Original Article

Received: 2024-11-15
Accepted: 2024-12-25

BCCR
2024, No 4, Vol 16 :183-195
www.bccrjournal.com

http://doi.org/10.18502/bccr.v16i4.20843

Monosodium Glutamate's Dose-Dependent Effects on Prostate Cancer Markers and Sperm Quality

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ABSTRACT

Monosodium glutamate (MSG) is a widely used flavor enhancer with controversial health effects. While high doses have been associated with oxidative stress and reproductive toxicity, low doses may exert protective effects. The objectives of this study were to investigate the effects of monosodium glutamate (MSG) on serum markers of prostate cancer and semen quality in male Wistar rats. Thirty-six male Wistar rats were randomly grouped into six groups (n = 6 per group) and orally administered varying doses of MSG (0, 15, 50, 100, 500, and 1000 mg/kg body weight) for 28 days. Serum total Prostate Specific Antigen (tPSA), free PSA (fPSA), Total Acid Phosphatase (TAP), Prostatic Acid Phosphatase (PAP), and Gamma-Glutamyl Transferase (GGT) were measured using ELISA. Sperm count, motility, viability, and morphology were assessed from epididymal samples. Our results showed that MSG exhibited a biphasic (hormetic) response.

15 mg/kg MSG reduced TAP by -64% ($p < 0.001$), fPSA by -60% ($p < 0.001$) and tPSA by -60% ($p < 0.001$), GGT by -19.4% ($p<0.05$) while 50–100 mg/kg MSG improved semen quality, boosting sperm count by +110% and +170% ($p < 0.01$, $p < 0.001$), sperm motility by +108% and +77% ($p < 0.001$, $p < 0.01$), and viability by +7% and +16% (ns, $p < 0.05$), respectively. In contrast, 1000 mg/kg MSG caused severe reproductive toxicity, with –65% sperm count, –100% motility, –23% morphology, and –37% viability (all $p < 0.05$). These results confirm MSG's hormetic behavior: low doses improved prostate health and fertility, while high doses induced prostate pathology and impaired spermatogenesis.

Low-dose MSG (15–100 mg/kg) demonstrated protective effects on prostate health and male fertility, while higher doses (≥ 500 mg/kg) showed potential for prostate pathology induction and reproductive toxicity. These findings suggest MSG's dual potential as both a therapeutic candidate for prostate cancer and a model compound for inducing prostate disease in experimental settings.

Keywords: Gamma Glutamyl Transferase; Monosodium Glutamate; Prostatic Acid Phosphatase (PAP); Prostate Cancer; Prostate Specific Antigen; Total Acid Phosphatase

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INTRODUCTION:

Monosodium glutamate (MSG), a sodium salt of glutamic acid, is a globally utilized flavor enhancer renowned for imparting the umami taste, first characterized by Professor Kikunae Ikeda in 1909 [1]. As a key component in processed foods, soups, and seasonings, MSG enhances palatability by releasing free glutamate, which stimulates taste receptors [2]. Despite its widespread culinary application, the safety profile of MSG remains contentious, with emerging evidence suggesting both beneficial and adverse health effects depending on dosage and duration of exposure [3]. Recent studies have linked excessive MSG consumption to oxidative stress, metabolic dysfunction, neurotoxicity, and reproductive impairments, while low doses may exhibit protective effects through modulation of antioxidant pathways and cellular signaling [4, 5]. These contradictory findings underscore the need to elucidate MSG's dose-dependent effects on specific physiological systems, particularly those with significant public health implications. Prostate cancer (CaP) ranks among the most prevalent malignancies affecting men worldwide, with early detection reliant on sensitive and specific biomarkers such as prostate-specific antigen (PSA), including free PSA (fPSA) and total PSA (tPSA), total acid phosphatase (TAP), prostatic acid phosphatase (PAP), and gamma-glutamyl transferase (GGT) [6, 7]. PSA, a serine protease produced by prostate epithelial cells, is the cornerstone of prostate cancer screening, with elevated levels indicating potential malignancy or benign prostatic hyperplasia. Complementary markers like TAP and PAP provide insights into prostate tissue integrity, while GGT, an enzyme involved in glutathione metabolism, reflects oxidative stress and cellular health [8]. The interplay between environmental factors, including dietary components like MSG, and these biomarkers is poorly understood, necessitating targeted research to assess whether MSG influences prostate pathology.

MSG has been associated with male reproductive issues beyond its potential effects on prostate health. Research indicates that high MSG doses can lead to testicular oxidative stress, damage to spermatogenic cells, and compromised semen quality, including decreased sperm count, motility, viability, and abnormal sperm shape [9]. On the other hand, some studies suggest that moderate MSG doses might improve sperm quality, potentially through glutamate-related metabolic processes [10]. This dose-dependent response reflects the toxicological principle of hormesis, where low doses of a substance may have beneficial or protective effects, while high doses become toxic [11]. The hormetic nature of MSG in both prostate and reproductive systems offers a valuable opportunity to investigate its potential as either a therapeutic tool or a contributor to health issues.

Previous studies on MSG have largely concentrated on its neurotoxic and metabolic effects, with less focus on how it influences prostate cancer markers and semen quality in a dose-dependent manner. For example, Egbuonu et al. [12] found that MSG triggers prostate damage in rats, while Armstrong et al. [13] showed that low-dose MSG decreases prostate-specific membrane antigen (PSMA) uptake, indicating a possible protective effect against prostate tumor development. Likewise, inconsistent results regarding semen quality underscore the need for detailed dose-response research to better understand MSG's impact on reproduction [8, 14]. The absence of thorough data on MSG's dual effects on these vital health aspects creates a notable research gap, especially given its common use in diets and potential for pharmaceutical purposes.

This study aims to investigate the dose-dependent effects of MSG (15 mg/kg to 1000 mg/kg body weight) on serum prostate cancer markers (fPSA, tPSA, TAP, PAP, GGT) and semen quality (sperm count, motility, viability, morphology) in male Wistar rats over a 28-day oral administration period. By employing a broad range of MSG doses, we seek to characterize its hormetic behavior, identifying thresholds for protective versus toxicological effects on prostate health and male fertility. The novelty of this research lies in its integrative approach, simultaneously evaluating MSG's impact on clinically relevant prostate cancer biomarkers and reproductive parameters within a single experimental framework. Unlike previous studies that focused on isolated outcomes, this work provides a comprehensive analysis of MSG's dual potential as a therapeutic agent for prostate cancer and male infertility at low doses, and as a tool for inducing prostate pathology at high doses. These findings have significant implications for food safety regulations, dietary recommendations, and the development of MSG-based chemotherapeutic or fertility-enhancing interventions, paving the way for future translational research in humans.

Materials and Methods:

Ethical Clearance

Ethical approval for this study was granted by the Faculty of Medical Sciences, Ahmadu Bello University, Zaria, under reference number ABUCUASR/2013/011.

Sample Collection

A commercial brand of monosodium glutamate (MSG) was obtained from the Foodstuff Section of the Community Market at Ahmadu Bello University (ABU), Zaria, Kaduna State, Nigeria. All other chemicals utilized during the study were of certified analytical grade.

Animals and Treatments

Thirty-six male Wistar rats, sourced from the Animal House of the Faculty of Pharmaceutical Sciences at Ahmadu Bello University, Zaria, Kaduna State, Nigeria, were housed in clean steel cages. They had unrestricted access to standard feed and drinking water, maintained under humid tropical conditions at room temperature with a 12-hour light/dark cycle. The rats were given a two-week acclimatization period before the start of the experiment.

All procedures complied with local guidelines for the care and use of laboratory animals.

Sample size Justification

Sample size (n=6/group) was based on prior MSG reproductive toxicology studies where n=5–8 was sufficient to detect biologically relevant differences.

Randomization and Blinding

The rats were randomly assigned to six groups, with each group consisting of six rats.

Laboratory personnel conducting biomarker assays and semen evaluations were blinded to group dose allocations.

- Group E (Control): Received 0 mg/kg body weight of MSG
- Group A: Administered MSG at 15 mg/kg body weight
- Group B: Administered MSG at 50 mg/kg body weight
- Group C: Administered MSG at 100 mg/kg body weight
- Group D: Administered MSG at 500 mg/kg body weight
- Group F: Administered MSG at 1000 mg/kg BW

The rats were orally given their respective MSG doses daily for 28 days, with consistent volumes across groups, while having free access to their regular food and water throughout the experiment.

Blood and Semen Collection and Preparation

Following the completion of the experimental period, blood samples were collected using the method outlined by Egbuonu et al. [15]. Briefly, after an overnight fast, the rats were anesthetized with a low concentration of chloroform and sacrificed by decapitation the following day. Blood was collected into individually labeled polystyrene centrifuge tubes and allowed to clot. The resulting sera were separated through centrifugation at 3000 rpm for 10 minutes, then stored in a deep freezer for later analysis of prostate cancer markers.

Semen samples, freshly obtained from the epididymis, were analyzed. Sperm count was determined using a hemocytometer under light microscopy. Motility was assessed as the percentage of progressively motile sperm cells per sample. Viability was evaluated by eosin–nigrosin staining, and morphology was assessed by following the WHO laboratory manual guidelines (2010), at the Anatomy Department of the Faculty of Medicine, Ahmadu Bello University, Zaria.

Biochemical Analysis

Levels of free PSA, total PSA, Total Acid Phosphatase (TAP), Prostatic Acid Phosphatase (PAP), and Gamma-Glutamyl Transferase (GGT) were measured using Diagnostic ELISA Kits at the Chemical Pathology Laboratory of ABU Teaching Hospital in Shika, following the manufacturer's protocols.

Test Principle

The ELISA kits included microtiter plates pre-coated with a PSA-specific antibody. Samples or standards were added to the designated wells, along with a biotin-conjugated polyclonal antibody specific to PSA. Horseradish Peroxidase (HRP)-conjugated avidin was then added to each well and incubated. A TMB (Trimethyl Benzidine) substrate solution was introduced, causing a color change in wells containing PSA, biotin-conjugated antibody, and enzyme-conjugated avidin. The reaction was stopped by adding a sulfuric acid solution, and the color intensity was measured spectrophotometrically at a wavelength of 450 nm ± 2 nm. PSA concentrations in the samples were calculated by comparing their optical density (O.D.) to a standard curve.

Data Analysis

Data were analyzed using one-way ANOVA followed by Tukey's post hoc test. Statistical significance was set at $p < 0.05$. And individual percentages and exact p-values are reported where relevant.

Results:

After the oral administration of varying doses of MSG for 28 days, the following results were obtained and expressed in the subsequent figures.

Effect of MSG on Serum Prostate Cancer Markers (fPSA, tPSA)

ANOVA revealed significant group effects for fPSA ($F(6,30) = 9.07$, $p = 1.10 \times 10^{-5}$) and tPSA ($F(6,30) = 7.42$, $p = 6.24 \times 10^{-5}$) across treatment groups. Post hoc Tukey's test confirmed that 15 mg/kg MSG produced a marked reduction in PSA levels compared to control (fPSA: 6.53 ± 0.90 → 2.62 ± 0.44 ng/mL, −59.8%, $p < 0.01$; tPSA: 8.99 ± 1.41 → 3.58 ± 1.47 ng/mL, −60.2%, $p < 0.01$). A moderate but significant reduction was also observed at 50 mg/kg (fPSA: −21.1%, $p < 0.05$; tPSA: −41.0%, $p < 0.01$). By contrast, doses of 100, 500, and 1000 mg/kg did not differ significantly from the control group, though trends indicated slight increases in PSA levels at 500 mg/kg (fPSA: +10.8%, tPSA: +6.2%). Figure 1 highlights that the strongest protective effect on prostate cancer markers occurred at the lowest dose (15 mg/kg), with diminishing benefits as the dose increased.

Effect of MSG on Total Acid Phosphatase (TAP):

Oral administration of MSG produced a clear dose-dependent effect on serum TAP levels in male Wistar rats (Figure 2). One-way ANOVA revealed a statistically significant difference among treatment groups ($F(6,30) = 11.93$, $p = 0.000003$). Compared to the control group (50.00 ± 5.73 ng/mL), the 15 mg/kg group showed a marked reduction to 18.00 ± 7.91 ng/mL (−64.0%, $p < 0.001$), while the 50 mg/kg group decreased to 33.00 ± 13.24 ng/mL (−34.0%, $p = 0.041$). In contrast, the 100 mg/kg (47.00 ± 12.10 ng/mL, −6.0%), 500 mg/kg (55.83 ± 6.27 ng/mL, +11.7%), and 1000 mg/kg (48.17 ± 8.23 ng/mL, −3.7%) groups were not significantly different from control ($p > 0.05$). Post hoc analysis confirmed that the 15 mg/kg group differed significantly from

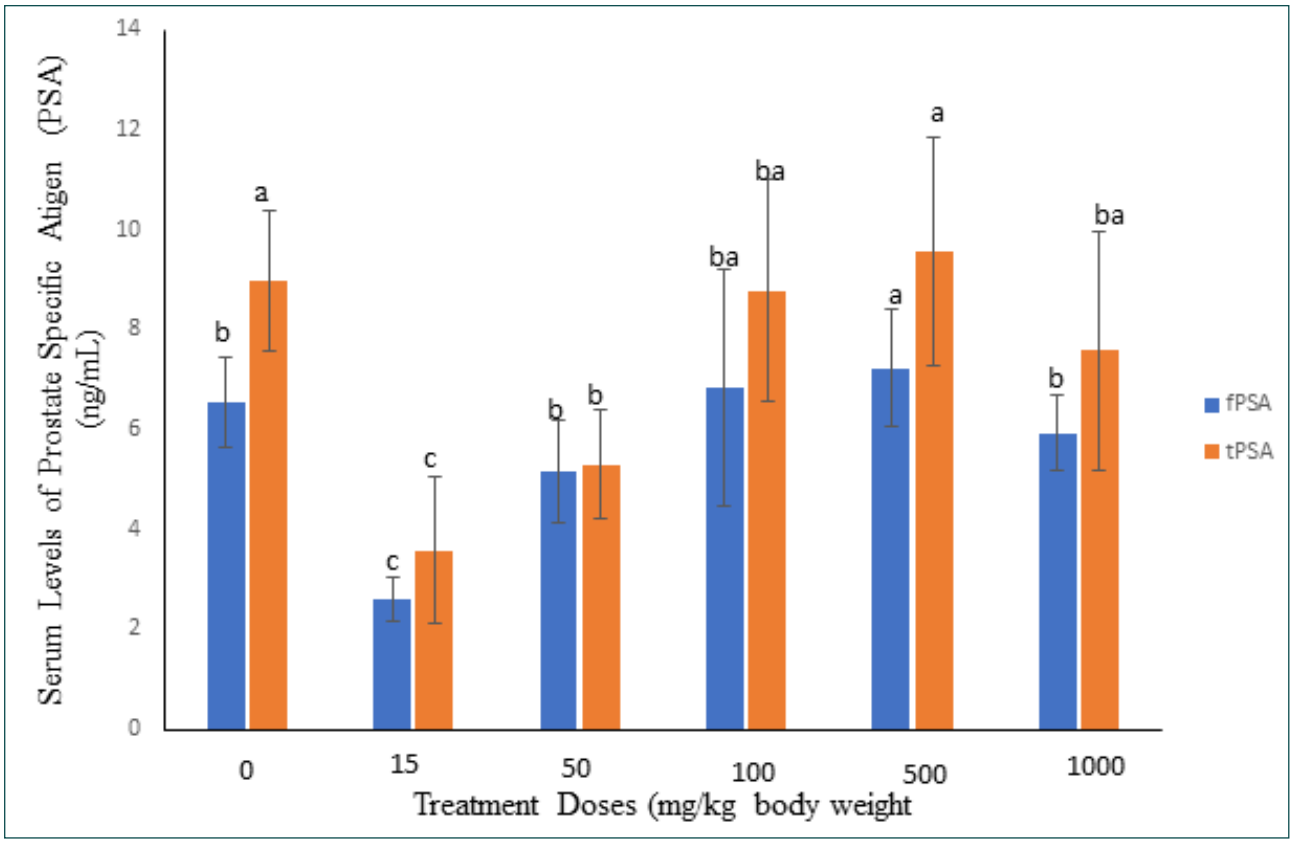

Figure 1: The Effect of varying doses of MSG on serum levels of free and total Prostate Specific Antigen (PSA) of male Wistar rats treated for 28 days
Data are presented as mean ±SD with n=6.
Means with the same superscripts are not significantly different (significance is at p<0.05 probability levels) when compared to the 0 mg treatment group

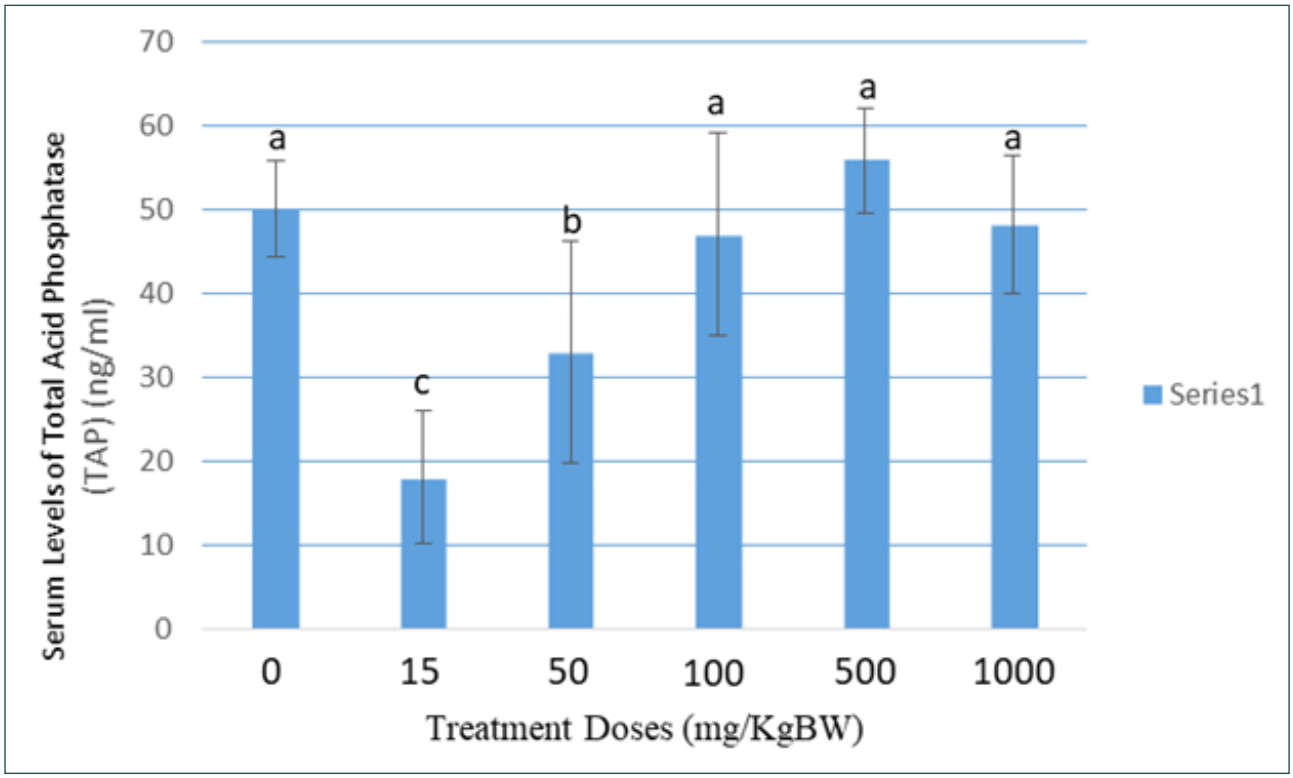

Figure 2: The Effect of varying doses of MSG on serum levels of Total Acid Phosphatase (TAP) of male wistar rats treated for 28 days
Data are presented as mean ±SD with n=6.
Means with the same superscripts are not significantly different (significance is at p<0.05 probability levels) when compared to 0mg treatment group

nearly all other doses ($p < 0.001$ vs control, 50 mg, and 500 mg), establishing it as the most effective in lowering TAP. These findings indicate that low-dose MSG, particularly at 15 mg/kg, exerts a protective influence on prostate health by significantly suppressing TAP activity, whereas higher doses do not confer similar benefits.

The Effect of varying doses of MSG on serum levels of Prostatic Acid Phosphatase (PAP) of male Wistar rats treated for 28 days

Oral administration of MSG produced a clear dose-dependent trend in serum Prostatic Acid Phosphatase (PACP) activity (Figure 3). Rats in the 15 mg/kg group showed a marked reduction in PACP levels (0.70 ± 0.33 ng/mL), representing a 48.1% decrease compared with controls (1.35 ± 0.59 ng/mL; $p < 0.05$). At 50 mg/kg and 100 mg/kg, PACP values were moderately reduced to 1.05 ± 0.36 ng/ml (22.2% decrease) and 1.17 ± 0.29 ng/mL (13.3% decrease), respectively, though these reductions were not statistically different from controls. In contrast, higher MSG doses caused a rebound effect: 500 mg/kg and 1000 mg/kg groups recorded elevated PACP activities of 1.55 ± 0.19 ng/mL and 1.57 ± 0.16 ng/mL, corresponding to 14.8% and 16.3% increases over control values.

Analysis of variance confirmed significant differences across treatment groups (ANOVA: $F(5,30) = 3.29$, $p = 0.018$). Post-hoc comparisons revealed that the reduction observed at 15 mg/kg was significantly lower than the elevations at 500 mg/kg and 1000 mg/kg ($p < 0.05$). This biphasic response pattern reinforces the hormetic nature of MSG, where low doses suppress prostate-related enzyme activity while higher doses induce an opposite trend.

Effect of varying doses of MSG on serum levels of Gamma Glutamyl Transferase (GGT)

Figure 4 shows that Gamma Glutamyl Transferase (GGT) followed a biphasic trend consistent with oxidative stress regulation. At 15 mg/kg and 50 mg/kg, serum GGT decreased significantly compared to control, reflecting improved antioxidant capacity and reduced prostatic stress ($p < 0.05$). However, animals at 500 and 1000 mg/kg doses exhibited elevated GGT levels relative to control ($p < 0.05$), suggesting

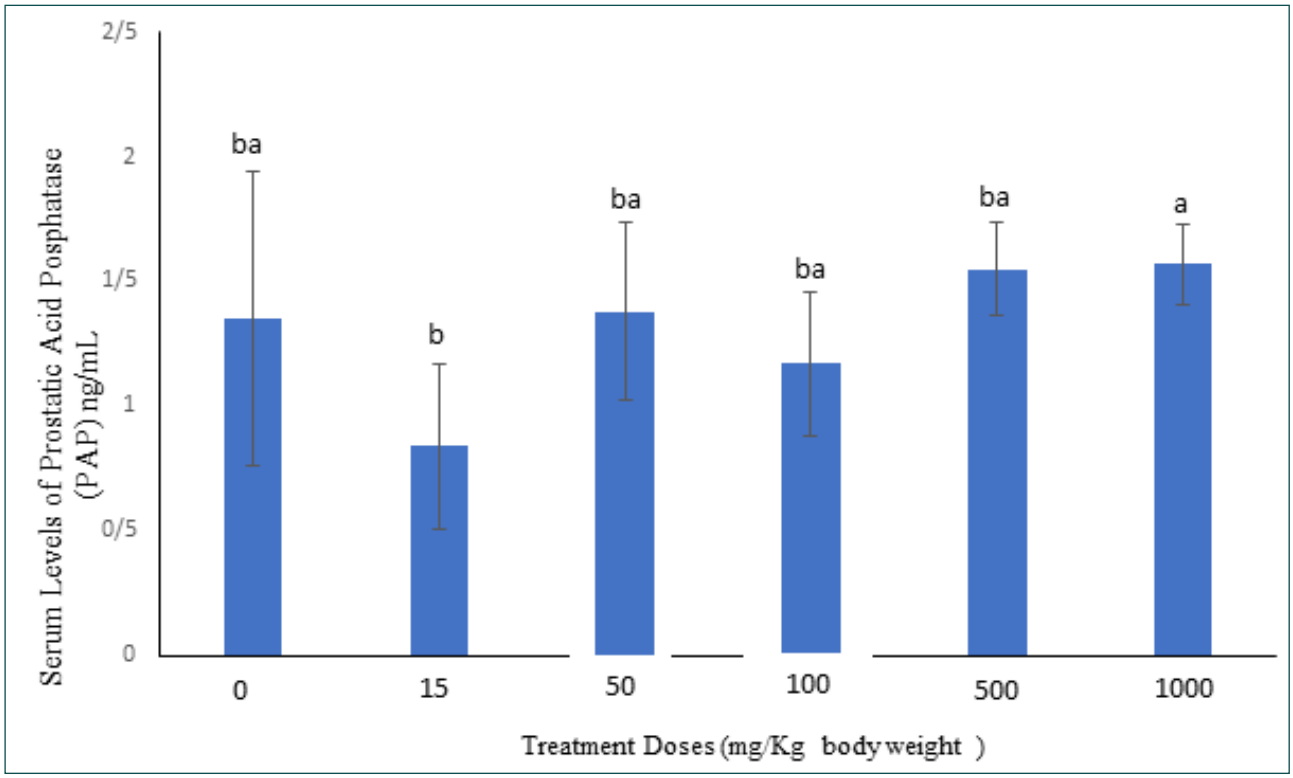

Figure 3: The Effect of varying doses of MSG on serum levels of Prostatic Acid Phosphatase (PAP) of male Wistar rats treated for 28 days
Data are presented as mean ±SD with n=6.
Means with the same superscripts are not significantly different (significance is at p<0.05 probability levels) when compared to 0mg treatment group

upregulation in response to oxidative stress burden at high MSG intake.

Effect of MSG on Semen Quality

MSG exerted a dose-dependent hormetic influence on sperm characteristics.

Figure 5 shows that Sperm count in controls averaged 10.0×10^6/mL. Counts increased steadily at 15 mg/kg (14.5×10^6/mL, +45%), 50 mg/kg (21.0×10^6/mL, +110%), and peaked at 100 mg/kg (27.0×10^6/mL, +170%, $p < 0.001$). Beyond this threshold, counts declined at 500 mg/kg (16.5×10^6/mL, +65%, $p < 0.05$) and dropped drastically at 1000 mg/kg (3.5×10^6/mL, −65%, $p < 0.001$).

Figure 6 shows Sperm motility mirroring this pattern. At 50 mg/kg, active motile cells increased to 67.5% compared with 32.5% in control (+108%, $p < 0.01$), whereas 1000 mg/kg eliminated all active motile sperm (0%, $p < 0.001$). Sluggish and non-motile fractions rose significantly at the highest dose, consistent with toxic impairment of sperm locomotion.

Figure 7 reveals that Sperm viability was highest at 100 mg/kg (62.5% viable vs 54% in control, +16%, $p < 0.05$), while the 1000 mg/kg group recorded only 34% viable cells (−37%, $p < 0.001$).

Similarly, Figure 8 shows that normal morphology was preserved at 50–100 mg/kg (≈60–61%), but declined at 1000 mg/kg (43%, −23%, $p < 0.01$), with increases in both head and tail defects.

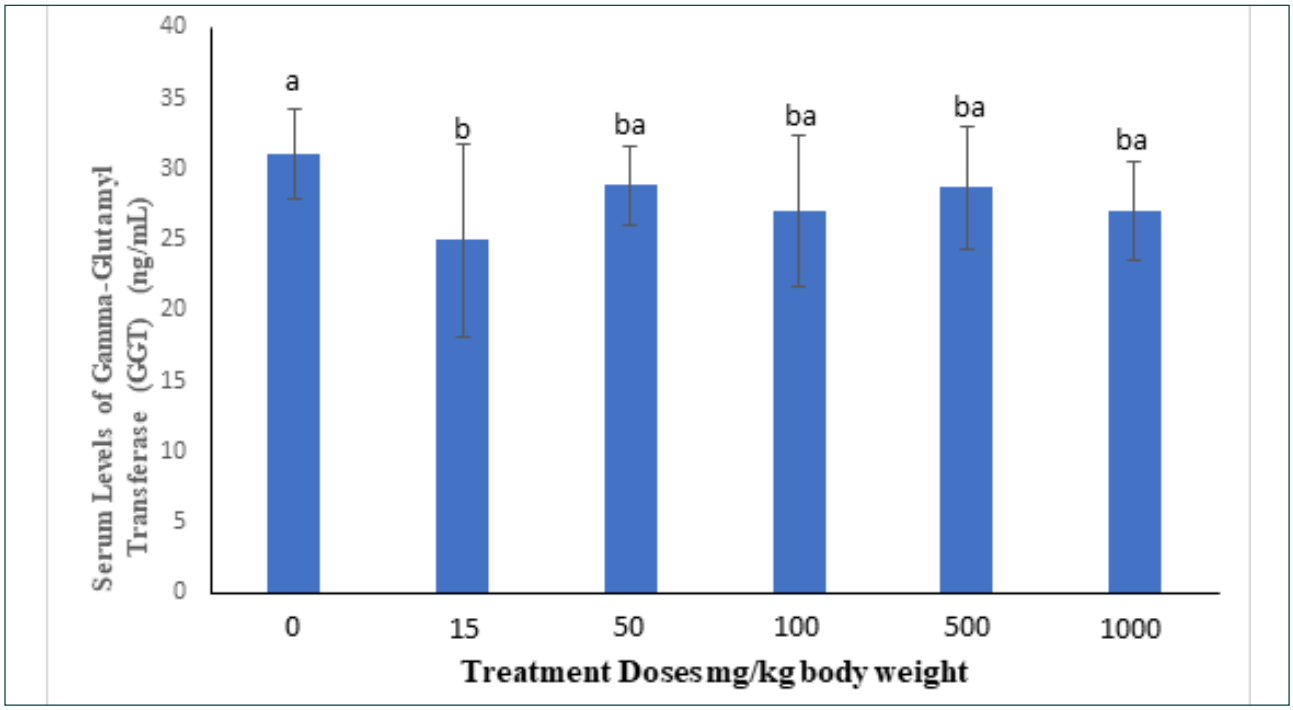

Figure 4: The Effect of varying doses of MSG on serum levels of Gamma Glutamyl Transferase (GGT) of male wistar rats treated for 28 days
Data are presented as mean ±SD with n=6.
Means with the same superscripts are not significantly different (significance is at p<0.05 probability levels) when compared to 0mg treatment group

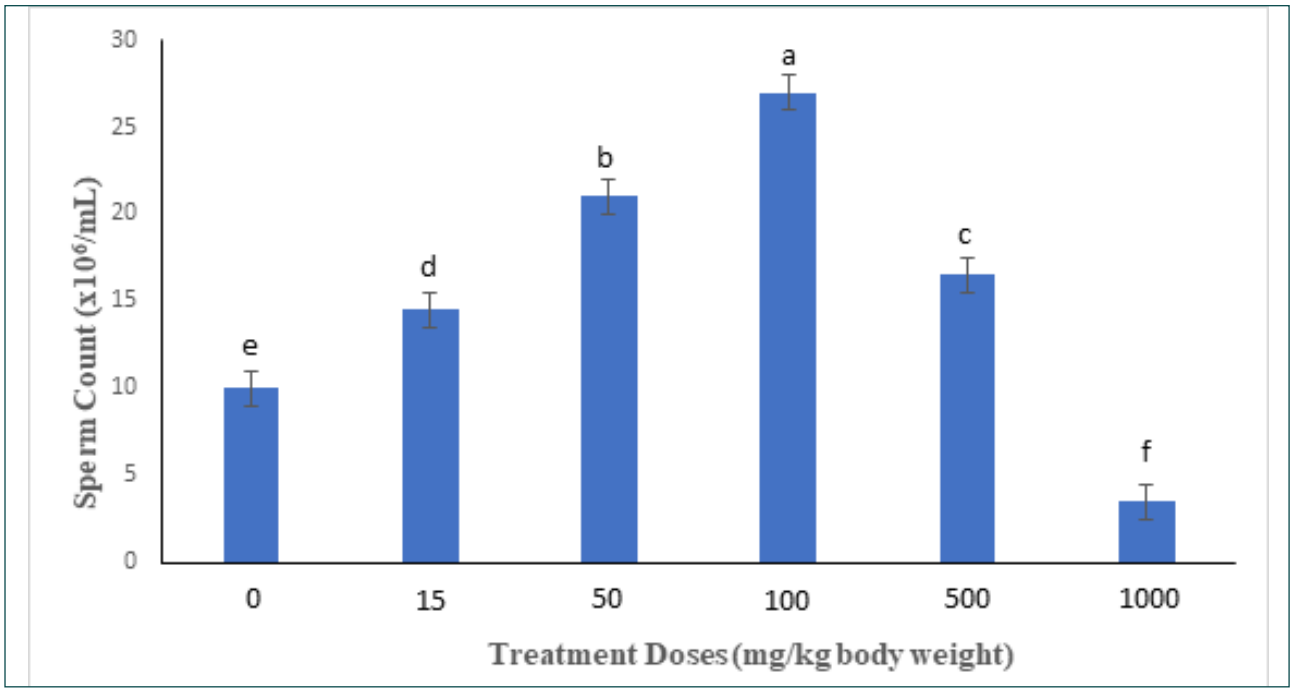

Figure 5: The Effect of varying doses of MSG on Sperm Count (x106/mL) of male wistar rats treated for 28 days
Data are presented as mean ±SD with n=6.
Means with the same superscripts are not significantly different (significance is at p<0.05 probability levels) when compared to 0mg treatment group

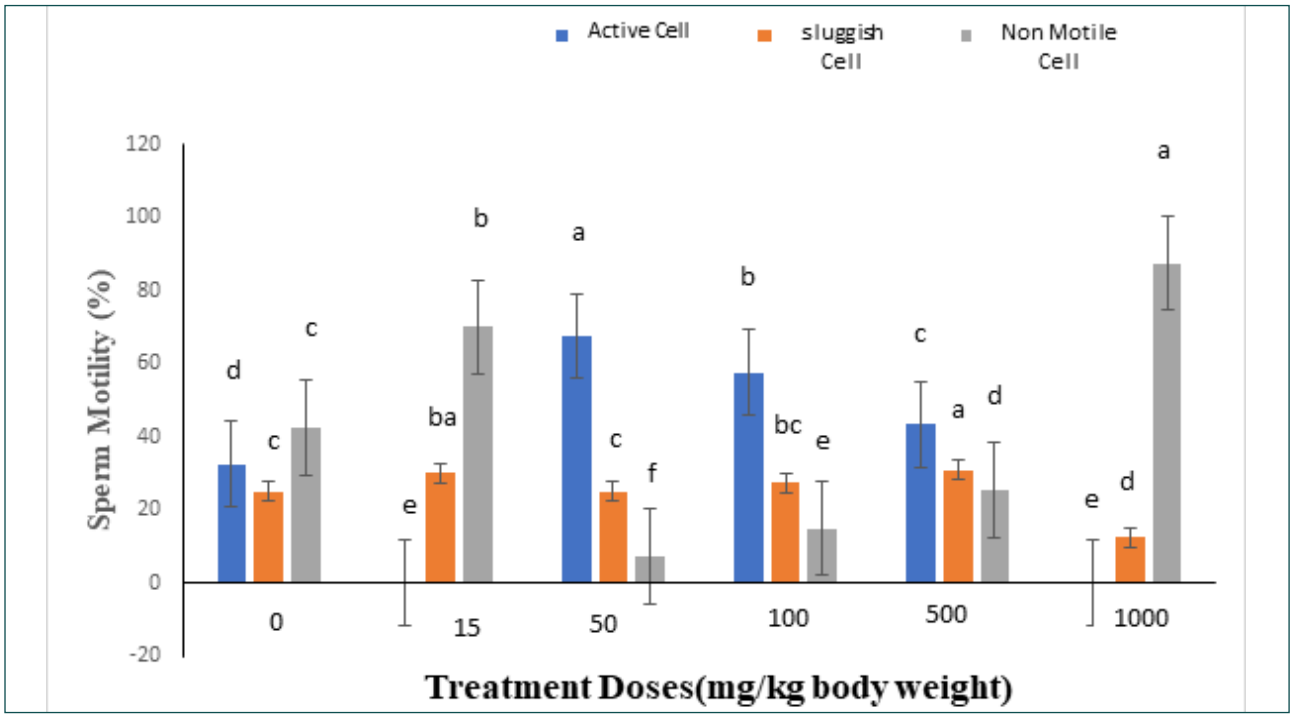

Figure 6: The Effect of varying doses of MSG on Sperm Motility (%) of male wistar rats treated for 28 days
Data are presented as mean ±SD with n=6.
Means with the same superscripts are not significantly different (significance is at $p<0.05$ probability levels) when compared to 0mg treatment group

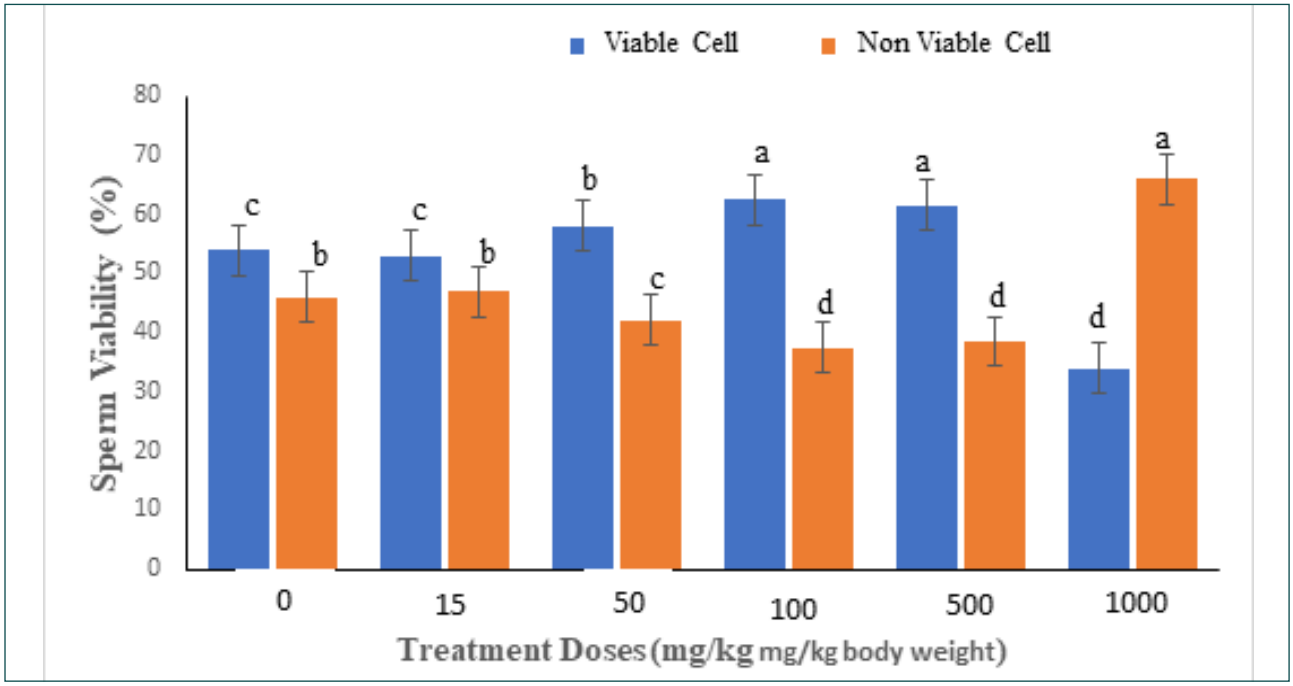

Figure 7: The Effect of varying doses of MSG on Sperm Viability (%) of male wistar rats treated for 28 days
Data are presented as mean ±SD with n=6.
Means with the same superscripts are not significantly different (significance is at $p<0.05$ probability levels) when compared to 0mg treatment group

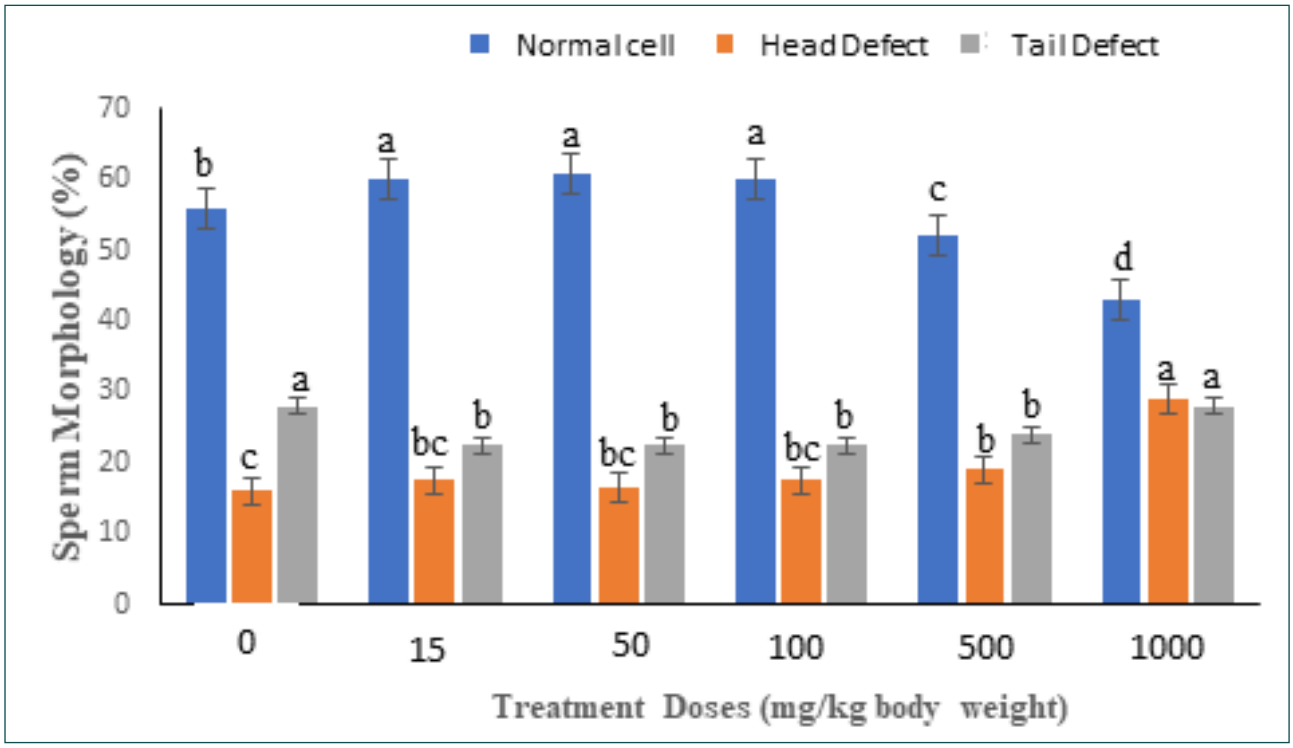

Figure 8: The Effect of varying doses of MSG on Sperm Morphology (%) of male wistar rats treated for 28 days
Data are presented as mean ±SD with n=6.
Means with the same superscripts are not significantly different (significance is at $p<0.05$ probability levels) when compared to 0mg treatment group

DISCUSSION:

The results of this study it show that the Null hypothesis at the beginning of the study, which states that MSG does not affect serum markers of prostate disease, is not true. This study shows that MSG has a dose-dependent, significant effect on serum diagnostic markers of prostate cancer. The outcomes of this research further revealed that lower doses of MSG (15, 50, 100 mg/kg body weight) used in this study lower the levels of serum prostate disease markers when compared to the control group. Clinically, a decrease in serum levels of TAP, PAP, and PSA shows that the Prostate health is good. In other words, the presence of MSG furnishes free glutamate, which is converted to GABA in the brain by glutamate decarboxylase. The presence of GABA also affects gamma-glutamyl transferase, which acts on reduced glutathione to furnish active glutathione for antioxidant functions. Invariably, the prostate gland is biochemically strengthened by the low dose of 15 mg/kg body weight to elicit a decrease in the serum level of prostate disease markers.

The reduction of serum GGT at low MSG doses can be explained by the concept of feedback inhibition and by the role of glutamate as both a substrate and regulator of glutathione metabolism. Normally, GGT is upregulated to cleave extracellular glutathione and liberate glutamate when cells are under oxidative stress. Exogenous glutamate supplied by MSG reduces the demand for GGT activity, supports cystine uptake through the Xc^- antiporter, and sustains intracellular GSH levels. This feedback lowers circulating GGT at 15–50 mg/kg body weight, reflecting reduced oxidative stress and a favorable biochemical environment for prostate health. At higher doses, however, oxidative stress increases, antioxidant defenses are overwhelmed, and GGT is upregulated again, demonstrating the biphasic hormetic response observed in this study.

This finding is in sync with a study done by Armstrong et al. [13] that shows that oral administration of MSG lowers 68Ga-PSMA in the salivary gland, showing that a low dose of MSG has a protective potential in lowering the serum levels of Prostate Membrane Antigen (PSMA) and shrinks tumour activities.

Also, the results from this study show that the higher doses deployed in this study, 500mg and 1000 mg/kg, show an elevation that is not significant (significance

is at $p<0.05$ probability levels), perhaps because of the short time of usage. This elevation of serum markers of prostate disease at these doses shows the propensity to induce this disease significantly with continuous use. This higher dose inductive potential is also in tandem with studies of Agada et al. (2023), who deployed doses higher than 1000 mg/kg body weight. Their studies show that 1000 mg/kg body weight and above shows a significant increase in serum markers of prostate disease and oxidative stress. Hence, the biphasic phenomenon of MSG to induce prostate cancer at certain medium to high doses and inhibit or treat prostate cancer at low doses even within a short period of use or treatment (28days).

The effect of MSG on the semen from this study confirms previous studies by Nayanatara et al. [14] and Igwebuike et al. [17] which established the fact that, MSG negatively influence the locomotor activity of the sperm cells (reduced active cells), decreasing sperm motility, reducing sperm viability and affecting sperm morphology at highest concentration of the administered doses with increased Tail and Head defect. From these studies, it was revealed that the lowest and the highest doses of 15mg/kg and 1000

mg/kg body weight, respectively, have the worst effects by reducing the number of active cells to zero. The Sperm Activity was 0% and the Sperm Count is 3.5×10^6 cells per mL for 1000mg/kg.

The sperm count increases upwards from the control as the concentration of MSG increases to 100mg/kg body weight and then begins to drop drastically until the lowest count is recorded at 1000 mg/kg body weight. Meanwhile, lower doses of MSG (15, 50 & 100 mg/kg body weight) tend to boost sperm count, sperm morphology in terms of increased normal sperm cells, sperm viability, and motility, except the 15mg/kg dose group, which significantly decreases sperm activity and viability at $p<0.05$ probability levels compared to the control group.

From the results above, 50 mg and 100 mg/kg body weight of MSG have shown more favorable outcomes on semen characteristics, but 50 mg/kg body weight is the best dose that supports better sperm motility, sperm morphology, sperm viability records, and increased sperm count when compared to the control groups.

It is worth noting that histopathological assessments were also performed on the liver, kidney, testes, and prostate during the experiment. The findings were consistent with the biochemical data. At low MSG doses (15–50 mg/kg BW), tissue architecture of the prostate and testes appeared largely preserved, in line with reduced GGT activity and improved semen quality. By contrast, higher doses (500–1000 mg/kg BW) revealed structural alterations, including focal necrosis and degeneration of spermatogenic cells, as well as mild hepatocellular and renal changes, which supported the biochemical trends. Representative micrographs are not included here, as they are being reserved for a separate future publication focusing on organ pathology. Nonetheless, these histological outcomes provide additional supportive evidence for the interpretations presented.

The impaired or reduced sperm count, as the concentration of MSG is highest, could be due to spermatogenic cell damage caused by MSG induced toxicity of the Testes in the presence of varying doses of MSG. These study results are in line with [18] and [16], where they observed alterations of seminiferous tubules, necrosis, and atrophy of the testicular cells after treatment with MSG. Also, [19] found that MSG induced histological changes in the testes of neonatal mice, showing that both germinal and Leydig cells were affected, which is also in line with the studies of [20].

The lowest dose (15 mg/kg body weight) used in this study, which is the average daily intake of 1.0g by an assumed 65kg body weight man as reported by Marshal 1994, this lowest dose has a significant effect on the serum markers of prostate cancer. From the 15 mg/kg body weight to the 1000 mg/kg body weight used all have a dose-dependent effect on the markers of prostate pathology and semen quality. While the low doses like 15 mg/kg significantly decrease the serum markers of prostate cancer, 500 mg has no significant increase at $p<0.05$ probability levels when compared to the control. That is, the 500mg/kg body weight altered serum markers increasingly, but the increase was not significantly different at $p<0.05$ probability levels when compared to the control group.

In a related behavior, 15mg has a dose-dependent significant decrease in sperm activity but an increase in sperm count when compared to the control, while 50 and 100 mg/kg body weight boosted the sperm count, sperm activity, sperm viability, and sperm morphology of the cells. This unique dose-dependent effect of MSG in these findings, both on the serum markers of prostate cancer and sperm quality, is best explained by the toxicological phenomenon called hormesis. Hormesis or hormetic behavior is an adaptive response

characterized by biphasic dose responses, where low doses of a substance can stimulate or enhance positive biological responses, while high doses inhibit or harm them. This adaptive response can manifest in two ways: Direct Stimulation Hormesis (DSH) - a direct response to low doses, resulting in enhanced biological activity. Or, an Overcompensation Response Hormesis (OCSH) – a response to initial disruption, leading to stimulation [21].

This biphasic or hormetic behavior of MSG was also observed to have a dose-dependent, positive effect on prostate health and sperm quality. It has a sperm boosting potential at 50 mg/kg body weight and 100 mg/kg body weight when compared to the low sperm count recorded at high dose (1000mg/Kg body weight) of the MSG in relation to the control. And, a most significant prostate cancer treatment capacity at 15 mg/kg body weight and a cancer-promoting potential with continuous use at 500 mg/kg body weight.

In all, MSG is not a food item but a biphasic dose-response toxicant with the potential to suppress and induce changes in the serum prostate cancer markers at low and high doses while also boosting sperm count and viability at 50 mg/kg body weight and 100 mg/kg body weight. It has also shown the potential to be a prostate cancer inducer within 28days, hence making it a viable and promising tool for cancer research and studies.

Taken together, the combination of reduced GGT activity, preserved GSH metabolism, and maintained tissue integrity at lower MSG doses suggests a potential protective effect on prostate health and reproductive function. However, the translational significance of these findings requires caution. Rodent models metabolize glutamate differently than humans, and the complexity of human prostate cancer etiology cannot be fully replicated in animal studies. While these results highlight mechanistic insights and possible therapeutic implications, controlled human studies are necessary before MSG or related compounds can be considered in the context of prostate health or fertility treatments.

CONCLUSION:

This work goes to show that the fears of Egbuonu et al 2010a that MSG may have a significant effect on serum markers of prostate cancer pathology are true. Of all the doses administered, (15 mg/kg body weight) of MSG has the most significant reduction effect on serum markers of prostate disease. Thus, showing that MSG has dual properties of protecting against prostate cancer at 15 mg/kg body weight and may induce prostate cancer (CaP) at 500 mg/kg body weight for a longer than 28days of oral administration.

Similarly, low dose (15 mg/kg) and high dose (1000 mg/kg) of MSG reduce semen activity to near zero, with 1000mg impairing sperm count significantly. Whereas, 50 mg/kg body weight stands out as the potentially most productive dose that significantly boosted the semen quality and characteristics far above the control.

Furthermore, it is significant to note that, while low doses of MSG 15 mg/kg body weight and 50 mg/kg body weight have therapeutic potential against prostate cancer evidenced by the significant reduction in serum markers of the disease, and a semen quality boosting capability, it is also significant to state that it may have a significantly toxic effect to the liver, kidney, and testes with protracted use.

Consequently, it is recommended that MSG usage as a food additive should be discouraged. Further research should, however, be encouraged to validate its use in humans, as a potential chemotherapeutic agent for prostate cancer and sperm quality-dependent male reproductive health treatment and research. It is also expedient to ascertain the best dose for treating prostate cancer, boosting semen quality, and its usage as a fertility drug that are aimed at treating semen quality-dependent infertility challenges through collaborative research.

Funding Information:

This study was funded by the authors only.

Author Contributions:

DUA conceptualized and planned the study. EEE and SD were involved in animal handling and sample collection. AJN, HCN, OBE, and AIA oversaw the laboratory procedures and data analysis. FM and ACN assisted with interpreting the results and reviewing the literature. All authors participated in drafting and revising the manuscript, and they all reviewed and approved the final version.

Conflicts of Interest:

The authors declare no conflict of interest

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