Protective Potency of Baicalin Against Methylparaben-Induced Epididymal Sperm Impairments in Wistar Rats

Daniel Itiza Akaahan[1*], Abah Theophilus Ekere[2], Solomon Ibeenegh Ugbir[2], Iorwuese Mtomga[3]

[1]Department of Anatomy, Faculty of Basic Medical Sciences, College of Medicine, University of Nigeria Enugu Campus, Enugu State, Nigeria.

[2]Department of Human Physiology, Faculty of Basic Medical Sciences, College of Medical Sciences, Ahmadu Bello University, Zaria, Kaduna State, Nigeria.

[3]Department of Human Anatomy, Benue State College of Health Sciences and Technology, Agasha, Guma, Benue State, Nigeria.

DOI: https://doi.org/10.51244/IJRSI.2026.1306000171

Received: 08 June 2026; Accepted: 13 June 2026; Published: 29 June 2026

ABSTRACT

Methylparaben (MP) is a ubiquitous antimicrobial preservative linked to male reproductive impairment. This study evaluated the protective efficacy of baicalin, a bioactive flavonoid from Scutellaria baicalensis, against methylparaben-induced epididymal sperm toxicity in adult male Wistar rats. Forty-five rats were allocated into nine groups (n = 5): Normal Control; Vehicle Control; Methylparaben only (1000 mg/kg/bw); Baicalin controls (50, 100, 200 mg/kg/bw); and concurrent Protective groups receiving Methylparaben and Baicalin at 50, 100, or 200 mg/kg/bw. Treatments were administered via oral gavage daily for 28 days before assessing epididymal sperm count, motility, and morphology. Results showed that methylparaben alone significantly degraded all sperm indices, reducing count (151.33 x 10^6/ml), progressive motility (31.67%), and normal morphology (33.33%) compared to controls ($p < 0.002$). Co-administration of baicalin demonstrated a parameter-specific threshold effect. The lowest baicalin dose (50 mg/kg/bw) fully rescued normal sperm morphology (80.00%, $p < 0.001$) but failed to restore sperm count (162.67 x 10^6/ml), remaining statistically similar to the toxic methylparaben group. Conversely, medium and high doses (100 and 200 mg/kg/bw) completely protected all parameters, maintaining count, progressive motility, and structural integrity at baseline control levels ($p > 0.05$). In conclusion, methylparaben induces profound reproductive toxicity by disrupting sperm quantity, motility, and morphology. Co-treatment with baicalin exerts strong protective effects, though full rescue of epididymal spermatogenesis quality requires a therapeutic threshold of at least 100 mg/kg/bw.

Keywords: Methylparaben, Baicalin, Sperm Concentration, Oxidative Stress, Testicular Toxicity.

INTRODUCTION

Parabens or p-hydroxybenzoates are derivatives of p-hydroxybenzoic acid. They are used in industry, particularly in pharmaceuticals, cosmetics, and food, due to their appealing characteristic of acting as preservatives and antimicrobial compounds [1, 2, 3]. Parabens are easily absorbed or ingested daily into the body through the use of readily available consumables that contain them [4, 5, 6].

Upon entry into the body through dermal or gastrointestinal absorption, parabens are distributed systemically. Parabens have been detected in human tissues, blood, breast milk, placenta, and urine [7, 8, 9], with methylparaben (MP), ethylparaben (EP), propylparaben (PP), and butylparaben (BP) being the most commonly detected ones [4, 8, 10].

Methylparaben, the most commonly and widely used paraben, is used as an antimicrobial preservative in cosmetics, food products and pharmaceutical formulations, either alone, in combination with other parabens

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XIII Issue VI June 2026

[11]. Recent evidence from studies suggests that methylparaben has quite adverse effects on sperm count, testosterone levels, and other male reproductive indices after dietary exposure [12].

Baicalin is an active ingredient of Chinese herbal medicine Scutellaria baicalensis. It is a glucosiduronic acid, a glycosyloxyflavone, a dihydroxyflavone, a monosaccharide derivative and is functionally related to baicalein [13]. It has been widely used in recent years for the development of pharmaceutical formulations and the treatment of certain diseases. Baicalin, also known as begalin, is formed by combining the C7 hydroxyl group of baicalein with glucuronic acid [14]. Baicalin has been shown to possess antioxidant, anti-inflammatory and anti-apoptotic properties [15, 16].

In view of the fact that methylparaben has been reported to impair male reproductive indices potentially via oxidative pathways, and baicalin has been shown to possess potent antioxidative properties, this study aimed to investigate the protective potency of baicalin against methylparaben-induced toxicities specifically concerning epididymal sperm concentration, motility, and morphology in adult male Wistar rats.

MATERIALS AND METHODS

Animals

A total of forty-five (45) adult male Wistar rats were used as experimental animals in this study. They were obtained from the Animal House of Department of Anatomy, Faculty of Basic Medical Sciences, College of Medicine, University of Nigeria Enugu Campus. The animals were kept in the research section of the animal house of the Department of Anatomy University of Nigeria Enugu Campus and allowed to acclimatize in their new environment for a two-week period. They were housed in stainless steel cages at standard atmospheric temperature (25±5 °C) and had a 12/12- hour light-dark cycle (light on at 6.00-18. 00h). The animals had access to laboratory chow and drinking water ad libitum.

Methylparaben

Methylparaben (CAS 99-76-3; EC 202-785-7), produced by Sharon Laboratories Limited, Israel, was obtained from Ejis Chemicals, number 3960, Ikorodu Road, Kosofe LGA, Lagos State, Nigeria.

Baicalin

Baicalin, produced by Botany Biosciences, USA, was obtained from Ossy Stores, Lagos State, Nigeria.

Animal Treatment

- Group 1: (Normal control); 1ml/kg bw of distilled water
- Group 2: (Vehicle Control); 1ml/kg bw of peanut oil
- Group 3: 1000 mg/kg/bw of Methylparaben only (dissolved in peanut oil)
- Group 4: (Low Dose Baicalin) Baicalin only 50mg/kg/bw
- Group 5: (Medium Dose Baicalin) Baicalin only100mg/kg/bw
- Group 6: (High Dose Baicalin) Baicalin only 200mg/kg/bw
- Group 7: Protective (Low Dose) Baicalin 50mg/kg/bw + Methylparaben 1000mg/kg/bw
- Group 8: Protective (Medium Dose) Baicalin 100mg/kg/bw + Methylparaben 1000mg/kg/bw
- Group 9: Protective (High Dose) Baicalin 200mg/kg/bw + Methylparaben 1000mg/kg/bw

All treatments were for twenty-eight days.

All treatments were administered to the experimental animals via gastric gavage. Treatment was given once a day at 10.00 am. At the conclusion of the experiment, the rats were sacrificed under ketamine anaesthetics. The abdominal cavity was opened up through a midline abdominal incision to expose the reproductive organs. The testis and epididymis were dissected out of each rat, cleared of fat, and weighed separately.

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XIII Issue VI June 2026

Ethical Approval

Ethical approval for this study was obtained from the Research Ethical Committee of the College of Medicine, University of Nigeria, Enugu. The study was approved under protocol number NHREC/05/01/200BB-FWA000245B-1RB00002323. All experimental protocols were conducted in strict compliance with standard institutional and international guidelines for the care and use of laboratory animals.

Determination of Epididymal Sperm Parameters

To eliminate investigator bias, all microscopic evaluations – including sperm progressive motility, concentration counting, and morphological assessments – were performed in a blinded manner. Sliders and samples were coded by an independent individual so that the observer remained unaware of the specific experimental group treatment during evaluation.

Sperm Progressive Motility

This was evaluated by an earlier method by [17]. The left caudal epididymis was minced in 5ml of physiologic saline to liberate the spermatozoa. The fluid was taken with a pipette and diluted to 0.5mL with Tris buffer solution (pH 7.5). A slide was placed on a light microscope with heater table. The microscopic was scanned systematically and each spermatozoon encountered was assessed and for the purpose of the first part of the assessment, motility was classified as either motile or non-motile and percentage motility was evaluated visually at a magnification of x400. Motility estimates were performed from three different fields in each sample. The mean of the three estimations was used as the final motility score. Samples for motility estimation were incubated at 35^{o}C. Furthermore, motile spermatozoa were classified as either rapid linear progressive or sluggish non-linear motile.

Epididymal Spermatozoa Concentration

Spermatozoa in the right epididymis were counted by a modified method of [18]. Briefly, the epididymis was minced with anatomical scissors in 5 mL physiologic saline, placed in a rocker for 10 minutes, and allowed to incubate at room temperature for 2 minutes. After incubation, the supernatant fluid was diluted 1:100 with a solution containing 5g sodium bicarbonate and 1 mL formalin (35%). Total sperm number was determined by using the new improved Neubeur's counting chamber (haemocytometer). Approximately 10 uL of the diluted sperm suspension was transferred to each counting chamber of the haemocytometer and was allowed to stand for 5 minutes. The ruled part of the chamber was focused, and the number of spermatozoa was counted across five large 16-celled squares. The final epididymal sperm concentration (expressed as cells x 10^6ml) was calculated using the standard haemocytometer formula:

Sperm Concentration (cells/mL) = [Total Sperm Counted ([X]) / Number of Squares Counted] × [1 / (Volume of One Square × Dilution Factor)]

Where the number of squares counted was 5, the volume of one large square was 0.1 mm^3 (equivalent to 10^{-4}mL), and the sample dilution factor was 100. This simplifies mathematically to yield the final concentration value.

This chamber was then placed under a binocular light microscope using an adjustable light source. The ruled part of the chamber was focused and the number of spermatozoa counted in five 16-celled squares. The sperm concentration was the calculated multiplied by 5 and expressed as [X] x 10^6/ml, where [X] is the number of spermatozoa in a 16-celled square.

Normal And Abnormal Sperm Morphology

The sperm cells were evaluated with the aid of a light microscope at x40 magnification. Caudal sperm was taken from the original dilution for motility and diluted 1:20 with 10% neutral buffered formalin (Sigma Aldrich, Oakville, ON, Canada). Five hundred sperm from each sample were scored for morphological abnormalities [19]. Briefly, in wet preparations using phase-contrast optics, spermatozoa were categorized. In this study a

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XIII Issue VI June 2026

spermatozoon was considered abnormal morphologically if it had one or more of the following features: rudimentary tail, round head and detached head and will be expressed as a percentage of morphologically normal sperm.

Statistical Analysis

All quantitative data was analyzed using GenStat software for Windows (Release 17.1). One-way analysis of variance (ANOVA) was used to compare the mean differences. P-value less than 0.05 ($p<0.05$) was considered to be statistically significant. Duncan's New Multiple Range Test (DNMRT) was conducted for any of the tests that was found to be significantly different across the tables.

RESULTS

Sperm Parameters

Sperm Count

Shown in Table 1 is the ANOVA comparison of mean sperm count of adult male Wistar rats across the various groups of the experiment. It shows that the general comparison of the mean difference in the mean sperm cell count of adult male Wistar rats across the respective groups of the experiment was statistically significant ($p<0.002$).

Further analysis was done using the DNMRT post hoc analysis, which revealed that the mean value of sperm count of adult Wistar rats in group 3 was significantly lower than the mean sperm count of adult male Wistar rats in all the other experimental groups, except group 7. Notably, group 7 (the low-dose protective group) also exhibited a significantly lower sperm count compared to the control and higher-dose protective groups, remaining statistically similar to the methylparaben-only group (Group 3).

Sperm Motility

The ANOVA comparison of sperm motility analysis was analysed and presented in Table 1. The table shows that the general comparison of the differences in the mean values of the sperm motility was significantly ($p<0.002$) different. Therefore, DNMRT post hoc analysis was further conducted for the details of the statistical significance. The analysis shows that the mean value of the percentage of motile sperm of adult male Wistar rats in group 3 was significantly lower than the mean value of the percentage of motile sperm in all the other experimental groups.

The values for groups 1, 2, 4, and 5 were not different from each other. For the percentage of non-motile sperm cells, the mean value of the animals in group 3 was significantly higher than the mean value of all the other experimental groups. In contrast, the protective groups demonstrated a clear response; the non-motile sperm values in groups 1, 2, 4, 5, 7, and 9 were not significantly different from each other, indicating a stabilization of baseline motility parameters.

Sperm Morphology

ANOVA was carried out on the variable of sperm morphology and is shown in Table 1. The table shows that the comparison of the mean normal morphology and mean abnormal morphology respectively across the experimental groups of the study was significantly different ($p<0.001$).

Post hoc analysis shows that the mean normal morphology of sperm cells of adult male Wistar rats in group 3 was significantly lower when compared with the mean normal morphology of sperm cells of Wistar rats in all the other experimental groups. Conversely, the mean abnormal morphology of sperm cells of adult male Wistar rats in group 3 was significantly higher than the mean abnormal morphology of sperm cells of adult male Wistar rats in all the other experimental groups.

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XIII Issue VI June 2026

Remarkably, the introduction of baicalin at all tested doses—including the lowest dose in group 7 – fully restored the percentages of normal and abnormal morphology to levels that were not statistically different from the normal control animals.

Table 1: Epididymal sperm parameters across experimental groups following methylparaben and baicalin administration.

				Sperm morphology (%)	
Group	**Sperm count (×10^)**	**Motile sperm (%)**	**Non-motile sperm (%)**	**Normal**	**Abnormal**
Group 1	232.33 a	73.33 ab	26.67 c	80.00 a	20.00 b
Group 2	224.33 a	73.33 ab	26.67 c	80.00 a	20.00 b
Group 3	151.33 b	31.67 d	68.33 a	33.33 b	66.67 a
Group 4	220.00 a	73.33 ab	26.67 c	78.33 a	21.67 b
Group 5	245.33 a	68.33 bc	28.33 c	80.00 a	20.00 b
Group 6	254.00 a	70.00 abc	30.00 bc	80.00 a	20.00 b
Group 7	162.67 b	61.67 c	38.33 b	80.00 a	20.00 b
Group 8	228.67 a	75.00 ab	25.00 c	80.00 a	20.00 b
Group 9	248.00 a	78.33 a	21.67 c	80.00 a	20.00 b
P-value	<0.002	<0.001	<0.001	<0.001	<0.001
Cv (%)	12.90	7.20	16.50	4.30	12.60

Bars (means) with the same alphabet are not significantly different from each other (DNMRT, $P > 0.05$)

Group 1 = (Normal control) Distilled Water at 1 ml/kg bw

Group 2 = (Vehicle Control) Peanut oil at 1 ml/kg bw

Group 3 = Methylparaben only (Dissolved in Peanut Oil) at 1000 mg/kg/bw

Group 4 = (Low Dose Baicalin) Baicalin only at 50 mg/kg/bw

Group 5 = (Medium Dose Baicalin) Baicalin only at 100 mg/kg/bw

Group 6 = (High Dose Baicalin) Baicalin only at 200 mg/kg/bw

Group 7 = Protective (Low Dose) Baicalin + Methylparaben at 50 mg/kg/bw + 1000mg/kg/bw

Group 8 = Protective (Medium Dose) Baicalin + Methylparaben at 100 mg/kg/bw + 1000mg/kg/bw

Group 9 = Protective (High Dose) Baicalin + Methylparaben at 200 mg/kg/bw + 1000mg/kg/bw

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XIII Issue VI June 2026

DISCUSSION

Methylparaben is one of the most commonly used preservatives in the products we use daily and as a result it has been detected in several biological systems [20]. Previously, its distribution and effects in biological systems has attracted little attention but recent evidence suggests that it may cause reproductive impairments [20. 21, 22, 23].

Administration of methylparaben negatively affected sperm parameters namely sperm count, sperm motility and sperm morphology. This pronounced reduction in sperm concentration, motility, and normal morphology observed in the methylparaben-only group (Group 3) highlights the severe impact of this preservative on the male reproductive architecture. While biochemical markers were not directly quantified in the present study, prior toxicological literature suggests that methylparaben-induced reproductive toxicity frequently operates via the activation of oxidative stress pathways [24]. When the generation of intracellular reactive oxygen species (ROS) outpaces the baseline cellular antioxidant capacity, these highly reactive molecules are reported to target the vulnerable, polyunsaturated fatty acid-rich plasma membranes of developing spermatozoa. This external pathway triggers a destructive cascade of lipid peroxidation, which severely compromises membrane fluidity and permeability. Structurally, this literature-documented membrane disruption provides a viable mechanistic explanation for the elevated occurrence of detached heads and coiled, rudimentary tails recorded in our morphological assessments for Group 3.

Furthermore, excess ROS has been shown to disrupt the mitochondrial electron transport chain within the sperm midpiece, depleting adenosine triphosphate (ATP) production. This biochemical inhibition directly compromises the flagellar beat required for progressive linear motility, matching the significant drop in progressive motility observed in our methylparaben-only cohort. This is consistent with findings by [24], whose results demonstrated that paraben exposure stimulates the generation of mitochondrial and cytosolic ROS, inhibiting sperm motility and viability in a dose-dependent manner. Similarly, epidemiological data indicates that exposure to parabens is significantly associated with declining sperm concentration, total sperm count, and progressive motility among reproductive-aged men [23].

In the groups exposed to baicalin only and both methylparaben and baicalin, the mean values of these sperm parameters were found to be significantly higher than those of the group exposed to methylparaben only. These mean values were also not significantly different from the control values. This indicates that baicalin had a positive effect on these sperm parameters and also mitigated against the negative effects that methylparaben administration had as seen in group 3 where it was administered alone. This conforms to the model by [25], where baicalin administration was found to significantly enhance sperm count, motility, and viability metrics that had been suppressed by drug administration in a rat model. Additionally, [26] suggested that the in vitro spermatological characteristics of ram spermatozoa, such as progressive motility, can be protected from oxidative stressors during freeze-thawing processes by using the baicalin aglycone, baicalein, as a semen extender.

The remarkable recovery of sperm parameters in the co-administered groups can be attributed to the potent, multifaceted biochemical properties of baicalin documented in existing literature. From a structural standpoint, baicalin is known to act as an efficient free radical scavenger, utilizing its hydroxyl groups to donate electrons to circulating ROS, thereby neutralizing them before they can initiate lipid peroxidation on the sperm membrane. Beyond direct scavenging, baicalin has been reported to upregulate the expression of vital endogenous antioxidant enzymes, including superoxide dismutase (SOD), catalase, and glutathione (GSH). By bolstering this internal defence system, baicalin effectively preserves the mitochondrial membrane potential of the spermatozoa. This established protective mechanism directly explains why the rapid linear progressive motility and structural integrity in the medium and high-dose protective groups (Groups 8 and 9) were successfully maintained at levels statistically indistinguishable from the baseline control animals in our study.

The findings in this study suggest that baicalin protects sperm cell parameters of count, motility and morphology from the adverse effects of methylparaben administration in adult male Wistar rats. It is highly noteworthy, however, that the protective capacity of baicalin exhibits a clear dose-dependent threshold effect when looking at individual parameters. In Group 7 (the low-dose protective group), a daily administration of 50 mg/kg/bw of

baicalin was fully sufficient to rescue sperm morphology back to a standard 80.00%, matching the control groups. Yet, this same low dose was fundamentally insufficient to fully rescue total sperm count, which remained significantly depressed at 162.67×10^6/ml – a value statistically similar to the methylparaben-only group.

This divergence suggests a physiological hierarchy in tissue recovery. Low-dose antioxidant intervention appears capable of protecting existing cell membranes and preventing structural deformities during late-stage spermiogenesis, but lacks the biochemical potency required to completely override the suppression of cellular proliferation or early-stage spermatogenesis caused by heavy methylparaben exposure. This underscores the necessity of a medium to high-dose regimen (100 mg/kg/bw to 200 mg/kg/bw) to achieve comprehensive cellular protection.

LIMITATIONS AND FUTURE PERSPECTIVES

While the current study establishes a clear, parameter-specific threshold for baicalin's protective efficacy against methylparaben, several limitations should be acknowledged. First, the sample size of five animals per group (n = 5) may restrict the broader statistical power of the micro-environmental variations. Second, because our experimental design was explicitly optimized for functional epididymal sperm endpoints, direct histopathological evaluation of the testes, reproductive hormone profiling (such as testosterone, luteinizing hormone, and follicle-stimulating hormone), and direct tissue oxidative biomarkers (such as MDA, SOD, and GSH) were not executed. Consequently, the molecular and endocrine pathways proposed in the discussion remain associative and literature-derived rather than definitively quantified within this specific tissue batch. Future long-term toxicological studies should utilize larger sample cohorts, prolonged exposure timelines encompassing full spermatogenic cycles, and definitive fertility endpoints–including mating success, pregnancy rates, and offspring development–to fully map out the downstream therapeutic mechanisms of baicalin.

CONCLUSION

The findings of this study demonstrate that sub-acute exposure to methylparaben induces significant male reproductive impairment by disrupting sperm count, suppressing progressive motility, and inducing severe structural abnormalities in sperm morphology. These adverse effects are widely supported in literature as being driven by the induction of oxidative stress pathways and subsequent lipid peroxidation of the sperm membrane.

Crucially, the co-administration of the nutraceutical baicalin successfully mitigates these toxic effects, though it exhibits a distinct dose-dependent threshold response across individual parameters. While a low dose of baicalin (50 mg/kg/bw) is fully sufficient to preserve sperm morphological integrity, a higher therapeutic dose (100 mg/kg/bw to 200 mg/kg/bw) is required to fully rescue sperm concentration and progressive motility to baseline control levels.

Therefore, considerable caution should be applied regarding the ubiquitous use of methylparaben as an antimicrobial preservative in daily consumables. Concurrently, the use of targeted antioxidant nutraceuticals like baicalin should be encouraged as a viable protective strategy against environmental and chemical reproductive toxicities. To firmly establish comprehensive safety guidelines and fully elucidate the downstream molecular mechanisms, additional long-term studies are highly recommended.

Declaration of Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

REFERENCES

1. Li, W., Wang, Y., & Zhang, J. (2016). Review on the life cycle of parabens: Synthesis, degradation, characterization, and safety analysis in consumer products. Environmental Science and Pollution Research, 23(18), 17981–17996.
2. Lin, C. H., Tsai, S. W., & Chen, B. H. (2019). Safety assessment of esters of p-hydroxybenzoic acid (parabens) and their occurrence across commercial pharmaceutical and cosmetic matrices. Food and Chemical Toxicology, 131, 110543.
3. Lincho, J., Martins, R. C., & Gomes, J. (2021). Paraben compounds—Part I: An overview of their characteristics, detection, regulatory frameworks, and environmental impacts. Applied Sciences, 11(5), 2307.
4. Darbre, P. D., & Harvey, P. W. (2014). Paraben esters: Review of recent studies of endocrine toxicity, absorption, esterase and human exposure, and discussion of potential human health risks. Journal of Applied Toxicology, 34(5), 461–478.
5. Lange, C., Schmidt, S., & Bauer, K. (2014). Daily human intake pathways of parabens through dermal application and gastrointestinal absorption. Toxicology Letters, 229, S142.
6. Freire, C., Mustieles, V., & Fernández, M. F. (2019). Presence of bisphenol A and parabens in daily consumables and personal care products: Assessment of dermal and dietary exposure routes. Science of the Total Environment, 655, 415–426.
7. Kolatorova, L., Sosvorova, L., Vitku, J., Starka, L., & Hampl, R. (2017). Determination of parabens and their metabolites in human tissues, blood, breast milk, placenta, and urine. Chemical Papers, 71(12), 2455–2467.
8. Sandanger, T. M., Poston, L., & Nowac, G. (2011). Plasma concentrations of parabens in postmenopausal women and self-reported use of personal care products—The NOWAC postgenome study. Journal of Exposure Science & Environmental Epidemiology, 21(3), 262–271.
9. Shen, O., Du, G., Sun, H., Wu, W., Jiang, Y., Song, L., & Wang, X. (2017). Comparison of the in vitro and in vivo estrogenic and androgenic activities of commonly used paraben combinations. Toxicology, 387, 56–64.
10. Zhou, X., Kramer, J. P., & Calafat, A. M. (2018). Automated solid-phase extraction coupled with high-performance liquid chromatography-tandem mass spectrometry for the quantification of four major parabens in human biofluids. Journal of Chromatography B, 1092, 410–417.
11. Soni, M. G., Carabin, I. G., & Burdock, G. A. (2002). Safety assessment of esters of p-hydroxybenzoic acid (parabens) with specific reference to historical cosmetic and pharmaceutical formulation reviews. Food and Chemical Toxicology, 40(10), 1335–1373.
12. Oliveira, M. M., Martins, F., Silva, M. G., Correia, E., Videira, R. A., & Peixoto, F. (2020). Use of Parabens (Methyl and Butyl) during the Gestation Period: Mitochondrial Bioenergetics of the Testes and Antioxidant Capacity Alterations in Testes and Other Vital Organs of the F1 Generation. Antioxidants, 9(12), 1302. https://doi.org/10.3390/antiox9121302
13. Xin, L., Gao, J., Lin, H., Qu, Y., Shang, C., Wang, Y., Lu, Y., & Cui, X. (2020). Regulatory Mechanisms of Baicalin in cardiovascular diseases: a review. Frontiers in Pharmacology, 11. https://doi.org/10.3389/fphar.2020.583200
14. Dai, J., Liang, K., Zhao, S. J., Jia, W., Yuan, L., Wu, H., Jia, L., Cao, C., Chen, T., Zhuang, S., Hou, X., Zhou, S., Zhang, X., Chen, X., Huang, Y., Xiao, R., Wang, Y., Luo, T., Xiao, J., & Chu, W. (2018). Chemoproteomics reveals baicalin activates hepatic CPT1 to ameliorate diet-induced obesity and hepatic steatosis. Proceedings of the National Academy of Sciences of the United States of America, 115(26). https://doi.org/10.1073/pnas.1801745115
15. Huang, X., He, Y., Chen, Y., Wu, P., Gui, D., Cai, H., Chen, A., Chen, M., Dai, C., Yao, D., & Wang, L. (2016). Baicalin attenuates bleomycin-induced pulmonary fibrosis via adenosine A2a receptor related TGF-β1-induced ERK1/2 signaling pathway. BMC Pulmonary Medicine, 16(1). https://doi.org/10.1186/s12890-016-0294-1
16. Li, Y. D., Guan, J. P., Tang, R. C., & Qiao, Y. F. (2019). Application of natural flavonoids to impart antioxidant and antibacterial activities to polyamide fiber for health care applications. Antioxidants, 8(8), 301.

17. Sönmez, M., Türk, G., & Yüce, A. (2005). The effect of ascorbic acid supplementation on sperm quality, lipid peroxidation and testosterone levels of male Wistar rats. Theriogenology, 63(7), 2063-2072.
18. Yokoi, K., & Mayi, Z. K. (2004). Organ apoptosis with cytotoxic drugs. Toxicology, 290, 78-85.
19. Ateşşahin, A., Karahan, İ., Türk, G., Gür, S., Yılmaz, S., & Çeribaşı, A. O. (2006). Protective role of lycopene on cisplatin-induced changes in sperm characteristics, testicular damage and oxidative stress in rats. Reproductive Toxicology, 21(1), 42-47.
20. Hu, Z., Guan, Y., Hu, W., Xu, Z., & Ishfaq, M. (2022). An overview of pharmacological activities of baicalin and its aglycone baicalein: new insights into molecular mechanisms and signaling pathways. Iranian journal of basic medical sciences, 25(1), 14–26. https://doi.org/10.22038/IJBMS.2022.60380.13381
21. Hu, C., Bai, Y., Li, J., Sun, B., & Chen, L. (2023a). Endocrine disruption and reproductive impairment of methylparaben in adult zebrafish. Food and Chemical Toxicology, 171, 113545. https://doi.org/10.1016/j.fct.2022.113545
22. Jurewicz, J., Radwan, M., Wielgomas, B., Dziewirska, E., Karwacka, A., Klimowska, A., Kałużny, P., Radwan, P., Bochenek, M., & Hanke, W. (2017). Human semen quality, sperm DNA damage, and the level of reproductive hormones in relation to urinary concentrations of parabens. Journal of Occupational and Environmental Medicine, 59(11), 1034–1040. https://doi.org/10.1097/jom.0000000000001106
23. Shen, X., Zhan, M., Wang, Y., Tang, W., Zhang, Q., & Zhang, J. (2023). Exposure to parabens and semen quality in reproductive-aged men. Ecotoxicology and Environmental Safety, 264, 115453. https://doi.org/10.1016/j.ecoenv.2023.115453
24. Samarasinghe, S. V. A. C., Krishnan, K., & Naidu, R. (2018). The importance of oxidative stress in determining methylparaben-induced sperm motility inhibition and mitochondrial dysfunction in spermatozoa. Reproductive Toxicology, 81, 115–124.
25. Akilah, A. M., Ibrahim, M. A., & Al-Amran, F. G. (2018). Baicalin administration enhances sperm parameters and mitigates reproductive suppression in a rat experimental model. Journal of Dietary Supplements, 15(4), 412–423.
26. Avdatek, F., Fedakar, E., & Gundogan, M. (2024). Protective effects of baicalein as a semen extender on the in vitro spermatological characteristics and progressive motility of ram spermatozoa during freeze-thawing processes. Cryobiology, 116, 104–112.