{a}
Group 2 (HCD)	32.25± 1.71^{b}	27.75± 1.89^{b}	21.75± 0.50^{b}	4.91 ± 0.08^{b}
Group 3 [HCD + HAERD] (200 mg/kg b.wt.)	39.00± 1.41^{c}	31.50± 1.29^{c}	21.00± 1.41^{b}	4.23 ± 0.07^{c}
Group 4 [HCD + HAERD] (500 mg/kg b.wt.)	39.25± 2.50^{c}	31.25± 2.87^{c}	22.00± 0.82^{b}	4.14 ± 0.05^{c}
Group 5 [Metformin] (150 mg/kg b.wt.)	42.75± 0.96^{c}	31.75± 1.71^{c}	23.00± 1.41^{c}	4.06 ± 0.07^{c}
Group 6 [HAERD 500 mg/kg b.wt.] (Toxicity/Safety Control)	54.50± 3.70^{d}	38.50± 1.29^{a}	30.00± 1.41^{d}	3.00 ± 0.17^{a}
F-value (within group)	38.45	19.72	42.18	156.89
p-value	< 0.0001	< 0.0001	< 0.0001	< 0.0001

Values are mean ± SD (n = 6/group). Different superscripts within columns indicate significant differences ($p < 0.05$, ANOVA with Tukey's test); same letters indicate no significance.

Table 5: Effect of Hot Water Infusion of Roasted Date Palm Seeds (HAERD) on Serum Liver Function Indices and Protein Profile in High-Carbohydrate Diet–Induced Hyperglycaemic Wistar Rats

Group	ALT (U/L)	AST (U/L)	ALP (U/L)	Total Protein (g/dL)	Albumin (g/dL)	Globulin (g/dL)	Total Bilirubin (mg/dL)
Group 1 (Normal Control)	22.00 ± 2.16^{a}	30.25 ± 2.06^{a}	67.50 ± 2.38^{a}	5.45 ± 0.16^{a}	2.84 ± 0.06^{a}	2.61 ± 0.10^{a}	0.65 ± 0.04^{a}
Group 2 (HCD)	92.50 ± 3.70^{b}	107.75 ± 3.86^{b}	147.00 ± 10.20^{b}	5.05 ± 0.11^{b}	2.37 ± 0.11^{b}	2.68 ± 0.04^{a}	1.19 ± 0.05^{b}
Group 3 [HCD + HAERD] (200 mg/kg b.wt.)	82.75 ± 2.87^{c}	91.50 ± 1.29^{c}	122.25 ± 5.38^{c}	5.55 ± 0.14^{a}	3.01 ± 0.02^{c}	2.69 ± 0.20^{a}	1.07 ± 0.07^{c}
Group 4 [HCD + HAERD] (500 mg/kg b.wt.)	81.50 ± 4.73^{c}	83.75 ± 3.59^{c}	117.50 ± 2.08^{c}	5.65 ± 0.13^{a}	3.01 ± 0.06^{c}	2.64 ± 0.18^{a}	1.03 ± 0.05^{c}
Group 5 [Metformin] (150 mg/kg b.wt.)	79.25 ± 2.75^{c}	80.25 ± 2.63^{c}	110.25 ± 2.22^{c}	5.63 ± 0.15^{a}	2.99 ± 0.03^{c}	2.61 ± 0.15^{a}	0.94 ± 0.04^{c}
Group 6 [HAERD 500 mg/kg b.wt.] (Toxicity/Safety Control)	23.25 ± 2.22^{a}	28.00 ± 2.16^{a}	69.00 ± 5.10^{a}	6.75 ± 0.24^{a}	3.24 ± 0.09^{c}	3.51 ± 0.25^{b}	0.64 ± 0.02^{a}
F-value (within group)	412.18	678.94	312.76	28.45	45.72	9.83	98.76
p-value	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001

Values are mean ± SD of liver function indices (n = 4/group). Different superscripts indicate significant differences among groups ($p < 0.05$, ANOVA with Tukey's test). Group 6 was the HAERD-only toxicity control (500 mg/kg, no HCD).

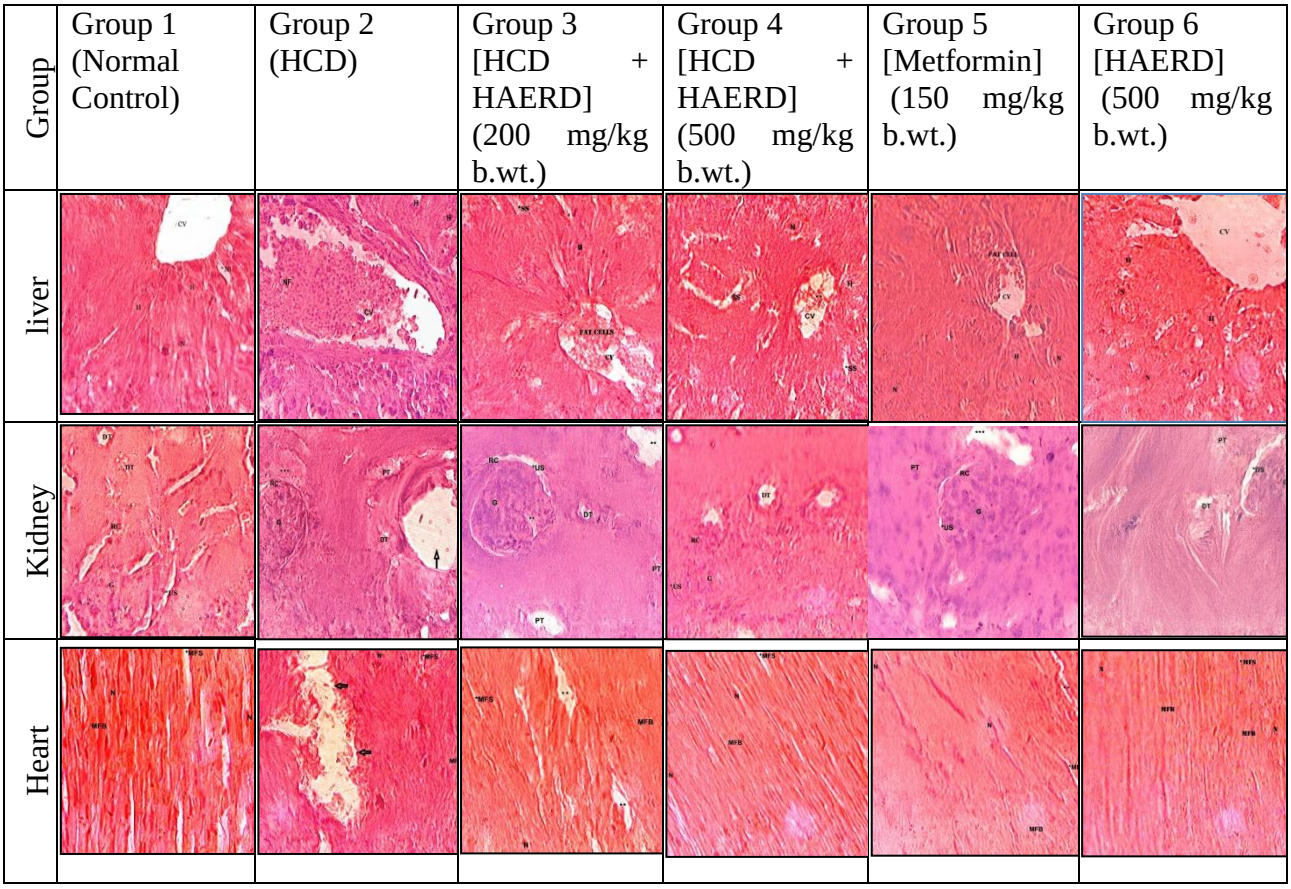

Figure 2: Histology of the liver, kidney and heart of Wistar rats with high-carbohydrate diet-induced hyperglycaemia treated with hot wer infusion of roasted date (HAERD) seeds (400 ×).

CV, central vein; DT, distal convoluted tubule; G, glomerulus; H, hepatocytes; H&E, hematoxylin and eosin; MFB, myofibrils; MFS, myofibrillar spaces; N, nucleus; NF, necrotic formations; PT, proximal convoluted tubule; RC, renal corpuscle; SS, sinusoids; HCD, high-carbohydrate diet; HAERD, hot water infusion of roasted *Phoenix dactylifera* seeds.

Discussion

The present study demonstrates that the hot water infusion of roasted *Phoenix dactylifera* seeds (HAERD) exerts significant dose-dependent antihyperglycaemic, insulin-sensitizing, hypolipidaemic, antioxidant, and multi-organ protective effects in high-carbohydrate diet (HCD)-induced hyperglycaemic Wistar rats. At the higher dose of 500 mg/kg, HAERD significantly reduced fasting blood glucose levels ($p < 0.05$), increased serum insulin concentration, improved the HOMA-IR index, normalised the serum lipid profile, restored antioxidant enzyme activities (GPx, SOD, and CAT), and decreased malondialdehyde (MDA) levels. These effects were

largely comparable to those of the standard antidiabetic drug metformin (150 mg/kg). The infusion-only group maintained normal biochemical and histological parameters, confirming the safety of HAERD at the tested dose. HAERD treatment produced progressive and significant reductions in fasting blood glucose, with the 500 mg/kg dose achieving near-normal values by the end of the 21-day treatment period. This antihyperglycaemic effect was accompanied by a dose-dependent increase in serum insulin levels and marked improvement in the HOMA-IR index, indicating enhanced insulin sensitivity. Concurrently, HAERD ameliorated HCD-induced dyslipidaemia by significantly lowering total cholesterol, triglycerides, LDL-C, and VLDL-C ($p < 0.0001$). These metabolic benefits were supported by strong antioxidant activity, evidenced by the restoration of endogenous antioxidant enzymes and substantial reduction in lipid peroxidation. The infusion also exerted hepatoprotective effects, as shown by significant decreases in ALT, AST, and ALP activities, reduced bilirubin levels, and recovery of total protein and albumin. Histopathological examination provided morphological corroboration of the biochemical findings. HCD feeding caused hepatic steatosis and necrosis, renal glomerular and tubular damage, and myocardial fibre disorganization. Treatment with HAERD, particularly at 500 mg/kg, resulted in clear dose-dependent regeneration, restoring near-normal tissue architecture in the liver, kidney, and heart, comparable to the metformin-treated group. The observed multi-target effects can be attributed to the phytochemical constituents of HAERD. Methyl oleate, the major compound in the infusion, showed strong binding affinity to pancreatic α-amylase (−7.2 kcal/mol), suggesting inhibition of carbohydrate digestion and reduced intestinal glucose absorption. Controlled roasting at 180°C enhances the release of bound phenolics and lipophilic compounds while generating Maillard reaction products with potent antioxidant properties (Al Juhaimi *et al*., 2018; Halabi *et al*., 2024). Phenolic compounds and unsaturated fatty acid derivatives likely act synergistically to scavenge reactive oxygen species, preserve β-cell function, and improve insulin signalling pathways (Alkhoori *et al*., 2022; Hasan and Mohieldein, 2016). This multi-target mechanism explains the simultaneous improvement in glycaemic control, insulin sensitivity, lipid metabolism, and organ protection. The HCD model employed in this study is particularly relevant because it closely mimics the diet-induced insulin resistance and progressive metabolic dysfunction seen in early-stage human type 2 diabetes, unlike chemical-induced models that cause rapid β-cell destruction (Skovsø, 2014; Ble-Castillo *et al*., 2012; Dupas *et al*., 2016). The ability of HAERD to counteract these changes highlights its potential for use in preventive and early-intervention strategies against metabolic disorders. The

present findings are consistent with previous reports demonstrating the hypoglycaemic, hypolipidaemic, and antioxidant activities of date palm seed infusions in different diabetic animal models (Mrabet *et al*., 2020; Hasan and Mohieldein, 2016). However, this study advances existing knowledge by utilising a traditionally relevant hot water infusion of roasted seeds in a high-carbohydrate diet model that reflects common dietary patterns in many African populations. It also complements findings from other Nigerian medicinal plants such as *Vernonia amygdalina* and *Gongronema latifolium* in similar models (Atangwho *et al*., 2012; Okon *et al*., 2022). Key strengths of this study include the use of a highly relevant diet-induced model, comprehensive evaluation of glycaemic control, insulin sensitivity, lipid profile, oxidative stress, liver function, and multi-organ histopathology, as well as the valorisation of an abundant agro-industrial waste. Limitations include the exclusive use of male rats, the relatively short treatment duration (21 days), calculation of LDL-C using the Friedewald formula, and the lack of molecular gene expression studies on pathways such as AMPK, GLUT4, or Nrf2. Future studies should address these gaps through longer-term experiments, inclusion of both sexes, inflammatory cytokine profiling, and clinical trials. The present study has some limitations that should be considered when interpreting the results. First, the study was conducted exclusively on male Wistar rats to minimise variability associated with the female estrous cycle. This precludes evaluation of potential sex differences in response to HAERD. Second, the treatment duration was limited to 21 days, which, while sufficient to demonstrate efficacy in this proof-of-concept study, may not fully reflect the long-term efficacy, safety, or sustainability of the extract in a chronic condition such as type 2 diabetes. Third, LDL-C values were calculated using the Friedewald formula rather than direct measurement, which may introduce some estimation errors. Furthermore, this study did not investigate the molecular mechanisms underlying the observed effects (e.g., expression of AMPK, GLUT4, or Nrf2) or profile key inflammatory cytokines such as TNF-α and IL-6. These important aspects warrant further investigation in future studies

Conclusion

In conclusion, the hot water infusion of roasted *Phoenix dactylifera* seeds (HAERD) exhibits robust multi-target efficacy in mitigating HCD-induced hyperglycaemia, insulin resistance, dyslipidaemia, oxidative stress, and tissue injury in Wistar rats. At 500 mg/kg, HAERD produced metabolic improvements approaching those of metformin. By transforming discarded date palm seeds into a safe, effective, and culturally acceptable nutraceutical, this study supports sustainable

approaches to managing type 2 diabetes and associated complications. Further mechanistic, bioactivity-guided, and clinical investigations are warranted to fully establish the therapeutic potential of HAERD.

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تأثير المستخلص المائي الساخن لبذور نخيل التمر المحمصة على تحسين حساسية الإنسولين وتخفيف فرط سكر الدم المستحث بالحمية عالية الكربوهيدرات في الجرذان

تشوكوما رافاييل إيكانيانوا * **نجوكو–هنري، دوريس أوبياغيري**

قسم الكيمياء الحيوية، جامعة ولاية إيمو، أوبري، ولاية إيمو، نيجيريا

*الباحث المراسل ekeanyanwu.chukwuma@imsuonline.edu.ng

الخلاصة

تم تقييم القدرة الخافضة لسكر الدم للمستخلص المائي الساخن لبذور نخيل التمر المحمصة (*Phoenix dactylifera*) (HAERD)في ذكور جرذان ويستر المصابة بفرط سكر الدم المستحث بالحمية عالية الكربوهيدرات (HCD). تم اختيار جرعات 200 و500 ملغم/كغم من وزن الجسم استناداً إلى دراسات سابقة حول مستخلصات بذور التمر ولإرساء علاقة واضحة بين الجرعة والاستجابة. بعد 8 أسابيع من تغذية HCD لإحداث فرط سكر الدم، عولجت الجرذان فموياً بـ HAERD (200 و500 ملغم/كغم)، أو الميتفورمين (150 ملغم/كغم)، أو بالمذيب (vehicle) لمدة 21 يوماً. أدى HAERD إلى انخفاضات معنوية معتمدة على الجرعة في سكر الدم الصائم($p < 0.05$) ، حيث أعادت جرعة 500 ملغم/كغم القيم إلى مستويات قريبة من الطبيعية بحلول الأسبوع السادس. كما حسّن المستخلص بشكل معنوي تراكيز الإنسولين في المصل ومؤشر HOMA–IR بشكل معتمد على الجرعة($p < 0.05$) ، مقترباً من تأثير الميتفورمين. علاوة على ذلك، قام HAERD بتطبيع ملف الدهون في المصل من خلال خفض معنوي لكل من الكوليسترول الكلي والدهون الثلاثية وكوليسترول LDL و VLDL ($p < 0.0001$). كما أعاد نشاط الإنزيمات المضادة للأكسدة (SOD, CAT, GPx) وخفّض بشكل ملحوظ مستويات المالونداليديهايد (MDA) ($p < 0.0001$). كما أدى العلاج بـ HAERD إلى خفض معنوي في إنزيمات الكبد (ALT, AST, ALP)ومستويات البيليروبين($p < 0.0001$) ، مترافقاً مع استعادة البروتين الكلي والألبومين. أظهر الفحص النسيجي تغيّرات تجددية معتمدة على الجرعة وبنية نسيجية شبه طبيعية في الكبد والكلى والقلب عند جرعة 500 ملغم/كغم، بما يتوافق مع مجموعة الميتفورمين. تُظهر هذه النتائج أن HAERD يمتلك فوائد أيضية متعددة الأهداف قوية تشمل تأثيرات خافضة لسكر الدم، وخافضة للدهون، ومضادة للأكسدة، وحامية لعدة أعضاء في حالات فرط سكر الدم المستحث بالحمية عالية الكربوهيدرات. وأظهرت جرعة 500 ملغم/كغم فعالية تقارب تأثير الميتفورمين ($p < 0.05$). وتدعم هذه النتائج الاستخدام التقليدي لمستخلص بذور نخيل التمر المحمصة وإمكاناته كمكمل غذائي مستدام ومنخفض التكلفة لإدارة فرط سكر الدم ومضاعفاته

الكلمات المفتاحية: نخيل التمر، بذور نخيل التمر، المستخلص المائي الساخن، حمية عالية الكربوهيدرات، فرط سكر الدم، خافض لسكر الدم، الميتفورمين.