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Original Research Article

OXIDATIVE STRESS AND HISTOPATHOLOGICAL ASSESSMENT OF LENS TISSUE IN MONOSODIUM GLUTAMATE-INDUCED DIABETIC MALE ALBINO RATS

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ABSTRACT

Monosodium glutamate is used as a food seasoning in different food cuisines. Unregulated consumption of MSG can lead to the production of oxidative stress, which can negatively influence ocular changes, such as cataracts. This study assessed the level of oxidative stress biomarkers and histopathological changes in MSG-induced diabetic Wistar rats. Ten male Wistar rats were randomly selected into two groups. It includes the control group (0.5 5ml distilled water) and the experimental group (750 mg/kg bodyweight MSG) administered orally daily for 28 days. The body weight and blood sugar level were measured weekly. The level of oxidative biomarkers was evaluated, which includes the Glutathione, Catalase (CAT), Malondialdehyde (MDA), Superoxide Dismutase (SOD) and Total protein content. Hematoxylin and eosin-stained lenses were examined for histopathological changes. Data were analysed using paired t-tests ($p<0.05$). The MSG-treated group showed an increase in body weight and the blood glucose level by week 4 as compared to the control group. The lens tissue showed elevated levels of GSH & MDA, decreased CAT activity, lower total protein content and reduced SOD activity. No structural damage was observed with the Histopathological analysis. MSG-induced diabetic lens revealed elevated levels of oxidative biomarkers, which can be detrimental to ocular health. Normal histopathological changes suggest that structural damage requires prolonged hyperglycemia. The findings imply the need for regulated MSG consumption among populations prone to diabetic and ocular diseases.

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KEYWORDS

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INTRODUCTION

The burden of Diabetes mellitus (DM) is becoming alarmingly increasing, with approximately 589 million adults aged 20–79 worldwide living with diabetes [1]. The prevalence is projected to rise to 853million by 2050 [2]. In Nigeria, it is reported that

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11 million people are living with diabetes. DM can lead to several ocular complications such as Diabetic retinopathy, diabetic papilledema, glaucoma, cataract and other ocular surface diseases (3). Diabetic patients are 2-5 times more at risk for cataract formation and more likely to get it at an earlier age (4).

Cataract is one of the major causes of visual impairment in diabetics; it is characterised by a decrease in the transparency of the lens. It is reported as one of the leading causes of blindness worldwide (5). In Nigeria, it accounts for about 43% of all blindness and 45.3% of severe visual impairment (6). Globally, the prevalence of diabetic cataract has been increasing as the number of diabetic patients has grown (7). Chronic hyperglycemia can induce oxidative stress, an imbalance between reactive oxygen species (ROS) production and antioxidant defences, leading to cellular damage in organs such as the eyes (8). The lens, which is critical for vision, is vulnerable to oxidative damage and to hyperglycemia-induced osmotic stress, which contributes to cataract formation, a leading cause of blindness (4). Excessive intake of MSG can lead to overstimulation of glutamate receptors, generating oxidative stress implicated in cataract formation and metabolic disorders such as diabetes (9;10). The lens comprises a collagenous capsule, epithelial cells and elongated fibres that maintain its transparency via crystalline proteins (11).

Diabetes disrupts the lens homeostasis through sorbitol accumulation, protein glycation and lipid peroxidation, thereby causing lens opacification (12). Preventing the development of cataract in diabetic patients remains a challenge, even though cataract surgery is the most effective treatment option for cataract worldwide. Diabetic and Diabetic-related cataract are significant health and economic burdens, especially in developing countries where access to diabetic treatment and cataract surgery is limited. This study evaluated the level of oxidative stress biomarkers and histopathological changes in MSG-induced diabetic Wistar rats.

MATERIALS AND METHODS

Materials

All chemicals and reagents were of analytical grade. MSG (99% purity, Ajinomoto Co., Inc., Nigeria); phosphate-buffered saline (PBS, 0.01 M, Ph 7.4, Sigma-Aldrich, USA, Malonialdehyde (MDA) assay kit, Catalase (CAT) activity assay kit, Superoxide Dismutase (SOD) assay kit, Formaldehyde (for tissue fixation), Paraffin (for embedding), Haematoxylin and Eosin (H&E) stains, Accu-Chek Active glucometer (Roche Diagnostics, Germany); glass-Teflon homogeniser (Potter-Elvehjem type, Sigma-Aldrich); automatic tissue processor (LEICA PT 1020, Germany); rotary microtome (LEICA RM 2135RT, Germany); light microscope (Olympus BX51, Japan).

Study Design

A controlled experimental study was conducted at the Physiology Laboratory, Department of Optometry and Vision Science, University of Ilorin, Nigeria, with ethical approval code UERC Approval Number: UERC/ASN/2024/3057 from the University of Ilorin Ethical Review Committee. A total of ten male Wistar rats were randomly selected into two groups (n+5 each). The grouping includes the control (0.5 5ml distilled water) and the experimental 750mg/kg body weight MSG) administered orally daily for 28 days.

Experimental Animals

Rats were purchased from a licensed breeder in Ogbomoso, Nigeria, and acclimatised for 6 weeks under standard conditions (12-hour light/dark cycle, 25 ± 2°C, 50-60% humidity, grower mesh feed, water ad libitum. Before MSG administration, all rats underwent a 1-week acclimatisation period with daily monitoring for behaviour, weight and the baseline FBS (< 5.6 mmol/L via Accu-Chek glucometer), ensuring no preexisting hyperglycemia or abnormalities.

MSG (99% purity, Ajinomoto Co., Inc., Nigeria) was dissolved in distilled water to achieve a concentration of 750mg/kg, calculated based on body weight, and administered via oral gavage using a 1 ml syringe with a curved cannula between 8:00 am – 11:00 am to minimise stress. The control group received 0.5 ml of distilled water. Diabetes was confirmed by fasting blood sugar levels (FBS) ≥5.6 mmol/L using an Accu-Chek Active glucometer (Roche Diagnostics, Germany).

Dosing Protocol

The dose was selected based on a previous study that demonstrated induced hyperglycemia and oxidative stress in rats using 750 mg/kg (13).

Data Collection

Body weight was measured weekly using a calibrated digital scale (500 g capacity, 0.01 g precision, Ohaus, USA). FBS was assessed after a 12-hour overnight fast via tail vein sampling. After 28 days, rats were anesthetized with ketamine (50 mg/kg, intraperitoneal) and euthanized by cervical dislocation. Lens tissues were excised under sterile conditions; one lens per rat was homogenized in 0.01 M phosphate-buffered saline (PBS, pH 7.4) for biochemical assays, and the contralateral lens was fixed in 10% formal saline for histopathology.

Biochemical Assays

Lens homogenates were prepared by rinsing lenses in 0.01 M cold phosphate-buffered saline (PBS, pH 7.4) using a glass-Teflon homogeniser, and centrifuging at 10,000×g for 10 minutes at 4°C (Eppendorf 5810R, Germany). Supernatants were stored at -20°C. Assays were performed in triplicate using a UV-Vis spectrophotometer (Jenway 7315, UK) with commercial kits (Sigma-Aldrich, USA) and validated with standards (intra-assay CV <5%):

- **Glutathione (GSH):** Measured by reaction with 5,5'-dithiobis-(2-nitrobenzoic acid) (DNTB) at 405 nm after 5-minute incubation at 25°C; quantified using a standard curve (14).

- **Catalase (CAT):** Quantified by H2O2 decomposition at 405 nm, stopped with ammonium molybdate after 1 minute; activity expressed as µmol H2O2/min/mg protein (15).
- **Malondialdehyde (MDA):** Assessed by thiobarbituric acid (TBA) reaction at 95°C for 60 minutes, measured at 532 nm; calculated using a molar extinction coefficient of 1.56 × 10^5 M^-1 cm^-1 [16].
- **Superoxide Dismutase (SOD):** Determined by inhibition of superoxide anion-mediated hydroxylamine oxidation at 550 nm; one unit inhibited 50% of the reaction [17].
- **Total Protein:** Measured using the biuret method at 550 nm after 10-minute incubation at 37°C, using bovine serum albumin standards [18].

Histopathological Analysis

Fixed lenses were processed using a LEICA PT 1020 Automatic Tissue Processor, dehydrated in ethanol (70–100%), cleared in xylene, and embedded in paraffin wax. Sections (5 µm) were cut using a LEICA RM 2135RT rotary microtome, stained with hematoxylin and eosin (H&E) using Mayer's hematoxylin (15 minutes), 1% acid-alcohol (10 seconds), and eosin (2 minutes), and mounted with dibutyl phthalate xylene (DPX) [19]. Slides were examined under a light microscope (Olympus BX51, Japan) at x10 (focusing) and x400 (detailed analysis) for cortex, nuclei, and fibre arrangement. A semi-quantitative scoring system (0–3; 0 = normal, 3 = severe disruption) was used by two blinded observers (inter-rater agreement >90%).

Statistical Analysis

Data were expressed as analysed using paired independent t-tests in Microsoft Excel 2016 ($p<0.05$). A priori power analysis (G*Power 3.1) confirmed n=5/group achieved 80% power to detect a 20% difference in biomarker levels ($\alpha=0.05$).

RESULTS

Body Weight Changes

The MSG-treated group showed a significant increase in body weight by week 4 compared with the control group, as shown in Figure 1.

Blood Glucose Levels

The MSG-treated group showed a significant increase in blood glucose levels by week 4 compared with the control group, as shown in Figure 2.

Glutathione (GSH)

The MSG-treated group showed a significant increase in GSH concentrations ($p<0.05$) by week 4 compared to the control group, as seen in Figure 3.

Catalase (CAT)

The MSG-treated group showed a significant decrease in CAT activity ($p<0.05$) by week 4 compared with the control group, as seen in Figure 4.

Malondialdehyde (MDA)

The MSG-treated group showed a significant increase in MDA concentrations ($p<0.05$) by week 4 compared with the control group, as seen in Figure 5.

Superoxide Dismutase (SOD)

The MSG-treated group showed a non-significant decrease in SOD concentrations ($p<0.05$) by week 4 compared with the control group, as shown in Figure 6.

Total Protein Concentration

The MSG-treated group showed a significant decrease in Total Protein concentrations ($p<0.05$) by week 4 compared to the control group, as seen in Figure 7.

Histopathological Findings

This revealed no structural changes between the treated group and the control group. Both groups displayed normal lens architecture, characterised by intact cortex, well-defined nuclei, and orderly arranged fibres as observed in (Figures 8 and 9).

DISCUSSION

An increase in body weight was observed in this study, corresponding to previous work showing that MSG promotes adiposity and metabolic dysregulation through hypothalamic injury and altered energy balance [4]. Similarly, the noticeable increase in blood glucose aligns with the findings that report MSG can impair pancreatic β-cell integrity and induce insulin resistance [9]. Chronic hyperglycemia can lead to the production of oxidative stress, which overwhelms the antioxidant defence mechanism [7]. In this study, there was a noticeable elevation in the level of lens glutathione (GSH) which revealed a compensatory approach by the lens to mitigate oxidative stress. More findings report that MSG exposure can activate antioxidant upregulation as a defensive mechanism before eventual reduction occurs under overwhelming oxidative burden [10]. The reduced level of catalase (CAT) and a non-significant decrease in superoxide dismutase (SOD) indicate that the enzymatic antioxidant system has been overwhelmed. Exposure of MSG can depletes the activity of CAT and SOD, indicating oxidative stress [20; 21]. In this study, the increased level of Malondialdeyde (MDA) confirms lipid peroxidation which is a central mechanism of oxidative lens injury. It corresponds with a study that reported MSG dose-dependent elevation of MDA concentration, supporting oxidative degradation of membrane lipids [20; 22].

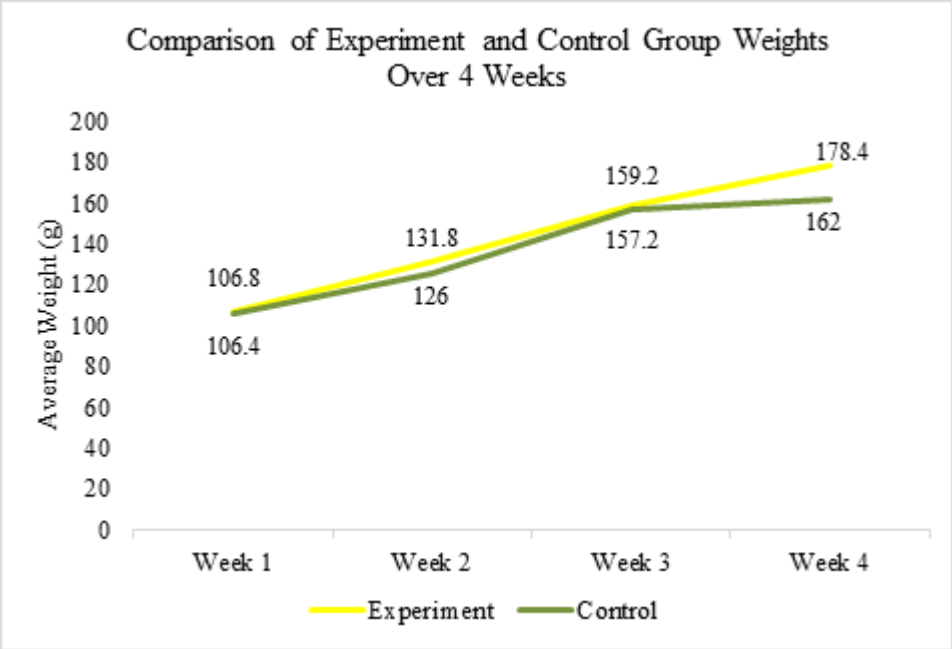

Figure 1: Average Body Weight (g) Over Four Weeks

Line graph comparing average blood glucose levels(mmol/L) over 4 weeks, depicting a significant increase in the MSG-treated group as compared to controls.

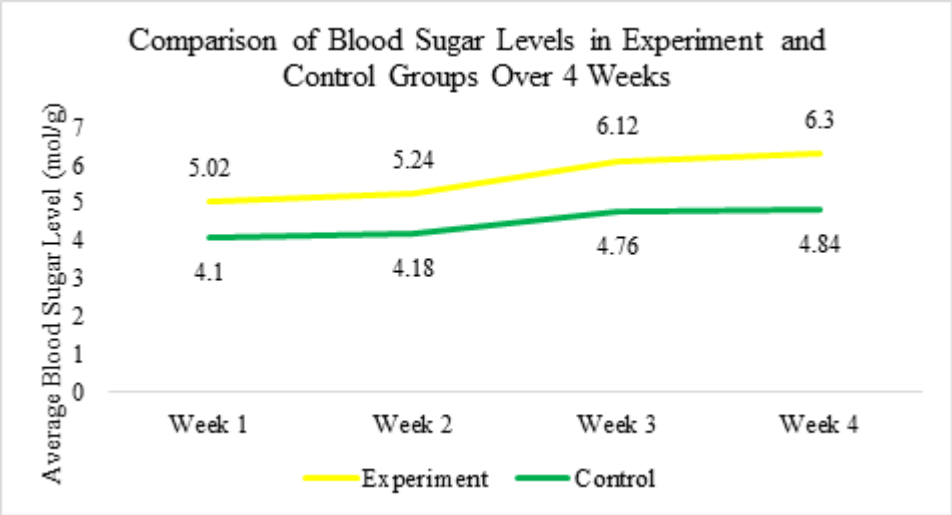

Figure 2: Average Blood Glucose Levels (mmol/L) Over Four Weeks

Line graph comparing average blood glucose levels(mmol/L) over 4 weeks, depicting a significant increase in the MSG-treated group as compared to controls.

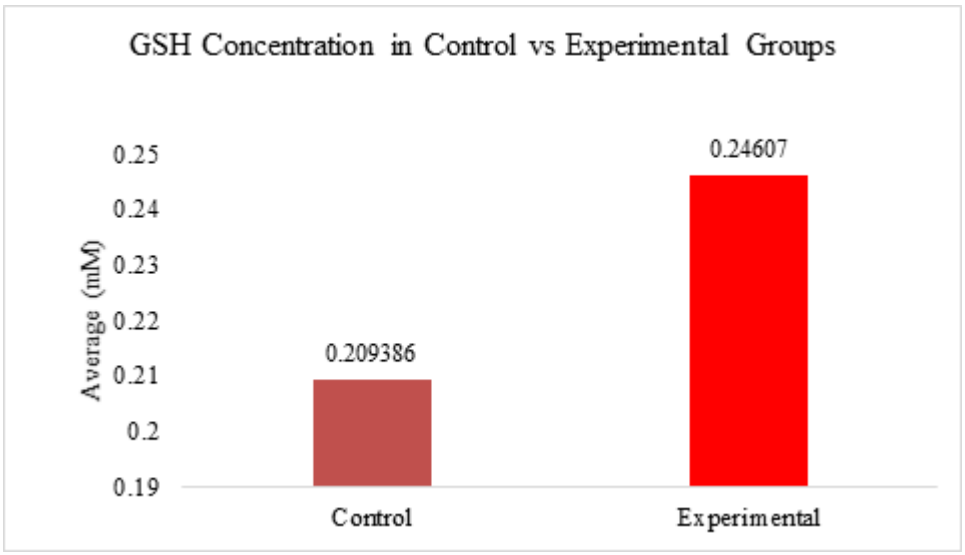

Figure 3: **Glutathione (GSH) Concentration.**
The bar graph shows a significantly increased GSH concentration in the MSG-treated group as compared to controls.

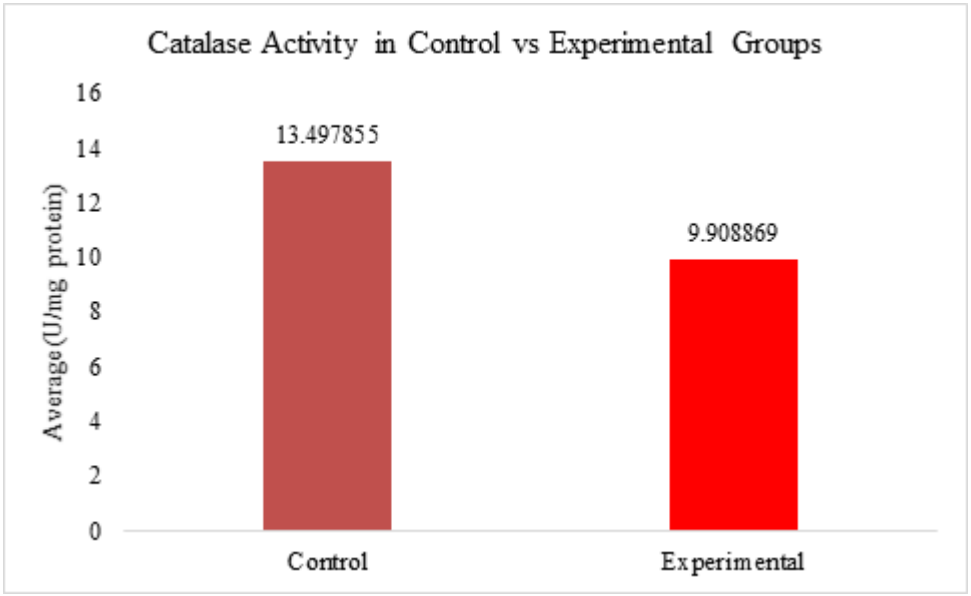

Figure 4: Catalase (CAT) Activity.
The bar graph shows a significantly decreased CAT activity in the MSG-treated group as compared to controls.

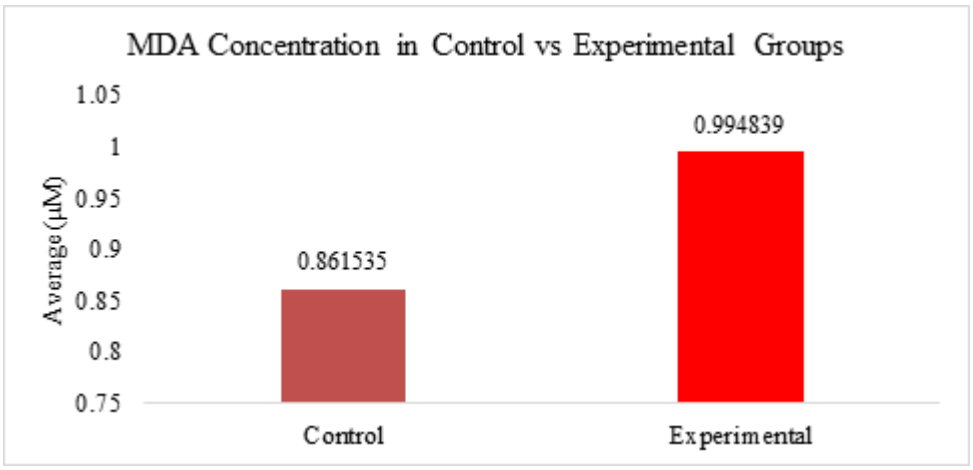

Figure 5: Malondialdehyde (MDA) Concentration.

The bar graph shows a significantly increased MDA concentration in the MSG-treated group as compared to controls.

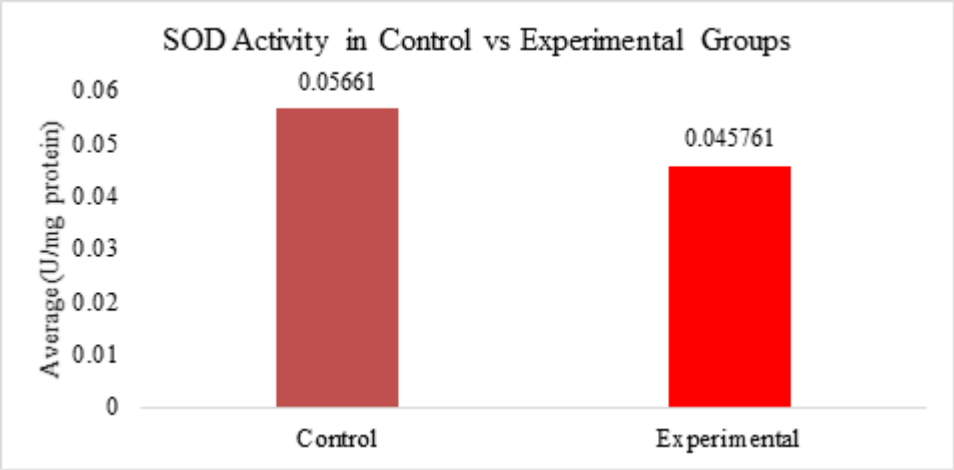

Figure 6: Superoxide Dismutase (SOD) Activity. *The bar graph shows a non-significantly decreased SOD activity in the MSG-treated group as compared to controls.*

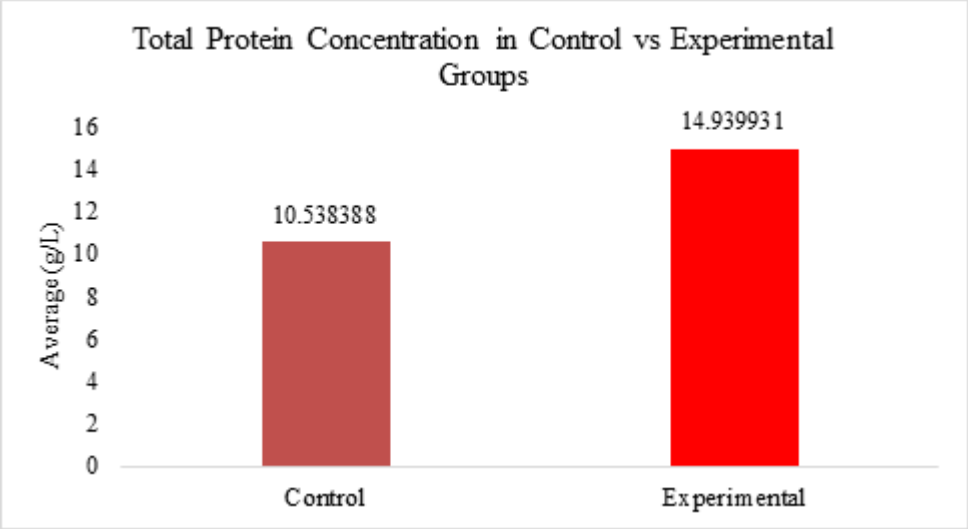

Figure 7*:* Total Protein Concentration.
The bar graph shows significantly decreased total protein concentration in the MSG-treated group as compared to controls.

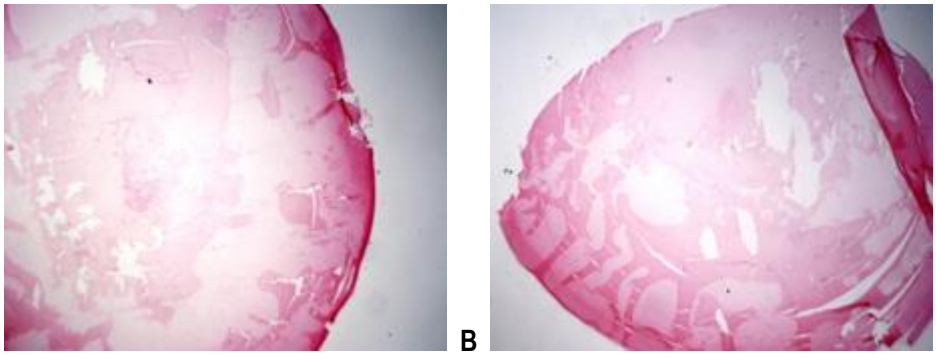

Figure 8: H&E-stained histological slides of the experimental group lens (x400), showed normal architecture with intact cortex, nuclei and orderly arranged lens fibers, with no pathological changes observed.

The lens has a high protein content and limited regenerative capacity, making it vulnerable to enzymatic compromise. Reduction in lens total protein concentration is consistent with early cataractogenesis [10]. Even though, few studies exist on

MSG's effect on the lens, the earlier neonatal MSG exposure reported cataract formation, disorganised lens morphology and retina damage [21], reinforcing its ocular toxicity potential. No structural damages observed, which aligned with the evidence that oxidative biochemical disruptions occur before morphological alterations [22]. In conclusion, this study shows that MSG exposure increases the level of oxidative biomarkers in the lens by altering the antioxidant systems, even when structural integrity is preserved. These findings support that MSG exposure under diabetogenic conditions may contribute to early lens changes during cataractogenesis. The short duration of the study, however, may not fully capture the long-term effects.

CONCLUSION

MSG-induced diabetic lens revealed elevated levels of oxidative biomarkers, which can be detrimental to ocular health. The normal histopathological changes suggest that structural damage requires prolonged hyperglycemia. The findings imply the need for regulated MSG consumption among populations prone to diabetic and ocular diseases.

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AUTHORS' CONTRIBUTION

IA: Conceptualized and supervised the study, guided experimental design, oversaw data analysis, and critically reviewed the manuscript. OOM.: Proofread and edited the manuscript, provided critical feedback on study design, and assisted with data interpretation. ASO: Conducted histopathological analysis, collected data, performed tissue processing/staining, and drafted the manuscript. AJA: Designed methodology, performed biochemical assays, collected oxidative stress data, and contributed to manuscript drafting.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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