Chapter 8

Nanotechnology in the Treatment of Infertility

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Abstract

With the increasing reproductive issues in all living beings worldwide, numerous problems related to fertility have emerged. Concurrently, the rising global population rates have led to a situation where the available food resources cannot meet the demand. Environmental factors, genetics, age, nutrition, stress, and global changes are some of the reasons that lead to infertility problems. Efforts are still underway to find methods in vivo or in vitro studies to eliminate reproductive problems by preventing structural abnormalities or changes in germ cells. In recent years, some nanoparticles have been utilized to address infertility issues caused by hormonal imbalances, metabolic disorders, or abnormalities in gamete cells, aiming to perform manipulations that could positively impact fertilization. Nanoparticles, used at non-toxic levels, have shown positive responses in fertility. Particularly in spermatological studies, nanoantioxidants have been observed to reduce reactive oxygen species, consequently preventing oxidative stress. Additionally, they are reported to benefit motility and sperm viability, while preserving DNA and gene expression. This section provides important insights into the potential of nanobiotechnology in addressing infertility issues in the years to come.

1. Introduction

Particles with a length or width of less than 100 nm in colloidal structures are referred to as Nanoparticles (NPs) (Khan et al., 2019). Depending on the type of material used, nanoparticles are classified into four categories: metallic nanoparticles (Au, Ag, Cu, Fe, Zn NPs), metal and metal oxide nanoparticles (FeO, VO, AlO, ZnO NPs), semiconductor nanoparticles (ZnS,

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CdSe, ZnSe, CdS NPs), and carbon-based (C) nanoparticles (Hong et al., 2022). These nanoparticles, which are produced in extremely small sizes, are also classified based on their dimensions (0D, 1D, 2D, and 3D) (Tiwari et al., 2012). Nowadays, researchers have discovered that nano-sized particles can alter the structural properties of a material. Recently, it has been reported that nano-sized particles are used in approximately 2000 products, and this number is rapidly increasing. These nanotechnological products are widely employed in biomedical, industrial, and agricultural fields. It is known that nanotechnology is used particularly in textile products, healthcare, sports equipment, the food industry, and many other products (Vance et al., 2015). The increasing utilization of nanotechnology in the past 30 years has raised the exposure level to nanomaterials. However, even though it may not be immediate, these products' positive or negative effects on living organisms are not yet fully understood. The current implications of this situation have been subject to investigation by some studies (Kwon et al.,2008; Nazar et al., 2016; Hong et al., 2017; Iftikhar et al., 2021; Klein et al., 2022; Öztürk and Ömür, 2022).

Nanomaterials, which have a multidisciplinary nature, have paved the way for a scientific discipline called nanobiotechnology with their applications in various fields of biology. It has been reported that various nanoparticles are used in the fields of biomedicine and veterinary science (Barkalina et al., 2014; Rath et al., 2015; Feugang, 2017; Falchi et al., 2018; Jain et al., 2018; Remião et al., 2018).

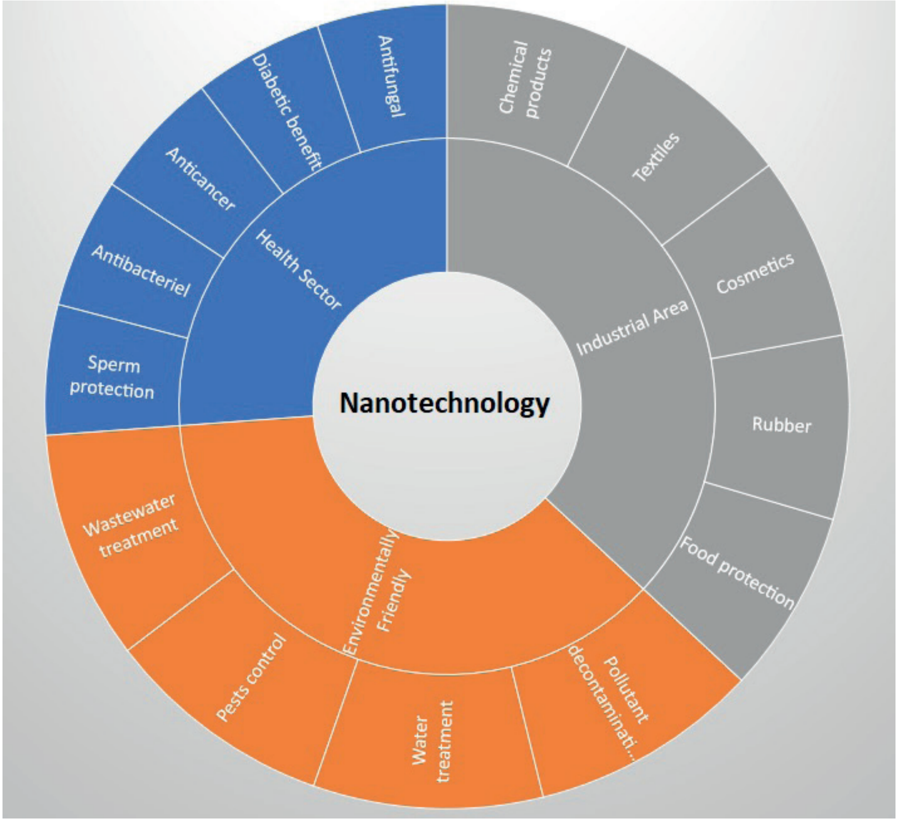

Figure 1. Current usage areas of Nanotechnology

With the rapid advancement of nanobiotechnology, nanoparticles, both physically, chemically, and biologically, are now increasingly present in the natural environment. According to recent research, it has been reported that nanoparticles can penetrate cells and lead to an increase in reactive oxygen species (ROS). Consequently, this may enhance intracellular oxidative stress, potentially disrupting biological structures and normal cellular functions (Nel et al., 2006). In some studies, the toxic effect of nanoparticles has been described to induce apoptosis or apoptosis-related tissue inflammation and perturb cellular redox status (Foldbjerg et al., 2009; Ahamed et al., 2010; Li et al., 2010). Finally, researchers have reported some nanoparticles to cross the blood-testis, placental, and blood-brain barriers, accumulating in different cells (Lan and Yang, 2012; Baghirov et al., 2016; Muoth et al., 2016).

In this section, the dose of nanoparticles administered to the living body through oral, parenteral, and inhalation routes, as well as their effects on fertility, will be discussed.

2. Use of Nanotechnology in Infertility Treatment

Approximately 15% of married couples worldwide experience infertility issues. Half of these infertility problems stem from males and the other half from females (Tahmasbpour et al., 2014). In pets, precise information about infertility rates has not been provided. We believe that urgent research should be conducted in this regard. Infertility problems, which are half caused by males, can arise either congenitally or due to environmental factors later in life.

The initial empirical studies have investigated the presence of the toxic effects of nanoparticles due to their small size and wide distribution. Research has been conducted in the veterinary field on reproduction and fertility, examining nanotoxicity effects (Jha et al., 2014; Falchi et al., 2018). Some researchers have reported that their studies in the field of reproductive biotechnology have preserved male fertility and sperm motility (Feugang et al., 2012; Odhiambo et al., 2014; Feugang et al., 2015; Falchi et al 2016; Durfey et al., 2017). One of the common causes of male infertility is asthenospermia. Astenospermia refers to an infertility problem where the motility (forward movement) of spermatozoa is below normal values (Nowicka-Bauer and Nixon, 2020). Progesterone hormone is commonly preferred in the treatment of asthenospermia. This hormone binds to mitochondrial membrane receptors, increasing the mitochondrial membrane potential, and assisting spermatozoa in gaining motility (Tantibhedhyangkul et al., 2014). The researchers focusing on this information obtained semen samples from 20 cases of asthenospermia. For the treatment, they used solid lipid nanoparticles to deliver the progesterone hormone. As a result, it has been shown to increase acrosomal reaction, sperm capacitation, and motility, as well as enhance the expression of protein kinase A, protein tyrosine kinase, P38MAPK, and SPACA1 genes in intracellular signaling pathways. It appears that progesterone-loaded solid lipid nanoparticles can be considered a significant and potent factor in sperm capacitation and acrosome reaction (Baranizadeh et al, 2022). Fifteen semen samples from asthenospermia cases were pooled and divided into 10 equal parts. They were then incubated with nanoliposomes containing testosterone, catalase, resveratrol, and resveratrol-catalase for 45 minutes. Before and after freezing, all spermatological parameters, sperm DNA, and gene expression were evaluated. They reported that nanoliposomes facilitated the delivery of antioxidants and testosterone into the cells. The nanoliposomes were found to enhance the effectiveness of antioxidants, leading to improvements in spermatological parameters and DNA integrity before and after freezing (Mohammadzadeh et al., 2021).

The researchers observed that sperm obtained from bulls could interact with polyvinyl alcohol-coated iron oxide nanoparticles after a 2-hour incubation. Following the investigations, they reported that the motility of spermatozoa improved, and their fertilization potential was preserved (Ben-David Makhluf et al., 2006). In another study conducted in humans and fish, conjugated iron oxide nanoparticles, utilized with a magnetic-activated cell sorting technique, facilitated increased usage for molecular-based targeting and removal (Gil et al., 2013; Valcarce et al., 2016). However, the spermatozoa capacity used in the study remains limited to 10^9 (Miltenyi et al., 1990; Feugang et al., 2019). In a similar study, researchers used iron oxide nanoparticles coated with a specific lectin or annexin-V to detect acrosome-reacted or abnormal spermatozoa in bull and pig sperm samples. Through this study, spermatozoa with impaired fertilization ability were eliminated. Spermatozoa with plasma membrane damage and mitochondrial membrane damage, exposed to oxidative stress, remained at low levels. Healthy offspring were obtained from mothers by performing simple and safe nanopurification, allowing for a normal gestation period (Odhiambo et al., 2014; Sutovsky, 2015; Durfey et al.,2017; Durfey et al.,2019).

The sperm cells obtained from broiler breed roosters can be damaged during cryopreservation. They have added soy lecithin in nanoparticle form (nano-SL) to the diluent at different ratios to enable minimal damage to germ cells during cryopreservation. The sperm samples, which underwent a freezing process, were examined after thawing. When the sperm parameters were checked, it was determined that the motility and viability rates of the sperm samples containing 1% nano-SL were higher compared to the other groups. In addition, the obtained sperm samples were used for artificial insemination in chickens to examine the hatchability rate. After this process, it was also determined that the sperm samples containing 1% nano-SL had the highest fertility rate (Sun et al., 2021). Another study on a nanoparticle containing lecithin was conducted in goat. The utilization of a Tris-based diluent containing 2% nano-SL for cryopreservation of goat sperm positively impacted the sperm parameters and motility rates compared to the other groups. They have also reported positive results in the sperm used for in vitro fertilization. (Nadri et al., 2019).

Afifi et al. (2015) investigated sperm parameters, oxidative stress, and testosterone levels in rats with experimentally induced Diabetes mellitus. For the treatment, they used zinc oxide (ZnONP) in nanoparticle form or a combination of ZnONPs with insulin. The results indicated a decrease in sperm motility and an increase in the presence of abnormal spermatozoa in rats with diabetes mellitus. They found that only ZnONPs or ZnONPs given in combination with insulin positively responded to the treatment, leading to an increase in sperm count and motility rate in the sperm cells. When interpreting these findings, it has been demonstrated that ZnONPs mitigate the harmful effects caused by diabetes.

3. Conclusion

In light of this information, we would like to report that nano-based particles, when administered in appropriate doses, yield positive responses in infertility. It would be accurate to say that there is a positive correlation in studies on fertility when using nanoparticles in sperm obtained from living organisms. In addition to the ease and effectiveness of the procedures, the easy integration of these processes into sperm cryopreservation protocols is of significant importance. Furthermore, we observe the need for an increase in studies on the female reproductive system, particularly in the areas of in vivo and in vitro fertilization (embryo production) processes. Furthermore, we observe the need for an increase in studies on the Due to their low costs and easy availability, we believe that nanoparticles should be further explored and utilized in more studies by experts. While initial studies in the reproductive field reported toxic effects, recent research has disproved this hypothesis, indicating that nanoparticles are not toxic in this context. However, it is not sufficient to state that there are still reliable results scientifically. Indeed, continuous and diligent research will be crucial in obtaining evidence-based information and revealing the truth.

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