JEB®

Journal of Environmental Biology

p-ISSN: 0254-8704 • e-ISSN: 2394-0379 • CODEN: JEBIDP

Journal website : www.jeb.co.in ★ **E-mail :** editor@jeb.co.in

Triveni Enterprises (Educational Services Set-up)

Editorial

DOI : http://doi.org/10.22438/jeb/44/2/Editorial

Nanoparticle toxicity may cause testicular dysfunction

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Nanotechnology is the science of designing, producing, and using structures and devices having one or more dimensions of about 100 millionth of a millimetre (100 nanometres) or less. It is going to be a major driving force behind the imminent technological revolution in the 21st century. Private and public sector companies are constantly in synthesizing nanomaterial based products. Nanotechnology has the potential of producing new materials and products that may revolutionize all areas of life. Meanwhile, its opponents believe that nanotechnology may cause serious health and environmental risks and advise that the prophylactic approach should command the blooming and distribution of such products. Nanotechnology pledges for producing novel materials with augmented properties and potential applications (Zeng and Sun, 2008).

Nanoparticles and nanomaterials both terms are used interchangeably in scientific literature. However, according to British Standards Institution for the scientific terms: "Nanomaterial is a material with any internal or external structures on the nanoscale dimension, while Nanoparticle a is nano-object with three external nanoscale dimensions. According to the European Commission, nanoparticles can be defined as a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate with one or more external dimensions is in the size range 1 nm – 100nm. The size of nanoparticles is comparable to the size of cell organelles. Nanoparticles can have amorphous or crystalline form and their surfaces can act as carriers for liquid droplets or gases. They have at least one dimension between 1 and 100 nanometers and a narrow size distribution. The nanometric dimensions of these materials make them ideal candidates for surface engineering and functionalization. Due to the development of nanotechnology in recent years, engineered nanoparticles are being used in various fields, particularly in biomedical field.

Various physico-chemical properties such as large surface area strength, mechanical, optical activity and chemical reactivity make nanoparticles unique and suitable candidates for various applications. Nanomaterials can be classified into natural and anthropogenic categories based on their origin. Natural sources include volcanic eruptions, forest fires, photochemical reactions, dust storms, etc., while anthropogenic sources include human activities, which can be of two types: Incidental nanomaterials that are generated unintentionally as a result of industrial activities. Combustion from vehicles, cooking, fuel petroleum and coal for power generation (Linak *et al*., 2000), aeroplanes engines, welding, ore refining and smelting are some of the incidental activities that lead to nanoparticle formation (Rogers *et al*., 2005). Engineered nanomaterials are designed and created intentionally for producing nanoparticles with specific characteristics. Due to its unusual tunable properties, these materials are widely used in electronics such as semiconductor chips, lighting technologies such as light-emitting diodes (LEDs), lasers, batteries, and fuel electronics etc. Scientists are using nanoparticles to target tumors, in drug delivery systems, and to improve medical imaging. Emerging engineered nanomaterials like quantum dots, nanobranches, nanocages, and nanoshells are presently being used in advance photovoltaic cells, drug delivery nanovehicles, and immunological sensing devices (Kahru and Dubourguier, 2010).

Nanomaterials are also classified on the basis of morphology (rod, flower shaped, fiber, sphere and sheet), crystalline mature (amorphous and cristaline), dimension (0D, 1D, 2D, and 3D), and chemical nature (metal, semi-metal and non-metal). There are more than 1800 market products containing nanomaterials, including drugs, food products, food preservatives, clothing, sports items, cosmetics and electronic appliances (Chou *et al*., 2008; Vance *et al.,* 2015). Nanoparticles are currently being used in biomedicine, bio-

imaging, targeted drug delivery, assisted rreproductive technologies (ART), etc. Nanoparticle exposure to humans may be either incidental or accidental or occupational to the natural and manmade nanomaterials. Nanoparticles enter human bodies through inhalation, ingestion and skin, accumulate in the body organs and cause toxic effects on the biological system. The highly activated surfaces of nanoparticles have great potential to induce cytotoxic, genotoxic and carcinogenic activities (Seaton *et al*., 2010). *In-vivo* studies specify that the lung, spleen, liver, and kidney are the major distribution sites and target organs for nanomaterial exposure (Wang *et al.*, 2013). They induce localized toxic effects such as cardiotoxicity, hepatotoxicity, nephrotoxicity, etc., in related organs (Du *et al*., 2013; Yan *et al*., 2012; Hussain *et al*. 2005).

Several reports have described the adverse effects of nanoparticles on human and animal health, especially in context of reproductive health. The reproductive toxicity of nanoparticles is becoming an important part of nano-science research (Ema *et al*., 2010). Exposure to nanoparticles adversely affects male reproductive system including both structural and functional aspects. Metallic nanoparticles, generally below 30 nm, owing to their spherical nature and diameter easily cross blood testicular barrier causing considerable toxic changes in the testicular tissue. Hong *et al*. (2015) reported decreased sperm production in testis accompanied with changes in expression of spermatogenesis regulating genes due to exposure of metallic nanoparticle titanium dioxide (TiO_2). A sub-chronic oral exposure of PVP-coated AgNPs to rats resulted in altered testicular histology and sperm morphological abnormalities. In a study, testicular toxicity due to silver nanoparticles was examined in Sprague Dawley rat. The results indicated a significant fall in testosterone level and hike in LH levels. Ultra structural examination revealed vaculations in Sertoli cells and abnormalities in spermatogenic cells, sperm viability and chromatin integrity were also affected adversely (Elsharkawy *et al.,* 2019).

Similarly, exposure to zinc oxide nanoparticles resulted in apoptosis in testicular cells and structural changes in seminiferous epithelium and sperm anomalies (Han *et al.,* 2016). Accumulation of copper oxide nanoparticles in testis of mouse may affect sperm morphology (Kadammattil *et al*., 2018). Spherical shaped nickel nanoparticles of 90 nm size can change motility and decrease FSH and testosterone levels in rats. At higher dose, nickel nanoparticles induced significant structural damage to the testis (Kong *et al*., 2014). Iron oxide nanoparticles of 20-80 nm size adverse by affected the sperm and Leydig cells in mouse (Nasri *et al.,* 2015). Recent testicular toxicity study conducted by Verma *et al.* (2022) demonstrated that low, medium and high doses (20, 40 and 80 mg kg^{-1}) of spherically shaped, with an average diameter of 15-20 nm, super paramagnetic IONPs (Fe_3O_4) injected intra-peritoneally decreased sperm counts and motility in spermatozoa.

With respect to the effects due to non-metallic or semi-metallic nanoparticles having different shapes, different outcomes have been reported. A study conducted by Nirmal *et al.* (2017) on Wistar rat, exposed to 2.0 and 10.0 mg kg^{-1} bwt doses of OH-f MWCNTs resulted in sperm dysfunction and degeneration in seminiferous tubules (Nirmal *et al*., 2017). In another study by the same group, Wistar rat exposed to high doses of nanoscale graphene oxide (NGO) intra-peritonially, showed reduced sperm motility and total sperm count and increased sperm abnormalities (Nirmal *et al.,* 2017). It is thus apparent that nanoparticles have a considerable negative impact on testicular tissue including damage to Leydig cells, Sertoli cells, spermatogenesis and sperm quality. Various studies have revealed that the testicular toxicity is caused due to combination factors. Oxidative stress is a key factor responsible for nanoparticle mediated damage. It becomes more harmful, especially to the testes because of high metabolism, continuous sperm production and presence of high amount of unsaturated fatty acids (Aitken and Roman, 2008).

With the expansion and production of nanometerials for industrial and medical applications, exposure chances are also increasing. Many research reports have documented the adverse effects of nanoparticles on animals and environment. The major concern with the widespread use of NPs is their toxicity to living cells. Therefore, alleviating or reducing NPs toxicity remains much coveted goal for researchers around the globe. It is the alertness and scientific awareness which can prevent these materials from becoming bane instead of boon for humanity.

This editorial is written as a tribute to my beloved teacher Dr. R. C. Dalela who has been my mentor since 1985, when I was student of M.Sc. Zoology (1985-1987) and Ph.D (1987-1993) in D.A.V. P.G. College, Muzaffarnagar. He has played a vital role in moulding my career, from an average post-graduate student to the academician and a researcher I am today. I deeply cherish his guidance, encouragement and support. It was my privilege to meet him last November, so close to his sudden demise. The values inculcated by him continues to inspire me in my onward journey.

I have been associated with JEB for the past 25 years as a reviewer and an Associate Editor. The articles published in this journal receive good citations, which reflect the popularity of this open access journal among the researchers of Environmental Biology and Toxicology. I must appreciate the present editorial team headed by Professor Divakar Dalela for their efforts in maintaining the standard of this journal. I wish all success and my sincere co-operation for the same in the coming years.

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