

Ameliorating Effects of *Cyperus esculentus* on the Cerebellum of Adult Male Wistar Rats Exposed to Both High-Fat Diet and Bisphenol A: A Comparative Histopathology Study

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Abstract

Exposure to a high-fat diet (HFD) and bisphenol A (BPA) has been reported to cause critical health conditions related to the cardiovascular and neuroendocrine systems. *Cyperus esculentus* (CE) has been used as a source of nutrients and also in traditional medicines due to its potent antioxidant, anti-inflammatory, and neuroprotective properties. However, the specific ameliorative effects of CE on the cerebellum under conditions of combined exposure to HFD and BPA remain unexplored. This study aimed to evaluate histopathologically the potential toxic effects of combined exposure of HFD and BPA on the cerebellum of adult male wistar rats, and the ameliorating effects of *Cyperus esculentus*. 24 adult male wistar rats were randomly divided into six groups (A-F) ($n=4$) as follows: Control (normal feed) – Group A; HFD only – Group B; BPA only – Group C; HFD+BPA – Group D; HFD+BPA+CE (50mg/kg) – Group E; and HFD+BPA+ CE (100mg/kg) – Group F. The HFD+BPA exposure lasted 12 weeks, followed by a 4-week treatment period with CE for Groups E and F. Cerebellar tissues were harvested, processed for histology, and stained with hematoxylin and eosin for microscopic examinations. Histopathological assessments revealed significant cerebellar damage under HFD+BPA combined exposure – Group D, characterized by severe Purkinje cell degeneration, granular layer congestion, vacuolization in the molecular layer, and general disorganization of cortical layers. Administration of CE extract, particularly at the 50mg/kg dose, attenuated these alterations, showing reduced vacuolation, less severe Purkinje cell degeneration, and improved cortical architecture. Notably, the 100mg/kg CE extract showed a less pronounced ameliorative effect. Combined exposure to HFD and BPA induces a marked histopathological injury in the rat cerebellum. CE extract demonstrates a dose-dependent, partial neuroprotective effect against this injury, with a 50mg/kg dose showing the most promising outcome in this study. These findings suggest that *Cyperus esculentus* has therapeutic potential, with a need for further studies on the precise molecular mechanisms involved.

Keywords: *Ameliorating effects, Bisphenol A, Cerebellum, Comparative study, Cyperus esculentus, High-fat diet, Histopathology, Neuroprotection, Wistar rats.*

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Introduction

The practice of consuming high-fat diets (HFDs), often referred to as fast food or junk food, keeps gaining more popularity due to its low cost, marketing strategies of vendors, and people's busy schedules to prepare a proper diet (Holmboe-Ottesen, 2000). This type of food often contains unhealthy high levels of total fat, saturated fat, and calories. Fat is an essential nutrient. However, the long-term consumption of inappropriate proportions of its bad derivatives, via HFD, has been reported to increase the prevalence of obesity, cardiovascular diseases, and related metabolic disorders (Banik and Hossain, 2014; Inya *et al.*, 2023a; Inya *et al.*, 2023b; Jones *et al.*, 2022).

Relatedly, obesity has been reported as one of the risk factors for multiple myeloma and non-Hodgkin lymphoma (Ikwuka, 2023e). Obesity is also one of the components of metabolic syndrome diseases (MSDs). MSDs include hypertension, obesity, diabetes mellitus, and dyslipidemia. These are interlinked diseases and often occur concurrently. MSDs are associated with very high economic costs, morbidity and mortality rates (Ikwuka, 2015; Ikwuka, 2017a; Ikwuka, 2017c; Ikwuka, 2023c; Ikwuka, 2023f; Ikwuka, 2024; Virstyuk, 2016). Various studies have also reported links between MSDs and increased levels of blood pressure, glucose and lipid metabolic disorders, asymptomatic hyperuricemia, systemic immune inflammation, and fibrogenesis – which are remarkable risk factors that may eventually lead to different types of renal pathologies (Ikwuka, 2017d; Ikwuka, 2017e; Ikwuka, 2018c; Ikwuka, 2018d; Ikwuka, 2019a; Ikwuka, 2019c; Ikwuka, 2022; Ikwuka, 2023d; Virstyuk, 2017a; Virstyuk, 2018a; Virstyuk, 2019; Virstyuk, 2021a; Virstyuk, 2021b).

On the other hand, the consumption of HFDs is often associated with bisphenol A (BPA) exposure (Li *et al.*, 2025). Bisphenols are a class of chemical compounds that have two hydroxyphenyl functional groups. The most widely used bisphenol A is used to make epoxy resins and polycarbonates, which are hard and usually clear plastics used in everyday life, such as in producing papers, toys, water pipes, electronic products, and other plastic materials (Vasiljevic and Harner, 2021). The frequent packing of hot HFDs in these polycarbonate plastics is the common route for HFD and BPA combined exposure, as it facilitates the diffusion of BPA from the plastic containers into the food (Almeida *et al.*, 2018; Li *et al.*, 2025).

Moreover, fat also promotes this process, as BPA is fat-soluble. The exposure to bisphenols in children has been documented to cause oxidative stress, insulin resistance, and endothelial dysfunction (Kataria *et al.*, 2017; Kougias *et al.*, 2018; Liu *et al.*, 2021). The major contributors to oxidative stress are free radicals such as superoxide anions, hydroxyl radicals, and hydroperoxyl radicals and all are significant physiologically. A non-radical which is significant physiologically is hydrogen peroxide (Aliu-Ayo *et al.*, 2023a; Aliu-Ayo *et al.*, 2023b; Ama *et al.*, 2023; Baysah *et al.*, 2023; Ikwuka, 2023b; Uche *et al.*, 2023). Increased oxidative stress could lead to alteration in the DNA sequence (Ikwuka, 2023a).

Other studies have also shown that girls with more BPA exposure in their meals are overweight and/or obese and are more at risk of cardiometabolic disorders than girls with a lower BPA exposure (Poojary *et al.*, 2024). HFD and BPA combined exposure presents a compounded health risk, which may exacerbate the negative effects on various biological systems, including the cardiovascular and neuroendocrine systems, due to their oxidative, inflammatory, and neurodegenerating properties. The cerebellum is particularly vulnerable to these combined insults, potentially leading to significant structural and functional impairments (Meli *et al.*, 2020).

Cyperus esculentus (Tiger nut) is a perennial plant belonging to the family Cyperaceae. The edible part of the plant is the spherical rhizome, located at the base of the tuber. The plant is a good source of edible oils that contain a lot of monounsaturated fatty acids, and the nutritional value of tiger nut oil is similar to olive oil (Gambo and Da'u, 2014; Roselló-Soto *et al.*, 2017). *Cyperus esculentus* contains bioactive



substances, including organic acids, alkaloids and phenols (Nina *et al.*, 2019), a lot of starch (Freire *et al.*, 2019), and protein, though relatively small, but is suitable for diabetic patients or those with digestive dysfunctions, and may prevent heart disease (Ogunlade *et al.*, 2015).

In addition, the pharmacologically active compounds that are bioavailable in *Cyperus esculentus* exert their actions by interacting with molecular targets, including receptors, enzymes, channels, and transporters. Regarding the central nervous system (CNS), modulation of neurotransmitter actions is its main target (Wiebe *et al.*, 2019). Changes in neurotransmitter activity induce changes in the downstream signaling cascade, which finally result in changes in ion channel conductance. Since the electric activity of single neurons depends on the set of momentarily active ion channels, communication between neurons is governed by ion channel activity. Thus, drug-induced changes in local field potentials reflect the changes in the underlying neurotransmission of local neural networks (Wiebe *et al.*, 2019).

The properties of *Cyperus esculentus* in preventing and managing diseases aligns it to be used in phytomedicine, also called herbal medicine. Phytomedicine is acknowledged as the most common form of alternative medicine, as numerous plants, including *Cyperus esculentus*, have been used medicinally (Ama *et al.*, 2023; Ekechi *et al.*, 2023a; Sadek *et al.*, 2018; Yu *et al.*, 2022). The World Health Organization (WHO) estimates that about 80% of the world's population relies on these unconventional plant-based medicines as their primary medical intervention, both in developing and developed countries (Nina *et al.*, 2019).

Emerging studies suggest that *Cyperus esculentus* possesses potent antioxidant, anti-inflammatory, and neuroprotective properties, which could counteract the damaging effects of HFDs and BPA (Vishe, 2023). However, despite the growing evidence of the risks associated with HFDs and BPA combined exposure, the specific ameliorative effects of *Cyperus esculentus* on the cerebellum under conditions of combined exposure to HFDs and BPA have been unexplored. This present study therefore, aimed to evaluate histopathologically the potential toxic effects of the combined exposure of HFDs and BPA on the cerebellum of adult male wistar rats, and the ameliorating effects of *Cyperus esculentus*.

Materials and Methods

Biological Materials

The biological materials used in this study are as follows: adult male wistar rats, *Cyperus esculentus* (tiger nut), water, King's oil, and high-fat diet (HFD) which constituted of a mixture of Devon margarine, BUA sugar, cooked egg yolk, and Chikun feed.

Chemical Materials

Bisphenol A (BPA) and 10% neutral buffered formalin were the chemicals used for this study.

Study Instruments

Instruments used in this study include cages, drinking containers, oral gavage for substance administration, measuring cylinder, distilled water, laboratory coats, timer, dissecting board, dissecting kits, hand gloves, tissue container, blood collecting tubes, syringe, histological processing materials and equipment, oven, paraffin wax, hematoxylin and eosin stains, Rotary microtome, centrifuge, light microscope with a camera Yw₅₀, microscope slides, and cover slips.

Composition of Original Rat Feed

The normal chow was purchased from Chikun feed, and it is composed of the following nutrients outlined in Table 1.

Table 1. Composition of Original Rat Feed

Nutrients	Composition (%) per 25 kg
Crude protein	17.00
Crude fat	4.00
Crude fibre	5.00
Calcium	0.85
Phosphorus	0.45
Lysine	0.90
Methionine	0.40

For this study, the HFD was constituted from a mixture of Devon margarine, BUA sugar, cooked egg yolk, and Chikun feed as shown in Table 2. According to the United States Department of Agriculture (USDA), 50g of cooked egg yolk has an equivalent 13.23g of fat.

Table 2. Composition of HFD Used for the Study

HFD composition	Percentage (%)	Composition (g)
Chikun feed	60	300
Margarine	20	100
Sugar	10	50
Cooked egg yolk	10	50
Total	100	500

Cyperus esculentus Extract Preparation

100 g of powdered *Cyperus esculentus* was added to a liter of distilled water (ratio 1:10 w/v). The mixture was heated at 60°C for 60 minutes, while stirring intermittently. The mixture was allowed to cool, and filtered using muslin cloth followed by filter paper. The filtrate was concentrated using a water bath at 40°C, dried to obtain a semi-solid or powdered extract, and stored at 4°C. Reconstitution for administration was done by dissolving the required extract dose in distilled water to form an aqueous extract.

Experimental Design and Substance Administration

This study involved 24 adult male wistar rats weighing from 330g to 630g, which were randomly divided into six (6) different groups (Groups A-F) as shown in Table 3. Each group has four (4) randomized rats, which were tagged and housed in separate cages. There was no need for acclimatization since the study setting was also in the same city where the animals were purchased. The rats were fed appropriately and closely monitored throughout the duration of this study. Administration of HFD was closely monitored through self-feeding by the rats in their cages. BPA and *Cyperus esculentus* extracts were administered with oral gavage to ensure accurate doses were given to the rats in each cage.

Table 3. Animal Grouping and Feeding with Normal Diet and High-Fat Diet

Group	Feeding	Duration (weeks)	Adult male wistar rats
A	Normal feed and water/oil	12	4
B	HFD only	12	4
C	BPA only	12	4
D	HFD and BPA only	12	4
E	HFD, BPA, and 50mg/kg of <i>Cyperus esculentus</i>	12 + 4	4

F	HFD, BPA, and 100mg/kg of <i>Cyperus esculentus</i>	12 + 4	4
	Total number of adult male wistar rats		24

Tissue Collection and Histological Preparation

On the 113th day (24 hours after the completion of the treatment period), the rats were euthanized using chloroform, and the brains were harvested for histological analysis. The cerebellum was carefully dissected from the rest of the brain and fixed in 10% neutral buffered formalin for 48 hours to ensure complete fixation.

Following fixation, the cerebellar tissues were dehydrated through graded ethanol concentrations: 70% ethanol for 7 hours, 80% ethanol for 2 hours, and two successive changes each of 90%, 95%, and 100% ethanol for 1 hour per change. Tissue clearing was performed in two changes of xylene, each lasting 1 hour. The tissues were then properly oriented and infiltrated with molten paraffin wax in an oven maintained at 58°C, using three changes at 1 hour per change. Subsequently, the tissues were embedded in paraffin wax and blocked, from which serial sections of 4 µm thickness were cut and mounted on clean glass slides.

The sections were deparaffinized in two changes of xylene for 10 minutes each, rehydrated through descending grades of ethanol (100%, 95%, and 80%) for 5 minutes each, and rinsed briefly in distilled water. Staining was carried out using hematoxylin for 10 minutes, followed by washing under running tap water. Differentiation was achieved using 1% acid alcohol for a few seconds, after which the sections were rinsed in running water for 1 minute and blued in 0.2% ammonia water for 30 seconds. Counterstaining was performed with eosin for 2 minutes.

After staining, the sections were dehydrated through ascending grades of ethanol (80%, 95%, and 100%) for 5 minutes each, cleared in two changes of xylene for 5 minutes per change, and mounted using DPX mounting medium. The prepared sections were examined under a light microscope at high-power magnification (×400), and photomicrographs were captured.

Data Analysis

All collected data were presented as Mean±Standard Error (S.E.), analyzed using one-way analysis of variance (ANOVA), and $p < 0.05$ was used as the significance level for comparisons (Ekechi *et al.*, 2023b; Udeh *et al.*, 2023a; Udeh *et al.*, 2023b).

Ethical Considerations

The ethical clearance for this study was sought from the Research and Ethics Committee of the Faculty of Basic Medical Sciences, Ebonyi State University, Abakaliki, Nigeria. The adult male wistar rats used in this study were handled in accordance with the guidelines of the Institute for Laboratory Animal Research concerning the care and use of laboratory animals (Institute for Laboratory Animal Research, 2011).

Results

Microscopic Findings of the Cerebellar Tissue

Photomicrographs of the section of the cerebellum of an adult male wistar rat in Group A, which is the control group that received normal feed and water/oil for 12 weeks, stained with hematoxylin and eosin with a magnification of x40 (a) and x100 (b). This section presented normal appearance of the histological layer of the cerebellum from outside moving inwards – Pia mater (PM), Molecular layer (ML), Purkinje cell layer (PCL), granular layer (GL), and white matter, all of which are found in a single folium (plate 1a)

of the cerebellum. The ML, which contains numerous basket (B) and stellate (S) cells [cells of the Molecular layer (CML)], showed no distortion. Flask-shaped cells of the Purkinje cell layer (CPL) showed a normal necklace appearance around the granular layer. Most of the CPLs are directed towards the CML. A normal, distinct, darker appearance of the CGL due to a higher density of nuclei of granular cells in this area was observed, as shown in Plate 1b.

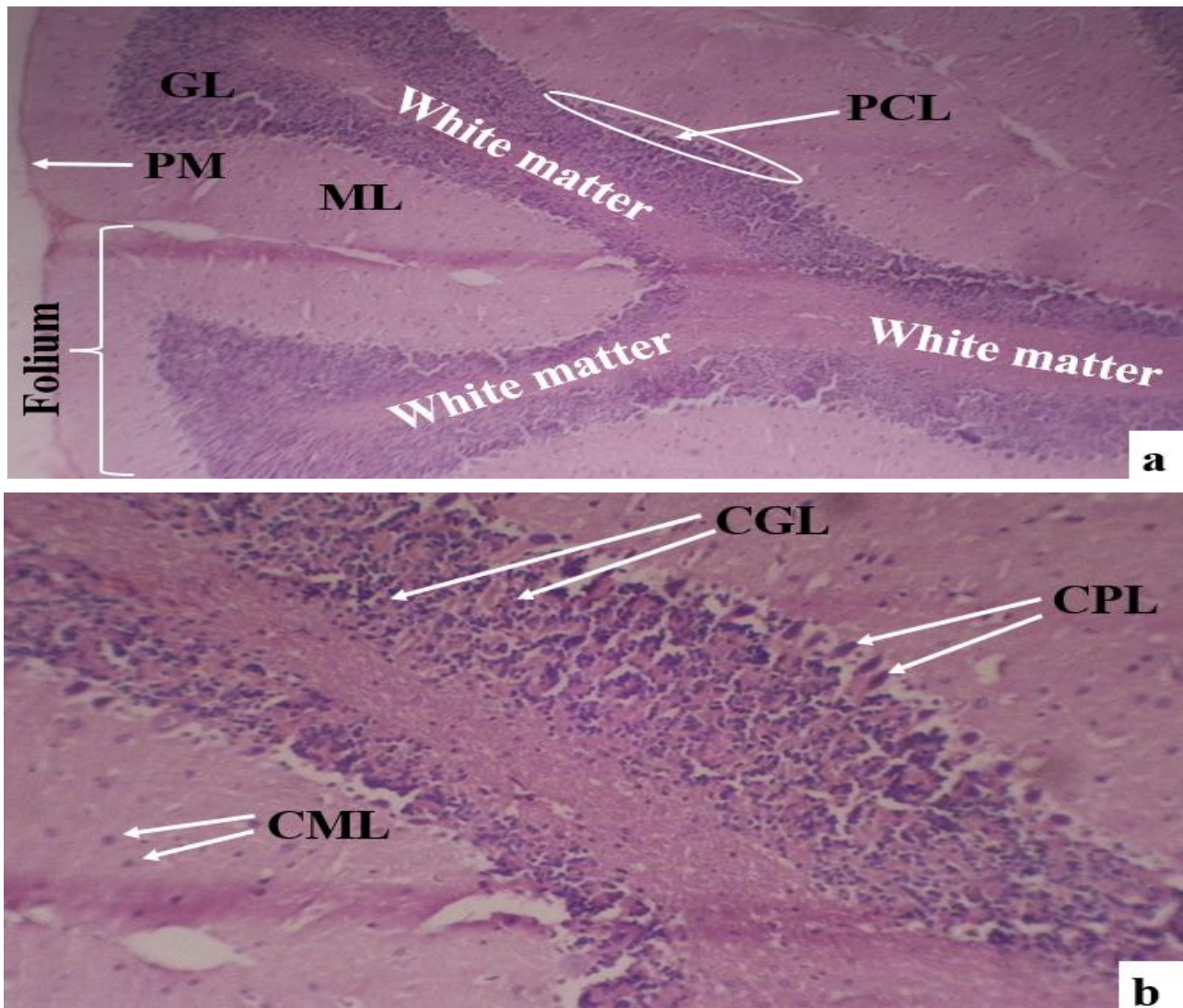


Plate 1. Normal Cerebellar Histology in Control Adult Wistar Rat

Plate 1a. Cerebellar Folium Showing Normal Layered Architecture (H&E, ×40)

Plate 1b. Granular and Purkinje Cell Layers with Normal Morphology (H&E, ×100)

Photomicrographs of a section of the cerebellum of an adult male wistar rat in Group B that received HFD only for 12 weeks, stained with hematoxylin and eosin with a magnification of x40 (c) and x100 (d). This section showed structural distortion of the flask-shaped cells or loss of structure of cells (LSCs) of PCL (Plates 2c and d), and some loss of Purkinje cells (LPCs) at the PCL (Plate 2c). It also indicated a reduction in the compactness of the ML and GL layers (Plate 2d). The presence of vacuoles (V) was also observed in the ML (Plate 2d).

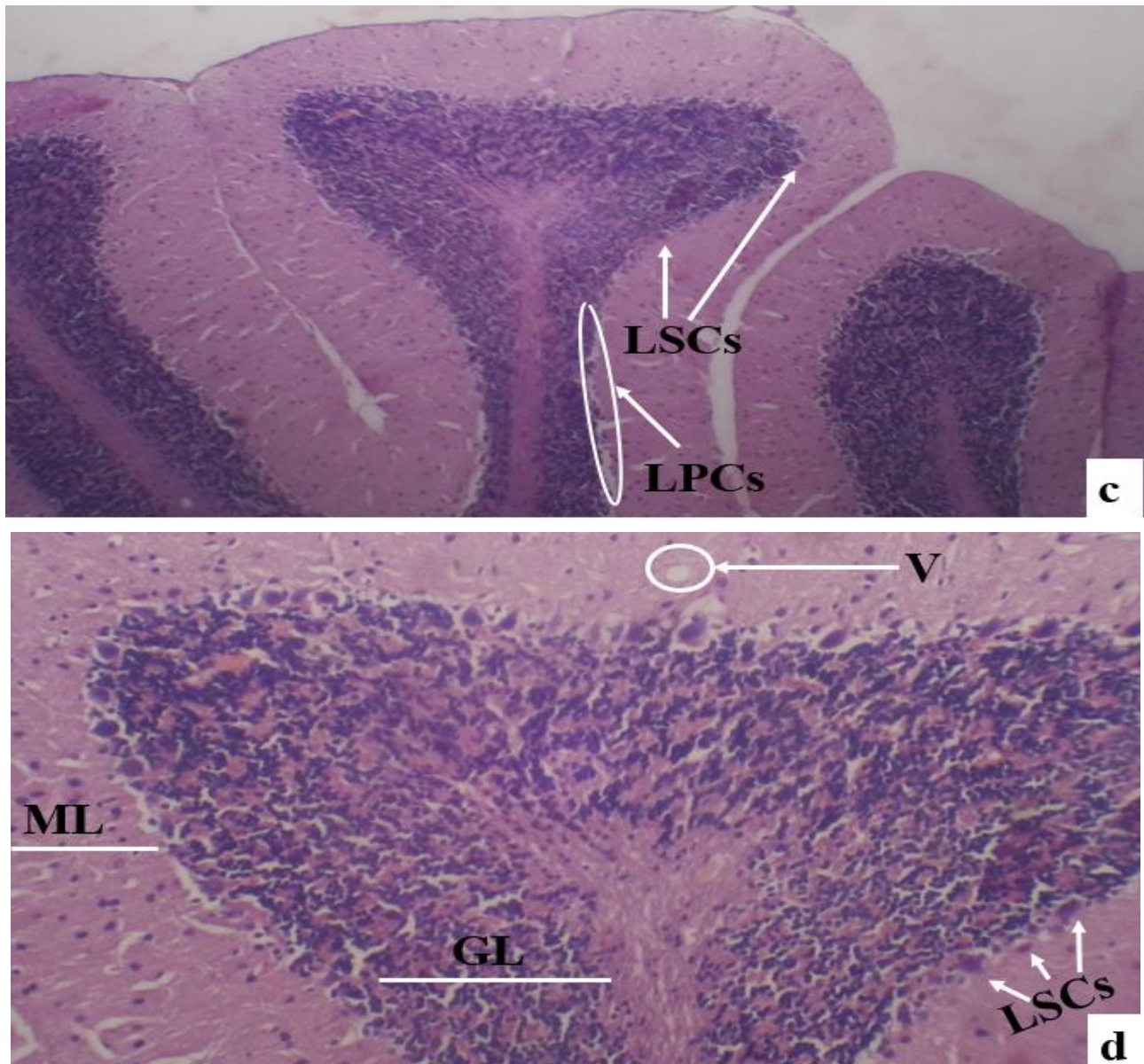


Plate 2. Cerebellar Changes in HFD Group

Plate 2c. Purkinje Cell Distortion and Loss (×40)

Plate 2d. Vacuoles and Reduced Compactness of ML/GL (×100)

Photomicrographs of a section of the cerebellum of an adult male wistar rat in Group C that received BPA only for 12 weeks, stained with hematoxylin and eosin with a magnification of x40 (e) and x100 (f). The section from this group indicated congestion of granular cells (CGCs) of the granular layer (GL) as well as a reduction in the thickness of the granular layer (RTGL) (Plate 3e) and severe degeneration of Purkinje cell layer (SDPCL) and associated Purkinje cells. The presence of vacuolization of some cells of the molecular layer (VCML) and severe reduction of the compactness of the ML (SRCML) was observed (Plate 3f).

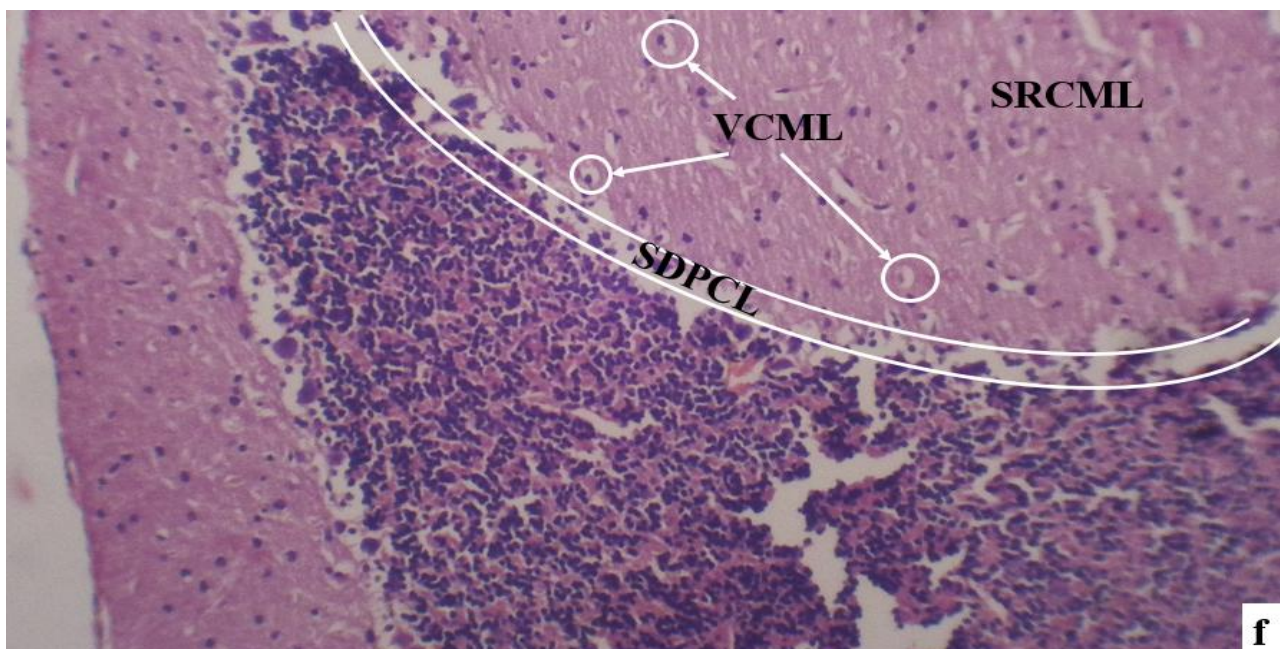
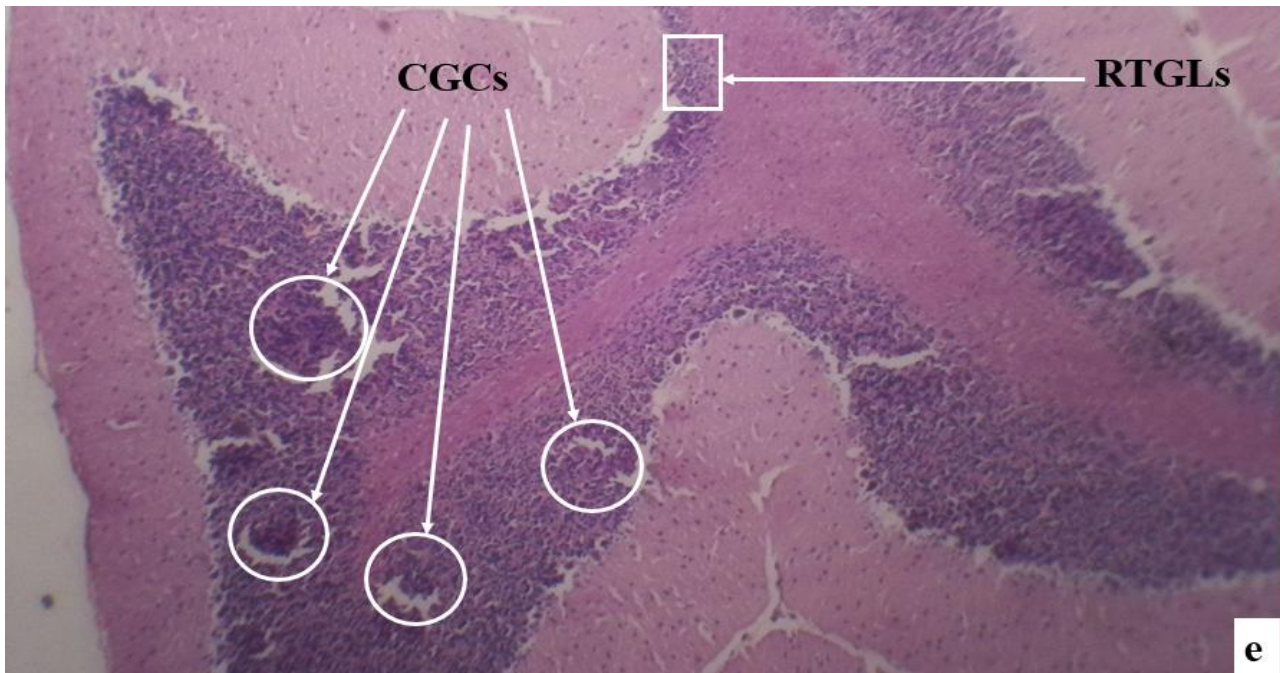


Plate 3. Cerebellar Histopathology in BPA-Exposed Adult Wistar Rat (Group C)
Plate 3e. Congested and Thinned Granular Layer with Granular Cell Crowding (×40)
Plate 3f. Severe Purkinje Cell Degeneration and Vacuolated Molecular Layer (×100)

Photomicrographs of a section of the cerebellum of an adult male wistar rat in Group D that received HFD and BPA only for 12 weeks, stained with hematoxylin and eosin with a magnification of x40 (g) and x100 (h). This section presented severe congestion of granular cells (SCGs) at the granular layer and severe degeneration of PCL (SDPCL) (Plate 4g). Presence of pyknotic Purkinje cells (PPCs) and structurally distorted Purkinje cells (SDPCs) with reduction of the compactness of the molecular layer (ML) were observed (Plate 4h).

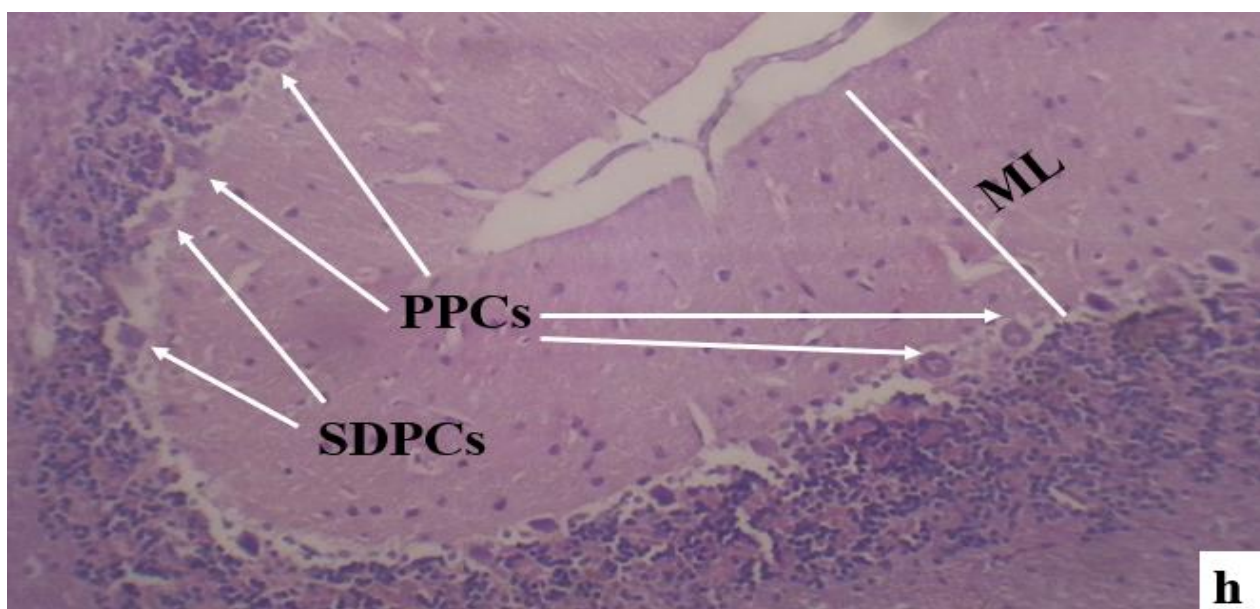
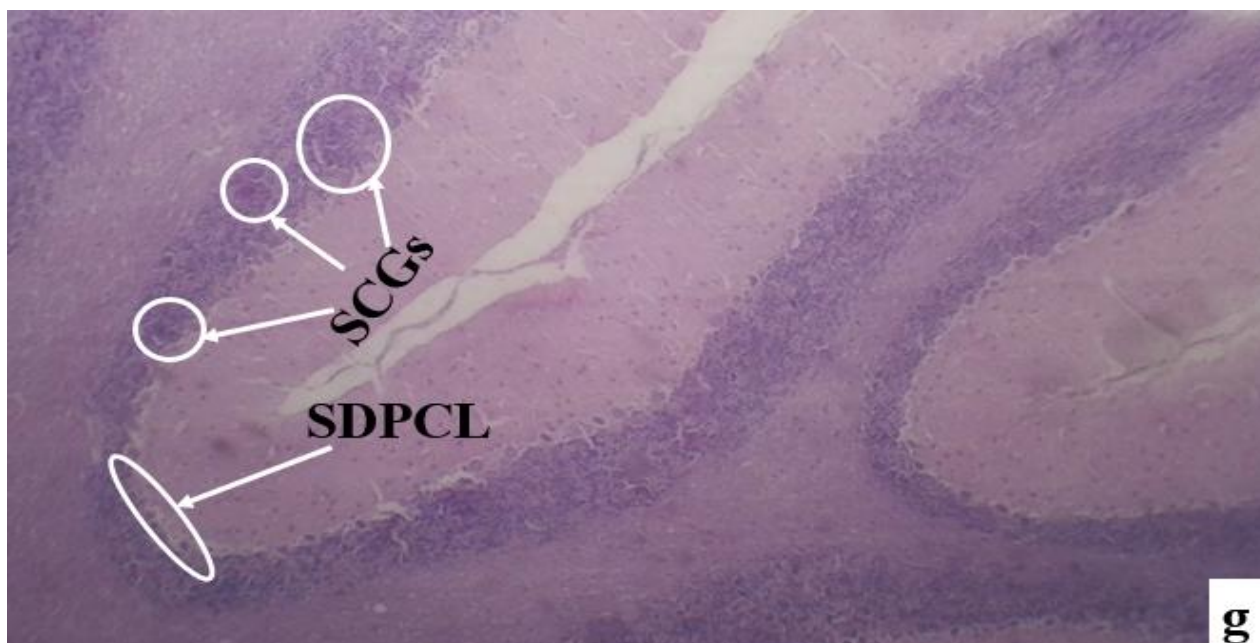


Plate 4. Cerebellar Histopathology in HFD + BPA–Exposed Adult Wistar Rat (Group D)
Plate 4g. Severe Granular Layer Congestion and Purkinje Cell Degeneration (×40)
Plate 4h. Pyknotic and Structurally Distorted Purkinje Cells with Reduced ML Compactness (×100)

Photomicrographs of a section of the cerebellum of an adult male wistar rat in Group E that received HFD, BPA, and 50mg/kg of *Cyperus esculentus* (CE) extract. HFD and BPA were given for 12 weeks and 50 mg/kg of *Cyperus esculentus* extract was given for 4 weeks. At the granular layer, there was the presence of a few congested granular cells (CGCs) and diminished thickness of the granular layer (DTGL). Cells of the molecular layer (CML) appeared normal and intact. Minimized degenerated Purkinje cell layer (DPCL) was observed with the presence of Purkinje cells (Plate 5i). It also showed minimal appearance

of degenerated Purkinje cell layer with reduced presence of abnormal Purkinje cells (RAPCs). The molecular layer (ML) showed minimized presence of vacuolated cells (VCs) (Plate 5j).

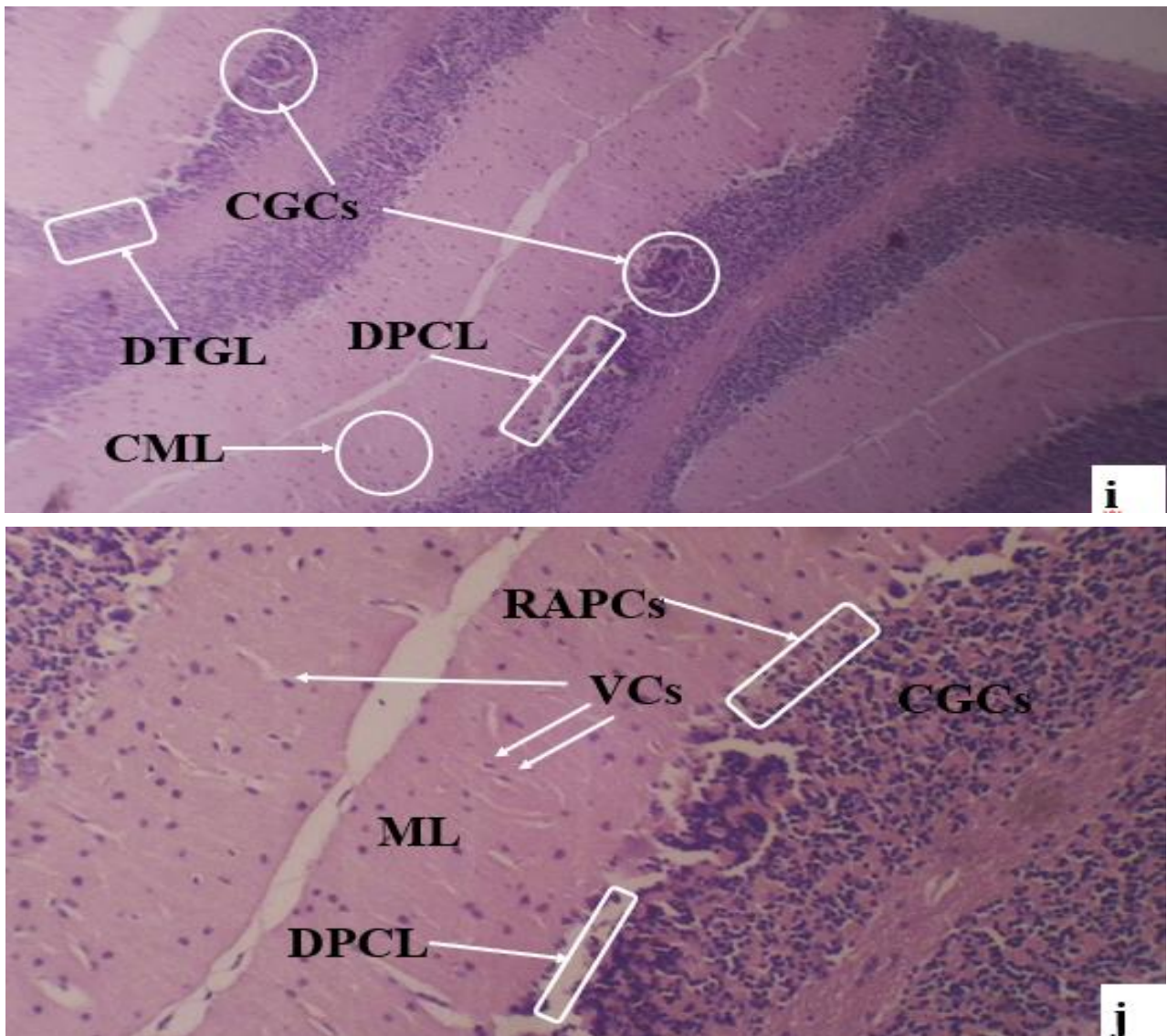


Plate 5. Cerebellar Histology in HFD + BPA Rats Treated With *Cyperus esculentus* Extract (Group E)

Plate 5i. Mild Granular Layer Congestion and Reduced Purkinje Cell Degeneration (×40)
Plate 5j. Minimal Purkinje Abnormalities and Reduced Vacuolization in the Molecular Layer (×100)

Photomicrographs of a section of the cerebellum of an adult male wistar rat in Group F, stained with hematoxylin and eosin with a magnification of x40 (k) and x100 (l). This section received HFD and BPA for 12 weeks and 100 mg/kg of *Cyperus esculentus* (CE) for 4 weeks. There was reduced molecular layer compactness (RMLC). There was an appearance of diminished thickness of the glandular layer (DTGL)

and degenerated Purkinje cell layer (DPCL) (Plate 6k). It also showed degeneration of the Purkinje cell layer (DPCL) and loss of Purkinje cells, but when present, the Purkinje cells (PCs) indicated abnormal cellular structure (ACS). Reduced molecular layer compactness (RMLC) due to vacuolations of molecular cells and reduced congestion of granular cells (RCGs) in the granular layer (GL) were also observed (Plate 6l).

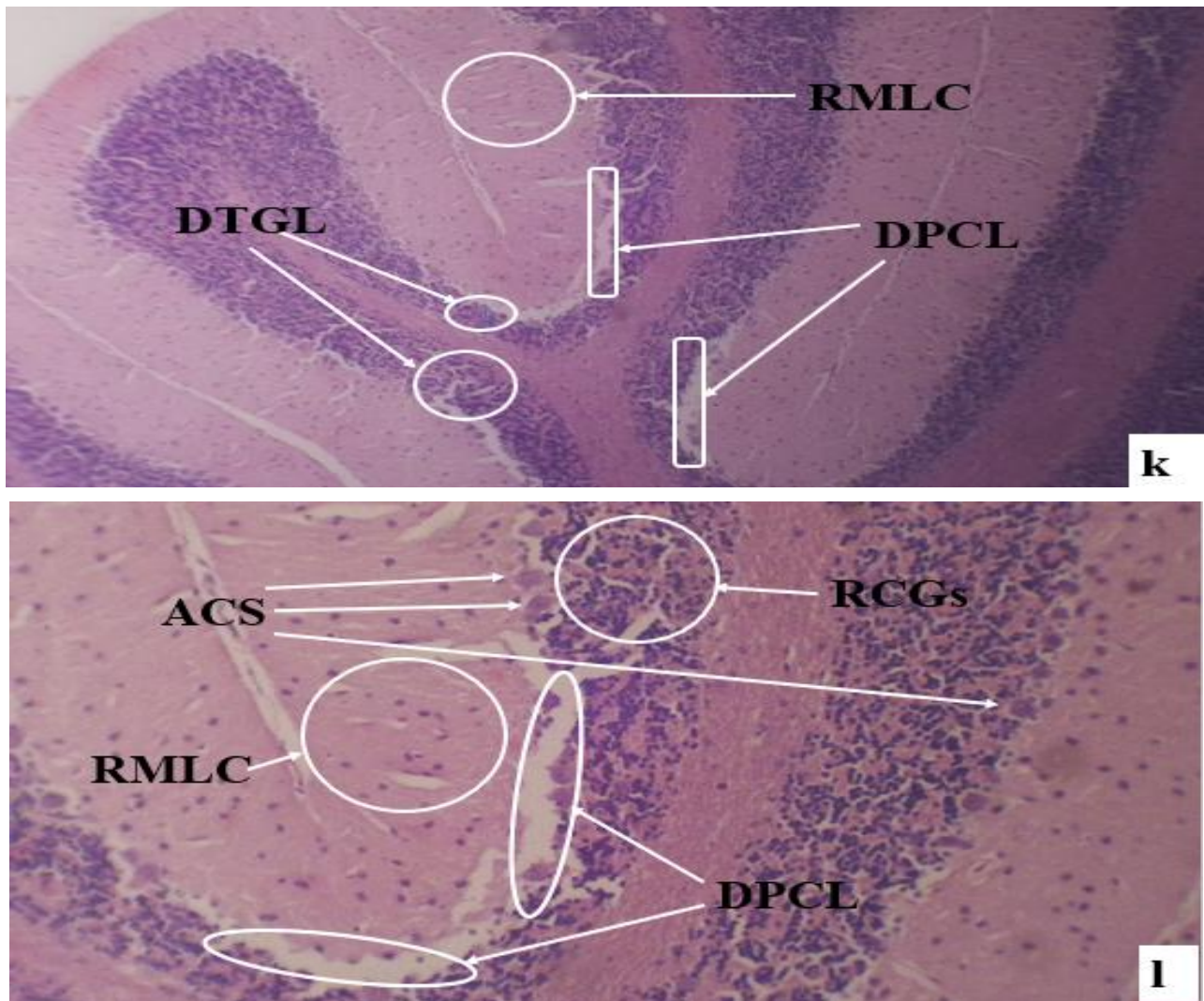


Plate 6. Plate 6. Cerebellar Histology in HFD + BPA Rats Treated With High-Dose *Cyperus esculentus* (100 mg/kg) (Group F)

Plate 6k. Reduced Molecular Layer Compactness and Thinned Granular Layer with Purkinje Degeneration (×40)

Plate 6l. Degenerated and Abnormal Purkinje Cells with ML Vacuolations and Reduced GL Congestion (×100)

Discussion

This study investigated the potential of *Cyperus esculentus* (CE) to mitigate cerebellar damage in adult male wistar rats exposed to both high-fat diet (HFD) and bisphenol A (BPA). The histopathological findings

demonstrate that exposure to both HFD and BPA induced clear structural alterations in the cerebellum, primarily characterized by degeneration and distortion of Purkinje cells, vacuolization in the molecular layer, congestion of the granular layer, and a general reduction in cortical compactness. These observations in Groups B, C, and D, particularly the pronounced pathology in the co-exposure group (D), align with established literature on the neurotoxic and pro-inflammatory effects of obesogenic diets and endocrine disruptors. HFDs are known to promote systemic neuroinflammation and oxidative stress, while BPA can disrupt endocrine signalling and induce neuronal apoptosis. The combination of HFD and BPA likely produces a synergistic insult to vulnerable cerebellar neurons (Lara-Aparicio *et al.*, 2021; Meli *et al.*, 2020).

The impact of heavy metals on the cerebellum of rats was examined and significant histopathological changes were found including Purkinje cell loss, and increased glial cell proliferation (Smith *et al.*, 2023). Interestingly, administration of CE markedly attenuated these histopathological alterations. The administration of CE extract, particularly at the 50mg/kg dose (Group E), appeared to attenuate the severity of these histopathological changes. Group E showed a minimized presence of vacuolated cells, a reduction in Purkinje cell degeneration, and a more preserved cortical architecture compared to the untreated co-exposure Group D. This partial amelioration is consistent with the known bioactive profile of CE, which is rich in polyphenols, flavonoids, and unsaturated fatty acids with documented antioxidant and anti-inflammatory properties (Nina *et al.*, 2019; Ogunlade *et al.*, 2015; Vishe, 2023).

Recent studies have demonstrated the neuroprotective effects of various natural and synthetic compounds on the cerebellum of rats exposed to neurotoxic agents (El Morsy & Ahmed, 2020). It was reported that curcumin supplements significantly reduced cerebellar damage in rats treated with a neurotoxin (Jones *et al.*, 2022). Another study reported that *Rauwolfia vomitoria* leaf can ameliorate the neurotoxicity associated with cisplatin-induced oxidative stress (Ekechi *et al.*, 2023a). Similarly, this present study has shown the neuroprotective effects of CE, which agrees with the reports of other studies (Khadrawy *et al.*, 2016; Sadek *et al.*, 2018).

It is noteworthy that the higher dose of CE (100mg/kg, Group F) did not demonstrate a superior protective effect in this present study, and some parameters (e.g., Purkinje cell loss) appeared less effective than the 50mg/kg dose. This suggests a non-linear, possibly biphasic, dose-response relationship, which is not uncommon in phytotherapeutic interventions (Calabrese, 2013).

On the other hand, and as earlier stated, metabolic syndrome diseases (MSDs) are diseases related to one another. MSDs contribute significantly to healthcare costs, morbidity, and mortality rates, thus requiring the search for new, effective, and innovative treatment options (Ikwuka, 2024). Innovative treatment options such as combining HMG-CoA reductase inhibitors, SGLT-2 inhibitors, and angiotensin II receptor blockers (type 1) i.e. A2RB (AT1), have shown clinical effectiveness indicated by marked improvements in the metabolic functions of the heart, liver, pancreas, and kidney (Ikwuka, 2017b; Ikwuka, 2018a; Ikwuka, 2018b; Ikwuka, 2021; Ikwuka, 2024; Virstyuk, 2017b; Virstyuk, 2018b; Virstyuk, 2018c). In addition, Glucagon-like Peptide 1 Receptor Agonists (GLP-1 RAs) such as liraglutide have been shown to improve the clinical outcomes in patients with type 2 diabetes mellitus and hypertension (Ikwuka, 2019b).

Finally, the precise molecular mechanisms underlying these protective effects of *Cyperus esculentus* (CE) are beyond the scope of this histopathology study, but these molecular mechanisms may involve complex interactions at the metabolic or receptor levels. It is possible that CE modulates signaling cascades, such as the Nrf2/ARE antioxidant pathway or inhibits apoptosis via caspase downregulation. Therefore, further studies incorporating immunohistochemical and biochemical assays to identify the precise molecular mechanisms underlying the observed damage and partial recovery, such as the degree of

oxidative stress, levels of pro-inflammatory cytokines (e.g., TNF- α , IL-1 β), or the activation of apoptotic pathways (e.g., caspase-3) are important.

Conclusion

This histopathology study demonstrates that exposure to both HFD and BPA induces significant structural pathology in the cerebellum of adult male wistar rats. The administration of *Cyperus esculentus* (CE) extract, particularly at a dose of 50mg/kg, showed a partial ameliorative effect, attenuating the severity of these histopathological alterations. The observed neuroprotective trend is likely attributable to the antioxidant and anti-inflammatory constituents of *Cyperus esculentus*. However, this neuroprotection is not complete and dose-dependent, with a higher dose (100mg/kg) showing a less pronounced effect. Therefore, *Cyperus esculentus* shows potential as a dietary agent that may help mitigate, but not fully prevent cerebellar damage induced by combined metabolic and environmental stressors.

Recommendations

These preliminary findings justify an in-depth investigation involving molecular and biochemical analyses to elucidate the underlying molecular mechanisms and potential translational applications of *Cyperus esculentus* in human neurodegenerative conditions. Quantitative histomorphometric analysis, such as Purkinje cell counts and layer thickness measurements, should also be incorporated in subsequent studies. Nevertheless, it is also recommended that the optimal therapeutic dose and therapeutic window for *Cyperus esculentus* should be investigated in subsequent studies because of its biphasic response observed in this study.

Conflict of Interest

The authors guarantee responsibility for all the data published in this manuscript. The authors confirm the absence of a conflict of interest and the absence of their financial interest in conducting this study and writing this manuscript. This manuscript was written from an original research work and has never been published, nor is it under consideration for publication elsewhere.

References

- Almeida, S., Raposo, A., Almeida-González, M., & Carrascosa, C. (2018). Bisphenol A: Food exposure and impact on human health. *Comprehensive Reviews in Food Science and Food Safety*, 17(6), 1503–1517. <https://doi.org/10.1111/1541-4337.12388>
- Aliu-Ayo, H. I., Adesina, K. T., Jimoh, A. A. G., Ikwuka, A. O., Udeh, F. C., Biliaminu, S. A., & Ayo, O. W. (2023a). Serum levels of thyroid hormones in infertile and fertile women attending a tertiary care hospital in North-Central Nigeria: A comparative reproductive medicine study. *American Journal of Medical Science and Innovation*, 2(2), 141–152. <https://doi.org/10.54536/ajmsi.v2i2.2044>
- Aliu-Ayo, H. I., Adesina, K. T., Jimoh, A. A. G., Ikwuka, A. O., Udeh, F. C., Biliaminu, S. A., & Ayo, O. W. (2023b). Correlation of thyroid gland functions with menstrual patterns amongst infertile and fertile women attending a tertiary care hospital in North-Central Nigeria. *World Journal of Clinical Medicine Research*, 3(1), 13–26. <https://doi.org/10.31586/wjcmr.2023.787>



- Ama, M. I., Ikwuka, A. O., Udeh, F. C., Ekechi, H. O., & Eteudo, A. N. (2023). Sperm parameters and testicular histology of male Wistar rats treated with *Phoenix dactylifera* after consumption of local mmahi salt. *American Journal of Bioscience and Bioinformatics*, 2(1), 41–51. <https://doi.org/10.54536/ajbb.v2i1.2275>
- Banik, S., & Hossain, M. S. (2014). A comparative overview on good fats and bad fats: Guide to control healthy body. *International Journal of Health*, 2(2), 41–44. <https://doi.org/10.14419/ijh.v2i2.2903>
- Baysah, P. V., Ikwuka, A. O., Udeh, F. C., Bleh, D. P., & Vilorio, T. (2023). Pathophysiological effects of alcohol and tobacco consumption on semen parameters of men attending a fertility clinic in West Africa. *American Journal of Biomedical and Life Sciences*, 11(4), 73–81. <https://doi.org/10.11648/j.ajbls.20231104.13>
- Calabrese, E. J. (2013). Biphasic dose responses in biology, toxicology and medicine: Accounting for their generalizability and quantitative features. *Environmental Pollution*, 182, 452–460. <https://doi.org/10.1016/j.envpol.2013.07.046>
- Ekechi, H. O., Ikwuka, A. O., Udeh, F. C., & Abraham, J. C. (2023a). Effects of ethanol extract of *Rauwolfia vomitoria* leaf on lipid profile and cerebellar histology in cisplatin-induced oxidative stress. *British Journal of Medical and Health Research*, 10(5), 16–39. <https://doi.org/10.5281/zenodo.8042521>
- Ekechi, H. O., Ikwuka, A. O., Udeh, F. C., Epete, M. A., & Uche, V. U. (2023b). Hepatorenal protective functions of coconut water in alloxan-induced type 1 diabetes mellitus. *World Journal of Current Medical and Pharmaceutical Research*, 5(4), 114–122. <https://doi.org/10.37022/wjcmpr.v5i4.276>
- El Morsy, E. M., & Ahmed, M. (2020). Protective effects of lycopene on hippocampal neurotoxicity and memory impairment induced by bisphenol A in rats. *Human and Experimental Toxicology*, 39(8), 1066–1078. <https://doi.org/10.1177/0960327120909882>
- Freire, C., Molina-Molina, J. M., Iribarne-Durán, L. M., Jiménez-Díaz, I., Vela-Soria, F., Mustieles, V., & Fernández, M. F. (2019). Concentrations of bisphenol A and parabens in socks for infants and young children in Spain and their hormone-like activities. *Environment International*, 127, 592–600. <https://doi.org/10.1016/j.envint.2019.04.013>
- Gambo, A., & Da'u, A. (2014). Tigernut (*Cyperus esculentus*): Composition, products, uses and health benefits: A review. *Bayero Journal of Pure and Applied Sciences*, 7(1), 56–61. <https://doi.org/10.4314/bajopas.v7i1.11>
- Holmboe-Ottesen, G. (2000). Global trends in food consumption and nutrition. *Tidsskrift for den Norske Lægeforening*, 120(1), 78–82.
- Ikwuka, A. O. (2015). Risk factors for the pathogenesis of diabetes mellitus type 2. In *Materials of the 84th Scientific and Practical Conference of Students and Young Scientists with International Participation "Innovations in Medicine"* (p. 19).
- Ikwuka, A. O. (2017a). Dyslipidemia risk severity in patients with diabetes mellitus type 2 and essential hypertension. In *Proceedings of the 21st International Medical Congress of Students and Young Scientists* (p. 59).
- Ikwuka, A. O. (2017b). Effectiveness of dapagliflozin in patients with diabetes mellitus type 2 and essential hypertension. In *Book of Abstracts of the 7th International Students' Scientific Conference of Young Medical Researchers* (p. 102).
- Ikwuka, A. O. (2017c). Influence of dyslipidemia in patients with diabetes mellitus type 2 and essential hypertension. *The Pharma Innovation Journal*, 6(3), 101–103.
- Ikwuka, A. O., & Haman, I. O. (2017d). Features of kidney damage in patients with diabetes mellitus type 2 and essential hypertension. In *Proceedings of the 86th Scientific Conference "Innovations in Medicine"* (p. 144).

- Ikwuka, A. O., Virstyuk, N. G., & Luchko, O. R. (2017e). Features of the functional state of kidneys in patients with diabetes mellitus type 2 and essential arterial hypertension. In *Babenkivski Readings* (p. 48).
- Ikwuka, A. O. (2018a). Clinical dynamics in patients with diabetes mellitus type 2 and concomitant essential hypertensive disease treated with dapagliflozin. In *Proceedings of the 22nd International Medical Congress* (p. 32).
- Ikwuka, A. O. (2018b). Clinical effectiveness of SGLT-2 inhibitors in patients with diabetes mellitus type 2 and essential hypertensive disease. *Endocrine Practice*, 24(1), 74. [https://doi.org/10.1016/S1530-891X\(20\)47129-0](https://doi.org/10.1016/S1530-891X(20)47129-0)
- Ikwuka, A. O. (2018c). Features of kidney damage in patients with arterial hypertension and type 2 diabetes mellitus and optimization of treatment.
- Ikwuka, A. O., & Paliy, Y. (2018d). Structural changes of the left ventricular myocardium in patients with essential arterial hypertension and diabetes mellitus type 2. In *Proceedings of the 87th Scientific Conference* (pp. 25–26).
- Ikwuka, A. O. (2019a). Clinical dynamics of nephropathy in patients with diabetes mellitus type 2 and concomitant essential hypertensive disease. *Clinical Medicine*, 19(2), S39. <https://doi.org/10.7861/clinmedicine.19-2-s39>
- Ikwuka, A. O. (2019b). Clinical effectiveness of GLP-1 receptor agonists in patients with metabolic syndrome diseases. *Endocrine Practice*, 25(1), 104–105. [https://doi.org/10.1016/S1530-891X\(20\)46611-X](https://doi.org/10.1016/S1530-891X(20)46611-X)
- Ikwuka, A. O., & Virstyuk, N. G. (2019c). Pattern of cardiac remodelling of the left ventricle in patients with essential hypertensive disease and concomitant type 2 diabetes mellitus. *Clinical Medicine*, 19(3), S92. <https://doi.org/10.7861/clinmedicine.19-3-s92>
- Ikwuka, A. O., & Virstyuk, N. G. (2021). Influence of SGLT2 inhibitor and A2RB (AT1) on fibrogenesis and heart failure in patients with essential hypertensive disease combined with diabetes mellitus type 2. <https://doi.org/10.13140/RG.2.2.26912.87047>
- Ikwuka, A. O., & Virstyuk, N. (2022). Prognostic markers of nephropathy in patients with dual metabolic syndrome diseases. *Endocrine Practice*, 28(5), S65–S66. <https://doi.org/10.1016/j.eprac.2022.03.164>
- Ikwuka, A. O. (2023a). *Dr. Aloy's Core Essential Series (DACES): Medical Genetics* (1st ed.). Science and Education Publishing.
- Ikwuka, A. O. (2023b). *Dr. Aloy's Core Essential Series (DACES): Immunology* (1st ed.). Science and Education Publishing.
- Ikwuka, A. O., & Virstyuk, N. (2023c). Patterns and influence of cardio-metabolic insufficiency in patients with essential hypertensive disease and concomitant type 2 diabetes mellitus. *Endocrine Practice*, 29(5), S32–S33. <https://doi.org/10.1016/j.eprac.2023.03.076>
- Ikwuka, A. O., Virstyuk, N. G., Luchko, O. R., & Kobitovych, I. (2023d). Heterogeneity of renal pathogenicity on the background of asymptomatic hyperuricemia in patients with dual metabolic syndrome diseases. *British Journal of Medical and Health Research*, 10(2), 1–9. <https://doi.org/10.5281/zenodo.7690636>
- Ikwuka, A. O. (2023e). *Dr. Aloy's Core Essential Series (DACES): Hematology* (1st ed.). Science and Education Publishing.

- Ikwuka, A. O., Omoju, D. I., & Mahanera, O. K. (2023f). Profiling of clinical dynamics of type 2 diabetes mellitus in patients: A perspective review. *World Journal of Current Medical and Pharmaceutical Research*, 5(5), 210–218. <https://doi.org/10.37022/wjcmpr.v5i5.294>
- Ikwuka, A. O., Virstyuk, N., Luchko, O., & Kobitovych, I. (2024). Optimization of treatment in MSD patients using a combination of HMG-CoA reductase inhibitor, SGLT-2 inhibitor and A2RB (AT1): Resultant clinical effectiveness. *Endocrine Practice*, 30(5), S60–S61. <https://doi.org/10.1016/j.eprac.2024.03.243>
- Institute for Laboratory Animal Research. (2011). *Guide for the care and use of laboratory animals* (8th ed.). National Academies Press.
- Inya, A. U., Achara, A. P., Ikwuka, A. O., Udeh, F. C., Chi-kadibia, U., & Onazi, O. (2023a). Patterns, peculiarities and associated risk factors of anemia in pregnancy: A case study of pregnant women attending antenatal clinic in North-Central Nigeria. *European Journal of Preventive Medicine*, 11(2), 21–31. <https://doi.org/10.11648/j.ejpm.20231102.12>
- Inya, A. U., Achara, A. P., Ikwuka, A. O., Udeh, F. C., Chi-kadibia, U., & Onazi, O. (2023b). Clinical dynamics of anemia in pregnancy: A 16-week cross-sectional study of pregnant women. *American Journal of Clinical Medicine Research*, 11(1), 1–9. <https://doi.org/10.12691/ajcmr-11-1-1>
- Jones, A. B., Roberts, C. D., & Williams, E. F. (2022). Curcumin attenuates neurotoxic effects in the cerebellum of rats treated with neurotoxins. *Journal of Neuroprotection*, 15(3), 210–222.
- Kataria, A., Levine, D., Wertenteil, S., Vento, S., Xue, J., Rajendiran, K., Kannan, K., Thurman, J. M., Morrison, D., Brody, R., & Urbina, E. (2017). Exposure to bisphenols and phthalates and association with oxidant stress, insulin resistance, and endothelial dysfunction in children. *Pediatric Research*, 81(6), 857–864. <https://doi.org/10.1038/pr.2017.16>
- Khadrawy, Y. A., Noor, N. A., Mourad, I. M., & AboulEzz, H. S. (2016). Neurochemical impact of bisphenol A in the hippocampus and cortex of adult male albino rats. *Journal of Toxicology and Environmental Health, Part A*, 79(17), 742–755. <https://doi.org/10.1080/10937404.2016.1212898>
- Kougias, D. G., Cortes, L. R., Moody, L., Rhoads, S., Pan, Y. X., & Juraska, J. M. (2018). Effects of perinatal exposure to phthalates and a high-fat diet on maternal behaviour and pup development and social play. *Endocrinology*, 159(2), 1088–1105. <https://doi.org/10.1210/en.2017-03047>
- Lara-Aparicio, S. Y., Laureani-Fierro, A. J., Morgado-Valle, C., Beltrán-Parrazal, L., Rojas-Durán, F., García, L. I., Toledo-Cárdenas, R., Hernández, M. E., Manzo, J., & Pérez, C. A. (2021). Latest research on the anatomy and physiology of the cerebellum. *Neurology Perspectives*, 2, 34–46. <https://doi.org/10.1016/j.neurop.2021.12.002>
- Li, J., Wu, D., Mu, Y., Wang, Y., Zhai, L., & Jia, L. (2025). The combined damage of bisphenol A and high fat diet to learning and memory in young male mice. *Environmental Research*, 276, 121538. <https://doi.org/10.1016/j.envres.2025.121538>
- Liu, X., Miao, M., Zhou, L., & Tan, H. (2021). Bisphenol A exposure and its effects on anxiety and activity levels in rodents. *Environmental Health Perspectives*, 129(6), 067002.
- Meli, R., Monnolo, A., Annunziata, C., Pirozzi, C., & Ferrante, M. C. (2020). Oxidative stress and BPA toxicity: An antioxidant approach for male and female reproductive dysfunction. *Antioxidants*, 9(5), 405. <https://doi.org/10.3390/antiox9050405>
- Nina, G. C., Ogori, A. F., Ukeyima, M., Hleba, L., Cisarova, M., Okuskhanova, E., Vlasov, S., Batishcheva, N., Goncharov, A., & Shariati, M. A. (2019). Proximate, mineral and functional properties

- of tiger nut flour. *Journal of Microbiology, Biotechnology and Food Sciences*, 9(3), 653–656. <https://doi.org/10.15414/jmbfs.2019/20.9.3.653-656>
- Ogunlade, I., Bilikis, A. A., & Olanrewaju, G. A. (2015). Chemical compositions, antioxidant capacity of tiger nut (*Cyperus esculentus*) and potential health benefits. *European Scientific Journal*, 11, 217–224.
- Poojary, S., Handady, G., & Rao, S. S. (2024). Bisphenol A exposure and its multifaceted effects on child health: A comprehensive review. *Journal of Chemical Health Risks*, 14(6), 1256–1263.
- Roselló-Soto, E., Poojary, M. M., Barba, F. J., Lorenzo, J. M., Mañes, J., & Moltó, J. C. (2017). Tiger nut and its by-products valorization. *Innovative Food Science & Emerging Technologies*, 45, 306–312. <https://doi.org/10.1016/j.ifset.2017.11.016>
- Sadek, S. A., Elshal, E. B., Abo-Ouf, A. M., & Abd El-Aal, M. T. (2018). Effect of bisphenol A on the cerebellar cortex of albino rats. *Medical Journal of Cairo University*, 86(7), 3643–3662.
- Smith, D. M., Johnson, G. H., & Thompson, L. K. (2023). Histopathological changes in the cerebellum of rats exposed to heavy metals. *Environmental Toxicology*, 38(2), 145–158.
- Uche, V. U., Ikwuka, A. O., Udeh, F. C., Okorochoa, A. E., Epete, M. A., Ekechi, H. O., Abraham, J. C., & Igwe, E. C. (2023). Associated risks and pathogenic effects of consumption of calcium carbide-ripened banana. *American Journal of Food Science and Technology*, 2(2), 54–64. <https://doi.org/10.54536/ajfst.v2i2.2197>
- Udeh, F. C., Ikwuka, A. O., Epete, M. A., & Igwe, E. C. (2023a). Effects of local tobacco snuff ingestion during pregnancy on renal functions. *American Journal of Medical Sciences and Medicine*, 11(1), 1–5. <https://doi.org/10.12691/ajmsm-11-1-1>
- Udeh, F. C., Ikwuka, A. O., Epete, M. A., & Igwe, E. C. (2023b). Effects of oral consumption of *Nicotiana tabacum* during pregnancy on the liver and prolactin levels. *European Journal of Veterinary Medicine*, 3(2), 1–5. <https://doi.org/10.24018/ejvetmed.2023.3.2.93>
- Vasiljevic, T., & Harner, T. (2021). Bisphenol A and its analogues in outdoor and indoor air. *Science of the Total Environment*, 789, 148013. <https://doi.org/10.1016/j.scitotenv.2021.148013>
- Virstyuk, N. G., Ikwuka, A. O., Haman, I. O., & Adebomi, M. S. (2016). Diabetes mellitus type 2, arterial hypertension and dyslipidemia. In *Proceedings of the 2nd International Scientific Conference* (pp. 46–47).
- Virstyuk, N. G., & Ikwuka, A. O. (2017a). Diagnostic and prognostic markers of diabetes mellitus type 2. *Precarpathian Journal Pulse*, 8(44), 53–62.
- Virstyuk, N. H., Ikwuka, A. O., Losyuk, L. V., Kobrynska, O. Ya., & Markiv, H. D. (2017b). Dapagliflozin utility in patients with diabetes mellitus type 2. *Actual Problems of Modern Medicine*, 4(60), 76–79.
- Virstyuk, N. G., & Ikwuka, A. O. (2018a). Features of asymptomatic hyperuricemia in patients with diabetes mellitus type 2. *Clinical and Experimental Pathology*, 17(1), 22–26. <https://doi.org/10.24061/1727-4338.XVII.1.63.2018.5>
- Virstyuk, N. G., Ikwuka, A. O., & Didushko, O. M. (2018b). Effect of dapagliflozin on uric acid levels. *Art of Medicine*, 1(5), 21–26.
- Virstyuk, N. H., & Ikwuka, A. O. (2018c). Dapagliflozin influence on clinical course of diabetes mellitus type 2. In *Recent Advances in Environmental Science* (pp. 2007–2008). https://doi.org/10.1007/978-3-319-70548-4_582
- Virstyuk, N. G., & Ikwuka, A. O. (2019). Nephropathic characteristics in patients with diabetes mellitus type 2. *Art of Medicine*, 1(9), 44–47. <https://doi.org/10.21802/artm.2019.1.9.44>

- Virstyuk, N. G., & Ikwuka, A. O. (2021a). Asymptomatic hyperuricemia and kidney function. *European Journal of Clinical Medicine*, 2(3), 100–104. <https://doi.org/10.24018/clinicmed.2021.2.3.65>
- Virstyuk, N. H., Ikwuka, A. O., Luchko, O. R., & Kocherzhat, O. I. (2021b). Peculiarities of renal insufficiency in patients with diabetes mellitus type 2. In *Conference Proceedings* (pp. 86–87).
- Vishe, T. S. (2023). Antioxidant and anti-inflammatory properties of tigernut extract. *International Journal of Agriculture and Nutrition*, 5(2), 103–105. <https://doi.org/10.33545/26646064.2023.v5.i2b.165>
- Wiebe, J. C., López-Ríos, L., Vega-Morales, T., Pérez-Machín, R., Mateos, C. J., & Gericke, N. (2019). Neurophysiological effects of *Cyperus esculentus* extract. *Journal of Herbal Medicine Research*, 4, 34. <https://doi.org/10.28933/jhmr-2019-09-2705>
- Yu, Y., Lu, X., Zhang, T., Zhao, C., Guan, S., Pu, Y., & Gao, F. (2022). Tiger nut (*Cyperus esculentus* L.): Nutrition, processing, function and applications. *Foods*, 11(4), 601. <https://doi.org/10.3390/foods11040601>