Influence of Nanomaterials on Milk Quality, Glands and Offspring's

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Abstract- **The studies on milk production are rapidly spread over the world due to high nutritional value contains which is very essential for us. Nanoparticle influence was reported on the animal performance, milk performance, mammary glands, milk yield and also affects the bread-fed offspring in the milk production. It was reported that the milk yield with Zn NPs treatment was reduced in the dams compared to the other zirconium and titanium. Infant nanomaterial exposure is a worldwide concern, breastfeeding transfer of transition metal-oxide nanoparticles to as well as their toxicity to offspring are still unclear. Infant nanomaterial exposure is a worldwide concern, breastfeeding transfer of transition metal-oxide nanoparticles to as well as their toxicity to offspring are still unclear. Breastfeeding transmits nutrition and immunity from mothers to their offspring; it also provides a portal for maternal toxins to enter offspring. Thus, a toxicology assessment of both mothers and their offspring should be established to monitor nanomaterial exposure during lactation. The food chain is an important pathway for investigation intake of NPs to high-trophic-level organisms.**
Keywords: Nanoparticles, Offspring, Milk, Titanium, Mammal, Toxicity, Animal.

I. INTRODUCTION

Milk is a product that needs to be kept cold until thermal processing, and milk that waits on the farm may not be kept cold at all times. Bacteria may grow before and during transport, even in thecooled tanks (psychrotrophic bacteria), and increases in the number of bacteria decreases milk quality. Toxic materials left by dead bacteria such as *Staphylococcus aureus* change milk's aroma,taste, and visual properties, and the toxic materials withstand pasteurization [1].

Particles <500 nm are called nanoparticles, and nanoparticles are measured in nanometers (1 nm = 10^{-9} m). An atom is ≥0.1 nm, viruses are ≥10 nm, bacteria are around 1,000 nm, and a human hair is 100,000 nm in diameter. Bizzarro et al. (2005) reported that the smaller the silver nanoparticles, the greater their antibacterial effects, largely due to the increased surface to volume ratio and crystal surface structure [2]. Normally, commercially available AgNP used for antibacterial purposes are around 50 nm in diameter.

Unique size dependent properties of nanoparticles have numerous diagnostic applications such as diagnostic biosensors, imaging Nano probes for magnetic resonance imaging contrast agents. Using nanotechnology multifunctional nanomaterial's can be designed to image a specific organ, target tissue, access deep molecular targets and providedrug at controlled release. Great advances have been and are being made in Nano biochip materials, Nano scale biomimetic materials, Nano motors, Nano composite materials, interface biomaterials and Nano biosensor with enormous prospect in veterinary medicine application [3].

Applications of nanotechnology and nanoparticles in food, animal breeding and animal productivity such as in meat production, milk production are emerging rapidly. It used to create materials and change structure, enhanced quality and texture of foodstuffs at the molecularlevel. This technology has a major impact on milk production in mammals.

Breast milk is known to be a rich source of exosomes, with early milk containing a greater exosome concentration compared to mature milk [4]. Proteins, microRNA and mRNA are encapsulated by exosomes within a phospholipid membrane to protect them from ribonuclease digestion, freeze–thaw cycles and acidity [5]. This stability allows exosome contents to reach the neonate's intestinal lumen intact and be absorbed, in order to exert their effects. Preterm mothers, however, are often unable to provide sufficient breast milk, which results in the use of milk banks. This milk is pasteurized, which is a process that has been shown to disrupt exosomal membranes and degrade contents, decreasing their concentration by approximately 50%, and preventing the infants from benefitting from the protective effects of these contents.

II. EFFECT ON ANIMAL PERFORMANCE

Nanoparticles (NPs) of essential minerals, which can be used as an alternative to conventional forms of elements in animal diet [6]. It is assumed that much smaller doses of nanoparticles will be required to cover animal requirements for elements than bulk minerals and thus the environmental impact caused by the high concentration of inorganic salts will be alleviated [7]. Other than this, reduction in the quantity of minerals supplemented to animal diet could reduce the feed cost as well. Additionally, nano-forms of elements can increase bioavailability to animals, due to their properties such as small size, good homogeneity, high surface area and physical reactivity. The biological properties of nanoparticles such as lesser dose, lower antagonism, greater absorption rate and better tissue distribution can also be beneficial to animals. It is well-known that nanoparticles have a great potential even at very low doses [8]. Different types of metal/metal oxide nanoparticles have already been tested as potential feed additives and most often tested are zinc, silver, and copper nanoparticles in poultry diet. Metal/metal oxide nanoparticles supplemented to animal diet can improve not only animal performance and productivity such as meat, milk, and eggs production, but also ameliorate the quality of the animal derived products [9].

Metal or metal oxide nanoparticles supplemented to animal diet can improve not only animal performance and productivity such as meat, milk, and eggs production, but also ameliorate the quality of the animal derived products. Usually, enrichment of animal products like meat or eggs with microelements was observed [10]. It was reported that nanoparticles can increase the bioavailability of nutrients to animals due to their nanoscale size. Absorption of nutrients in the gut may be enhanced and can exert strengthened biological effects in the target tissues of animals. Minerals in the nanoparticle form can pass through the stomach wall and into body cells faster than common inorganic salts with a larger particle size. Bunglavan et al. (2014) showed that in the case of selenium, its nano-form transfer from the intestinal lumen to the body was significantly higher than for sodium selenite with significantly lower intestinal retention of nano-Se than for the inorganic form [11]. It was observed thar retention of nano-Se in the body was more efficient than sodium selenite. Metal containing nanoparticles can be a solution for nutrient deficiencies in animals and can enrich animal products with microelements. Additionally, minerals in the form of nanoparticles are believed to reduce intestinal minerals antagonism and thus minimize their excretion and environmental pollution [12].

Role of Zn in the animal system was well realized and documented, however Zn from conventional sources is less available to the body and thus mostly excreted to the environment causing environmental pollution. Apart from being highly bio-available, reports have pointed out the growth promoting, antibacterial, and immune-modulatory and many other beneficial effects of nano Zn. Thus, nano Zn may be used at lower doses in livestock feed to provide better results than the conventional Zn sources and indirectly prevents environmental contamination also. So, thorough and systematic studies were also recommended for elucidating toxic effects, in any, dose fixation and also for economic production procedures to take nano-Zn journey to logical conclusions [13].

III. EFFECT ON MAMMARY GLAND

Nanoparticles can be distributed to the breast milk of lactating mice without producing apparent damage to the mammary gland. It was reported that the mammary gland structure can be impaired to different degrees by the nanoparticle exposure depending on the category of the nanoparticle and the exposure route. All of the nanoparticle exposures induced high apoptosis rates for the mammary gland, suggesting they play harmful roles in the mammary gland. Other than this, cytotoxicity of nanoparticles was observed for human breast cells and their mammary tumorigenesis traits. The evidences suggested that when dams were exposed to nanoparticles via different pathways, the potential toxicological impacts on offspring were different from each other. The mammary gland is a key system in processing and delivering nutrients from the mother to her offspring [14]. Reichmuth et al., reported that SCC elevation has been linked with an animal's innate immune response in preparation for calving and to enhance the mammary gland defense mechanism at this critical calving time. Supplementation of zinc to pregnant goats at pre kidding period had improved the humoral as well as cell-mediated immunity and the effect of nano zinc was better than inorganic zinc [15].

As the sole nutritional source for newborns, it is extremely important to fortify specific milk components when they are scarce to promote healthy growth of neonates. Because the way that milk is fortified through maternal manipulation depends largely on the concentration of milk substrates de-livered to the mammary glands and the supply of most nutritional components in breast milk such as lipid, protein, vitamin, and other micronutrients (e.g., nicotinamide) can be enhanced by increasing maternal nutrient supplements either orally or intravenously [16].

Another study reported similar to what was seen with other Cd forms, Cd associated with inhaled CdO NP results in renal injury to both directly exposed dam and offspring. As commercial uses for nanotechnology continue to expand throughout the world, risks for unintentional exposure in the workplace increase. Given the large number of women in the industrial workforce, care needs to be taken to protect these already vulnerable populations [17]. Other than this, Cd levels in a study reported below detectable limits in the developing fetus, whole-body Cd levels in offspring had Cd burdens ranging between 0.08 and 0.5 ng Cd/mg body weight (Blum et al., 2012). The study suggested that mammary glands are a site for preferential deposition of Cd during pregnancy, and thus any CdO NP-induced kidney injury in the neonate could be a result of lactational exposure [18]

IV. EFFECT ON MILK YIELD

Generally, the milk yield is determined by offspring weights and weight gains during the peak lactation period according to the previous method [19]. In brief, each day was divided to continuous 6 h and during each period, mother and offspring were separated for 4 h before re-uniting suckling intervals. Daily milk yield was determined based on offspring weight gain during suckling intervals for each day and were further corrected with offspring weight loss. The milk yield with Zn NPs treatment was reduced in the dams compared to the control, whereas other treatments as zirconium and titanium did not alter the milk yield of dams. In terms of milk composition, the Zr and Zn NPs dams had lower milk fat concentrations than the control-dams. The ROS concentrations in the milk of Ti and Zn NPs dams were higher than in those of the control animals. However, the concentrations of albumin, IgA, lactose, protein, SC count, and β-casein in the blood were not affected by nanoparticle exposure. The lower milk fat concentration may be attributed to the lower fat biosynthesis in dams induced by the consumption of Zn and Zr NPs. Relative to dams exposed to nanoparticles through the airway routes, dams exposed to nanoparticles through the oral route showed a lower fat biosynthesis rate, possibly due to a dysfunction of gastrointestinal microbes, which greatly contribute to the supply of milk fat precursors [20]. Finally, exposure to Zn NPs and Ti NPs may lead to increased oxidative stress in mice, which further increased the ROS accumulation in the milk.

Various studies have been done to investigate the effect of dietary supplementation of zinc in lactating animals. In most of the studies, zinc was used either as inorganic form (oxide, sulfate) or organically bound chelated form. There has been an equivocal response of zinc supplements on the yield and composition of milk. Some researchers reported that supplementation of Zn in the diet of lactating dairy animals increased the milk production while others observed no effect of the supplementation. Similarly, a varying response has been reported with respect to concentration of milk constituents [21].

A number of studies have been done to investigate the effect of zinc supplementation on udder health and somatic cell count (SCC). Milk zinc concentration has also been another conflicting area with diverse results. To our knowledge, very rare work has been done to study the effect of nano zinc supplementation in periparturient goats. During periparturient period, animals undergo a series of well-orchestrated metabolic and physiological adaptations to meet the extra demands of body, fetus, and lactation. So, there may be increased demand for zinc due to its role in cell proliferation, tissue growth and maintenance, DNA synthesis, and RNA transcription. The average yield (g/day) of fat, protein, and lactose was statistically similar among all the groups at 30th and 45th presenting no effect of inorganic zinc or nano zinc supplementation. There was no significant effect of inorganic zinc or nano zinc supplementation on milk constituents (%) like fat, protein, lactose, SNF, and ash. The supplementation of Zn either as inorganic ZnO or as nano zinc particles had no effect on milk yield and composition. The results were in agreement with previous studies, wherein there was no effect of zinc supplementation from different sources on milk yield and milk composition in dairy goats or cows was reported [22]. However, contradictory results were also reported in some studies. Hassan et al. reported that milk yield and fat-corrected milk (FCM) were significantly increased for zinc methionate rations compared with inorganic Zn ration. They contributed it to improving of nutrient composition and its digestibility and hence the feeding values of ration. Extra supplementation of zinc has no effect on milk yield and composition [23].

V. NANOMATERIAL IN MAMMAL MILK

Yang et al. also found that the injection of quantum dots in lactating rats reduced the weight gain of their neonates [24]. The biological effect of nanoparticles (TiO_2, ZrO_2, and ZnO) on the health of dams and neonates depends on the particle size. Zhang et al. showed that titanium dioxide nanoparticles injure the mammary gland, which leads to distribution of the nanoparticles to breast milk [25]. Fullerenes were also reported to be distributed to breast milk after intravenous injection to lactating rats, and Ag nanoparticles and titanium dioxide nanoparticles were reported to be distributed to breast- fed pups after maternal exposure during lactation; however, no histologic examination of the mammary gland was performed in these studies. Maternal exposure to titaniumdioxide nanoparticles during lactation has been reported to have biological effects on breast-fed pups [26]. Considering that nanoparticles may be distributed to breast milk, more-detailed safety information, such as information about the properties that determine whether nanoparticles are distributed to breast milk and about whether nanoparticles can transfer to breast milk without injuring the mammary gland, must be collected. Unfortunately, exhaustive studies ofthis nature have not been conducted.

When lactating dams were intravenously injected with Ag nanoparticles, these were distributed to breast milk and subsequently to breast-fed pups. Smaller Ag nanoparticles were more readily distributed to breast milk than were larger nanoparticles. Au nanoparticles could also be distributed to breast milk. Orally administered Ag NPs was also distributed to breast milk and then distributed to and retained in the pups' brains. Despite the retention of Ag in the brain, the offsprings' neuromuscular strength, depression-related behavior, locomotor activity, anxiety-like behavior, pain sensitivity, social interaction, motor ability, motor learning, acoustic startle response, pre- pulse inhibition, gait function, and context memory were not affected by maternal exposure to nAg10 or Ag^+ during lactation [27].

Another study analyzed the transfer of metallic silver nanoparticles through the placenta and breast milk in an in vivo experiment. The accumulation of NPs in rat fetuses and infant rats consuming their mother's breast milk was evaluated. In all cases, authors observed a penetration of the Ag NPs through the placenta and their entry into the mother's milk. The average level of accumulation of NPs in fetuses was 0.085-0.147% of the administered dose, which was comparable to the accumulation of the label in the liver, blood, and muscle carcass of adult animals and exceeded the penetration of NPs across the hematoencephalic barrier into the brain of females. In lactating females, accumulation of Ag NPs into the milk was reported and other absorbed into the gastrointestinal tract of infant rats [28].

VI. CONCLUSIONS

The studies on milk production are rapidly spread over the world due to high nutritional value contains which is very essential for us. Nanoparticle influence was reported on the animal performance, milk performance, mammary glands, milk yield and also affects the bread-fed offspring in the milk production. It was reported that the milk yield with Zn

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REFERENCES

[1] Cenci-Goga, B. T., Karama, M., Rossitto, P. V., Morgante, R. A., & Cullor, J. S. (2003). Enterotoxin production by Staphylococcus aureus isolated from mastitic cows. Journal of food protection, 66(9), 1693-1696.

[2] Bizzarro, M., Baker, J. A., Haack, H., & Lundgaard, K. L. (2005). Rapid timescales for accretion and melting of differentiated planetesimals inferred from 26Al-26Mg chronometry. The Astrophysical Journal, 632(1), L41.

[3] Tiwari A. Frontiers in Bio-Nanocomposites. Adv Mat Lett. 2011.

[4] Torregrosa Paredes P, Gutzeit C, Johansson S, et al. Differences in exosome populations in human breast milk in relation to allergic sensitization and lifestyle. Allergy 2014.

[5] Garcia C, Duan RD, Brevaut-Malaty V, et al. Bioactive compounds in human milk and intestinal health and maturity in preterm newborn: an overview. Cell Mol Biol 2013.

[6] Szuba-Trznadel, A., Rząsa, A., Hikawczuk, T., & Fuchs, B. (2021). Effect of zinc source and level on growth performance and zinc status of weaned piglets. Animals, 11(7), 2030.

[7] Silva, A. L. P., Prata, J. C., Walker, T. R., Duarte, A. C., Ouyang, W., Barcelò, D., & Rocha-Santos, T. (2021). Increased plastic pollution due to COVID-19 pandemic: Challenges and recommendations. Chemical Engineering Journal, 405, 126683.

[8] Matuszewski, S., Hall, M. J., Moreau, G., Schoenly, K. G., Tarone, A. M., & Villet, M. H. (2020). Pigs vs people: the use of pigs as analogues for humans in forensic entomology and taphonomy research. International journal of legal medicine, 134(2), 793-810.

[9] Mekonnen, Z. K., Ashraf, D. C., Jankowski, T., Grob, S. R., Vagefi, M. R., Kersten, R. C.,... & Winn, B. J. (2021). Acute invasive rhino-orbital mucormycosis in a patient with COVID-19-associated acute respiratory distress syndrome. Ophthalmic plastic and reconstructive surgery, 37(2), e40.

[10] Safarzadeh Kozani, P., Safarzadeh Kozani, P., Hamidi, M., Valentine Okoro, O., Eskandani, M., & Jaymand, M. (2021). Polysaccharide-based hydrogels: Properties, advantages, challenges, and optimization methods for applications in regenerative medicine. International Journal of Polymeric Materials and Polymeric Biomaterials, 1- 15.

[11] Bunglavan, S. J., Garg, A. K., Dass, R. S., & Shrivastava, S. (2014). Effect of supplementation of different levels of selenium as nanoparticles/sodium selenite on blood biochemical profile and humoral immunity in male Wistar rats. Veterinary World, 7(12).

[12] Amalraj, A., Pius, A., Gopi, S., & Gopi, S. (2017). Biological activities of curcuminoids, other biomolecules from turmeric and their derivatives–A review. Journal of traditional and complementary medicine, 7(2), 205-233.

[13] Jiang, L., Shestov, A. A., Swain, P., Yang, C., Parker, S. J., Wang, Q. A., ... & DeBerardinis, R. J. (2016). Reductive carboxylation supports redox homeostasis during anchorage-independent growth. Nature, 532(7598), 255-258.

[14] Sachs, H. C., Committee on Drugs, Frattarelli, D. A., Galinkin, J. L., Green, T. P., Johnson, T., ... & Van den Anker, J. (2013). The transfer of drugs and therapeutics into human breast milk: an update on selected topics. Pediatrics, 132(3), e796-e809.

[15] Southall, B. L., Finneran, J. J., Reichmuth, C., Nachtigall, P. E., Ketten, D. R., Bowles, A. E., ... & Tyack, P. L. (2019). Marine mammal noise exposure criteria: Updated scientific recommendations for residual hearing effects. Aquatic Mammals, 45(2), 125-232.

[16] Famouri, F., Shariat, Z., Hashemipour, M., Keikha, M., & Kelishadi, R. (2017). Effects of probiotics on nonalcoholic fatty liver disease in obese children and adolescents. Journal of pediatric gastroenterology and nutrition, 64(3), 413-417.

[17] Stevens, E., Jason, L. A., Ram, D., & Light, J. (2015). Investigating social support and network relationships in substance use disorder recovery. Substance abuse, 36(4), 396- 399.

[18] Blum, K., Chen, A. L., Giordano, J., Borsten, J., Chen, T. J., Hauser, M., & Barh, D. (2012). The addictive brain: all roads lead to dopamine. Journal of psychoactive drugs, 44(2), 134-143.

[19] Bergin, I. L., & Witzmann, F. A. (2013). Nanoparticle toxicity by the gastrointestinal route: evidence and knowledge gaps. International journal of biomedical nanoscience and nanotechnology, 3(1-2).

[20] Shrivastava, D., Singhai, A. K., & Yadav, R. K. (2014). Effect of lime and rice husk ash on engineering properties of black cotton soil. Int. J. Eng. Res. & Sci. & Technology, 3(2), 292-296.

[21] Wu, Y., Liang, D., Wang, Y., Bai, M., Tang, W., Bao, S., & Li, J. (2013). Correction of a genetic disease in mouse via use of CRISPR-Cas9. Cell stem cell, 13(6), 659-662.

[22] Mousavi, S. S., YAZDI, S. B., Naghavi, M. R., Zali, A. A., Dashti, H., & Pourshahbazi, A. (2008). Introduction of new indices to identify relative drought tolerance and resistance in wheat genotypes.

[23] Hassan, M. K., Sanchez, B., & Yu, J. S. (2011). Financial development and economic growth: New evidence from panel data. The Quarterly Review of economics and finance, 51(1), 88-104.

[24] Liu, H., Simonyan, K., & Yang, Y. (2018). Darts: Differentiable architecture search. arXiv preprint arXiv:1806.09055.

[25] Zhang, C.; Zhai, S.; Wu, L.; Bai, Y.; Jia, J.; Zhang, Y.; Zhang, B.; Yan, B. Induction of Size-Dependent Breakdown of Blood-Milk Barrier in Lactating Mice by TiO2 Nanoparticles. PLoS One 2015, 10, e0122591.

[26] Gao, X.; Yin, S.; Tang, M.; Chen, J.; Yang, Z.; Zhang, W.; Chen, L.; Yang, B.; Li, Z.; Zha, Y., et al. Effects of Developmental Exposure to TiO2 Nanoparticles on Synaptic Plasticity in Hippocampal Dentate Gyrus Area: An in Vivo Study in Anesthetized Rats. Biol. Trace Elem. Res. 2011, 143, 1616-1628.

[27] Fujiwara, S., Yarai, H., Kobayashi, T., Morishita, Y., Nakano, T., Miyahara, B., ... & Une,H. (2016). Small-displacement linear surface ruptures of the 2016 Kumamoto earthquake sequence detected by ALOS-2 SAR interferometry. Earth, Planets and Space, 68(1), 1-17.

[28] Melnik, E. A.; Buzulukov, Y. P.; Demin, V. F.; Demin, V. A.; Gmoshinski, I. V.; Tyshko, N. V.; Tutelyan, V. A. Transfer of Silver Nanoparticles through the Placenta and Breast Milk During in Vivo Experiments on Rats. Acta Naturae 2013, 5, 107-115.