

微纳米塑料对雄性生殖的毒性作用及机制研究进展

谭 昱, 杨 青*

湖南农业大学动物医学院, 湖南 长沙

收稿日期: 2024年11月10日; 录用日期: 2024年12月29日; 发布日期: 2025年1月3日

摘 要

微纳米塑料是一种新型的环境污染物, 不仅造成环境污染, 对动物和人类健康也造成极大威胁。研究发现微纳米塑料在人和动物的生殖系统中积累, 并产生毒性作用。本文主要介绍了微纳米塑料对雄性生殖毒性及其潜在的作用机制, 为防控微纳米塑料引起的雄性生殖毒性提供理论基础, 维护生殖健康。

关键词

微纳米塑料, 雄性, 生殖毒性, 作用机制

Research Progress in Reproductive Toxicity of Micro- and Nanoplastics on Males and Its Mechanisms

Yu Tan, Qing Yang*

College of Veterinary Medicine, Hunan Agricultural University, Changsha Hunan

Received: Nov. 10th, 2024; accepted: Dec. 29th, 2024; published: Jan. 3rd, 2025

Abstract

Micro- and Nanoplastics are a new type of environmental pollutant that not only cause environmental pollution, but also pose a great threat to animal and human health. Research has found that micro- and nanoplastics accumulate in the reproductive system of human and animals, and exhibit reproductive toxicity. This article mainly introduces the reproductive toxicity of micro- and

*通讯作者。

nanoplastics on males and their potential mechanisms, providing a theoretical basis for preventing and controlling the reproductive toxicity caused by micro- and nanoplastics in males and maintaining reproductive health.

Keywords

Micro- and Nanoplastics (MNPs), Male, Reproductive Toxicity, Mechanism

Copyright © 2025 by author(s) and Hans Publishers Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

1. 微纳米塑料概述

微纳米塑料(micro- and nanoplastics, MNPs)是指尺寸小于 5 mm 的微塑料(MPs)和 1 μm 的纳米塑料(NPs),由塑料制品经光照、加热、生物降解、机械切割等作用形成的一种新型环境污染物,具有分布广、数量多、难降解、体积小、比表面积大以及吸附污染能力强等特点[1][2]。常见的微纳米塑料主要有聚氯乙烯(PVC)、聚苯乙烯(PS)、聚乙烯(PE)、聚丙烯(PP)、聚氨酯与聚酰胺(PA)等类型。微塑料可进一步降解为粒径更小、毒性作用更大的纳米塑料[3][4]。

2. 微纳米塑料的生物学毒性

微纳米塑料可通过食物摄取、饮水、呼吸和皮肤接触等途径沉积在人和动物体内,因其体积小,容易被各种生物体摄入,摄入后其物理成分及有毒化学物质对生物体产生有害影响[5]。微塑料可先积聚在生物体内,随后通过内部磨损对生物体的组织和器官造成物理性损伤[6]。与物理损伤相比,微纳米塑料的化学毒性损伤更为严重,与多种癌症的发生有关,并干扰内分泌系统的正常功能[7]。除释放内源性有毒化学物质外,微纳米塑料比表面积大且具有疏水性,可以快速吸附细菌、病毒、藻类以及非生物物质,吸附的这些污染物可进一步导致机体复杂的毒理学效应,从而引起间接毒性[8]。

在整个生态系统食物链中,微纳米塑料从最低的携带者到最高的捕食者之间传播[9],它们被生物富集和扩增,生物毒性随之放大,对生物多样性造成严重威胁,导致生殖和胚胎发育毒性[10]、神经毒性[11]和内分泌毒性[12]以及免疫毒性[13]等。研究发现在胎盘、卵泡液、子宫内膜、精液及睾丸等多种生殖器官和组织中均可检测到微纳米塑料,引起多种动物的生殖毒性[14]-[16]。

3. 微纳米塑料对雄性动物的生殖毒性作用

研究表明微纳米塑料暴露损伤睾丸组织结构和功能、减少生殖内分泌激素的分泌、影响精子质量,导致雄性生殖毒性[4][17]。MNPs 在生殖器官中的蓄积与其粒径大小密切相关。当小鼠暴露在不同粒径大小的微纳米塑料时,诱发生精障碍,表现为生精小管萎缩、各级生精细胞数减少、排列疏松、脱落,附睾中精子数显著减少且畸形率升高;睾丸炎症和血睾屏障(BTB)损伤,细胞层发生紊乱;睾酮水平降低等[18]-[20]。口服聚苯乙烯纳米塑料(PS-NPs)时引起小鼠睾丸和精子毒性,降低睾丸指数,损伤生精小管外壁,导致生育能力降低甚至不育[21]。一定浓度的 PS-NPs 可穿透 BTB,导致生精小管中的生精细胞功能异常[22]。在斑马鱼中,微纳米塑料可在母体内积累并转移给其子代,改变 F1 代斑马鱼的抗氧化系统[23]。微纳米塑料严重影响子代小鼠生殖系统的发育,Huang 等研究发现妊娠期和哺乳期母体暴露 PS-NPs 导致子代小鼠出生重下降,降低子代小鼠睾丸重量、破坏生精上皮并减少精子数量[24]。睾丸是 MNPs 潜在作

用的靶器官, 暴露后引起其生精功能障碍程度与 MNPs 粒径大小、暴露时间和浓度等密切相关[4] [14]。

MNPs 通过内吞作用进入睾丸细胞并影响其微观结构, 可减少睾丸支持细胞数量、间质细胞面积以及成熟精母细胞数[20] [25]。睾丸间质细胞分泌的睾酮对精子发生至关重要。MNPs 暴露可干扰下丘脑 - 垂体 - 性腺轴(HPG)的正常功能, 导致多种内分泌激素分泌紊乱, 如减少血清中睾酮、卵泡刺激素(FSH)以及促黄体素(LH)水平, 增加雌激素水平[10] [26]。体外研究发现, 微纳米聚苯乙烯处理显著抑制间质细胞的活力, 并呈剂量依赖, 通过下调类固醇生成酶, 如 3β -羟基类固醇脱氢酶(3β -HSD)、 17β -羟基类固醇脱氢酶(17β -HSD)和类固醇生成急性调节蛋白(StAR)等的表达, 降低睾丸间质细胞分泌睾酮的能力[26] [27]。MNPs 的暴露也可能通过激活支持细胞中抑制素的表达而间接影响 FSH 的分泌[28]。在一项人体细胞实验中发现, 聚酰胺相关化学物质可适度激活芳烃受体(AhR)并引发抗雄激素活性[29]。Qu 等研究也证实了 PS-MPs 具有抗雄激素特性, 暴露后在睾丸中蓄积并被内化至细胞质中, 不仅破坏睾丸的组织形态和超微结构, 还降低间质细胞的活力和血清中促性腺激素释放激素、LH、FSH 和睾酮的水平[30]。此外, MNPs 可通过吸附作用降低睾酮的生物利用度, 进而导致精子质量下降。Zhang 等用 0.5 mg/d 剂量的聚酰胺微塑料(PA-MPs)暴露小鼠 28 天后, 发现 PA-MPs 对睾酮表现出单层均匀吸附过程, 导致血清睾酮浓度显著降低, 但使睾丸内睾酮浓度显著增加[14]。

精子浓度、活力和形态等是评估精子质量的主要参数, 决定卵母细胞成功受精的关键。已经证实多种 MNPs 在哺乳动物组织中的生物累积显著影响啮齿动物的精子数量和存活率。人类可通过消化道、呼吸道以及皮肤等多种途径摄入 MNPs, 并在体内蓄积。研究表明附睾和精囊中的积聚是 MNPs 进入精液的潜在入口。Montano 等人在部分男性精液样本中检测到多种球形或不规则形状的有色微塑料, 进一步检测发现为聚乙烯(PE)、PS、聚氯乙烯(PVC)等[31]。Zhao 等人也在人睾丸和精液中均检测到 PS、PE 和 PVC 等多种 MPs。因此, MNPs 对雄性生殖的威胁需引起高度关注[32]。

4. MPs 对雄性动物生殖毒性作用的机理

研究表明 MNPs 通过诱导氧化应激和炎症, 干扰内分泌, 改变代谢等引起生殖损伤。由于 MNPs 表面积大, 可吸附释放至其表面的氧化物(如金属)或炎症反应过程中释放的活性氧(ROS), 造成炎症、免疫损伤甚至 DNA 结构改变, 导致细胞坏死[33] [34]。ROS 与多种信号通路有关, PS-MPs 以剂量依赖的方式诱导氧化应激, 在 PS-MPs 暴露的小鼠中, 通过中和 ROS 可以抑制睾丸间质细胞的衰老[35]-[37]。当雄性大鼠通过饮食暴露 PS-MPs 三个月时, 睾丸组织中过氧化氢酶活性增加, 超氧化物歧化酶活性降低, 导致大比例的空泡化生精小管出现, 生殖功能发生严重障碍[38]。PS-MPs 诱导猪生精细胞产生大量的 ROS, 促进丝裂原活化蛋白激酶(MAPK)通路相关基因的磷酸化, 并激活缺氧诱导因子[39]。PS-MPs 通过 ROS 介导 mTORC1 的活性升高, 而 mTORC2 的活性下降, 使两者失衡, 改变肌动蛋白结合蛋白的表达谱, 导致 F-actin 的解体, 减少 BTB 中连接蛋白的表达减少, 最终破坏 BTB 的完整性, 使精子发生功能障碍[40]。PS-MPs 诱导产生的过量 ROS 引起氧化应激, 激活 MAPK 信号通路, 破坏 BTB 的完整性, 诱导小鼠的生殖毒性, 使精子数量和活力下降, 精子畸形率升高[40] [41]。此外, 微纳米塑料诱导产生的 ROS 使精子 DNA 片段化, 导致睾丸激素水平下降, BTB 完整性遭到破坏[42]。

PS-MPs 可引起大鼠睾丸组织中多种炎症因子升高, 包括 IL-6、NF- κ B、IL-1 β 、TNF- α 和环氧合酶 2 (COX-2)的活性, 使用抗炎物质干预时可缓解相关炎症所导致的损伤[27] [43]。PS-MPs 诱导小鼠睾丸炎症后, 增加睾丸中的炎症因子, 使精子发生障碍和 BTB 结构受损[18]。当公鸡饮用含有 PS-MPs 的水后, 睾丸内出现炎症浸润和间质出血, BTB 的完整性受到破坏, 相关紧密连接蛋白 Claudin3 和 Occludin 的表达减少[44]。此外, PS MP 暴露可诱导睾丸组织中 JNK 和 p38 MAPK 的磷酸化, 引起炎症反应和 BTB 结构损伤[45]。许多研究表明氧化应激和 MP 引起的炎症反应之间具有相互作用, 机体暴露于 MPs 时会消

耗抗氧化能力, 导致炎症。

生殖系统的发育和调节依赖于 HPG, 在雄性动物中, HPG 轴负责睾酮的分泌和精子发生的调节。MPs 含有多钟内分泌干扰化学物质(EDCs)和其他有害化合物, 许多 EDCs 的结构与特定的激素受体具有相似性[17]。研究表明 MPs 在雄性小鼠中的暴露降低血清中 FSH、LH 和睾酮的浓度, 并下调睾酮生成相关基因的表达, 升高雌二醇水平, 破坏 HPG 轴[10] [46] [47]。在精子发生过程中, 睾丸支持细胞产生大量的丙酮酸并传递给各级生精细胞, 为初级精母细胞和精子细胞的减数分裂提供所需的能量[48]。在 MNPs 暴露的精母细胞中, 细胞中一些特异基因表达的变化可能在不同水平上改变精母细胞的丙酮酸代谢, 其中 PS-MPs 暴露后丙酮酸代谢和甲状腺激素代谢的改变主要导致精子发生障碍, 而视黄酸代谢途径的改变与 PS-NPs 暴露减少精母细胞密切相关[49]。在水生动物中, PS-MPs 通过减少能量产生和细胞活力来影响精子游泳性能, 从而降低配子碰撞的可能性, 影响牡蛎的受精率[50]。

5. 展望

MNPs 作为一种新型的环境污染物, 威胁着人类和动物的健康, 通过氧化应激、炎症反应、干扰内分泌、改变代谢等途径损害雄性动物的生殖系统。不同类型、大小以及剂量的 MNPs 所发挥不同的作用机制, 但这些研究结合实际还存在一定的局限性。首先, 许多研究中使用的 MNPs 的浓度远高于环境中暴露的浓度, 且商品化的 MNPs 不能反映其在实际环境中所诱导的生物效应。其次, MNPs 种类繁多, 不同来源、化学成分、形状和粒径等对雄性生殖毒性作用机理需进一步开展研究。此外, 不同动物所处的环境差异大, 所暴露的 MNPs 也存在很大差异, 对生殖毒性的影响也需进一步研究。

参考文献

- [1] Thompson, R.C., Olsen, Y., Mitchell, R.P., Davis, A., Rowland, S.J., John, A.W.G., *et al.* (2004) Lost at Sea: Where Is All the Plastic? *Science*, **304**, 838-838. <https://doi.org/10.1126/science.1094559>
- [2] Sarkar, B., Dissanayake, P.D., Bolan, N.S., Dar, J.Y., Kumar, M., Haque, M.N., *et al.* (2022) Challenges and Opportunities in Sustainable Management of Microplastics and Nanoplastics in the Environment. *Environmental Research*, **207**, Article ID: 112179. <https://doi.org/10.1016/j.envres.2021.112179>
- [3] Lu, H., Xu, P., Sun, G., Chen, B., Zheng, Y., Zhang, J., *et al.* (2024) Early-Life Exposure to Polystyrene Micro- and Nanoplastics Disrupts Metabolic Homeostasis and Gut Microbiota in Juvenile Mice with a Size-Dependent Manner. *Science of the Total Environment*, **955**, Article ID: 176802. <https://doi.org/10.1016/j.scitotenv.2024.176802>
- [4] Lin, Z., Li, Z., Ji, S., Lo, H.S., Billah, B., Sharmin, A., *et al.* (2024) Size-Dependent Deleterious Effects of Nano- and Microplastics on Sperm Motility. *Toxicology*, **506**, Article ID: 153834. <https://doi.org/10.1016/j.tox.2024.153834>
- [5] 王英雪, 徐嫚, 王立新, 崔建升. 微塑料在哺乳动物的暴露途径、毒性效应和毒性机制浅述[J]. 环境化学, 2021, 40(1): 41-54.
- [6] Thompson, R.C., Courtene-Jones, W., Boucher, J., Pahl, S., Raubenheimer, K. and Koelmans, A.A. (2024) Twenty Years of Microplastic Pollution Research—What Have We Learned? *Science*, **386**, ead12746. <https://doi.org/10.1126/science.ad12746>
- [7] Stevens, S., McPartland, M., Bartosova, Z., Skåland, H.S., Völker, J. and Wagner, M. (2024) Plastic Food Packaging from Five Countries Contains Endocrine- and Metabolism-Disrupting Chemicals. *Environmental Science & Technology*, **58**, 4859-4871. <https://doi.org/10.1021/acs.est.3c08250>
- [8] Gutow, L., Eckerlebe, A., Giménez, L. and Saborowski, R. (2015) Experimental Evaluation of Seaweeds as a Vector for Microplastics into Marine Food Webs. *Environmental Science & Technology*, **50**, 915-923. <https://doi.org/10.1021/acs.est.5b02431>
- [9] Santos, R.G., Machovsky-Capuska, G.E. and Andrades, R. (2021) Plastic Ingestion as an Evolutionary Trap: Toward a Holistic Understanding. *Science*, **373**, 56-60. <https://doi.org/10.1126/science.abh0945>
- [10] Wei, Z., Wang, Y., Wang, S., Xie, J., Han, Q. and Chen, M. (2022) Comparing the Effects of Polystyrene Microplastics Exposure on Reproduction and Fertility in Male and Female Mice. *Toxicology*, **465**, Article ID: 153059. <https://doi.org/10.1016/j.tox.2021.153059>
- [11] Shan, S., Zhang, Y., Zhao, H., Zeng, T. and Zhao, X. (2022) Polystyrene Nanoplastics Penetrate across the Blood-Brain

- Barrier and Induce Activation of Microglia in the Brain of Mice. *Chemosphere*, **298**, Article ID: 134261. <https://doi.org/10.1016/j.chemosphere.2022.134261>
- [12] Amereh, F., Eslami, A., Fazelipour, S., Rafiee, M., Zibaii, M.I. and Babaei, M. (2019) Thyroid Endocrine Status and Biochemical Stress Responses in Adult Male Wistar Rats Chronically Exposed to Pristine Polystyrene Nanoplastics. *Toxicology Research*, **8**, 953-963. <https://doi.org/10.1039/c9tx00147f>
 - [13] Wang, J., Wang, X., Zhang, C. and Zhou, X. (2022) Microplastics Induce Immune Suppression via S100A8 Downregulation. *Ecotoxicology and Environmental Safety*, **242**, Article ID: 113905. <https://doi.org/10.1016/j.ecoenv.2022.113905>
 - [14] Zhang, P., Zhang, Y., Li, P., Tu, D. and Zheng, X. (2024) Effects of the Adsorption Behavior of Polyamide Microplastics on Male Reproductive Health by Reduction of Testosterone Bioavailability. *Ecotoxicology and Environmental Safety*, **269**, Article ID: 115747. <https://doi.org/10.1016/j.ecoenv.2023.115747>
 - [15] Amereh, F., Amjadi, N., Mohseni-Bandpei, A., Isazadeh, S., Mehrabi, Y., Eslami, A., *et al.* (2022) Placental Plastics in Young Women from General Population Correlate with Reduced Foetal Growth in IUGR Pregnancies. *Environmental Pollution*, **314**, Article ID: 120174. <https://doi.org/10.1016/j.envpol.2022.120174>
 - [16] Liu, H., Li, H., Liu, Y., Zhao, H. and Peng, R. (2024) Toxic Effects of Microplastic and Nanoplastic on the Reproduction of Teleost Fish in Aquatic Environments. *Environmental Science and Pollution Research*, **31**, 62530-62548. <https://doi.org/10.1007/s11356-024-35434-9>
 - [17] Ullah, S., Ahmad, S., Guo, X., Ullah, S., Ullah, S., Nabi, G., *et al.* (2023) A Review of the Endocrine Disrupting Effects of Micro and Nano Plastic and Their Associated Chemicals in Mammals. *Frontiers in Endocrinology*, **13**, Article ID: 1084236. <https://doi.org/10.3389/fendo.2022.1084236>
 - [18] Hou, B., Wang, F., Liu, T. and Wang, Z. (2021) Reproductive Toxicity of Polystyrene Microplastics: *In Vivo* Experimental Study on Testicular Toxicity in Mice. *Journal of Hazardous Materials*, **405**, Article ID: 124028. <https://doi.org/10.1016/j.jhazmat.2020.124028>
 - [19] Jin, H., Ma, T., Sha, X., Liu, Z., Zhou, Y., Meng, X., *et al.* (2021) Polystyrene Microplastics Induced Male Reproductive Toxicity in Mice. *Journal of Hazardous Materials*, **401**, Article ID: 123430. <https://doi.org/10.1016/j.jhazmat.2020.123430>
 - [20] Gao, L., Xiong, X., Chen, C., Luo, P., Li, J., Gao, X., *et al.* (2023) The Male Reproductive Toxicity after Nanoplastics and Microplastics Exposure: Sperm Quality and Changes of Different Cells in Testis. *Ecotoxicology and Environmental Safety*, **267**, Article ID: 115618. <https://doi.org/10.1016/j.ecoenv.2023.115618>
 - [21] Xu, W., Yuan, Y., Tian, Y., Cheng, C., Chen, Y., Zeng, L., *et al.* (2023) Oral Exposure to Polystyrene Nanoplastics Reduced Male Fertility and Even Caused Male Infertility by Inducing Testicular and Sperm Toxicities in Mice. *Journal of Hazardous Materials*, **454**, Article ID: 131470. <https://doi.org/10.1016/j.jhazmat.2023.131470>
 - [22] Fu, X., Han, H., Yang, H., Xu, B., Dai, W., Liu, L., *et al.* (2024) Nrf2-Mediated Ferroptosis of Spermatogenic Cells Involved in Male Reproductive Toxicity Induced by Polystyrene Nanoplastics in Mice. *Journal of Zhejiang University-Science B*, **25**, 307-323. <https://doi.org/10.1631/jzus.b2300138>
 - [23] Pitt, J.A., Trevisan, R., Massarsky, A., Kozal, J.S., Levin, E.D. and Di Giulio, R.T. (2018) Maternal Transfer of Nanoplastics to Offspring in Zebrafish (*Danio Rerio*): A Case Study with Nanopolystyrene. *Science of the Total Environment*, **643**, 324-334. <https://doi.org/10.1016/j.scitotenv.2018.06.186>
 - [24] Huang, T., Zhang, W., Lin, T., Liu, S., Sun, Z., Liu, F., *et al.* (2022) Maternal Exposure to Polystyrene Nanoplastics during Gestation and Lactation Induces Hepatic and Testicular Toxicity in Male Mouse Offspring. *Food and Chemical Toxicology*, **160**, Article ID: 112803. <https://doi.org/10.1016/j.fct.2021.112803>
 - [25] Xiao, M., Li, X., Zhang, X., Duan, X., Lin, H., Liu, S., *et al.* (2023) Assessment of Cancer-Related Signaling Pathways in Responses to Polystyrene Nanoplastics via a Kidney-Testis Microfluidic Platform (KTP). *Science of the Total Environment*, **857**, Article ID: 159306. <https://doi.org/10.1016/j.scitotenv.2022.159306>
 - [26] Hamza, A., Ijaz, M.U. and Anwar, H. (2023) Rhamnetin Alleviates Polystyrene Microplastics-Induced Testicular Damage by Restoring Biochemical, Steroidogenic, Hormonal, Apoptotic, Inflammatory, Spermatogenic and Histological Profile in Male Albino Rats. *Human & Experimental Toxicology*, **42**. <https://doi.org/10.1177/09603271231173378>
 - [27] Jin, H., Yan, M., Pan, C., Liu, Z., Sha, X., Jiang, C., *et al.* (2022) Chronic Exposure to Polystyrene Microplastics Induced Male Reproductive Toxicity and Decreased Testosterone Levels via the LH-Mediated LHR/cAMP/PKA/StAR Pathway. *Particle and Fibre Toxicology*, **19**, Article No. 13. <https://doi.org/10.1186/s12989-022-00453-2>
 - [28] Amereh, F., Babaei, M., Eslami, A., Fazelipour, S. and Rafiee, M. (2020) The Emerging Risk of Exposure to Nano(micro)plastics on Endocrine Disturbance and Reproductive Toxicity: From a Hypothetical Scenario to a Global Public Health Challenge. *Environmental Pollution*, **261**, Article ID: 114158. <https://doi.org/10.1016/j.envpol.2020.114158>
 - [29] Alijagic, A., Kotlyar, O., Larsson, M., Salihovic, S., Hedbrant, A., Eriksson, U., *et al.* (2024) Immunotoxic, Genotoxic,

- and Endocrine Disrupting Impacts of Polyamide Microplastic Particles and Chemicals. *Environment International*, **183**, Article ID: 108412. <https://doi.org/10.1016/j.envint.2023.108412>
- [30] Qu, J., Wu, L., Mou, L. and Liu, C. (2024) Polystyrene Microplastics Trigger Testosterone Decline via GPX1. *Science of the Total Environment*, **947**, Article ID: 174536. <https://doi.org/10.1016/j.scitotenv.2024.174536>
- [31] Montano, L., Giorgini, E., Notarstefano, V., Notari, T., Ricciardi, M., Piscopo, M., *et al.* (2023) Raman Microspectroscopy Evidence of Microplastics in Human Semen. *Science of the Total Environment*, **901**, Article ID: 165922. <https://doi.org/10.1016/j.scitotenv.2023.165922>
- [32] Zhao, Q., Zhu, L., Weng, J., Jin, Z., Cao, Y., Jiang, H., *et al.* (2023) Detection and Characterization of Microplastics in the Human Testis and Semen. *Science of the Total Environment*, **877**, Article ID: 162713. <https://doi.org/10.1016/j.scitotenv.2023.162713>
- [33] Kelly, F.J. and Fussell, J.C. (2020) Toxicity of Airborne Particles—Established Evidence, Knowledge Gaps and Emerging Areas of Importance. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences*, **378**, Article ID: 20190322. <https://doi.org/10.1098/rsta.2019.0322>
- [34] Yu, P., Liu, Z., Wu, D., Chen, M., Lv, W. and Zhao, Y. (2018) Accumulation of Polystyrene Microplastics in Juvenile Eriocheir Sinensis and Oxidative Stress Effects in the Liver. *Aquatic Toxicology*, **200**, 28-36. <https://doi.org/10.1016/j.aquatox.2018.04.015>
- [35] Ijaz, M.U., Shahzadi, S., Samad, A., Ehsan, N., Ahmed, H., Tahir, A., *et al.* (2021) Dose-Dependent Effect of Polystyrene Microplastics on the Testicular Tissues of the Male Sprague Dawley Rats. *Dose-Response*, **19**. <https://doi.org/10.1177/15593258211019882>
- [36] Hu, Y., Shen, M., Wang, C., Huang, Q., Li, R., Dorj, G., *et al.* (2024) A Meta-Analysis-Based Adverse Outcome Pathway for the Male Reproductive Toxicity Induced by Microplastics and Nanoplastics in Mammals. *Journal of Hazardous Materials*, **465**, Article ID: 133375. <https://doi.org/10.1016/j.jhazmat.2023.133375>
- [37] Zhang, Y., Hou, B., Liu, T., Wu, Y. and Wang, Z. (2023) Probiotics Improve Polystyrene Microplastics-Induced Male Reproductive Toxicity in Mice by Alleviating Inflammatory Response. *Ecotoxicology and Environmental Safety*, **263**, Article ID: 115248. <https://doi.org/10.1016/j.ecoenv.2023.115248>
- [38] Ilechukwu, I., Ehigior, B.E., Ben, I.O., Okonkwo, C.J., Olorunfemi, O.S., Modo, U.E., *et al.* (2022) Chronic Toxic Effects of Polystyrene Microplastics on Reproductive Parameters of Male Rats. *Environmental Analysis Health and Toxicology*, **37**, e2022015. <https://doi.org/10.5620/eaht.2022015>
- [39] Wang, X., Zhang, X., Sun, K., Wang, S. and Gong, D. (2022) Polystyrene Microplastics Induce Apoptosis and Necrosis in Swine Testis Cells via ROS/MAPK/HIF1 α Pathway. *Environmental Toxicology*, **37**, 2483-2492. <https://doi.org/10.1002/tox.23611>
- [40] Wei, Y., Zhou, Y., Long, C., Wu, H., Hong, Y., Fu, Y., *et al.* (2021) Polystyrene Microplastics Disrupt the Blood-Testis Barrier Integrity through ROS-Mediated Imbalance of mTORC1 and mTORC2. *Environmental Pollution*, **289**, Article ID: 117904. <https://doi.org/10.1016/j.envpol.2021.117904>
- [41] Xie, X., Deng, T., Duan, J., Xie, J., Yuan, J. and Chen, M. (2020) Exposure to Polystyrene Microplastics Causes Reproductive Toxicity through Oxidative Stress and Activation of the P38 MAPK Signaling Pathway. *Ecotoxicology and Environmental Safety*, **190**, Article ID: 110133. <https://doi.org/10.1016/j.ecoenv.2019.110133>
- [42] Zhang, C., Wang, Z., Ma, S., Chen, R., Wang, S., Zhang, H., *et al.* (2023) Repair Mechanism of Yishen Tongluo Formula on Mouse Sperm DNA Fragmentation Caused by Polystyrene Microplastics. *Pharmaceutical Biology*, **61**, 488-498. <https://doi.org/10.1080/13880209.2023.2168705>
- [43] Rizwan, A., Ijaz, M.U., Hamza, A. and Anwar, H. (2023) Attenuative Effect of Astilbin on Polystyrene Microplastics Induced Testicular Damage: Biochemical, Spermatological and Histopathological-Based Evidences. *Toxicology and Applied Pharmacology*, **471**, Article ID: 116559. <https://doi.org/10.1016/j.taap.2023.116559>
- [44] Hou, L., Wang, D., Yin, K., Zhang, Y., Lu, H., Guo, T., *et al.* (2022) Polystyrene Microplastics Induce Apoptosis in Chicken Testis via Crosstalk between NF- κ B and Nrf2 Pathways. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, **262**, Article ID: 109444. <https://doi.org/10.1016/j.cbpc.2022.109444>
- [45] Li, S., Wang, Q., Yu, H., Yang, L., Sun, Y., Xu, N., *et al.* (2021) Polystyrene Microplastics Induce Blood-Testis Barrier Disruption Regulated by the MAPK-Nrf2 Signaling Pathway in Rats. *Environmental Science and Pollution Research*, **28**, 47921-47931. <https://doi.org/10.1007/s11356-021-13911-9>
- [46] Wang, J., Li, Y., Lu, L., Zheng, M., Zhang, X., Tian, H., *et al.* (2019) Polystyrene Microplastics Cause Tissue Damages, Sex-Specific Reproductive Disruption and Transgenerational Effects in Marine Medaka (*Oryzias melastigma*). *Environmental Pollution*, **254**, Article ID: 113024. <https://doi.org/10.1016/j.envpol.2019.113024>
- [47] Sun, Z., Wen, Y., Zhang, F., Fu, Z., Yuan, Y., Kuang, H., *et al.* (2023) Exposure to Nanoplastics Induces Mitochondrial Impairment and Cytoplasmic Destruction in Leydig Cells. *Ecotoxicology and Environmental Safety*, **255**, Article ID: 114796. <https://doi.org/10.1016/j.ecoenv.2023.114796>

-
- [48] Rato, L., Alves, M.G., Socorro, S., Duarte, A.I., Cavaco, J.E. and Oliveira, P.F. (2012) Metabolic Regulation Is Important for Spermatogenesis. *Nature Reviews Urology*, **9**, 330-338. <https://doi.org/10.1038/nrurol.2012.77>
- [49] Wen, Y., Cai, J., Zhang, H., Li, Y., Yu, M., Liu, J., *et al.* (2024) The Potential Mechanisms Involved in the Disruption of Spermatogenesis in Mice by Nanoplastics and Microplastics. *Biomedicines*, **12**, Article No. 1714. <https://doi.org/10.3390/biomedicines12081714>
- [50] Shi, W., Sun, S., Han, Y., Tang, Y., Zhou, W., Zhang, W., *et al.* (2022) Microplastics Hamper the Fertilization Success of a Broadcast Spawning Bivalve through Reducing Gamete Collision and Gamete Fusion Efficiency. *Aquatic Toxicology*, **242**, Article ID: 106049. <https://doi.org/10.1016/j.aquatox.2021.106049>