Chapter 1

The Positive Effects of In Vivo/In Vitro Suplementation of Nanoparticles on Semen

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Abstract

Nanoparticles (NPs) are small size molecules. It is divided into organic and inorganic. Organic NPs have many clinical uses, from inoculation to homeostasis, long-term storage and delivery to the system, and absorption of topically used drugs into the skin. Inorganic NPs can be used in intraoperative lymphatic scanning, tumors, and anemia treatments. NPs have a favorable effect on sperm motility, kinematic parameters or membrane integrity rates, they can also be used as antibacterial, antiviral and antifungal in genital organ diseases. There are many studies in which the addition of NPs can be beneficial or harmful to sperm. Researchers have stated that it may be beneficial or cytotoxic depending on in vivo (such as airway, skin or injection) or in vitro use. It has been reported that NPs have positive effects on motility, kinematic parameters, plasma membrane integrity, DNA damage and acrosomal integrity and can be used as an antioxidant. In addition, it has been reported that it can be used in sexsorting, bioimaging and nanopurification, and that more studies on NPs will increase in the coming years.

1. Introduction

Nanoparticles (NPs) are small size molecules (Falchi et al. 2018a) and with sizes in the range of 10-1000nm (Mohanraj and Chen 2006). Although it is not named as a nanoparticle, nanoparticle studies date back to the 1950s. And nowadays scientific studies are more focused on NPs (Kreuter 2007). Because NPs have many particle-based formulations and technologies, they are widely researched preclinically. They are proven methods approved by the Food and Drug Administration (FDA) for the distribute of NPs, based upon the desired application or targeted site, delivered as oral, local, topical

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and systemic administration (Wagner et al. 2006; Torchilin 2014, Min et al. 2015). Treatment and identical NPs generally fall into two categories such as inorganic nanoparticles (e.g., gold, silica, iron oxide, etc.) and organic nanoparticles (e.g., polymeric, liposomes, micelles, etc.) (Anselmo and Mitragotri 2016). It has been stated that inorganic NPs can be used in intraoperative lymphatic scanning, tumors, and anemia treatments. (McCarthy and Weissleder 2008; Huang et al. 2011; Anselmo and Mitragotri 2015). In addition, organic NPs have many clinical uses, from inoculation to homeostasis, long-term storage and delivery to the system, and absorption of topically used drugs into the skin (Anselmo and Mitragotri 2016).

NPs have been highly used in the area of drug for treatment and they contain both lipophilic and some hydrophilic compounds. But hydrophobic drugs remains still a seriously trouble for clinical application (Falchi et al. 2018a).

There are in vivo studies showing that NPs cross the blood testicular barrier more easily than larger molecules of the same element. Researchers attributed the main reason for this to the fact that these particles received an inflammatory response when passing through Sertoli cells (Lan and Yang 2012).

There are many studies in which the addition of NPs can be beneficial or harmful to sperm. Researchers have stated that it may be beneficial or cytotoxic depending on in vivo (such as airway, skin or injection) or in vitro use (Park et al. 2010; Shi et al. 2010; Shi et al. 2011).

2. Positive Effect of Addition of Nanoparticles

Nowadays, there are nanoparticle technologies used for antioxidant, antiinflammatory and antimicrobial properties. (Stevanović et al. 2014; Lee et al. 2016; Kim et al. 2017). This case has enabled for most researchers in its in vivo and in vitro use for reproductive functions research (Barkalina et al. 2014).

NPs have a positive effect on sperm motility, kinematic parameters or sperm functionality, they can also be used as antibacterial, antiviral and antifungal in genital organ diseases (Samad et al. 2009; Mohamed et al. 2017; Raghunath and Perumal 2017; Gurunathan et al. 2018; Hassanein and El-Amir 2018; Siddiqi et al. 2018). Considering the antioxidative effects of NPSs, it can improve sperm functions and male fertility by eliminating the negative effects of reactive oxygen species (ROS) that occur in cooling or freezing reconstituted semen (Khalil et al. 2018). For example; Cerium oxide ($CeO2$) NPs have used as a ROS scavenger during cooling in ram semen. There is a study reporting that the addition of CeO2 nanoparticle to ram semen extender has a positive effect on sperm velocity parameters, DNA integrity and plasma membrane integrity even after 96 hours at +5 ^{o}C, as well as a significant decrease in ROS level compared to the control group (Falchi et al. 2018b).

Gold NPs(nano-Au) with DNA conjugated and nanosensors have been used to research for hormonal assesment and for accumulating semen production. For imaging method, liposome which is called emulsions have been loaded with large payloads, such as doxorubicin and magnetic NPs to make possible application and reveal with actual imaging tools. Despite these NPs to increase male fertility through intratesticular application, their use in livestock is limited yet. NPs containing antioxidant enzymes to decrease the effect of oxidative stress have the potential to improve male fertility. The benefit of such NPs have showed in a cultured mouse Sertoli cell line, so there is potential for an affect on the fertility of males (Feugang et al. 2019). Although magnetic nanoparticles accumulate in Leydig cells in mice as a result of inhalation of magnetic nanoparticles (Kwon et al. 2008), there are studies showing that Fe3O4, one of the magnetic nanoparticles, can be put into semen extenders as an equivalent to antibiotics in boar (Tsakmakidis et al. 2020). It was also stated that magnetic nanoparticles used to separate X and Y chromosomes in rams before sperm freezing did not have any effect on sperm motility, viability rates, membrane integrity, abnormal sperm ratios and MDA levels (Moradi et al. 2022). It was also shown in a study conducted for fertilization in both unsorted and sexsorted semen that magnetic NPs used to remove DNA damage to the extender in bull semen had a positive effect on semen parameters and did not have a negative effect on the blastocyst cleavage rate (Farini et al. 2016). It was also stated that the addition of magnetic NPs to the semen extender in bulls did not adversely affect motility and other parameters undergo acrosome reaction (Makhluf et al. 2006). In addition, polivinil alcohol (PVA) iron oxide (Fe3O4), which are magnetic NPs, can get into sperm and the intracellular antibody is still active in binding the cellular antigen. The similarity among regular immunocytochemical analysis regarding the localization of proteins and the use of antibody-bound particles can be used as a very good tool for protein localization of antibody-bound particles in living cells (Makhluf et al. 2008). When using magnetic NPs for molecular-based selection of wild swine sperm, results have indicated that the nanoselected sperm cells have raised velocity characteristics with increased progressive motility (Durfey et al. 2017). Others studies have used NPs from FeO conjugated with annexin V in order to designate the apoptosis of boar and bull spermatozoon (Odhiambo et al. 2014; Feugang et al. 2015). In a study conducted in rats to examine the time-dependent distribution of nano-Au in the testicles, it was stated that residues could be seen in the testicles even after 2 months. (Balasubramanian et al. 2010). Another studied rats that were injected intravenously with a single dose nano-Au showed that there may be residue in the testis even after one day. Even small doses of Nano-Au are given injectable, there may be a large amount of residue in the testis. (De Jong et al. 2008). Nano-Au added Tris-based extender have improved goat semen freezing by retaining the sperm membrane and acrosome integrity post-thawing. In addition, nano-Au has increased antioxidant level and ultimately have scavenged ROS in a goat semen extender (Ismail et al. 2020).

In a study examining the effects of nanoselenium(nano-Se) addition to rooster semen after thawing, it was stated that it increased total motility, progressive motility, sperm viability and total antioxidant capacity, and significantly decreased the abnormal rate of sperm and the level of malondialdehyde, which is end product of lipid peroxidation (Safa et al. 2016). Similarly, it was stated that the addition of nano-Se to the bull semen extender increased the progressive motility, viability rate, membrane integrity rate and TAC level after thawing, in addition to decreasing sperm chromatin damage, sperm apoptosis rate and abnormal sperm rate (Khalil et al. 2019). It has been stated that nano-Se added to the sperm extender in rams reduces lipid peroxidation and DNA damage after thawing, and positively increases sperm motility and membrane integrity (Hozyen et al. 2019; Nateq et al. 2020). In a study conducted in fish, it was stated that nano-Se added to the extender increased total and progressive motility, increased mitochondrial membrane integrity, plasma membrane integrity, and decreased ROS at 72 hours at +4^{o}C (Zhu et al. 2023). In another study given orally to male rats nano-Se, after its reproductive toxicity was induced by bisphenol, there is a study stating that it is beneficial as an antioxidative to the damage caused by toxicity, rearranges COX-2 and ER-2 genes and reduces DNA damage (Khalaf et al. 2019). In addition, orally administered nano-Se also preserved motility and DNA integrity and reduces oxidative stress (Rezvanfar et al. 2013). When given orally in goats, nano-Se increasing antioxidant levels and sperm quality when compared with other compound of selenium (Shi et al. 2010; Shi et al. 2011).

Addition of bull semen extender with nanoparticles of Zinc Oxide(nano-Zn) reduces MDA level and improved mitochondrial activity (Yazdanshenas et al. 2016). In addition, it was stated that it increased plasma membrane and acrosomal integrity and reduced DNA damage after thawing in frozen bull semen (Farhadi et al. 2022; Jahanbin et al. 2015). There is also the opinion that it will be beneficial in reaching the blastocyst stage by developing the cumulus oocyte complex in the embryo obtained by using bull semen with nano-Zinc added (Jahanbin et al. 2021). In a study given orally to rams, nano-Zn has been shown to increase the level of superoxide dismutase and TAC, motility, viability, semen volume and density, as well as plasma membrane integrity in semen. They are also added it when there was a decrease in the rate of abnormal sperm (Abaspour Aporvari et al. 2018). In addition to the study supplementation of the diet with nano-Zn increase epididymal semen quality, seminal plasma antioxidant levels and superoxide dismutase (SOD) in rams (Zhang et al. 2015). In another study added to the diet of rams, researchers have stated that after 72 hours at +4^{o}C, epididymal sperms increased total motility, viability, and plasma membrane and DNA integrity (Soltani et al. 2022). In diabetic rats, nano-Zinc have been expressed to raise the antioxidant activity in the testicular tissue, to increase spermatological parameters against harmful of oxidative stress (Afifi et al. 2015). In addition, there are studies showing that the addition of nano-Zn to sperm in humans protects the sperm chromatin structure and nano-Zn reduces oxidative stress in testicular tissue in mice (Snow Lisy et al. 2014; Sabanegh et al. 2014; Isaac et al. 2017).

A water-soluble nanotechnological method has been developed without using any solvent or stabilizer to produce C60 fullerene (C60HyFn). Chemically, C60HyFn water molecules are highly hydrophilic (Özer Kaya et al. 2021). In a study conducted to investigate whether hydrated C60 fullerene (C60HyFn) could prevent testicular dysfunction diabetic rats, researchers have stated that by preventing the negative effect of STZ, these NPs increase total motility and preserve sperm density (Bal et al. 2011). It has stated that C60HyFn added to ram semen extender was better for spermatological parameters between 100 nM and 40 μM doses at +5 ^{o}C at the end of the 144th hour (Özer Kaya et al. 2021). In addition, there are studies stating that C60HyFn added to semen extender in rams increases total and progressive motility after thawing, decreases abnormal sperm rate, decreases MDA levels, and increases vitamin A, K and amino acid levels (Türk et al. 2022).

It has been known that the progesterone hormone as a NPs increases the acrosome integrity, sperm capacitation and TAC level, as well as increases the expression of PTK PKA, SPACA1 and P38MAPK genes in the study conducted in asthenospermic humans (Baranizadeh et al. 2022).

In addition, there is a study stating that heparin-containing gold nanoparticle may be useful as a biomarker during sperm preparation in in vitro fertilization (Vidya and Saji 2018).

Plant extract nanoformulations such as mint, thyme, and curcumin increase progressive motility, vitality, and plasma membrane integrity ratios and antioxidative level, chromatin decondensation and also decreased apoptosis in goat semen. Curcumin NPs increase sperm motility and antioxidative level, while decreased apoptotic and necrotic spermatozoa in rabbit semen (Saadeldin et al. 2020).

Vitamin E NPs have preserved the acrosome integrity, decreased cell death ratio, and decreased ROS and LPO and hence improved sperm kinematic parameters in red deer epididymal sperm (Sanchez Rubio et al. 2020).

3. Conclusions

As a result, NPs not only have positive effects on sperm motility, membrane integrity, sperm morphology and antioxidant effects on sperm in vivo or in vitro addition, but also can be used in bioimaging, sexsorting and purification on sperm and that more studies on NPs will increase in the coming years.

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