



Toxic Effects of Nanoparticles on Reproductive System of Animals: A Review

Hanan Waleed Kasim Agwaan¹, Afrah Younis Jasim²

10.18805/ag.RF-407

ABSTRACT

This review was designed to shed light on the application of nanoparticles (NPs) and their toxic effects of on the reproductive health of males and females. The use of nanoparticles (NPs) has increased in recent years in various industries due to its small size and physical and chemical properties. This article reviews the effect of different types of metal-based (e.g., silver, gold, zinc oxide) and carbon-based (e.g., graphene oxide) affect reproductive systems in animal models. In males Scientific studies indicate that exposure to various types of nanoparticles (NPs) leads to decreased sperm quality, testicular damage, oxidative stress, hormonal imbalance, programmed cell death in reproductive tissues, weak sperm formation, reduced sperm count and motility. In females, research has indicated that exposure to nanoparticles (NPs) causes hormonal disturbance and decreased fertility due to the formation of reactive oxygen species (ROS) and impact on the functions of the endocrine glands also exposure to nanoparticles (NPs) leads to oxidative stress and cellular damage in ovarian tissue, which disrupts follicle formation and hormone regulation, as well as causing morphological changes in the reproductive organs and preventing uterine implantation.

Key words: Cell death, Nanoparticle (NPs), Oxidative stress, Reproduction, Toxicity.

One of the key biological processes is reproduction, which functions to create a new organism (Alkhashab *et al.*, 2021; Agwaan, 2023; Tirpák *et al.*, 2021), reproductive efficiency plays an important role in livestock breeding systems and affects farm production and profitability (Alkhashab *et al.*, 2021). The rate of animal reproduction determines the effectiveness of milk and meat production (Smith *et al.*, 2018). Nanoparticles (NPs) have been used in recent years, as research has indicated their toxicity to female reproductive organs (Blum *et al.*, 2012), the use of nanoparticles (NPs), as their small size gives them unique characteristics that enhance medical procedures and technological processes (Massányi *et al.*, 2020; Rasool *et al.*, 2025). Despite the many benefits of nanoparticles NPs, information about their impact on health and the environment is limited (Massányi *et al.*, 2020). Numerous studies have shown that nanoparticles have negative effects on gametes of male and female reproductive organs, as nanoparticles are toxic to testicular tissue, reduce sperm quality and their ability to fertilize, disrupt the endocrine function of males and females, alter the level of sex hormones, increase programmed cell death and damage the ovaries in females (Brohi *et al.*, 2017). Nanoparticles (NPs) are made with very small sizes on the nanometer scale and have a high surface area (Taha and Ismail, 2023), they are made from minerals, polysaccharides and proteins (Falchi). The size of nanoparticles ranges between 1-100 nanometers and they exist in the natural environment due to physical, chemical and biological processes (Khan *et al.*, 2019). Nanoparticles enter cells and cause functional disorders such as increased oxidative stress inside cells or the production of a type of reactive oxygen species (ROS) (Xuan *et al.*, 2023). Nanoparticles

¹Department of Animal Production, College of Agriculture and Forestry, University of Mosul, Iraq.

²Department of Anesthesia Techniques, Mosul Medical Technical Institute, Northern Technical University, Mosul, Iraq.

Corresponding Author: Hanan Waleed Kasim Agwaan, Department of Animal Production, College of Agriculture and Forestry, University of Mosul, Iraq.
Email: hanan_agwaan@uomosul.edu.iq

How to cite this article: Agwaan, H.W.K. and Jasim, A.Y. (2026). Toxic Effects of Nanoparticles on Reproductive System of Animals: A Review. *Agricultural Reviews*. **47(4)**: 609-617. doi: 10.18805/ag.RF-407.

Submitted: 19-09-2025 **Accepted:** 26-05-2026 **Online:** 17-06-2026

accumulate in a variety of cell types and are distinguished by their capacity to cross the blood-brain barrier and the placenta. Over time, the toxicity of nanoparticles increases upon reproduction (Karthik *et al.*, 2024). Nanoparticles are characterized as relatively complex molecules with three layers and their properties are determined by their central components (Khan *et al.*, 2019). Numerous chemical and physical characteristics of nanoparticles include their large surface area, sensitivity and magnetic, optical and thermal properties (Gupta *et al.*, 2022). Through the circulatory and lymphatic systems, nanoparticles are absorbed and transported to numerous organs, including the reproductive system (Ober). In the laboratory, nanoparticles generate reactive oxygen species (ROS), which are harmful (Mahmoudi *et al.*, 2010). The large surface areas and small size of nanoparticles help them pass easily through the cell membrane (Gopinath *et al.*, 2008). Research has found that the toxicity of iron oxide nanoparticles causes changes in the acidity and concentration of serum (Nel *et al.*, 2006).

The chemical nature, shape and size of nanoparticles are responsible for the toxicity of nanoparticles, the large surface areas and ability to penetrate cells are the cause of the toxic effects of nanoparticles (Santacruz-Márquez *et al.*, 2021).

Nanoparticle mechanism

Different nanoparticles have different physical and chemical properties, as well as differ in their size, shape and surface properties (Taha and Ismail, 2023), they travel through the blood stream to vital organs like the liver and spleen, where the cells of the spleen's reticuloendothelial system (RES) capture them (Liu *et al.*, 2008). They produce reactive oxygen species (ROS) that contribute to the toxicity of the spleen and their accumulation leads to inflammation, cellular stress, DNA damage and programmed cell death (Oberdörster *et al.*, 2005; Capasso *et al.*, 2014). Cu NPs characterized by its small size, large surface areas and ability to penetrate cells, causing severe toxic effects (Santacruz-Marquez *et al.*, 2021). According to some studies (Santacruz *et al.*, 2021; Sengul and Asmatulu, 2020), Nanoparticles possess the capability to traverse the blood-brain barrier as well as the placental barriers, enabling them to infiltrate the brain, reproductive systems and possibly the fetus. This can result in mitochondrial damage, alterations to DNA and cell death. Furthermore, they are also able to reach vital organs such as the liver, kidneys and lungs.

The general mechanism by which nanoparticles cause toxicity

Internalization of nanoparticles

Nanoparticles can trigger a significant inflammatory response, which may impact the biological testis barrier (BTB) and they are capable of breaching various biological barriers that influence the reproductive system. Furthermore, the genes that are crucial for the development of the BTB (tight junction genes found in Sertoli cells) are also components of the BTB and the accumulation of

nanoparticles leads to their crossing the BTB barrier and infiltrating spermatogenic cells. In some studies, it was found that nanoparticles accumulate in ovarian cells and works to damage the local cellular environment of the developing follicles and prevent egg formation (Gao *et al.*, 2012; Sun *et al.*, 2013) nanoparticles interfere with the development of oocytes (oogenesis) and negatively affect the surrounding cellular environment of developing follicles (Fig 1).

Oxidative stress

An imbalance between the body's defense mechanisms' production of antioxidants and metabolism's production of reactive oxygen species (ROS) causes oxidative stress. (Bhardwaj, 2020) decreased levels of CAT (catalase), GPx (glutathione peroxidase), SOD (superoxide dismutase) and glutathione reductase (GR), as well as diminished intracellular concentrations of antioxidants such as GSH (reduced glutathione) and ascorbic acid, were attributed to TiO₂ NPs, which led to heightened ROS production and increased malondialdehyde (MDA) levels, while also diminishing the activity of antioxidant enzymes (Gurr *et al.*, 2005; Ramkumar *et al.*, 2012). Research has indicated that nano-TiO₂ can harm the DNA of sperm, resulting from the direct impact of reactive oxygen species (ROS) on genetic material through oxidative stress reactions mediated by cells (Gao *et al.*, 2012; Hong *et al.*, 2015). In sperm cells, the discharge of electrons *via* the electron transport chain. The combination of the one-electron reduction of molecular oxygen results in the generation of reactive oxygen species (ROS) (An *et al.*, 2021).

DNA damage

As nanoparticles in the nucleus cause DNA damage by interacting with it or with proteins associated with it, increased exposure to nanoparticles results in the generation of ROS, DNA damage, oxidative stress and subsequent genetic and reproductive toxicity. It has the ability to enter the nucleus and inhibit the process of

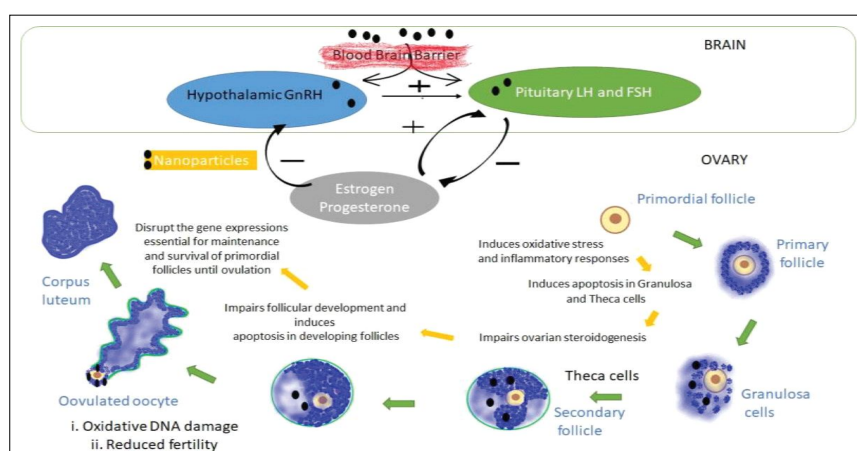


Fig 1: Nanoparticles induced female reproductive toxicity (Bhardwaj and Rathee, 2023).

replication, transcription and cell proliferation, thus damaging DNA (Geiser *et al.*, 2005). Exposure to nanoparticles causes DNA damage to sperm and male infertility (Meena *et al.*, 2015). It was found that some species produce oxidizing substances to DNA, which causes instability in the DNA structure and single-strand breaks. The pressure resulting from oxidative stress caused by nanoparticles leads to loss of fertility. In the laboratory, nanoparticles also damage DNA and oxidative stress in follicular cells and eggs, an increase in DNA damage was found (Courbiere *et al.*, 2013) and colleagues found that exposure to CeO₂ nanoparticles causes DNA damage in granulosa cells. When zebrafish (*Danio rerio*) larvae and adults were exposed to plasmonic nanoparticles, particularly gold and silver, DNA damage and ROS production were reported (d'Amora *et al.*, 2021).

Cell apoptosis

Some research (Wang *et al.*, 2018; Li *et al.*, 2009; Afifi *et al.*, 2016) has indicated that nanoparticles weaken the function of mitochondria, causing the rupture of mitochondria and an increase in ROS levels, which in turn leads to programmed cell death.

Route of entry of nanoparticles in animals

Ingestion

Nanoparticles pass through the air way with the help of ciliated mucous cells and reach the stomach and spread through the bloodstream to all organs of the body and affect the movement of the digestive system and the mucous layer lining the intestines (Geiser *et al.*, 2005).

Inhalation/animal breath

Nanoparticles may gain entry into the body via inhalation of aerosols, powder, or artificial, nanoparticles move to different lung sites depending on their size, when they reach the respiratory system, they cause toxic effects due to the lack of rapid mechanisms for eliminating them (Wickett and Visscher, 2006).

Skin penetration

The skin plays a major role in protecting against external chemicals and ultraviolet rays, modifying the immune response and controlling temperature (Kumar *et al.*, 2023; Rajamani *et al.*, 2025).

Nanoparticle induced reproductive toxicity

Nanoparticles can enter blood, placenta and epithelial obstructions to ensure regenerative tissues, but they can moreover gather within the regenerative region, causing damage to reproductive organs just like the ovaries, uterus and gonads, nanoparticles too cause harm to germinal stem cells, Sertoli cells and Leydig cells and adversely influence semen and the number, shape and development of sperm, in expansion to decreasing the number of developed eggs and influencing the method of arrangement of essential and auxiliary follicles (Brohi *et al.*, 2017).

Female reproductive toxicity

The function of the female reproductive system is to maintain the growth of the fetus, the system is considered fragile compared to other systems due to the limited number of female gametes compared to male gametes, the sensitivity of this system to foreign bodies, the effect of stress on female hormones and the occurrence of abnormal growth of the fetus when a female reproductive disorder occurs (Sun *et al.*, 2013). The underlying mechanisms of nanoparticle toxicity in biological systems are unclear, the production of reactive oxygen species is the cause of nanoparticle toxicity and the accumulation of reactive oxygen species causes inflammation, cellular stress, DNA damage and apoptosis (Oberdörster *et al.*, 2005; Capasso *et al.*, 2014). Nanoparticles also have a toxic effect on ovarian cells, causing damage to oocyte formation, follicle maturation and altered sex hormone levels (Iavicoli *et al.*, 2013). Some studies (Zhou *et al.*, 2019) have indicated that exposure to nano-TiO₂ causes a decrease in the number of ovarian follicles and hinders their development due to the destruction of the ovary, there is also a significant decrease in the number of eggs, fertilization rate, pregnancy rates and the number of births. Recent studies have shown that prolonged exposure to nano-TiO₂ has a negative impact on fertility and follicle development due to its effect on the level of sex hormones (Gao *et al.*, 2012), (Zhao *et al.*, 2013). It has been confirmed that exposure of mice to nanoparticles reduces the level of the hormone FSH, LH, Uterine tissues become fibrotic as a result of exposure to MNPs. Which causes an increase in the level of reactive oxygen species, thus causing oxidative stress, which raises collagen and fibronectin levels in the uterus, the ovaries and uterus also become fibrotic as a result of the accumulation of reactive oxygen species and thus an increase in the expression of proteins associated with fibrosis and tissue damage (Wu *et al.*, 2022). Zhou *et al.* (2019) gave female mice a dose of TiO₂ (2.5, 5, 10 mg/kg) for 90 days and observed a decrease in body weight and the relative weight of the ovary and a decrease in fertility, also deposition in the ovary caused an increase in the number of follicles and an increase in the level of sex hormones (Zhao *et al.*, 2013). It was noted that giving a dose of TiO₂ (10 mg/kg) for 90 days inside the stomach caused ovarian damage, a change in functional gene expression, an imbalance in mineral distribution, a decrease in the progesterone hormone, an increase in gene expression of the gene associated with estradiol synthesis, a decrease in the fertility and pregnancy rate and an increase in oxidative stress (Gao *et al.*, 2012). It is imperative to note that TiO₂ was infused into pregnant mice through intravenous infusion at a dosage of 0.8 mg/mouse which led to a decrease in uterine weight and an increase in the rate of fetal absorption and that smaller nanoparticles accumulate more than larger particles in the uterus (Yamashita *et al.*, 2011). According to one study nanometer gold nanoparticles, specifically 1.4 nm gold NPs (AuNPs),

accumulated on the uterine divider at concentrations two orders of magnitude greater than those of 18 nm nanoparticles (3 g/rat) or 80 nm nanoparticles (27 g/rat) when managed intravenously at a dosage of 5 g per microgram (Semmler-Behnke *et al.*, 2014). Concurring to Yang *et al.* (2017), oxide attractive NPs (IOMNs) with a estimate of 10 nm are more likely to enter the uterus of a mouse than nanoparticles with sizes of 20, 30 and 40 nm. Ovarian dysfunction, changes in gene expression patterns and changes in the expression of genes involved in inflammatory and immune reactions, oxidative stress, ion transport and cell diffusion and the transcription and activity of ovary oxidoreductase are all induced when animals are subjected to TiO₂ nanoparticles (5-6 nm) at a dosage of 10 mg/kg body weight. The researcher Wei *et al.* (2021) indicated that when silver nanoparticles are injected into the stomachs of pregnant mice using an intravenous feeding needle, they are transferred from the mother to the fetus and through breastfeeding. Pregnant mice uncovered to cadmium oxide (CdO) nanoparticles at a day-by-day measurement of 230 g/m³ by inward breath encounter changes within the weights of the placenta and uterus, changes within the expression levels of uterine estrogen receptors (ER) and ER and a diminish within the sum of 17-estradiol, according to the research. By altering the hormonal environment of the uterus, the cadmium ions that are produced by CdO nanoparticles hinder the process of blastocyst implantation (Blum *et al.*, 2012).

Exposure to MNPs through the digestive system causes a decrease in estradiol and progesterone level and an increase in the level of FSH, LH hormones in the serum and female endocrine disorders (Wei *et al.*, 2022), it causes oxidative stress by raising hydrogen peroxide levels and lowering antioxidant enzyme levels; the effect is dose-dependent (Haddadi *et al.*, 2022; Wei *et al.*, 2022; An *et al.*, 2021). Through an increase in inflammatory cytokines and reduce in anti-inflammatory cytokines, MNPs also impair the structure of the ovaries, uterus and endocrine glands (Hou *et al.*, 2021; Afonina *et al.*, 2017). By decreasing such as the thickness of uterus and number and diameter of uterine arteries, MNPs prevent embryos from implanting. These nanoparticles can also move from mother's body to fetus and reach different fetal tissues, brain, liver, kidneys, lungs and heart, disrupting immunological and metabolic processes (Jeong *et al.*, 2022). Agreeing to investigate, fetuses amass Cuco NPs after brief introduction, this phenomenon also occurs during oxidative stress, along with the production of reactive oxygen species (ROS) (He *et al.*, 2020).

Effect of nano on the male reproductive system

Nanoparticles affect reproductive health and reduce fertility (Pinho *et al.*, 2020), due to its tiny stature, it can accumulate in the testicles, prostate and epididymis through blood or be administered directly to these organs, resulting in organ poisoning (Wang *et al.*, 2018). Studies have shown the negative effects of TiO₂ on the male reproductive system

(Morgan *et al.*, 2017) and its ability to generate reactive oxygen species (ROS) and damage DNA and programmed cell death (Iftikhar *et al.*, 2021). When administered by injection at a dose of 40 mg/kg/B.W. for 35 days, silver nanoparticles (Ag-NPs) modify the structural composition, functionality and sexual behavior of testicular tissue, as well as affect testicular function when infused at a dosage of 40 mg/kg of body weight over a period of 35 days. Silver nanoparticles when administered intravenously to male rats the concentration of luteinizing hormone in plasma and sex hormone in the testes are changed (Dziendzikowska *et al.*, 2016). Male mice given water soluble carbon nanotubes (MWCNTs) intravenously experienced increased oxidative stress, decreased seminiferous tubule thickness and accumulation in the testis (Knez, 2013). Male mice were given intravenous gold nanoparticles (Au NPs) Testicular aggregation in BALB/c mice has been connected to negative impacts on the male regenerative system, including alterations in testicular histology, 0.5 ml of 20 and 40 mg/kg/B.W. of copper nanoparticles (Cu NPs) administered intraperitoneally for 3, 6 and 9 days caused a decrease in body weight and an increase in the weight of the reproductive organs (prostate gland, seminal vesicle, testes and epididymis). Additionally, it was discovered that the weight of tunica albuginea had significantly increased (Al-Bairuty *et al.*, 2016). Nanoparticles have harmful impacts on Leydig cells (Fig 2) causing a disruption in the production of testosterone produced by Leydig cells, excessive or insufficient production of this hormone is considered harmful (Zirkin and Papadopoulos, 2018). The production of testosterone is influenced by tit zinc oxide nanoparticles (70 nm at concentrations of 5-20 µg/ml for durations of 3-24 hours), which build up in the cytoplasm and nucleus of Leydig cells. According to research done by (Takeda *et al.*, 2009). When titanium dioxide nanoparticles (TiO₂-400 mg dose) with a diameter of less than 300 nm were infused, which comes about appeared a critical diminish in sperm generation, a mutilated testicular morphology, extended seminiferous tubules and a lower sertoli cell number.

Exposure to unique dosages of silver nanoparticles (3000 mg/kg/B.W., 4000 mg/kg/B.W., 5000 mg/kg/B.W. and 6000 mg/kg/B.W.) administered consecutively for five days, followed by observation for thirty days reduced Sertoli cells, abnormalities in testicular shape, Expanded seminiferous tubules and diminished sperm generation were observed following a period of 90 days during which subjects received 85 and 20 µg/kg/B.W./day, fresh semen was subjected to exposure of 44 mg/ml of Au NPs (9 nm) in a recent experiment; about 25% of the spermatozoa lost their ability to move. A treatment involving 20 nm Mn3O4 nanoparticles over the course of a year results in a decline in fertility among mice due to poor sperm quality, as supported by subsequent research (Zhang *et al.*, 2020; Hashemi *et al.*, 2016). The ability of SSCs to regenerate their stem cell population and produce self-progenitor cells

that undergo spermatogenesis to generate sperm is limited by silver nanoparticles (Griswold, 2016). According to one study, nano-TiO₂ can penetrate the blood-testis barrier and build up in the testicles, which reduce sperm motility and quantity while increasing the proportion of sperm exhibiting abnormalities, resulting in a lower fertility rate of offspring (Komatsu *et al.*, 2008; Gao *et al.*, 2013). The number of spermatocytes and spermatid cells dramatically dropped after five days of intraperitoneal injection of TiO₂ nanoparticles at doses of 50, 100 and 150 mg/kg (Dehghani and Noori, 2014). Gao *et al.* (2013) gave mice 2.5, 5 and 10 mg/kg of TiO₂ nanoparticles intragastric for 90 days. This caused the nanoparticles to accumulate in the testicles, resulting in abnormalities in the sperm, testicular lesions, changes in the serum level of sex hormones and changes in the expression of genes linked to sperm formation. Hong *et al.* (2015) illustrated that male mice were subjected to intragastric administration of TiO₂

nanoparticles at doses of 2.5, 5, 10 and 30 mg/kg over duration of 60 consecutive days.

Overall summary

The growing use of nanoparticles (NPs) in several industries and their possible harmful effects on both male and female reproductive health are highlighted in this review. It looks at the effects of several kinds of metal-based NPs (such silver, gold and zinc oxide) and carbon-based NPs (like graphene oxide) on the reproductive systems of animals. Male NP exposure has been associated with reduced sperm quality, testicular injury, oxidative stress, hormonal imbalances and reproductive tissue cell death, which results in decreased motility, sperm count and sperm production (Fig 3). Exposure to NPs in female's results in oxidative stress, which damages ovarian tissue, interferes with follicle growth and impacts endocrine functioning, as well as hormonal imbalances and lower fertility. Safety considerations in general.

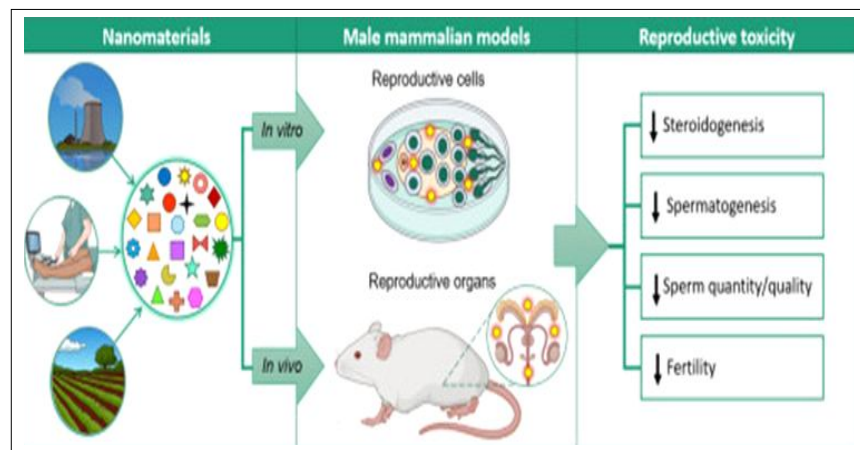


Fig 2: Nanomaterials induce reproductive toxicity in male mammals (Souza *et al.*, 2021).

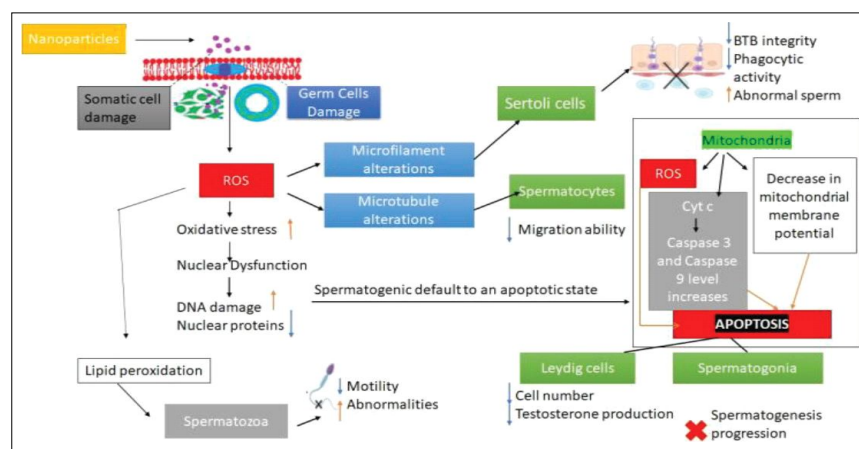


Fig 3: Nanoparticle-induced male reproductive toxicity (Bhardwaj and Rathee, 2023).

RECOMMENDATIONS

Implementing thorough safety precautions is crucial due to the increasing use of nanoparticles (NPs) in a variety of industries and their possible negative effects on reproductive health. To reduce occupational and environmental exposure, regulatory bodies should set stringent rules for the manufacture, processing and disposal of NPs. To determine acceptable exposure thresholds and clarify the mechanisms underlying NP-induced reproductive harm, more investigation is required. To maximize the safe use of nanoparticles while preserving reproductive health, a multidisciplinary strategy combining toxicology, reproductive biology and nanotechnology is necessary. By putting these suggestions into practice, we can better strike a balance between health protection and technology development.

While the primary focus of this review is on the toxic effects of nanoparticles on the reproductive systems of animals, it is highly encouraged to incorporate discussions on physiology, health and nutrition to provide a comprehensive understanding of the biological impacts. Including online supplementary materials such as datasets, videos, or interactive modules related to these topics could greatly enhance the educational value and engagement for readers. In addition, the inclusion of fundamental elements of culture, biodiversity and ecological management may give a larger perspective to the environmental effects of exposure to nanoparticles. This interrelationship of these factors, can lead to a more comprehensive understanding of nanotoxicology, thereby raising awareness for sustainable practices and ecological preservation.

CONCLUSION

Due to their potential health risks, the toxic effects of nanoparticles on male and female reproductive systems have received increasing scientific attention, because of their diminutive size and elevated reactivity, nanoparticles are able to easily break through biological barriers and alter cellular and molecular structures in reproductive tissues. Exposure to nanoparticles has been linked to decreased male sperm motility, DNA damage and sperm quality, ultimately affecting fertility. Testicular tissue may experience oxidative stress, inflammation and apoptosis as a result of these particles, causing testosterone synthesis and spermatogenesis to be disrupted. Similarly, in females, nanoparticles may interfere with ovarian function by inducing oxidative stress, follicular atresia and hormonal imbalances, which can compromise ovulation and overall reproductive health. Furthermore, nanoparticles have the potential to cross placental barriers, posing risks to fetal development, including teratogenic effects and growth retardation. The mechanisms underlying these detrimental effects include inflammation, reactive oxygen species production and disruption of cellular signaling pathways that are critical for reproductive processes. A number of variables, including particle size, dosage, exposure time and

nanoparticle makeup, affect how toxic a substance is. The potential reproductive risks necessitate cautious evaluation and regulation of nanoparticle exposure, despite promising applications in industry and medicine. In conclusion, while nanoparticles hold significant technological promise, their adverse impacts on reproductive health warrant comprehensive research to establish safe exposure limits and protective strategies, ensuring both male and female reproductive integrity are preserved.

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

- Afifi, M., Abu, Z.O.A., Ali, H. and Couderchet, M. (2016). Zinc nanoparticles induced brain lesions and behavioral changes in *Tilapia nilotica* and *Tilapia zillii*. *Indian Journal of Animal Research*. **50(5)**: 764-768. doi: 10.18805/ijar.10269.
- Afonina, I.S., Zhong, Z., Karin, M., Beyaert, R. (2017). Limiting inflammation-the negative regulation of NF- κ B and the NLRP3 inflammasome. *Nat Immunol*. **18(8)**: 861-86s9. <https://doi.org/10.1038/ni.3772>.
- Agwaan, H.W.K. (2023). Effect of coated methionine and lysine and their combination on fertility of awassi male sheep. *Basrah J. Agric. Sci*. **36(1)**: 201-213. <https://doi.org/10.37077/25200860.2023.36.1.17>.
- Al-Bairuty, G.A. and Taha, M.N. (2016). Effects of copper nanoparticles on reproductive organs of male albino rats. *Int. J. Sci. Technol*. **11(3)**: 17-24. <https://doi.org/10.12816/0034940>.
- Alkhashab, A.T., Al-Hassan, F.H. Al-dabbagh, S.F., Kassim, H.W. and Albak, T.M.A. (2021). Effect of protected methionine supplementation on body weight, testicular parameters, semen characteristics and testosterone hormone of awassi ram lambs. *Plant Archives*. **21(1)**: 1238-1242. <https://www.researchgate.net/publication/349731868>.
- An, R., Wang, X., Yang, L., Zhang, J., Wang, N. and Xu, F. (2021). Polystyrene micro- plastics cause granulosa cells apoptosis and fibrosis in ovary through oxidative stress in rats. *Toxicology*. **449**: 152665. <https://doi.org/10.1016/j.tox.2020.152665>.
- Bhardwaj, J.K., Panchal, H. and Saraf, P. (2020). Ameliorating effects of natural antioxidant compounds on female infertility: A review. *Reprod. Sci*. **28(5)**: 1227-1256. <https://doi.org/10.1007/s43032-020-00312-5>.
- Bhardwaj, J.K. and Rathee, V. (2023). Toxicological impact of nanoparticles on reproductive system: A review. *Toxicology International*. **30(4)**: 605-628. <https://doi.org/10.18311/ti/2023/v30i4/33893>.
- Blum, J.L., Xiong, J.Q., Hoffman, C. and Zelikoff, J.T. (2012). Cadmium associated with inhaled cadmium oxide nanoparticles impacts fetal and neonatal development and growth. *Toxicol. Sci*. **126(2)**: 478-486. <https://doi.org/10.1093/toxsci/kfs008>.
- Brohi, R.D., Wang, L. Talpur, H.S.; Wu, D., Khan, F.A., Bhattarai, D., Rehman, Z.U. Farmanullah, F. and Huo, L.J. (2017). Toxicity of nanoparticles on the reproductive system in animal models: A review. *Front. Pharmacol*. **8**: 908-931. <https://doi.org/10.3389/fphar.2017.00606>. eCollection 2017.

- Capasso, L., Camatini, M. and Gualtieri, M. (2014). Nickel oxide nanoparticles induce inflammation and genotoxic effect in lung epithelial cells. *Toxicol. Lett.* **226(1)**: 28-34. <https://doi.org/10.1016/j.toxlet.2014.01.040>.
- Courbiere, B., Auûan, M., Rollais, R., Tassistro, V., Bonnefoy, A., Botta, A., Rose, J., Orsiere, T. and Perrin, J. (2013). Ultrastructural interactions and genotoxicity assay of cerium dioxide nanoparticles on mouse oocytes. *Int. J. Mol. Sci.* **14(11)**: 21613-21628. <https://doi.org/10.3390/ijms141121613>.
- d'Amora, M., Raffa, V., De Angelis, F. and Tantussi, F. (2021). Toxicological profile of plasmonic nanoparticles in zebrafish model. *Int. J. Mol. Sci.* **22(12)**: 6372. <https://doi.org/10.3390/ijms22126372>.
- Dehghani, N., Noori, A. and Modaresi, M. (2014). Investigating the effect of titanium dioxide nanoparticles on the growth and sexual maturation of male rats. *International Journal of Basic Sciences and Applied Research.* **3(11)**: 772-776.
- Dziendzikowska, K., Krawczynska, A., Oczkowski, M., Krolkowski, T., Brzoska, K., Lankoff, A., Dziendzikowski, M., Stepkowski, T., Kruszewski, M. and Gromadzka-Ostrowska, J. (2016). Progressive effects of silver nanoparticles on hormonal regulation of reproduction in male rats. *Toxicol Applied Pharmacol.* **313**: 35-46. <https://doi.org/10.1016/j.taap.2016.10.013>.
- Gao, G., Ze, Y., Li, B., Zhao, X., Zhang, T. and Sheng, L. (2012). Ovarian dysfunction and gene-expressed characteristics of female mice caused by long-term exposure to titanium dioxide nanoparticles. *J. Hazard Mater.* **243**: 19-27. <https://doi.org/10.1016/j.jhazmat.2012.08.049>.
- Gao, G., Ze, Y., Zhao, X., Sang, X., Zheng, L., Ze, X. *et al.* (2013). Titanium dioxide nanoparticle-induced testicular damage, spermatogenesis suppression and gene expression alterations in male mice. *J. Hazard Mater.* **15**: 258-259: 133-143. <https://doi.org/10.1016/j.jhazmat.2013.04.046>.
- Geiser, M., Rothen-Rutishauser, B., Kapp, N., Schurch, S., Kreyling, W., Schulz, H., Semmler, M., Hof, V.I., Heyder, J. and Gehr, P. (2005). Ultrafine particles cross cellular membranes by nonphagocytic mechanisms in lungs and in cultured cells. *Environ. Health Perspect.* **113(11)**: 1555-1560. <https://doi.org/10.1289/ehp.8006>.
- Gopinath, P., Gogoi, S.K., Chattopadhyay and Ghosh, S.S. (2008). Implications of silver nanoparticle induced cell apoptosis for *in vitro* gene therap. *Nanotechnology.* **19(7)**: 075104. <https://doi.org/10.1088/0957-4484/19/7/075104>.
- Griswold, M.D. (2016). Spermatogenesis: The commitment to meiosis. *Physiol. Rev.* **96(1)**: 1-17. <https://doi.org/10.1152/physrev.00013.2015>.
- Gupta, G., Hamawandi, B., Sheward, D.J., Murrell, B., Hanke, L., McInerney, G., Blossi, M., Costa, A.L. and Toprak, M.S. (2022). Silver nanoparticles with excellent biocompatibility block pseudotyped SARS CoV-2 in the presence of lung surfactant. *Front. Bioeng. Biotechnol.* **10**: 1083232. <https://doi.org/10.3389/fbioe.2022.1083232>.
- Gurr, J.R., Wang, A.S., Chen, C.H. and Jan, K.Y. (2005). Ultrafine titanium dioxide particles in the absence of photoactivation can induce oxidative damage to human bronchial epithelial cells. *Toxicology.* **213(1-2)**: 66-73. <https://doi.org/10.1016/j.tox.2005.05.007>.
- Haddadi, A., Kessabi, K., Boughammoura, S., Rhouma, M.B., Mlouka, R. and Banni, M. (2022). Exposure to microplastics leads to a defective ovarian function and change in cytoskeleton protein expression in rat. *Environ. Sci. Pollut. Res. Int.* **29(23)**: 34594-34606. <https://doi.org/10.1007/s11356-021-18218-3>.
- Hashemi, E., Akhavan, O., Shamsara, M., Daliri, M., Dashtizad, M. and Farmany, A. (2016). Synthesis and cyto-genotoxicity evaluation of graphene on mice spermatogonial stem cells. *Colloids Surf B: Biointerfaces.* **146**: 770-776. <https://doi.org/10.1016/j.colsurfb.2016.07.019>.
- He, H., Zou, Z., Wang, B., Xu, G., Chen, C., Qin, X., Yu, C. and Zhang, J. (2020). Copper oxide nanoparticles induce oxidative DNA damage and cell death via copper ion-mediated P38 MAPK activation in vascular endothelial cells. *Int. J. Nanomed.* **8(15)**: 3291-3302. <https://doi.org/10.2147/IJN.S241157>. eCollection 2020.
- Hong, F., Si, W., Zhao, X., Wang, L., Zhou, Y. and Chen, M. (2015). TiO2 nanoparticle exposure decreases spermatogenesis via biochemical dysfunctions in the testis of male mice. *J. Agric. and Food Chem.* **63(31)**: 7084-7092. <https://doi.org/10.1021/acs.jafc.5b02652>.
- Hou, J., Lei, Z., Cui, L., Hou, Y., Yang, L. and An, R. (2021). Polystyrene microplas-tics lead to proptosis and apoptosis of ovarian granulosa cells via NLRP3/caspase-1 signaling pathway in rats. *Ecotoxicol. Environ Saf.* **212(1)**: 112012. <https://doi.org/10.1016/j.ecoenv.2021.112012>.
- Iavicoli, I., Fontana, L., Leso, V. and Bergamaschi, A. (2013). The effects of nanomaterials as endocrine disruptors. *Int. J. Mol. Sci.* **14(8)**: 16732-16801. <https://doi.org/10.3390/ijms140816732>.
- Iftikhar, M., Noreen, A., Uzair, M., Jabeen, F., Abdel Daim, M. and Cappello, T. (2021). Perspectives of nanoparticles in male infertility: Evidence for induced abnormalities in sperm production. *Int. J. Environ. Res. Public Health.* **18(4)**: 1758. <https://doi.org/10.3390/ijerph18041758>.
- Jeong, B., Baek, J.Y., Koo, J., Park, S., Ryu, Y.K. and Kim, K.S. (2022). Maternal exposure to polystyrene nanoplastics causes brain abnormalities in progeny. *J. Hazard Mater.* **426**: 127815. <https://doi.org/10.1016/j.jhazmat.2021.127815>.
- Karthik, K.K., Cheriyan, B.V., Rajeshkumar, S. and Gopalakrishnan, M. (2024). A review on selenium nanoparticles and their biomedical applications. *Biomed Technol.* **6**: 61-74. <https://doi.org/10.1016/j.bmt.2023.12.001>.
- Khan, I., Saeed, K. and Khan, I. (2019). Nanoparticles: Properties, applications and toxicities. *Arab. J. Chem.* **12(7)**: 908-931. <https://doi.org/10.1016/j.arabjc.2017.05.011>.
- Knez, J. (2013). Endocrine-disrupting chemicals and male reproductive health. *Reprod Biomed Online.* **26(5)**: 440-448. <https://doi.org/10.1016/j.rbmo.2013.02.005>.
- Komatsu, T., Tabata, M., Kubo-Irie, M., Shimizu, T., Suzuki, K. and Nihei, Y. (2008). The effects of nanoparticles on mouse testis leydig cells *in vitro*. *Toxicol in vitro.* **22(8)**: 1825-1831. <https://doi.org/10.1016/j.tiv.2008.08.009>.
- Kumar, P., Singh, P., Chauhan, S., Swaroop, M.N., Bhardwaj, A., Datta, T.K. and Nayan, V. (2023). Nanotechnology for animal sciences-new insights and pitfalls: A review. *Agricultural Reviews.* **46(2)**: 210-219. doi: 10.18805/ag.R-2620.

- Li, C., Taneda, S., Taya, K., Watanabe, G., Li, X., Fujitani, Y., Tamie, N. and Suzuki, A.K. (2009). Effects of in utero exposure to nanoparticle- rich diesel exhaust on testicular function in immature. male rats. *Toxicol Lett.* **185(1)**: 1-8. <https://doi.org/10.1016/j.toxlet.2008.11.012>.
- Liu, Z., Chen, K., Davis, C., Sherlock, S., Cao, Q., Chen, X. *et al.* (2008a). Drug delivery with carbon nanotubes for *in vivo* cancer treatment. *Cancer Res.* **68(16)**: 6652-6660. <https://doi.org/10.1158/0008-5472.CAN-08-1468>2008.
- Mahmoudi, M., Simchi, A., Imani, M., Shokrgozar, M.A., Milani, A.S., Hafeli, U.O. and Stroeve, P. (2010). New approach for the *in vitro* identification of the cytotoxicity of superparamagnetic iron oxide nanoparticles. *Colloids Surf B Biointerfaces.* **75(1)**: 300-309. <https://doi.org/10.1016/j.colsurfb.2009.08.044>.
- Massányi, P., Massányi, M., Madeddu, R., Stawarz, R. and Lukács, N. (2020). Effects of cadmium, lead and mercury on the structure and function of reproductive organs. *Toxics.* **8(4)**: 94. <https://doi.org/10.3390/toxics8040094>.
- Meena, R., Kajal, K. and Paulraj, R. (2015). Cytotoxic and genotoxic effects of titanium dioxide nanoparticles in testicular cells of male wistar rat. *Appl. Biochem. Biotechnol.* **175(2)**: 825-840. <https://doi.org/10.1007/s12010-014-1299-y>.
- Morgan, A.M., Ibrahim, M.A. and Noshay, P.A. (2017). Reproductive toxicity provoked by titanium dioxide nanoparticles and the ameliorative role of tiron in adult male rats. *Biochem. Biophys. Res. Commun.* **486(2)**: 595-600. <https://doi.org/10.1016/j.bbrc.2017.03.098>.
- Nel, A., Xia, T., Madler, L. and Lin, N. (2006). Toxic potential of materials at the nano level. *Science.* **311**: 622-627. <http://dx.doi.org/10.1126/science.1114397>.
- Oberdörster, G., Maynard, A. and Donaldson, K. (2005). Principles for characterizing the potential human health effects from exposure to nanomaterials: Elements of a screening strategy. *Particle and Fibre Toxicology.* **8**: 1-35. <https://doi.org/10.1186/1743-8977-2-8>.
- Pinho, A.R., Rebelo, S. and Pereira, M.D.L. (2020). The impact of zinc oxide nanoparticles on male (in) fertility. *Materials.* **13(4)**: 849. <https://doi.org/10.3390/ma13040849>.
- Ramkumar, K.M., Manjula, C., Kumar, G.G. and Kanjwal, M.A. (2012). Oxidative stress mediated cytotoxicity and apoptosis induction by TiO₂ nanofibers in HeLa cells. *Eur. J. Pharm. Biopharm.* **81(2)**: 324-33. <https://doi.org/10.1016/j.ejpb.2012.02.013>.
- Rajamani, P., Bagthasingh, C., Baskaran, V., Rani, V., Shalini, R. and David, E.P. (2025). Brine shrimp lethality assay for *in vitro* toxicity assessment of eco-friendly synthesized ZnO nanoparticles. *Indian Journal of Animal Research.* **59 (Special Issue)**: 126-129. doi: 10.18805/IJAR.B-5692.
- Rasool, A., Sakthivel, J., Veerappa, V.G., Abhonkar, R.M. and Misal, S. (2025). Applications of nanotechnology in animal reproduction: An overview. *The Indian Journal of Animal Reproduction.* **46(3)**: 15-23. <https://doi.org/10.48165/ijar.2025.46.03.2>.
- Santacruz-Márquez, R., González-De los Santos, M. and Andez-Ochoa, I.H. (2021). Ovarian toxicity of nanoparticles. *Reprod Toxicol.* **103**: 79-95. <https://doi.org/10.1016/j.reprotox.2021.05.001>.
- Semmler-Behnke, M., Lipka, J., Wenk, A. and Hirn, S. (2014). Size dependent translocation and fetal accumulation of gold nanoparticles from maternal blood in the rat. *Part Fibre Toxicol.* **10(11)**: 33. <https://doi.org/10.1186/s12989-014-0033-9>.
- Sengul, A.B. and Asmatulu, E. (2020). Toxicity of metal and metal oxide nanoparticles: A review. *Environmental Chemistry Letters.* **18(2)**: 1659-1683. <https://doi.org/10.1007/s10311-020-01033-6>.
- Smith, M.F., Geisert, R.D. and Parrish, J.J. (2018). Reproduction in domestic ruminants during the past 50 years: Discovery to application. *J. Anim. Sci.* **96(7)**: 2952-2970. <https://doi.org/10.1093/jas/sky139>.
- Souza, M.R., Mazaro-Costa, R. and Rocha, T.L. (2021). Can nanomaterials induce reproductive toxicity in male mammals? A historical and critical review. *Science of The Total Environment.* **769**: 144354. <https://doi.org/10.1016/j.scitotenv.2020.144354>.
- Sun, J., Zhang, Q., Wang, Z. and Yan, B. (2013). Effects of nanotoxicity on female reproductivity and fetal development in animal models. *Int. J. Mol. Sci.* **14(5)**: 9319-9337. <https://doi.org/10.3390/ijms14059319>.
- Taha, A.N. and Ismail, H.K. (2023). The impact of nano zinc oxide particles on the histology of the male reproductive system of adult male rabbits. *Iraqi J. Vet. Sci.* **37(1)**: 105-113. <https://doi.org/10.33899/ijvs.2022.133632.2270>.
- Takeda, K., Suzuki, K.I., Ishihara, A., Kubo-Irie, M., Fujimoto, R., Tabata, M., Oshio, S., Nihei, Y., Ihara, T. and Sugamata, M. (2009). Nanoparticles transferred from pregnant mice to their offspring damage the genital and cranial nerve systems. *Journal of Health Science.* **55(1)**: 95-102. <https://doi.org/10.1248/jhs.55.95>.
- Tirpák, F., Halo, M., Tokárová, K., Binkowski, L.J., Vašíček, J., Svoradová, A., Błaszczyk, A.M., Kováčik, A. and Tvrdá, E.P. (2021). Composition of stallion seminal plasma and its impact on oxidative stress markers and spermatozoa quality. *Life.* **11(11)**: 1238. <https://doi.org/10.3390/life11111238>.
- Wang, R., Song, B., Wu, J., Zhang, Y., Chen, A. and Shao, L. (2018). Potential adverse effects of nanoparticles on the reproductive system. *Int. J. Nanomed.* **13**: 8487-8506. <https://doi.org/10.2147/IJN.S170723>.
- Wei, S.M., Wang, Y.H., Tang, Z.S., Xu, H.B., Wang, Z., Yang T. *et al.* (2021). A novel green synthesis of silver nanoparticles by the residues of Chinese herbal medicine and their biological activities. *RSC. Adv.* **11**: 1411-1419. <https://doi.org/10.1039/D0RA08287B>.
- 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**: 153059. <https://doi.org/10.1016/j.tox.2021.153059>.
- Wickett, R.R. and Visscher, M.O. (2006). Structure and function of the epidermal barrier. *Am. J. Infect. Control.* **34(10)**: 98. <https://doi.org/10.1016/j.ajic.2006.05.295>110.
- Wu, H., Xu, T., Chen, T., Liu, J. and Xu, S. (2022). Oxidative stress mediated by the TLR4/NOX2 signalling axis is involved in polystyrene microplastic-induced uterine fibrosis in mice. *Sci. Total Environ.* **838(Pt 2)**: 155825. <https://doi.org/10.1016/j.scitotenv.2022.155825>.

- Xuan, L., Ju, Z., Skonieczna, M., Zhou, P.K. and Huang, R. (2023). Nanoparticles-induced potential toxicity on human health: Applications, toxicity mechanisms and evaluation models. *Med. Comm.* **4(4)**: e327. <https://doi.org/10.1002/mco2.327>.
- Yamashita, K., Yoshioka, Y., Higashisaka, K., Mimura, K. and Morishita, Y. (2011). Silica and titanium dioxide nanoparticles cause pregnancy complications in mice. *Nat. Nanotechnol.* **6(5)**: 321-328. <https://doi.org/10.1038/nnano.2011.41>.
- Yang, J., Hu, S., Rao, M., Hu, L., Lei, H., Wu, Y., Wang, Y., Ke, D., Xia, W. and Zhu, C. (2017). Copper nanoparticle-induced ovarian injury, follicular atresia, apoptosis and gene expression alterations in female rats. *Int. J. Nanomed.* **12**: 5959-5971. <https://doi.org/10.2147/IJN.S139215>. eCollection 2017.
- Zhang, X., Yue, Z., Zhang, H., Liu, L. and Zhou, X. (2020). Repeated administrations of Mn₃O₄ nanoparticles cause testis damage and fertility decrease through PPAR-signaling pathway. *Nanotoxicology.* **14(3)**: 326-40. <https://doi.org/10.1080/17435390.2019.1695976>.
- Zhao, X., Ze, Y., Gao, G., Sang, X., Li, B. and Gui, S. (2013). Nanosized TiO₂ induced reproductive system dysfunction and its mechanism in female mice. *Plos One.* **8(4)**: e59378. <https://doi.org/10.1371/journal.pone.0059378>.
- Zhou, Y., Hong, F., Wu, N., Ji, J., Cui, Y. and Li, J. (2019). Suppression of ovarian follicle development by nano TiO₂ is associated with TGF β mediated signaling pathways. *Journal of Biomedical Materials Research.* **107(2)**: 414-422. <https://doi.org/10.1002/jbm.a.36558>.
- Zirkin, B.R. and Papadopoulos, V. (2018). Leydig cells: Formation, function and regulation. *Biol. Reprod.* **99(1)**: 101-111. <https://doi.org/10.1093/biolre/i0y059>.