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Commentary

Navigating nanotoxicity, ethical challenges, and policy imperatives in human and livestock reproductive research and therapy

Amit Kumar[1], Jerome Andonissamy[2], Avijit Dey[3]

[1]School of Genome Engineering, ICAR-Indian Institute of Agricultural Biotechnology, Ranchi, Jharkhand, [2]Department of Physiology and Reproduction, [3]Department of Animal Nutrition and Feed Technology, ICAR-Central Institute for Research on Buffaloes, Hisar, Haryana, India.

***Corresponding author:**
Amit Kumar,
School of Genome Engineering,
ICAR-Indian Institute of
Agricultural Biotechnology,
Ranchi, Jharkhand, India.

amitkajal7@gmail.com

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ABSTRACT

Nanotechnology has emerged as a transformative tool in reproductive research and therapy for both humans and livestock. In human medicine, nanomaterials are being explored for targeted drug delivery to treat infertility, enhance assisted reproductive technologies, and improve *in vitro* embryo production outcomes. These approaches hold significant potential to address infertility, which affects around 15% of couples worldwide. In the livestock sector, nanotechnology offers promising applications for boosting agricultural productivity by optimizing breeding outcomes, improving semen quality, and enabling precise genetic modifications for the production of genome-edited animals. This commentary explores the complex interplay of nanotoxicity, ethical challenges, and policy imperatives in the context of human and livestock reproductive research and therapy. By examining the mechanisms and risks of nanotoxicity, ethical dilemmas in clinical and agricultural settings, and the need for comprehensive regulatory frameworks, we aim to provide a roadmap for navigating this rapidly evolving field. The goal is to balance innovation with safety, ensuring that nanotechnology's benefits are realized without compromising health, welfare, or public trust.

Keywords: Ethical challenges, Human, Livestock, Nanotoxicity, Research

INTRODUCTION

Nanotechnology has emerged as a transformative tool in reproductive research and therapy for humans and livestock. In human medicine, nanoparticles (NPs) have been explored for targeted drug delivery to treat infertility, enhance assisted reproductive technologies (ARTs), and improve *in vitro* embryo production. These approaches hold significant potential to address infertility, which affects around 15% of couples worldwide. In the livestock sector, nanotechnology offers promising applications for boosting agricultural productivity by optimizing breeding outcomes, improving semen quality, and enabling precise genetic modifications for the production of genome-edited animals.

Overall, nanotechnology presents immense potential to tackle critical challenges in both sectors – infertility in human medicine and sustainable food production. For addressing these issues, nanomaterials such as liposomes, metal NPs, and polymeric carriers have been used for semen purification, oocyte maturation, gene transfer, and cryopreservation.[1] However, nanotechnology is tempered by significant risks, particularly nanotoxicity, which can adversely affect reproductive organs and cells.

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Unlike conventional drugs, NPs interact at the molecular level with unique biological pathways, resulting in unpredictable or transgenerational effects. As the field advances, there is a pressing need to establish robust frameworks that ensure the safe and ethical integration of nanotechnology into reproductive healthcare for both humans and animals. The objective of this commentary is to explore the complex interplay of NPs and their toxicity, ethical challenges, and policy imperatives in human and livestock reproductive research and therapy.

NANOTOXICITY IN REPRODUCTIVE RESEARCH AND THERAPY

Mechanisms of nanotoxicity

NPs, because of their extremely small size, can interact with biological systems in ways distinct from larger particles. In the reproductive system, NPs are capable of penetrating cell membranes, accumulating within gametes (sperm and oocytes), and crossing the placental barrier, thereby posing potential risks. Metallic NPs primarily induce oxidative stress, which damages cellular components and deoxyribonucleic acid, leading to compromised genetic integrity and disrupted cellular signaling pathways. For example, silver NPs have been reported to cause mitochondrial dysfunction, reduce sperm motility, and lower fertilization potential. Similarly, carbon-based nanomaterials such as fullerenes have been linked with embryonic toxicity in animal studies. The toxicity profile of NPs is strongly influenced by their physicochemical properties, including size, shape, surface charge, and chemical composition. However, variability in these characteristics complicates risk assessment, as different types of NPs may exert diverse biological effects. This highlights the need for rigorous and standardized testing to better understand nanotoxicity in reproductive research and therapeutic applications.

Nanotoxicity on gametes and embryos

While NPs offer promising applications in ARTs, their use beyond optimal concentrations may result in substantial toxicity risks. Due to their ability to interact with gametes and embryos in complex ways, careful evaluation of NP-associated risks in reproductive systems is essential. Metallic NPs, which are commonly studied in reproductive biology, present several limitations, including low stability, a tendency to aggregate, uncontrolled ion release, biomagnification, and compositional changes. Their nanoscale dimensions enable them to cross biological barriers, such as the blood–testis barrier, which may impair spermatogenesis and compromise male fertility. In addition, metallic NPs such as iron oxide, zinc oxide, and silver have demonstrated dose-dependent reproductive toxicity *in vitro* by inducing oxidative stress, impairing oocyte maturation, and disrupting ovarian cell structures. Embryos exposed to chitosan NPs have also shown reduced developmental competence, diminished mitochondrial activity, and down regulated expression of pluripotency-related genes. These observations underscore the importance of defining safe concentration ranges and thoroughly investigating NP-induced reproductive risks before advancing their use in clinical or veterinary ARTs.

Knowledge gaps

Despite the emerging evidence of nanotoxicity, critical knowledge gaps still remain unanswered as present review focus on acute toxicity, with limited data on chronic, low-dose, or transgenerational exposure effects. The diversity of NP, routes of exposure and their biological interactions complicates the establishment of universal safety guidelines. In addition, a lack of standardized testing protocols across species impedes comparative analysis. Addressing these challenges demands a collaborative, interdisciplinary research approach integrating toxicology, reproductive biology, nanomaterial science, as well as computational modeling. Such efforts are essential to design safer NPs having predictive toxicity models, and guide regulatory decisions for the protection of human and animal reproductive health.

ETHICAL CONSIDERATIONS

The application of nanotechnology in animal ARTs holds significant promise for enhancing reproductive efficiency and promoting genetic diversity in livestock. However, its use, particularly during pregnancy and embryonic development, has raised critical safety concerns. Certain nanomaterials, such as metallic NPs and quantum dots, have been shown to exert potentially harmful effects on embryos. Emerging evidence suggests that nano-mediated interventions during early embryonic stages can result in transgenerational changes that may persist across generations. Environmental risks are also a growing concern, particularly for metallic NPs that may be released into the ecosystem through waste, posing a threat to non-target organisms and disrupting ecological balance. Moreover, if animals developed using nanotechnologies enter the food chain, there is a potential risk of bioaccumulation, raising questions about food safety and public health. Another concern involves possible epigenetic modifications caused by NP exposure, which could lead to unanticipated health outcomes.[2,3] Regulatory and societal acceptance of nanotechnology in ART depends heavily on transparent communication, comprehensive risk-benefit analyses, and the establishment of robust oversight mechanisms. A thorough evaluation of long-term health impacts is essential to ensure the responsible application of nanomaterials in reproductive research. In parallel, the capability of nanotechnology to facilitate gene editing in

embryos, particularly in humans, intensifies the ethical debate, given the implications of heritable genetic alterations. Addressing these ethical considerations is critical to balancing the scientific advantages of nanotechnology in animal ART with the need for environmental sustainability, food safety, and social responsibility.[1,4]

POLICY GUIDELINES

Present regulatory frameworks are highly inconsistent across countries, often lacking specific guidelines for reproductive applications. For example, the U.S. food and drug administration (FDA) regulates nanomaterials in medical products; it does not offer detailed protocols for assessing their safety in reproductive contexts.[5] In veterinary medicine, regulatory gaps are even wider, with limited oversight of the use of NPs in livestock. This fragmented landscape risks the regulatory arbitrage, where weaker jurisdictions become testing grounds for unvetted products.[6] Establishing standardized safety protocols is imperative and should include both *in vitro* and *in vivo* assessments.[7] Global organizations, namely the World Health Organization and the Food and Agriculture Organization, can bridge disparities, especially in low-resource settings (WHO, 2021). Ethical guidelines must address issues of germline manipulation, animal welfare, and informed consent, requiring interdisciplinary collaboration.[4,8] There should be inclusive policy-making processes involving scientists, ethicists, and the public to promote culturally sensitive frameworks. Besides, transparent public engagement through education, forums, and open reporting can aid to build trust and preventing misinformation.[3,9] Clear communication about benefits and risks, without oversimplifying science, is vital to societal acceptance and through coordinated international efforts, ethical foresight, and participatory governance, can nanotechnology be responsibly integrated into reproductive health research and therapy.

FUTURE DIRECTIONS

Nanotechnology holds remarkable promise to transform reproductive research and therapy in both humans and livestock, yet its progress must be balanced with careful consideration of nanotoxicity, ethical concerns, and policy imperatives. Future applications may include nano-enabled semen purification, gamete evaluation, embryo manipulation, and the development of species-specific media and cryoprotectants that enhance bioavailability and improve *in vitro* maturation, fertilization, and embryo development.[1] However, due to their unique physicochemical characteristics, NPs must be rigorously examined for biosafety, bioaccumulation, and reproductive toxicity, highlighting the necessity for defined exposure limits and harmonized testing protocols across species. Besides, ethical challenges related to embryo manipulation, germline modifications, and animal welfare require transparent guidelines and responsible innovation to prevent misuse. Policy frameworks must evolve to regulate nanotechnology use in reproductive biology, ensuring safety, efficacy, and equitable application while safeguarding biodiversity and food security. Ultimately, the future of nanotechnology in reproductive sciences depends on multidisciplinary collaboration among researchers, ethicists, and policymakers to harness its transformative potential while minimizing risks to health, society, and the environment.[10]

CONCLUSION

Rapid application of nanotechnology needs to be strengthened by rigorous safety evaluations, considering the sensitivity of reproductive tissues and developmental stages. The ethical implications of manipulating reproductive systems with NPs necessitate thoughtful oversight and public transparency. The present policy frameworks are inadequate to address the unique challenges posed by NPs in reproductive applications. Therefore, a unified, one-health-based approach integrating science, ethics, and regulation is vital. Long-term futuristic studies on nanotoxicity, especially transgenerational effects, must be prioritized and responsible innovation will ensure the benefits of nanotechnology are realized without compromising health, welfare and trust.

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