



Research Article

Phytochemicals and Nanotechnology in the Management of Infertility

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Abstract

Reproductive medicine is a multidisciplinary field that involves the assessment and treatment of male and female reproductive systems. Advances in reproductive medicine and assisted reproductive technologies have enhanced fertility management and increased opportunities for parenthood for millions of people. Regardless of fertility-sparing strategies, gamete and embryo selection, cryopreservation, and other approaches in infertility management, this condition remains a social and health issue, and increased precision is needed in managing this disease due to the limitations of conventional pharmacological and assisted reproductive technologies. Bioactive compounds isolated from medicinal plants have gained attention due to their therapeutic potential, although they have certain limitations, which nanotechnology has shown great potential in improving through targeted delivery of phytochemicals, enhancing bioavailability and stability. The use of nanotechnology has been explored to preserve fertility and gamete quality, support diagnosis, develop targeted nanomedicines, and create cellular therapeutics. The current review will highlight the role of nanotechnology in the targeted delivery of phytochemicals for the management of infertility. The article will focus on the application of nanocarriers in counteracting the low bioavailability of phytochemicals and discuss the potential of various nanomedicines. The review will also assess the role of nanotechnology, identify novel phytochemical formulations for the treatment of infertility, and evaluate the translational potential of nanomedicine in this field. Overall, the application of nanotechnology in phytochemical delivery offers a promising avenue for developing innovative and potentially more effective treatments for infertility.

Keywords

Infertility, Phytochemicals, Nanotechnology, Nanocarriers, Drug Delivery, Curcumin, Oxidative Stress

1. Introduction

Infertility is a major global reproductive health problem affecting approximately 17.5% of adults worldwide, or about one in six people [1]. It has psychological, social, and

economic consequences and may result from male, female, combined, or unexplained factors. Infertility is associated with genetic, endocrine, infectious, immunological, environmental,

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Received: 13 August 2026; **Accepted:** 26 August 2026; **Published:** 18 September 2026



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and reproductive tract abnormalities, while approximately 30–40% of infertile men have no clearly identifiable cause and are classified as having idiopathic infertility, and about 10-17% in women [2]. Although advances in assisted reproductive technologies have improved fertility outcomes, their cost, accessibility, variable success rates, and procedural demands continue to present challenges.

Oxidative stress is an important contributor to reproductive dysfunction. Excessive production of reactive oxygen species (ROS) can disrupt the balance between oxidants and antioxidant defenses, resulting in lipid peroxidation, mitochondrial dysfunction, impaired sperm motility, apoptosis, and sperm DNA damage [3]. Oxidative imbalance has also been implicated in female reproductive disorders, including ovarian insufficiency, endometriosis, and polycystic ovary syndrome (PCOS) [4]. These mechanisms have increased interest in therapeutic agents capable of simultaneously addressing oxidative stress and inflammation.

Phytochemicals have therefore attracted attention as potential complementary approaches to infertility management because of their antioxidant, anti-inflammatory, and metabolic activities. Compounds such as curcumin, lycopene, resveratrol, and epigallocatechin gallate (EGCG) have demonstrated biological activities relevant to reproductive health [4, 5]. However, promising biological effects do not necessarily translate into clinical efficacy. Many phytochemicals are limited by poor aqueous solubility, chemical instability, rapid metabolism, and low bioavailability, which can restrict their therapeutic application [6].

Nanotechnology offers a potential solution to these limitations by enabling phytochemicals to be encapsulated or incorporated into nanoscale delivery systems. Nanocarriers such as micelles, liposomes, nanoemulsions, nanostructured lipid carriers, and polymeric nanoparticles can improve stability, solubility, bioavailability, cellular uptake, and controlled release of poorly absorbed compounds [7, 8]. This approach has demonstrated promising reproductive applications. For example, a randomized clinical trial reported that curcumin nanomicelle supplementation improved sperm count, concentration, motility, antioxidant capacity, and inflammatory biomarkers in infertile men [3]. Experimental studies have also investigated nanoformulated curcumin and resveratrol for PCOS and ovarian tissue preservation [9-11].

Despite these advances, the application of nano-enabled phytochemicals in infertility remains largely experimental. Important challenges include nanoparticle safety and biocompatibility, biological barriers, formulation and manufacturing requirements, reproducibility, regulatory considerations, and limited clinical evidence [12, 13]. Therefore, this review examines the potential of nanotechnology-enabled phytochemical delivery in infertility management, focusing on the reproductive mechanisms and therapeutic potential of selected phytochemicals, nanocarrier systems, evidence from male and female infertility studies, and the challenges that must be addressed for clinical translation.

2. Phytochemicals in Infertility Management

2.1. Why Phytochemicals are Relevant to Infertility

Phytochemicals are increasingly investigating infertility management due to their antioxidant, anti-inflammatory, metabolic, and cellular effects. This is especially relevant because oxidative stress is an important contributor to reproductive dysfunction. Reactive oxygen species (ROS) may cause lipid peroxidation, mitochondrial dysfunction, impaired sperm motility, and DNA damage, with spermatozoa being especially susceptible to oxidative stress due to the high polyunsaturated fatty acid content of their cell membranes and limited antioxidant defense mechanisms [4, 5].

The use of herbal medicines is also common among individuals seeking treatment for infertility. For example, 76.2% of women attending an infertility clinic in Uganda had used herbal medicines while seeking treatment, and 63.8% of them did not disclose this information to their clinicians [14]. This highlights the potential of phytochemicals in infertility management while also underscoring the need to identify specific compounds with proven efficacy and safety profiles.

Several phytochemicals have demonstrated beneficial effects on reproductive function. For example, curcumin has antioxidant and anti-inflammatory properties and has been investigated in clinical studies involving infertile men. A randomized controlled trial found that oral administration of 80 mg of curcumin nanomicelles for 10 weeks improved sperm count, concentration, and motility, as well as antioxidant and inflammatory biomarkers in men with infertility [3]. Other phytochemicals, including EGCG and lycopene, also have antioxidant and anti-inflammatory properties and may be beneficial in the management of infertility [4, 5].

However, the therapeutic potential of phytochemicals is limited by their pharmacokinetic properties. Clinical evidence for most of these compounds is also limited, and their effects should be interpreted with caution. Further research is needed to determine the most promising doses and formulations and evaluate the efficacy and safety of these treatments in clinical practice [6]. Additionally, many phytochemicals have poor solubility, stability, and bioavailability, which limits their therapeutic application. This is an important consideration for the review because the role of nanotechnology in improving the delivery of phytochemicals is discussed in detail later in the paper. The rationale for using nanotechnology is even stronger for phytochemicals with poor solubility, instability, and bioavailability.

2.2. Major Phytochemicals and Their Reproductive Effects

The review focuses on phytochemicals with proven or

potential therapeutic benefits for the management of infertility. The most relevant compounds include curcumin, epigallocatechin-3-gallate (EGCG), and lycopene, which have been investigated in clinical trials and are of particular interest due to their formulation challenges and promising results.

2.2.1. Curcumin

Curcumin is the most studied bioactive constituent of *Curcuma longa* (turmeric) and has been linked with a variety of fertility processes. The mechanisms through which curcumin may play a role in the treatment of infertility are related to its antioxidant and anti-inflammatory effects. In particular, male infertility is closely associated with increased levels of oxidative stress, which disrupts normal sperm cell membrane structure and function, mitochondrial activity, motile ability, and DNA integrity. In particular, a clinical study conducted has demonstrated that oral nanomicelle curcumin administration positively influenced the number of sperm, their concentration, and motility, as well as reduced oxidative stress and inflammation in infertile men [3]. Thus, curcumin may be a substance with a considerable impact on the outcomes of male infertility by addressing the key underlying mechanisms. Nevertheless, its low oral bioavailability requires special consideration, which has prompted the development of novel formulations, such as nano curcumin.

2.2.2. EGCG

EGCG is another phytochemical from *Camellia sinensis* (green tea) with antioxidant and anti-inflammatory properties that may help reduce oxidative stress and related infertility mechanisms. It is the major catechin in green tea extract and can impact oxidative stress, inflammatory signaling, cellular proliferation, and apoptosis [4, 5]. However, EGCG is also associated with formulation challenges, including poor stability and bioavailability.

2.2.3. Lycopene

Lycopene is a lipophilic carotenoid with strong antioxidant properties. It can help reduce oxidative damage to reproductive cells, which is especially relevant for spermatozoa, given their susceptibility to oxidative stress. However, the solubility and stability of lycopene are limited, which decreases its bioavailability and therapeutic efficacy. Nanoencapsulation can help improve the solubility and stability of lycopene and reduce its sensitivity to oxygen, light, and temperature [15, 16]. Other phytochemicals, including flavonoids, carotenoids, and polyphenols, also have antioxidant, anti-inflammatory, metabolic, and cellular effects that may help address infertility mechanisms [4, 5]. For example, phytochemicals such as resveratrol, crocin, cinnamaldehyde, and compounds from *Nigella sativa* have been associated with improvements in oxidative stress, hormonal regulation, sperm quality, folliculogenesis, and other reproductive parameters [17]. However, the evidence is most compelling for curcumin, EGCG, and

lycopene, and these three phytochemicals were selected for further discussion.

2.3. Mechanisms of Action of Phytochemicals in Infertility

The reviewed studies highlight the potential of phytochemicals in the management of infertility. Most of the investigated compounds have antioxidant, anti-inflammatory, metabolic, and cellular effects that may help reduce oxidative stress and related reproductive dysfunction. Specifically, phytochemicals can impact several mechanisms of male infertility, including oxidative stress, inflammation, mitochondrial dysfunction, apoptosis, and impaired reproductive signaling [4, 5].

Oxidative stress is a major contributor to infertility, and antioxidant phytochemicals can reduce oxidative damage to sperm cell membranes, DNA, and mitochondria. Phytochemicals can also reduce inflammation, which often occurs alongside oxidative stress. For example, the treatment with curcumin nanomicelles reduced C-reactive protein, tumor necrosis factor-alpha, and other inflammatory biomarkers in infertile men [3]. Phytochemicals can also help reduce mitochondrial dysfunction and apoptosis, which are also related to oxidative stress. Finally, phytochemicals can impact reproductive and metabolic signaling pathways and have direct cellular effects. Therefore, these compounds can address multiple mechanisms of infertility, and their combined anti-inflammatory and antioxidant effects may help reduce oxidative stress and related reproductive dysfunction [4, 5].

2.4. Limitations of Conventional Phytochemicals: Rationale for Nanotechnology

The review discusses the mechanisms of phytochemicals and their potential role in the management of infertility. However, most of these compounds have significant limitations, and their therapeutic use is currently limited by pharmacokinetic and formulation-related challenges. Phytochemicals typically have poor solubility, stability, and bioavailability and are subject to rapid degradation or metabolism after administration [4, 5]. This significantly limits their clinical application and therapeutic efficacy.

For example, curcumin has poor aqueous solubility and oral bioavailability, which is why it was formulated as nanomicelles to improve its solubility and bioavailability [3]. Similar challenges are reported for lycopene, which has limited solubility in water and is subject to photodegradation and isomerization [15, 16]. EGCG also has stability and bioavailability challenges that limit its therapeutic use [4, 5].

Another limitation of conventional phytochemical formulations is the lack of control over the release and distribution of active compounds after administration. The use of nanocarriers can help address this issue and improve the therapeutic efficacy of phytochemicals by enhancing their solubility,

stability, and bioavailability and controlling the release of the active compounds [12, 13].

Finally, the clinical evidence for most phytochemicals is limited, and the reported effects vary significantly. Biological activity does not always translate into clinically relevant efficacy, and individual patient characteristics, including genetic and physiological variability, can impact the observed treatment outcomes. Therefore, phytochemicals require additional preclinical and clinical research to determine the most promising formulations and doses and evaluate their efficacy and safety in clinical practice [6]. Thus, the reviewed studies highlight the potential of phytochemicals in the management of infertility but also demonstrate the importance of optimizing their delivery to improve therapeutic efficacy and safety.

3. Nanotechnology as a Strategy for Phytochemical Delivery

Nanotechnology can help to overcome the physicochemical and pharmacokinetic limitations of phytochemicals through their incorporation into nanocarriers. The latter can improve dispersion, stability, and bioavailability and control the release of the active compounds, contributing to enhanced performance and reduced off-target effects [13, 19]. Curcumin and lycopene are among the phytochemicals that can potentially benefit from nanoformulation. For example, curcumin nanomicelles have been reported to restore semen parameters and reduce oxidative and inflammatory biomarkers in infertile males [3]. They can also be used to achieve a targeted effect in the ovaries, since, in a PCOS rat model, curcumin encapsulated in nanoparticles demonstrated a prolonged release and increased ovarian efficacy as compared to the free drug [9, 18]. Similar advantages of nanoencapsulation have been demonstrated for resveratrol in reproductive tissues, with polymeric nanoparticles enhancing follicular viability and ovarian tissue integrity [10, 11].

Generally, nanoformulation can improve the pharmacokinetic properties of phytochemicals, including targeting, bio-distribution, cellular uptake, and tissue accumulation, which are critical for achieving therapeutic concentrations in the relevant tissues [12, 13, 20].

4. Nanotechnology-Enabled Delivery of Phytochemicals

4.1. Types of Nanocarriers

The described advantages can be achieved through the use of various nanocarriers, including micelles, liposomes, nanoemulsions, nanostructured lipid carriers (NLCs), and polymeric nanoparticles [7, 8, 12]. They can encapsulate bioactive compounds, thus protecting them from the environment, enhancing dispersion and stability, and controlling the release

rate to improve efficacy and reduce toxicity.

Micelles can be beneficial for the delivery of hydrophobic phytochemicals, such as curcumin, since their hydrophobic core can incorporate the latter, thus facilitating solubilization and increasing bioavailability [12, 13]. On the other hand, lipid-based nanocarriers, such as nanoemulsions and NLCs, have also been considered for hydrophobic and unstable molecules, such as lycopene. NLCs have been proposed as carriers for lycopene due to their reduced lipid crystallinity as compared to other lipid nanoparticles [15, 21].

As for polymeric nanoparticles, they can be used to carry resveratrol and demonstrate improved ovarian tissue preservation capacity [10, 11].

4.2. Enhancement of Bioavailability and Stability

Nanoencapsulation can increase the bioavailability of poorly soluble and unstable phytochemicals. For example, curcumin nanomicelles have been shown to improve multiple semen parameters and reduce oxidative and inflammatory stress markers in men with infertility [3].

NLCs can also be used to encapsulate lycopene and enhance its stability and bioaccessibility while controlling its release [9, 10]. Similar advantages of nanoformulation have been described for resveratrol, with polymeric nanoparticles demonstrating enhanced accumulation in reproductive tissues, thus improving follicular viability and ovarian structure [10, 11].

4.3. Targeted and Controlled Delivery

Nanoparticles can also be used to control the release of the encapsulated phytochemicals to enhance targeting and ensure prolonged presence in the target tissues. This can be beneficial for reproductive tissues, where enhanced exposure to the active compounds is required [12, 13].

For example, self-assembled chitosan–curcumin nanoparticles have been shown to prolong curcumin release and increase cellular uptake in a PCOS rat model [9]. Moreover, compared to free curcumin, these nanoparticles enhanced estrous cyclicity, folliculogenesis, corpus luteum formation, reproductive hormone levels, and ovarian morphology.

Another example is resveratrol-loaded polymeric nanoparticles, which have been shown to enhance follicular viability and ovarian tissue preservation in bovine follicles and ovarian cortical slices [10, 11]. Together, the described preclinical evidence demonstrates that nanoformulation can be useful for the application of phytochemicals in reproductive medicine beyond conventional systemic administration.

5. Applications in Infertility

Nano-enabled phytochemicals are explored for male and female infertility. The available preclinical and clinical evidence

demonstrates that both systemic and local administration can be beneficial in male and female reproductive disorders. However, with few exceptions, most applications of nano-phytochemicals have been explored in the preclinical setting.

5.1. Male Infertility

Male infertility can be caused by multiple factors, including oxidative stress, inflammation, impaired spermatogenesis, and poor sperm quality. Consequently, there is an interest in using antioxidant phytochemicals, such as curcumin, for their potential protective and regenerative effects on the male reproductive system.

The only clinical trial evidence so far comes from the study which investigated the effect of curcumin nanomicelles on infertile males with asthenoteratospermia. The intervention, which comprised 80 mg daily for 10 weeks, improved sperm count, concentration, and motility. It also increased total antioxidant capacity and decreased malondialdehyde, C-reactive protein, and tumor necrosis factor-alpha [3].

In parallel, multiple nanoparticle formulations have been explored for their potential beneficial effects on sperm function and selection, as well as antioxidant effects. These include formulations with EGCG and other polyphenols, as well as inorganic and organic nanoparticles [12]. However, evidence directly linking them to improved pregnancy or fertility outcomes is lacking.

5.2. Female Infertility

As in males, oxidative stress, inflammation, and hormonal dysregulation can disrupt female reproductive function and contribute to infertility. Thus, nano-enabled phytochemicals have been investigated for their potential antioxidant effects on the ovaries and ovarian tissues, such as follicles.

One of the first examples is a study that developed curcumin nanoparticles which demonstrated prolonged release and enhanced cellular uptake in the PCOS rat model. The intervention was able to restore estrous cyclicity, folliculogenesis, corpus luteum formation, reproductive hormone levels, and ovarian morphology [9].

Another example is resveratrol-loaded polymeric nanoparticles, which have been shown to improve follicular viability and ovarian tissue preservation in bovine follicles and ovarian cortical slices [10, 11]. Again, the evidence comes from in vitro and animal studies, with resveratrol studies in females being largely extrapolated from bovine follicles to human ovarian tissue. Thus, the available evidence on nano-enabled phytochemicals in female infertility is also primarily preclinical. However, it highlights the potential of nanoformulation to improve follicular function for enhancing fertility.

6. Challenges and Future Perspectives

The evidence described above suggests that nano-enabled

phytochemicals have the potential to be beneficial for male and female infertility. However, there are currently significant biological, pharmaceutical, and clinical challenges to their safe and effective use. The majority of the published studies vary significantly in the design, nanocarriers, doses, routes of administration, model systems, and outcome parameters, which complicates the interpretation and comparisons.

6.1. Biological Barriers and Safety

First, biological barriers to nanoparticle administration should be considered, including stability in the in vivo environment, ability to reach the target tissues, and interactions with gametes, embryos, and reproductive tissues [22]. Moreover, nanoformulation can impact absorption, biodistribution, cellular uptake, and persistence in the body, which should be considered when interpreting the safety of the free form of a phytochemical compared to its nanoencapsulated form [23]. Moreover, the safety of nano-enabled phytochemicals should be considered in the context of nanoparticle accumulation, unintended interactions, and toxicity. These are of particular concern for reproduction, where the health of gametes, embryos, and fetuses should be taken into account. Thus, long-term reproductive and offspring safety should be assessed in appropriate models before clinical investigations.

6.2. Manufacturing and Formulation

Another challenge pertains to the manufacturing and formulation process, as nanoparticles should possess desirable characteristics for clinical applications. Specifically, their size, shape, surface charge, encapsulation efficiency, drug loading, and release profiles should be optimized for target-specific delivery and enhanced efficacy. At the same time, reproducibility is of paramount importance, and scale-up procedures should be developed to ensure consistency and cost-effectiveness.

6.3. Clinical Translation and Regulation

A major limitation in the current literature pertains to the relevance of the findings to clinical practice. While the majority of the studies are primarily preclinical, there is currently limited clinical evidence on the efficacy and safety of phytochemical-loaded nanoparticles. In fact, only one clinical trial has been conducted to date, investigating curcumin nanomicelles in males with infertility [3]. Therefore, future clinical studies, including randomized controlled trials, are needed to demonstrate the efficacy and safety of nano-enabled phytochemicals in both genders.

Moreover, when designing such trials, it will be critical to determine the optimal formulation, dose, and route of administration, as well as evaluate pharmacokinetics and long-term safety. Particular consideration should be given to reproductive outcomes beyond standard biomarkers and infertility parameters, such as pregnancy, implantation capability, embryo

development, and live birth rates.

6.4. Future Directions

Nanoparticle research into reproductive disorders and infertility should be expanded to include mechanistic preclinical studies and clinical investigations. More specifically, there is a need for targeted nanoparticle formulations capable of enhanced accumulation in specific reproductive tissues. Moreover, nanoparticles with prolonged release properties can reduce the frequency of administration and ensure consistent tissue exposure. Since the causes of infertility can be diverse, future studies should consider the heterogeneity of the condition and identify the patient's populations and mechanisms that can benefit from nano-enabled phytochemicals.

Ultimately, the critical areas of investigation should include standardized preclinical protocols, long-term reproductive safety studies, direct comparisons of free and nano-formulated compounds, and collaborative studies across disciplines to ensure the clinical translation of the most promising findings.

7. Conclusion

Phytochemicals with proven antioxidant and anti-inflammatory activity are attractive agents for counteracting oxidative stress, inflammation, and impaired reproductive function. However, the low solubility, stability, and bioavailability of phytochemicals and the inability to control their targeting to specific cells are significant limitations for their efficient use in the reproductive system. Nanotechnology is a promising approach to deliver various phytochemicals and improve their biological activity in targeted cells.

The study of curcumin and resveratrol nano-formulation preclinical and clinical trials have yielded promising results for treating semen quality, PCOS, and ovarian function [3, 9, 10, 11]. However, most of the research used curcumin and resveratrol nano-formulations in preclinical studies, and there is a need for further trials to determine their safety and effectiveness in humans.

Abbreviations

ROS	Reactive Oxygen Species
PCOS	Polycystic Ovary Syndrome
EGCG	Epigallocatechin-3-Gallate
NLCs	Nanostructured Lipid Carriers
DNA	Deoxyribonucleic Acid
TNF- α	Tumor Necrosis Factor-Alpha
CRP	C-Reactive Protein
MDA	Malondialdehyde

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Conflicts of Interest

The authors declare no conflicts of interest.

References

- [1] Njagi, P., Groot, W., Arsenijevic, J., Dyer, S., Mburu, G., & Kiari, J. (2023). Financial costs of assisted reproductive technology for patients in low- and middle-income countries: A systematic review. *Human Reproduction Open*, 2023(2), hoad007. <https://doi.org/10.1093/hropen/hoad007>
- [2] Ehsani, M., Mohammadnia-Afrouzi, M., Mirzakhani, M., Esmailzadeh, S., & Shahbazi, M. (2019). Female unexplained infertility: A disease with imbalanced adaptive immunity. *Journal of Human Reproductive Sciences*, 12(4), 274–282. https://doi.org/10.4103/jhrs.JHRS_30_19
- [3] Alizadeh, F., Javadi, M., Karami, A. A., Gholaminejad, F., Kavianpour, M., & Haghighian, H. K. (2017). Curcumin nanomicelle improves semen parameters, oxidative stress, inflammatory biomarkers, and reproductive hormones in infertile men: A randomized clinical trial. *Phytotherapy Research*, 32(3), 514–521. <https://doi.org/10.1002/ptr.5998>
- [4] Liu, X., Zeng, T., Zhang, E., Bin, C., Liu, Q., Wu, K., Luo, Y., & Wei, S. (2025). Plant-based bioactives and oxidative stress in reproduction: anti-inflammatory and metabolic protection mechanisms. *Frontiers in Nutrition*, 12, 1650347. <https://doi.org/10.3389/fnut.2025.1650347>
- [5] Noh, S., Go, A., Kim, D. B., Park, M., Jeon, H. W., & Kim, B. (2020). Role of Antioxidant Natural Products in Management of Infertility: A Review of Their Medicinal Potential. *Antioxidants*, 9(10), 957. <https://doi.org/10.3390/antiox9100957>
- [6] Bratchikov, O. I., Tyuzikov, I. A., & Grekov, E. A. (2023). Modern possibilities of phytotherapy for male infertility from the standpoint of evidence-based medicine. *Research Results in Pharmacology*, 9(4), 93–103. <https://doi.org/10.18413/rpharmacology.9.10060>
- [7] Boulaiz, H., Alvarez, P. J., Ramirez, A., Marchal, J. A., Prados, J., Rodriguez-Serrano, F., et al. (2011). Nanomedicine: Application areas and development prospects. *International Journal of Molecular Sciences*, 12, 3303–3321. <https://doi.org/10.3390/ijms12053303>
- [8] Patra, J. K., Das, G., Fraceto, L. F., Campos, E. V. R., Rodriguez-Torres, M. D., Acosta-Torres, L. S., et al. (2018). Nano based drug delivery systems: Recent developments and future prospects. *Journal of Nanobiotechnology*, 16, 71. <https://doi.org/10.1186/s12951-018-0392-8>

- [9] Raja, M. A., Maldonado, M., Chen, J., Zhong, Y., & Gu, J. (2021). Development and Evaluation of Curcumin Encapsulated Self-assembled Nanoparticles as Potential Remedial Treatment for PCOS in a Female Rat Model. *International Journal of Nanomedicine*, 16, 6231–6247. <https://doi.org/10.2147/IJN.S302161>
- [10] Costa, F. D. C., De Assis, E. I. T., Nascimento, D. R., De Lima Neto, M. F., Silva, A. A., Azevedo, V. A. N., Ribeiro, R. P., Silva, B. R., Donato, M. A. M., Reis, A. V. F., Eloy, J. O., & Silva, J. R. V. (2026). Decellularized ovarian bioscaffolds and resveratrol-loaded polymeric nanoparticles support in vitro viability and ultrastructural preservation of bovine preantral follicles. *Journal of Assisted Reproduction and Genetics*, 43(5), 1605–1620. <https://doi.org/10.1007/s10815-026-03823-3>
- [11] Catunda, M. B. A., Costa, F. D. C., Bezerra, V. S., Caetano Filho, F. F., Ribeiro, R. P., Silva, A. A., Martins, S. D., Araújo, V. R., Reis, A. V. F., Eloy, J. O., & Silva, J. R. V. (2026). Effects of Resveratrol-Loaded Nanoparticles on Follicular Survival, Stromal Integrity and Activity of Endogenous Free-Radical Scavengers in Bovine Ovarian Cortical Slices Cultured In Vitro. *Reproduction in Domestic Animals*, 61(2), e70158. <https://doi.org/10.1111/rda.7015>
- [12] Mukherjee, A. G., Mukherjee, A. G., Gopalakrishnan, A. V., Mukherjee, A., & Mukherjee, A. (2024). The application of nanomaterials in designing promising diagnostic, preservation, and therapeutic strategies in combating male infertility: A review. *Journal of Drug Delivery Science and Technology*, 92, 105356. <https://doi.org/10.1016/j.jddst.2024.105356>
- [13] Shandilya, R., Bhargava, A., Bunkar, N., Tiwari, R., Goryacheva, I. Y., & Mishra, P. K. (2019). Nanobiosensors: Point-of-care approaches for cancer diagnostics. *Biosensors and Bioelectronics*, 130, 147–165. <https://doi.org/10.1016/j.bios.2019.01.034>
- [14] Kaadaaga, H. F., Ajeani, J., Ononge, S., Alele, P. E., Nakasujja, N., Manabe, Y. C., & Kakaire, O. (2014). Prevalence and factors associated with use of herbal medicine among women attending an infertility clinic in Uganda. *BMC Complementary and Alternative Medicine*, 14, 27. <https://doi.org/10.1186/1472-6882-14-27>
- [15] Ma, Y., Li, C., Xiu, W., & Wang, X. (2022). In vivo and in vitro evaluation of stability and antioxidant activity of lycopene-nanostructured lipid carriers. *Food Science and Biotechnology*, 32(6), 833–845. <https://doi.org/10.1007/s10068-022-01219-4>
- [16] Alam, M. A. U., Khatun, M., & Alam, M. A. U. (2022). Recent trend of nanotechnology applications to improve bio-accessibility of lycopene by nanocarrier: A review. *Journal of Food Chemistry and Nanotechnology*, 8(4). <https://doi.org/10.17756/jfcn.2022-138>
- [17] Chorosh, S. H., Malik, N., Panesar, G., Kumari, P., Jangra, S., Kaur, R., Al-Ghamdi, M. S., Albishi, T. S., Chopra, H., Singh, R., & Murthy, H. C. A. (2023). Phytochemicals: Alternative for infertility treatment and associated conditions. *BioMed Research International*, 2023, 1–27. <https://doi.org/10.1155/2023/1327562>
- [18] Sharma, K., Bhardwaj, S., & Nagarajan, K. (2025). A review on herbal interventions and nanotechnological advancements for managing polycystic ovarian syndrome. *JBRA Assisted Reproduction*, 29(4), 744–763. <https://doi.org/10.5935/1518-0557.20250042>
- [19] Ramos, A. P., Cruz, M. A. E., Tovani, C. B., & Ciancaglini, P. (2017). Biomedical applications of nanotechnology. *Biophysical Reviews*, 9, 79–89. <https://doi.org/10.1007/s12551-016-0246-2>
- [20] Chenthamara, D., Subramaniam, S., Ramakrishnan, S. G., Krishnaswamy, S., Essa, M. M., Lin, F. H., et al. (2019). Therapeutic efficacy of nanoparticles and routes of administration. *Biomaterials Research*, 23, 20. <https://doi.org/10.1186/s40824-019-0166-x>
- [21] Mishra, D. K., Shandilya, R., & Mishra, P. K. (2018). Lipid based nanocarriers: A translational perspective. *Nanomedicine*, 14, 2023–2050. <https://doi.org/10.1016/j.nano.2018.05.021>
- [22] Mishra, D. K., Balekar, N., & Mishra, P. K. (2017). Nanoengineered strategies for siRNA delivery: From target assessment to cancer therapeutic efficacy. *Drug Delivery and Translational Research*, 7, 346–358. <https://doi.org/10.1007/s13346-016-0352-5>
- [23] Wong, X. Y., Sena-Torralba, A., Alvarez-Diduk, R., Muthoosamy, K., & Merkoci, A. (2020). Nanomaterials for nanotheranostics: Tuning their properties according to disease needs. *ACS Nano*, 14, 2585–2627. <https://doi.org/10.1021/acsnano.9b08133>