

Research Article

Antioxidant, hypolipidaemic and hepatoprotective potentials of perinatal *Thaumatococcus daniellii* leaf supplemented diet in male offspring of Sprague-Dawley rats

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Catalase, Cholesterol, Perinatal, *Daniellii* *thaumatococcus*

ABSTRACT

Background: *Thaumatococcus daniellii* (Benn.) Benth is one of the monocotyledonous herbs found in rain forests and coastal areas of West and Central Africa. This study investigated the antioxidant, hypolipidaemic and hepatoprotective roles of perinatal *Thaumatococcus daniellii* leaf supplemented diet in offspring of Sprague-Dawley rats. **Methods:** Twenty-four (24) pregnant Sprague-Dawley rats were used and fed either a control diet or *Thaumatococcus daniellii* leaf supplemented diet (TDLSD). The dams were given TDLSD diet up to parturition (in-utero group, IUG), or from birth to post-natal day 21 (lactation group, LG) or for a period covering both, combined (CG). On postnatal day 90, blood sample was collected via retro-orbital puncture to obtain serum sample for the determination of cholesterol (CHOL), triglyceride (TG), high density lipoprotein (HDL) and low-density lipoprotein (LDL) and hepatic lipase (HL). Aspartate amino transferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) was investigated. Superoxide dismutase (SOD) reduced glutathione (GSH), catalase (CAT), malonaldehyde (MDA) were investigated. **Results:** There was no significant difference ($p < 0.05$) in CHOL, LDL, and HDL levels in LG and CG offspring while TG significantly ($p < 0.05$) decreased in IUG, and CG compared with control. HL increased significantly ($p < 0.05$), ALT, AST and ALP significantly decrease ($p < 0.05$) while GSH, SOD and CAT upregulated in IUG, LG and CG compared with CONT. MDA downregulated ($p < 0.05$) in IUG, LG and CG compared with CONT. **Conclusion:** This study provides evidence that perinatal *Thaumatococcus daniellii* leaf supplemented diet possesses antioxidant, lipid lowering and hepatoprotective potentials in offspring of Sprague-Dawley rats though it was observed that in-utero exposure produced more effect hence, it's dependent on the window of exposure.

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INTRODUCTION

The origin of chronic diseases has been traced to a combination of early life nutritional exposure and lifestyle changes (Petry *et al.*, 2000). While this hypothesis on developmental programming and chronic diseases is not entirely new, it has however given rise to a recurring interest on the effect of in-utero environment on foetal / neonatal growth and

development (Armitage *et al.*, 2000). Foetal programming as a theory suggests that the environment surrounding the foetus during its developmental phase, plays a formative role in determining its disease risk during the later stages. There is ample evidence in literature that demonstrates a beneficial relationship between optimal in- utero nutritional exposure and postnatal development; as well as increased risk to diseases in the presence of an insult to the maternal environment (Kapoor *et al.*, 2006; Dai *et al.*, 2012; Babu *et al.*, 2014). The use of plants in traditional medicine referred to as herbalism or botanical medicine (Trease and Evans, 2002) falls outside the mainstream of the Western or Orthodox medicine. It has been estimated that about 75% of the world's population

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(mainly in the developing countries) rely on traditional medicine as their primary form of health care (Summer, 2000). Plants contain active components such as flavonoids, glycosides, saponins, tannins, etc., which possess medicinal properties that are harnessed for the treatment of different diseases (Eujoba, 2005). The active ingredients for a vast number of pharmaceutically derived medications contain components originating from phytochemicals. These active substances that contain the healing property are known as the active principles and are found to differ from plant to plant. The significance of plants in the treatment of diseases can be traced back to the prehistoric times (Ankita *et al.*, 2012) and medicinal herbs are being increasingly studied by medical researchers. More than 80% of the world's populations, rely on herbal medicine for their primary health care, majority of which use plants or their active principles (Gupta *et al.*, 2005).

Thaumatococcus daniellii (Benn.) Benth is one of the monocotyledonous herb found in rain forests and coastal areas of West and Central Africa (Onwueme *et al.*, 1979; Nwonuma *et al.*, 2016; Adeogun *et al.*, 2016). It is a large rhizomatous flowering herb which grows to about 3-4 m in height with large papery leaves (Adedosu *et al.*, 2017). It bears pale purple flowers and a soft crimson-coloured fruits containing a few shiny black seeds (Adedosu *et al.*, 2017). It is commonly referred to as miraculous fruit, miraculous berry, serendipity berry and katamfe/katempfe. In Nigeria, it is popular referred to as soft cane (Segun *et al.*, 2015). It was one of the underutilized and neglected plant species in Nigeria, which grows wildly mainly in cocoa growing areas of Southwest Nigeria (Adedosu *et al.*, 2017; Oluwatayo and Ojo, 2014). It is categorized as a non-woody fibre (NWF) plant used to supplement to wood fibre in paper manufacturing (Oluwadare, 2016). The plant, commonly known as "ewe eran" in Southwest Nigeria (Ekpo *et al.*, 2012) is popular for being the natural source of thaumatin, a globally traded protein sweetener (Boadi *et al.*, 2014; Oluwadare *et al.*, 2014; Arowosoge and Popoola, 2006). This low-calorie sweetener is about 2000 times sweeter than sucrose and suitable for diabetic patients (Olabanji *et al.*, 2014). Thaumatin is found in the arils which are located at the top of the seeds (Boadi *et al.*, 2014; Yeboah *et al.*, 2003). The seeds are black, hard and impervious, wrapped around by a transparent sticky gel-like sac (Chinedu *et al.*, 2014). The seed was used by locals in ethnomedicine as an emetic and in treating pulmonary problems (Lim, 2012). The jelly on the seed can be used as a substitute for agar (Abiodun *et al.*, 2014). Nonetheless, it has little to no antimicrobial effect

(Ojekale, 2007). The medicinal significance of *Thaumatococcus daniellii* (Benn) can't be overemphasized owing to the presence of several bioactive compounds, fats, minerals protein and several mineral elements, the role of which on offspring metabolism and effect in later life have not been reported.

During pregnancy, the developing foetus is completely dependent on his/her mother and maternal environment for nutrition. Several experimental investigations revealed that offspring stands a good chance of survival if diet exposed to during pregnancy is the same as the post-natal exposure. Pre-natal environment has been suggested as a factor influencing the risk of metabolic disorders such as obesity, dyslipidaemia, glucose intolerance and insulin resistance in adulthood. Several experimental and observational investigations revealed that maternal diet is a major influencer of the development systems' regulation in the offspring before and after birth. However, it remains to be defined the role of perinatal *Thaumatococcus daniellii* supplemented diet on offspring's oxidative balance, lipid metabolism and hepatic functions. In this study, we investigated the influence of early life perinatal *Thaumatococcus daniellii* supplemented diet on markers of oxidative balance such as GSH, SOD, CAT and MDA lipid peroxidation's index, markers of hepatic functions such as aspartate amino transferase (AST), alkaline amino transferase (ALT), alkaline phosphatase (ALP) and albumin (ALB), lipid metabolism's indices such as cholesterol (CHOL), high density lipoprotein (HDL), low density lipoprotein (LDL), triglyceride (TG) and hepatic lipase (HL) and whether the effect is dependent on windows of exposure.

METHODS

Experimental animals

Twenty-four (24) female and 12 male Sprague- Dawley rats weighing between 120-150 g were obtained from animal house of the College of Medicine of the University of Lagos, Idi-Araba. Experimental animals were housed in a room with controlled temperature (25 ± 1 °C) and with artificial dark-light cycle 12h light/dark cycle and acclimatized for two weeks before the experiment. The animals were well fed with standard rodent diet and water ad libitum. The experimental procedures adopted were in accordance with the provisions of the Experimentation Ethics Committee on Animals Use of the College of Medicine of the University of Lagos, Lagos State and the United States National Academy of

Sciences Guide for the Care and Use of Laboratory Animals.

Plant collection

Fresh leaves of *Thaumatococcus daniellii* were obtained from a farm in Itori-Ewekoro Local Government Area, Ogun state. The fresh leaves were identified and deposited at the herbarium of the Department of Science Laboratory Technology, D.S Adegebnro ICT Polytechnic, Eruku-Itori, Ewekoro, Ogun state. The fresh leaves of *Thaumatococcus daniellii* were air dried until constant weight was obtained. The air dried leaves were powdered using blender. Approximately 800g of the dried leaves was pelletized with 40kg of normal rat chow to form the *Thaumatococcus daniellii* supplemented diet (TSDS).

Ethical clearance

Ethical clearance was sought and given to conduct this research from the Animal Use and Care Committee of the Department of Science Laboratory Technology, D.S Adegebnro ICT polytechnic, Eruku-Itori, Ewekoro Ogun state to conduct this study.

Phytochemical screening

The phytochemical screening of the plant was carried out on dried sample as described by Harbone, (1973) to identify the active components present in *Thaumatococcus daniellii*

Mating and grouping

Female Sprague-Dawley rats were mated overnight with confirmed male breeders and a smear from vaginal which was washed with normal saline solution (NaCl, 0.9%w/v) was taken to determine the presence of spermatozoa (Chisari *et al.*, 2015). Pregnant rats were individually housed in plastic cages and allocated at random to one of four groups which was fed with either a control diet or TSDS diet. Food and water were made available to all animals

Grouping

Control group (CONT) were fed with normal rat chow throughout the experiment and the treated groups were fed thus: In-utero TSDS group (IUG) were fed with TSDS only during gestation starting from gestation day 0; lactational TSDS group (LG) were exposed to TSDS only during lactation starting from postnatal day 21 and ended at postnatal day 42; and the last group, combined TSDS group (CG) received TSDS throughout gestation and lactation. Control group was fed with normal rat diet throughout the experiment.

Litters were reduced to 8 – 12 pups on postnatal day (PND) 1 (birth, day 0). They were weaned on PND 21 and housed in groups of four to six male rats per cage. All male pups were transitioned to control diet, except control group, until the end of the experiment (PND 90). For consistency, only male offspring were used for this study.

Collection of blood sample

The rats were lightly anesthetized with isoflurane (5 % for 2 min) and after seizure of movement and unconsciousness in the rats, the eyelid is pulled back to proptose the eye for retro-orbital bleeding. Five (5 ml) of blood sample was collected and allowed to clot for 1 hour at 4 °C and centrifuged at 3,000 rpm for 10 min to obtain serum. Serum samples obtained were kept at -20 °C until analyses (Morakinyo *et al.*, 2018). This procedure on was performed on PND 90.

Collection of tissue sample

On PND 91 the rats were sacrificed using cervical dislocation following light anaesthesia. The animals were dissected; the liver tissue was removed and washed in an ice cold and rinsed with 1.15 % KCl, blotted after which the tissue was weighed.

Lipid profile

Cholesterol, triglyceride, high density and low density lipoproteins levels were carried out from the serum and liver homogenate samples with the aid of an automated analyzer (Mindray BS-120, Chema Diagnostica, Italy).

Liver functions

Albumin, alkaline phosphatase (ALP), alkaline amino transferase (ALT) and aspartate amino transferase (AST) were determined using both serum and liver homogenate samples by an automated analyzer (Mindray BS-120, Chema Diagnostica, Italy)

Oxidative stress

Oxidative analyses were carried out using both serum samples (Igbayilola *et al.*, 2021).

Determination of superoxide dismutase (SOD) activity

Briefly, SOD activity was measured by the inhibition autoxidative capacity of pyrogallol. The SOD activity was evaluated using a spectrophotometer at 420 nm. A calibration curve was constructed using SOD as standard. A 50% inhibition of autoxidation of pyrogallol was defined as one SOD unit (DinizVilela, 2016).

Determination of reduced glutathione (GSH) activity

The protein content of the samples was initially precipitated by metaphosphoric acid (MPA) at the ratio

of 1:1 (homogenate/MPA). The samples were centrifuged at 3000rpm for 10 minutes. The supernatant was collected and mixed with sodium phosphate buffer (0.1M, pH 7.4), containing EDTA (5mM) and orthophthaldialdehyde (1 mg/mL in methanol). The mixture was incubated in the dark at room temperature for 15 min and fluorescence was measured at 350 nm (excitation) and 420 nm (emission). A standard curve of GSH (0.001–0.1 mM) was used for linear regression (DinizVilela, 2016; Igbayilola *et al.*, 2021)

Determination of catalase (CAT) activity

Briefly, sample (1ml) was mixed with 49 ml of distilled water to give a 1 in 50 dilution of the sample. The assay mixture contained 4ml of H₂O₂ solution (800 μmoles) and 5ml of Phosphate buffer in a 10ml flat bottom flask. 1ml of properly diluted enzymes preparation was rapidly mixed with the reaction mixture by a gentle swirling motion. The reaction was run at room temperature. A 1ml portion of the reaction mixture was blown into 2ml of dichromate acetic acid reagent at 60s intervals. Catalase (CAT) activity was determined by measuring the exponential disappearance of H₂O₂ at 240nm and expressed in units/mg of protein (Igbayilola *et al.*, 2021; Morakinyo *et al.*, 2011; Aebi, 1984).

Determination of malonaldehyde (MDA) activity

Briefly, the most abundant individual aldehyde resulting from lipid peroxidation breakdown in biological systems, MDA was estimated with the method of Uchiyama and Mihara which is based on its interaction with thiobarbituric acid (TBA) to form pink complex with absorption at 535nm. Absorbance was read using Microlab 300 recording spectrophotometer (UV 160) in all measurements (Igbayilola *et al.*, 2021; Uchiyama *et al.*, 1978).

Determination of hepatic lipase (HL)

HL was determined in liver and adipose tissue homogenates respectively thus: The assay system (final volume 1 ml) contained 0.1 ml of glyceride emulsion, 0.2 ml of serum albumin, 0.6 ml of 0.1 M phosphate buffer (pH 7.4). 0.1 ml of enzyme approximately 200 pg of lipase protein was dissolved in glass-distilled water. Incubations lasted were for 60 min at 37 °C in a shaking water bath (Igbayilola *et al.*, 2021).

Statistical Analysis

Data were recorded as mean and standard error of the Mean. Statistical difference between the means was determined by one-way ANOVA. Any significant difference between means was assessed by and P<0.05 was accepted as the significant level.

RESULTS

*Proximate analysis of dried *Thaumatococcus daniellii* leaf extract*

Result from the proximate analysis revealed the presence of moisture (8.35), fat (1.16), ash (4.8), fibre (12.37), protein (12.96), Carbohydrate (60.32). Table 1.

Table 1

Parameters	Values (%)
Moisture content	8.35
Fat content	1.16
Ash content	4.84
Crude fibre	42.37
Crude protein	32.96
Carbohydrate	10.32

Table 2

VITAMINS VALUES	
	(μg/100g)
A	27.016
B1	2.058
B6	1.041
C	4.473
D	0.210
E	0.082

Table 3

MINERALS	VALUES
	(mg/100g)
Calcium(Ca)	13.99
Magnesium (Mg)	14.97
Manganese (Mn)	0.023
Iron(Fe)	0.24
Sodium (Na)	1.203
Potassium (K)	146.73
Silicon(Si)	0.03
Sulphur (S)	0.07
Zinc(Zn)	0.19
Fluoride(F)	1.29

Table 1: Proximate analysis of dried *Thaumatococcus daniellii* leaf. All the values are in g/100g sample. The sample was in the same condition as submitted

Table 2: Vitamin compositions of dried *Thaumatococcus daniellii* leaf

Table 3: Mineral compositions of dried *Thaumatococcus daniellii* leaf

*Vitamin compositions of dried *Thaumatococcus daniellii* leaf*

Table 2 shows the result of the vitamin compositions and value for each vitamin are presented in the table.

*Mineral elements of dried *Thaumatococcus daniellii* leaf*

Result of the mineral compositions revealed the presence of both water- and fat-soluble vitamins and these are presented in table 3.

*Serum activities of reduce glutathione (GSH), superoxide dismutase (SOD), catalase (CAT) and malonaldehyde (MDA) level in offspring exposed to perinatal *Thaumatococcus daniellii* leaf supplemented diet*

Results from antioxidant assay showed a significant increase ($p < 0.05$) in GSH activity in IUG (156.5 ± 4.36), LG (169.0 ± 5.81) and CG (175.3 ± 3.02) compared with CONT (141.0 ± 3.32) and a significant increase ($p < 0.05$) in CG (175.3 ± 3.02) compared with IUG (156.5 ± 4.36), (Figure 1). A significant increase ($P < 0.05$) was observed in SOD activity in IUG (1.2 ± 0.16), LG (1.27 ± 0.01) and CG (1.5 ± 0.17) compared with CONT (0.5 ± 0.11) and increased ($P > 0.05$) in CG (1.5 ± 0.17) compared with IUG (1.2 ± 0.16) ($p < 0.05$) (Figure 2). Figure 3 showed a significant increase ($P < 0.05$) in CAT activity only in CG (8.5 ± 0.62) compared with CONT (4.7 ± 0.37) and significantly increased ($P < 0.05$) in CG (8.5 ± 0.62), compared with IUG and LG respectively (5.2 ± 0.58) and (5.4 ± 0.41). *Thaumatococcus daniellii* leaf supplemented diet produced a significant decrease ($p < 0.05$) in MDA level in IUG (6.6 ± 0.86), LG (6.8 ± 0.38) and CG (3.9 ± 0.14) with a significant decrease ($p < 0.05$) in CG (3.9 ± 0.14) compared with CONT (11.0 ± 1.02) ($p < 0.05$) (Figure 4).

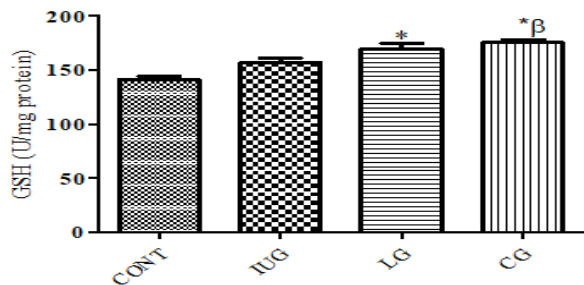


Fig. 1: GSH activity in CONT and offspring of dams exposed to *Thaumatococcus daniellii* leaf supplemented diet. Values represent Mean \pm SEM. n=6. Significant ($*p < 0.05$ vs. group A, $\#p < 0.05$ vs. group C).

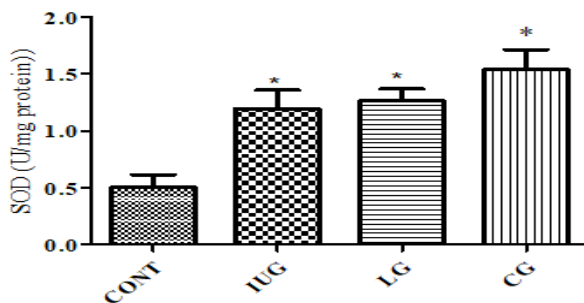


Fig. 2: SOD activity in CONT and offspring of dams exposed to *Thaumatococcus daniellii* leaf supplemented diet. Values represent Mean \pm SEM. n=6. Significant ($*p < 0.05$ vs. group A, $\#p < 0.05$ vs. group C).

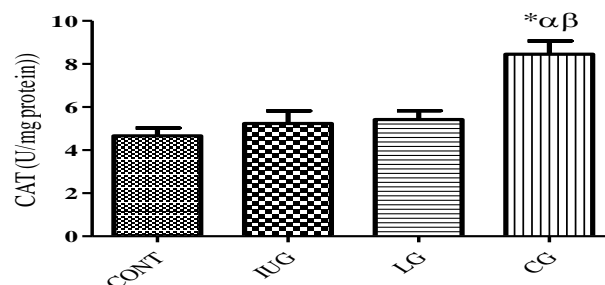


Fig. 3: CAT activity in CONT and offspring of dams exposed to *Thaumatococcus daniellii* leaf supplemented diet. Values represent Mean \pm SEM. n=6. Significant ($*p < 0.05$ vs. group A, $\#p < 0.05$ vs group B, $\alpha p < 0.05$ vs. group C)

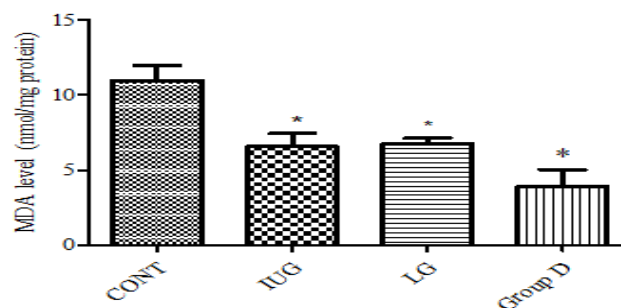


Fig. 4: MDA level in CONT and offspring of dams exposed to *Thaumatococcus daniellii* leaf supplemented diet. Values represent Mean \pm SEM. n=6. Significant ($*p < 0.05$ vs. group A)

*Serum levels of cholesterol (CHOL), triglycerides (TG), high density lipoprotein (HDL), low density lipoprotein (LDL) and hepatic lipase (HL) activity in offspring exposed to perinatal *Thaumatococcus daniellii* leaf supplemented diet*

Results from lipid profile assay showed a decrease ($p > 0.05$) in CHOL level in IUG (1.9 ± 0.04), LG (1.9 ± 0.06) and CG (1.9 ± 0.04) compared with CONT (2.1 ± 0.08) (Figure 5). There was a significant decrease ($p < 0.05$) in TG levels in IUG (0.9 ± 0.05) and CG (1.2 ± 0.11) compared with CONT (1.2 ± 0.09) and significantly increase ($p < 0.05$) in LG (1.2 ± 0.07) and CG (1.2 ± 0.11) compared with IUG (0.9 ± 0.05). (Figure 6). Figure 7 shows a significant increase ($p < 0.05$) in HDL in IUG (1.1 ± 0.04), with a decrease ($P > 0.05$) in LG and CG (0.8 ± 0.04), (0.8 ± 0.06) respectively compared with CONT (0.8 ± 0.07). HDL showed a significant decrease ($p < 0.05$) in LG (0.8 ± 0.04), and CG (0.8 ± 0.06) compared with IUG (1.1 ± 0.04). *Thaumatococcus daniellii* leaf supplemented diet produced a decrease ($p > 0.05$) in LDL levels in IUG (0.5 ± 0.02), LG (0.5 ± 0.04) and CG (0.4 ± 0.02) compared with CONT (0.5 ± 0.02) (Figure 8). However, there was a significant increase ($p < 0.05$) in hepatic lipase activity in groups IUG, LG and CG compared with CONT.

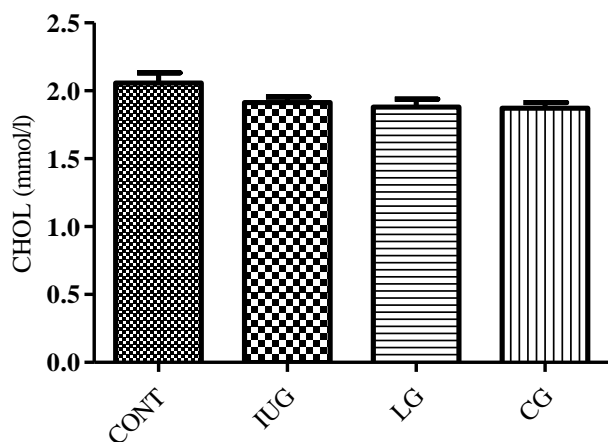


Fig. 5: CHOL level in CONT and offspring of dams exposed to *Thaumatococcus daniellii* leaf supplemented diet. Values represent Mean \pm SEM. n=6.

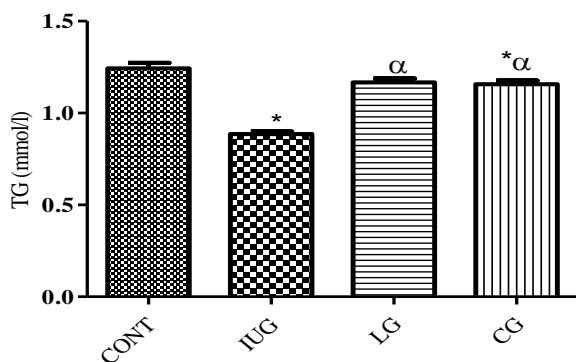


Fig. 6: TG level in CONT and offspring of dams exposed to *Thaumatococcus daniellii* leaf supplemented diet. Values represent Mean \pm SEM. n=6. Significant (*p<0.05 vs. group A)

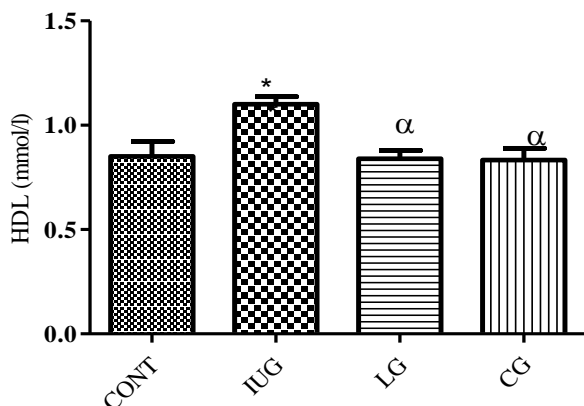


Fig. 7: HDL level in CONT and offspring of dams exposed to *Thaumatococcus daniellii* leaf supplemented diet. Values represent Mean \pm SEM. n=6. Significant (*p<0.05 vs. group A, α p<0.05 vs group B, β p<0.05 vs. group C)

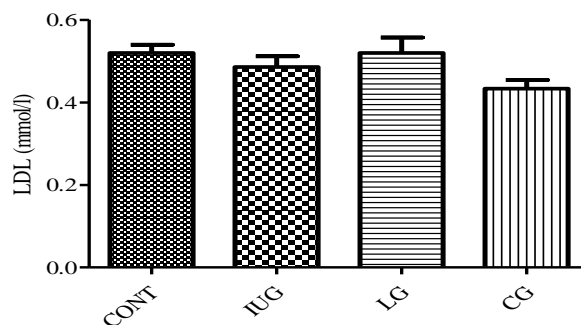


Fig. 8: LDL level in CONT and offspring of dams exposed to *Thaumatococcus daniellii* leaf supplemented diet. Values represent Mean \pm SEM. n=6.

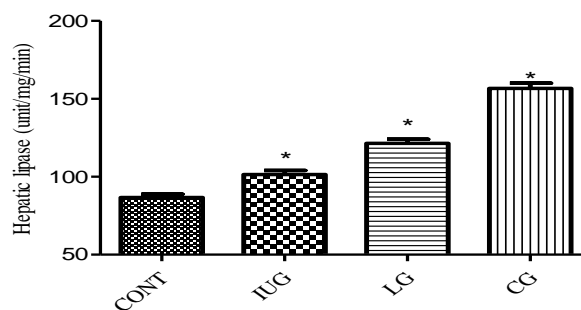


Fig. 9: HL level in CONT and offspring of dams exposed to *Thaumatococcus daniellii* leaf supplemented diet. Values represent Mean \pm SEM. n=6. Significant (*p<0.05 vs. group A)

Serum levels of AST, ALP and ALT in offspring exposed to perinatal Thaumatococcus daniellii leaf supplemented diet

Results from liver function assay showed a significant decrease (p<0.05) in AST level in IUG (69.00 \pm 2.61), LG (67.00 \pm 5.50) and CG (74.83 \pm 1.76) compared with CONT (86.14 \pm 3.87). Table 3. A significant decrease (P<0.05) was observed in ALP level in IUG (19.17 \pm 0.54) compared with CONT (23.14 \pm 1.26). ALTP decrease (p>0.05) in LG (21.86 \pm 0.77) and CG (22.71 \pm 0.84) compared with CONT (23.14 \pm 1.26) and IUG (19.17 \pm 0.54). Table 3. Table 3 showed a significant decrease (P<0.05) in ALT activity in IUG (70.00 \pm 2.44), LG (11.57 \pm 0.43) and CG (12.33 \pm 0.50), compared with CONT (80.40 \pm 5.00) and significantly decreased (P<0.05) in LG (11.57 \pm 0.43) and CG (12.33 \pm 0.50) compared with IUG (70.00 \pm 2.44).

DISCUSSION

Thaumatococcus daniellii is a plant, commonly known as “ewe eran” in Southwest Nigeria (Ekpo et al., 2012) is popular for being the natural source of thaumatin, a globally traded protein sweetener (Boadi et al., 2014; Oluwadare et al., 2014; Arowosoge and Popoola,

Table 4: Aspartate amino transferase (AST), alkaline phosphatase (ALP) and alanine amino transferase (ALT) levels in offspring of dams exposed to *Thaumatococcus daniellii* leaf supplemented diet

Parameters (u/l)	Group A	Group B	Group C	Group D
AST	86.14±3.87	69.00±2.61*	67.00±5.50*	74.83±1.76
ALP	23.14±1.26	19.17±0.54*	21.86±0.77	22.71±0.84
ALT	80.40±5.00	70.00±2.44*	11.57±0.43* ^α	12.33±0.50* ^{αβ}

Values represent Mean ± SEM. n=6. Significant (*p<0.05 vs. group A, ^αp<0.05 vs group B, ^βp<0.05 vs. group C).

2006). This low-calorie sweetener is about 2000 times sweeter than sucrose and suitable for diabetic patients (Olabanji et al., 2014). The significance of plants in the treatment of diseases can be traced back to the prehistoric times (Ankita et al., 2012) and medicinal herbs are being increasingly studied by medical researchers. More than 80% of the world's populations, rely on herbal medicine for their primary health care, majority of which use plants or their active principles (Gupta et al., 2005)

The SOD and GSH properties were investigated in this study because of their synergistic ability to work hand in hand and the result from oxidative stress study in the rats exposed to perinatal *Thaumatococcus daniellii* leaf supplemented diet shows a significant increase in GSH, SOD and CAT activities suggestive of increased oxidative balance in the male offspring. A significant reduction was observed in MDA's lipid peroxidation in all the offspring exposed to perinatal *Thaumatococcus daniellii* leaf supplemented diet suggestive of a decrease in oxidative stress. MDA has been shown to be a biomarker of oxidative stress, excessive production of which has been linked to dyslipidaemia and atherosclerosis. Oxidative stress results when the antioxidant system is overwhelmed by the generation of excess reactive oxygen species (ROS) (Halliwell and Gutteridge, 1999). These reactive species like superoxide radical anion (O⁻²), hydrogen peroxide (H₂O₂) and hydroxyl radicals (HO⁻) cause severe damage to macromolecules, tissues and organs through the process of lipid peroxidation (LPO), protein modification and DNA strand breaks (Sun and Chen, 1998). Oxidative stress resulting from the generation of these free radicals is known to contribute immensely to several pathological conditions like aging, cancer, cardiovascular disorder, neurodegenerative diseases among others (Halliwell and Gutteridge, 1999).

In the current study, decreased in LDL and increased HDL levels were observed which is suggestive of lipid lowering effect of *Thaumatococcus daniellii*. It was also observed that the *Thaumatococcus daniellii* possessed hypotriglyceridaemic effect with the significant reduction of TG in all the groups exposed to perinatal

Thaumatococcus daniellii leaf supplemented diet. The significance of serum lipids in atherosclerosis and coronary heart disease has been proved by many researchers. Emerging evidence has demonstrated the cardiovascular disease risk to be positively associated with TC and TG, and inversely associated with HDL (Cziraky et al., 2009; Cooney et al., 2008). Lipids are essential for energy homeostasis, reproductive and organ physiology, and numerous aspects of cellular biology. They are also associated to many pathological processes, such as obesity, diabetes, heart disease, and inflammation. To meet the different demands from a variety of tissues, the human body has evolved a sophisticated lipoprotein transport system to deliver cholesterol and fatty acids to the periphery exemplified by the metabolic syndrome, or syndrome X, which refers to patients who are insulin-resistant (hyperinsulinemic), dyslipidemic (elevated TG and decreased HDL-cholesterol levels), and at high risk for developing coronary artery disease (CAD) (Nguyen et al., 2008). Hyperlipidemia is a heterogeneous group of disorders characterized by high level of lipids in the bloodstream. It may be caused by disorders of some endocrine glands, kidneys, effects of certain drugs, dietary intake containing high amount of fat, risky life style and ageing (Durrington, 1998). It is one of the risk factors in development of atherosclerosis (Nwodo et al., 2014).

Fibre has been reported to decrease LDL by interrupting cholesterol and bile acid absorption and increasing LDL receptor activity (Xiao-Qian et al., 2012). LDL has been shown to facilitate transport of cholesterol into cell thus, the reduction in LDL is suggestive and justifies the cholesterol lowering effect of perinatal *Thaumatococcus daniellii* supplemented diet observed in this study which may further reduce the risk of metabolic disorder such as obesity and dyslipidaemia. The lipid lowering effect of perinatal *Thaumatococcus daniellii* supplemented diet may be attributed to large fibre content present in this plant and this was evident in the proximate composition. There have also been reports on the lipid profile of various plants including *Thaumatococcus daniellii* and some of which is in accordance with the present study (Harword

et al., 2008; Ikeda et al., 2008). Thus, there could be alterations in the concentration of the various lipid metabolism and predisposition of the heart to atherosclerosis and its associated coronary heart diseases.

Furthermore, the current study is the first study on perinatal *Thaumatococcus daniellii* supplemented to understudy the roles of hepatic lipase (HL) on lipid metabolism. HL is a lipolytic enzyme synthesized mostly by hepatocytes and found localized at the surface of liver sinusoidal capillaries. It can be considered as a lipase of the vascular compartment, together with lipoprotein lipase (LPL), with which it shares number of structural and functional similarities. HL exerts both triglyceride lipase and phospholipase A1 activities and is involved at different steps of lipoprotein metabolism (Gabory et al., 2008). The results showed upregulation in HL activity in offspring exposed to the supplemented diet which is suggestive of improved lipid metabolism. Furthermore, perinatal *Thaumatococcus daniellii* leaf supplemented diet produced a significant decrease in significant downregulation in all the liver enzymes' such as AST, ALP and ALT in all the offspring suggestive of hepatoprotective effect of *Thaumatococcus daniellii* leaf.

CONCLUSION

This study provides evidence that perinatal *Thaumatococcus daniellii* leaf supplemented diet possesses antioxidant, lipid lowering and hepatoprotective potentials in male offspring of Sprague-Dawley rats though it was observed that in-utero exposure produced more beneficial effect. This showed that in-utero window of exposure is most important to offspring metabolism and any alteration during this window may compromise health in later life.

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REFERENCES

Abiodun, O.A., R. Akinoso, O.O. Olosunde, J.A. Adegbite and O.A. Omolola, (2014). Nutritional quality and essential oil compositions of *Thaumatococcus daniellii* (Benn.) tissue and seed. *Food Chem.*, 160: 286-291.

Adedosu, O.T., J.A. Badmus, G.E. Adeleke and G.O. Olalere, (2017). *Thaumatococcus daniellii* extract modulates glibenclamide activity and ameliorates hematological disorders, oxidative stress and dyslipidemia associated with diabetes mellitus in rats. *Br. J. Pharm. Res.*, 16: 1-12.

Adeogun, O., A. Adekunle and A. Ashafa (2016). Chemical composition, lethality and antifungal activities of the extracts of leaf of *Thaumatococcus daniellii* against foodborne fungi. *Beni-Suef Univ. J. Basic Applied Sci.*, 5: 356-368.

Aebi, H. (1984). Catalase in vitro. *Methods Enzymology*. 105:121-126.

Ankita, S., Kaur, P., Gupta., R (2012). Phytochemical screening and antimicrobial assay of various seeds extracts of Cucurbitaceae Family. *International Journal of Applied Biology and Pharmaceutical Technology*; 3 (3) 401-409.

Armitage J.A., Taylor P.D., Poston L. (2005). Experimental models of developmental programming: consequences of exposure to an energy rich diet during development. *J Physiol*. 565: 3-8.

Arowosoge, O.G.E. and L. Popoola, (2006). Economic analysis of *Thaumatococcus daniellii* (Benn.) Benth. (Miraculous berry) in Ekiti State, Nigeria. *Nig. J. Food Agric. Environ.*, 41: 264-269.

Babu, M.B., Rajasekhar, D., Vanajakashamma, V., Babu, S (2014). Study of relationship between metabolic syndrome Score and Angiographic severity of coronary artery diseases according to the presence of Diabetes. *Indian Heart Journal*. 66(12): S46-S47. DOI: 10.1016/j.hj.2014.10.131

Boadi, S., M. Baah-Acheamfour, F. Ulzen-Appiah and G.M. Jamro, (2014). Nontimber forest product yield and income from *Thaumatococcus daniellii* under a mixed tree plantation system in Ghana. *Int. J. For. Res.* 10.1155/2014/524863.

Chinedu, S.N., A.Y. Oluwadamisi, S.T. Popoola, B.J. David and T. Epelle (2014). Analyses of the leaf, fruit and seed of *Thaumatococcus daniellii* (Benth.): Exploring potential uses. *Pak. J. Biol. Sci.* 17: 849-854.

Chisari, A.N., Podaza, E., Echarte, E.M. (2015). A low maternal protein diet during pregnancy and lactation induce liver offspring dysfunction, in the rat. *Am Nutr Disord & Ther*. 2(1):1020.

Cooney, M.T., Dudina, A., de Bacquer, D., Wilhelmsen, L., Sans., S., Mentotti, A., de Bacquer, G., Jousilahti, P., Keil, U., Thomsen, T., Whincup, P., Graham, I.M., Score investigators. *Atherosclerosis*; 2009. 206: 611-616.

- Cziraky, M.J., Watson, K.E., Talbet, R.L (2008). Targeting low HDL-cholesterol to decrease residual cardiovascular risk in the managed care setting. *J. Mang. Care Pharm*; 14: S3-S8.
- Dai, Y., Thamotharan, S., Garg, M., Shin B.C., Devaskar, S.U. (2012). Superimposition of postnatal calorie restriction protects the aging male intrauterine growth-restricted offspring from metabolic maladaptations. *Endocrinology*; 45:435-449
- Durrington, P.M., Hunt, I., Ishola, M., Arrol, S., Bhatnagar, D (1998). Apolipoproteins (a), AI, and B and parental history in men with early onset ischaemic heart disease. *Lancet*; 1:1070-1073
- Ekpo, I.A., R.B. Agbor, E.C. Okpako, A.N. Osuagwu, B.E. Ekanem and P.A. Otu, 2012. Effect of crude oil and simulated acid rain on the growth and physiology of *Thaumatococcus daniellii*. *J. Biodivers. Environ. Sci.*, 2: 21-25.
- Eujoba, A.A., Odeleye, O.M., Ogunyemi, C.M (2005). Traditional medicine development for medical and dental primary health care delivery system in Africa. *African Journal of Traditional, Complementary and Alternative Medicines*; 2(1): 46-61.
- Gabory A, Attig L, Junien C (2009). Sexual dimorphism in environmental epigenetic programming. *Mol Cell Endocrinol*; 304: 8-18.
- Gupta, M.P, Sol s, P.N., Calder, A.I., Guinneau-Sinclair, F., Correa, M., Galdames, C., Guerra, C., Espinosa, A., Alvenda, G.I., Robles, G. and Ocampo, R (2005). Medical ethnobotany of the Teribes of Bocas del Toro, Panama. *Journal of Ethnopharmacology*; 96:389-401.
- Halliwell B, Gutteridge JMC (1999). editors. *Free radicals in biology and medicine*. Oxford, UK: Oxford University Press; 284-330.
- Harword, H.J. Jr., Chandler, C.E., Pellarin, L.D., Bangerter, F.W., Wilkins, R.W., Long C.A (2005). Pharmacologic consequences of cholesterol absorption inhibition: alteration in cholesterol concentration induced by the synthetic saponin β -tigogenin in cellobioside (CP-88818; tiqueside). *J. Lipid. Res*; 2005. 34: 377-95.
- Igbayilola Y.D, Aina O.S, Saka W.A, Oyabambi A.O, Mofolorunso A.M, Moshood A.A. (2021). Beneficial effect of co-administration of Coconut water and Honey on glucose storage, hepatic functions and oxidative balance in Sprague-Dawley rats. *Int J Basic Appl Physiol*. 10(1): 23-34
- Igbayilola Y.D, Morakinyo A.O and Iranloye B.O (2021). Adverse effects of perinatal protein restriction on regulators of lipid metabolism and hepatic function in offspring of Sprague-Dawley rats. *Niger J Exp Clin Biosci*. 9(2): 74-81
- Ikeda, I., Sugano, M., Imoh, E.U., Julia, O.M (2005). Nutrient requirement for the growth of water leaf (*Talinum triangulare*) in Uyo Metropolis, Nigeria. *The Environ*; 2005. 21; 153-159.
- Kapoor, A., Dunn, E., Kostaki, A., Andrews, M.H., Matthews, S.G (2006). Fetal programming of hypothalamo-pituitary-adrenal function: Prenatal stress and glucocorticoids. *J. Physiol*. 572 (1): 31-44
- Kayode, A.A., and Kayode, O.T (2011). Some medicinal values of *Telfairia occidentalis*: American Journal of Biochemistry and Molecular Biology; 2: 36-42. Leaf, Wikipedia, the free encyclopedia, retrieved on 19th July. <http://en.wikipedia.org/wiki/leaves>
- Lim, T.K., (2012). *Edible Medicinal and Non-Medicinal Plants, Volume 6. Fruits*. Springer, New York, ISBN: 978-94-007-5627-4, pp: 259-264.
- Morakinyo, A.O., Iranloye B.O., Ogunsola, O.A. (2018). Glucometabolic effects of single and repeated exposure to forced-swimming stressor in Sprague-Dawley rats. *EndocrRegul*. 52 (2):85-92. doi: 10.2478/enr-2018-0010.
- Morakinyo, A.O., Iranloye, B.O., Daramola, A.O. and Adegoke, O.A. (2011). Antifertility effect of calcium channel blockers on male rats: association with oxidative stress. *Advances in Medical Sciences*. 56: 1-8.
- Nguyen, P., Leray, V., Diez, M., Serisier, M., Le Bloc'h, J., Siliart, B., Dumon, M (2008). Liver lipid metabolism. *Journal of Animal Physiology and Animal Nutrition*; 272-283. DOI: 10.1111/j.1439-0396.2007.00752x
- Nwodo, N.J., Nnadi, C.O., Ibezim, A., Mbah, C.J (2014). Plants with hypolipidaemic effects from Nigeria flora. In *Tech. Chapt*; 10: 241-255.
- Nwonuma, C.O., E.O. Irokanulo, C.E. Iji, O.O. Alejolowo and C.O. Adetunji. (2016). Effect of *Thaumatococcus daniellii* leaf rat-feed on potassium bromate induced testicular toxicity. *Asian Pac. J. Reprod.*, 5: 500-505.
- Ojekale, A.B., S.C.O. Makinde and O. Osileye (2007). Phytochemistry and anti-microbial evaluation of *Thaumatococcus danielli*, Benn. (Benth.) leaves. *Nig. Food J.*, 25: 176-183.
- Olabanji, S.O., G.A. Osinkolu, D.A. Pelemo, E.I. Obiajunwa and A.T. Oladele, (2014). PIXE analysis of *Thaumatococcus danielli* in Osun State of Nigeria. *Nucl. Instruments Methods Phys. Res. Sect. B: Beam Interact. Mater. Atoms*, 318: 182-186.
- Oluwadare, A.O. (2016). Pulp sheet properties of soda pulp of miraculous berry (*Thaumatococcus daniellii* Benth.) stalk as a global fibrous raw material for papermaking. *Egerton J. Sci. Technol.*, 15: 190-203.

- Oluwadare, A.O., A.F. Gilbert and O.A. Sotannde (2014). A comparison of soda and soda-ethanol pulps of *Thaumatococcus daniellii* Benth (Miraculous Berry) stalks. *Br. J. Applied Sci. Technol.*, 4: 2181-2193.
- Oluwatayo, I.B. and A.O. Ojo (2014). Socioeconomic contributions of neglected and underutilized species to livelihood security in rural southwest Nigeria: *Thaumatococcus daniellii* as a test case. *Mediterr. J. Social Sci.*, 5: 311-317.
- Onwueme, I.C., B.E. Onochie and E.A. Sofowora, (1979). Cultivation of *Thaumatococcus daniellii*-the sweetener. *World Crops*, 31: 321-335.
- Petry, C.J and Hales, C.N. (2000). Long-term effects on offspring of intrauterine exposure to deficits in nutrition. *Hum Reprod Update*; 6: 578-586.
- Segun, A.A., F.O. Samuel and A.T. Aminat (2015). Assessment of antibacterial activity of essential oil extracted from leaves of *Thaumatococcus daniellii* (Benn.) Benth. in light of its inhibitory impact on extracellular protease of *Shigella dysenteriae*. *Int. J. Biochem. Res. Rev.*, 5: 9-19.
- Sumner, J (2000). *The Natural History of Medicinal Plants*. 1st ed. Timber Press. Portland; P 235.
- Toxicology; 1: 167-175.
- Sun, A. Y., and Chen, Y. M (1998). Oxidative stress and neurodegenerative disorders. *J. Biomed. Sci*; 5: 401-414.
- Trease, G.E. and Evans, W.C (2002). *Trease and evans pharmacognosy*. 15th ed. London: WB Saunders. 419-473.
- Uchiyama, M. and Mihara, M. (1978). Determination of malondialdehyde precursor in tissues by thiobarbituric acid test. *Anal of Biochemistry*. 86: 271-278.
- Xiao-Qian, H.U., Jie, X.U., Yong, X.U.E., Zhao-Jie, L.I., Jing-Feng, W., Jia-Hui, W., Chang-Hu, X.U.E., YuMing, W (2012). Effects of bioactive components of sea cucumber on the serum liver, lipid profile and lipid absorption. *Journal of Bioscience Biotechnology and Biochemistry*; 76(12): 2214-2218.
- Yeboah, S.O., T.H. Hilger and J. Kroschel, (2003). *Thaumatococcus daniellii* (Benn.) Benth.-A natural sweetener from the rain forest zone in West Africa with potential for income generation in small scale farming. *J. Applied Sci.*, 6: 854-859.