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EFFECT OF NANOMATERIAL ON ANIMAL AND HUMAN HEALTH : A REVIEW

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Abstract

Nanotechnology is science that deals with the applications, which related to the scientific knowledge of the control and manipulation at in nanometric (1-100) nanometer at molecular, atomic and cell level. The nanostructures showed specific chemical and physical properties and it revealed high solubility, stability and reactivity. All nanoparticles application is depended on the Nanobiotechnology that has an important role in the diagnosis of the diseases, drug manufacturing. Nanotechnology has an important role in veterinary medicine, animal health and diseases treatment. It used in control some diseases such as FMD in the ruminants in the United Kingdom. By using smart drug delivery applications this will provide the complete program in the determination of the time and dose of drugs.

There are also silver nanoparticles used for coating and applied to many medical devices such as wound dressing drains and catheters for reduction the contamination during the operation. Although silver nanoparticles cause genotoxicity, oxidative stress, a disorder in production of the cytoskeleton, stimulation of lysosomal AcP and activation of the phagocytosis in RBC and increase the activity of the MXR transport and inhibition of sodium-potassium-ATPase in the fish. In addition, the fishes affected by the side effect of silver nanoparticles that included pathological change of the gills due to inhibition of sodium+ potassium+ ATPase.

In doges, prostate cancer is a dangerous disease but there is a new formulation of gold nanoparticles for the disease treatment. That new have very small dose, it smaller than the chemotherapy, so do not lead to tissues damage.

Key words: nanomaterial side effect, nanoparticles, public health, nanotechnology.

Nanomaterial Preparation:

There are many methods for the preparation of the nanomaterial. Its synthesis is developed within the time due to the continuous studies that discuss the topic. Each method required specific material, particular geometry. With the development of the shape and size of the material, will results in the production of new synthetic methods. The artificial methods classified to bottom-up and top-down approaches. There are four generic methods for making the nanomaterial:

1. The wet chemical methods
2. The mechanical processes
3. The form-insitu
4. The gas-phase deposition

Based on the chosen method and material type result in the material have different chemical and physical properties (Jackson *et al*., 1998; Kunzmann *et al*., 2008).

Effects of nanoparticles on Terrestrial Animals Species:

On Mammals:

The mammals exposed to nanoparticle silver every day and can get in the body by skin and inhalation (Oberdörster *et al.,* 2005 and Teli *et al.,* 2010). After it, penetrate the body, nanoparticle silver gets inside the cell. When the nanoparticle silver inhaled, it reaches to the nervous tissues especially the olfactive epithelium tissue. Nanoparticle silver reaches to the blood, lung and brain. In addition, it reaches to spleen, bone marrow, heart and lymph nodes. Nan particle silver causes activation of the inflammation, antioxidant component, mitochondrial distribution and oxidative stress (Oberdörster *et al.,* 2005 and Ramos *et al.,* 2017).

There are harmful effects of nanoparticle silver in mice and rat brain. Exposure to the Cu-nanoparticles at (40-60) Nanometer in the rat causes multiplication of the

brain endothelial cells if administrated at (1.5) μg/mL. It is given at (50) μg/mL leading to increase of prostaglandin E2. ILβ and TNFα were produced at large amount (Trickler *et al.,* 2012). Exposure of the rat to Ag-nanoparticles for one day showed an increase of the proinflammatory reaction, brain inflammation (Trickler *et al.,* 2010). Nanoparticle silver (25-40) nanometer caused cytotoxic effects (Trickler *et al.,* 2010).

Ag-nanoparticles (7.5) nm in the adult rat causes a decrease in the locomotor activity (Zhang *et al.,* 2013). Harmful effects of nanoparticles on the brain of the rat have included an increase in permeability of brain-blood barrier, production of cerebral oedema and disorder in the brain blood fluxes. There is a large change in glial cells, increase neurons injuries and decrease of the myelin fiber. Cu-nanoparticle and P and Ag-nanoparticles at (50-60) nm were more important from Al-nanoparticle at (50-60) nm in mouse and rat (Sharma *et al.,* 2009).

In pigs, there are pathological changes (25, 40, 80) nm Ag-nanoparticle, (40, 60) Cu-nanoparticles and (3-5) nm Au-nanoparticles on the barrier between the blood and the brain (Trickler *et al.,* 2014). Acetylcholine disorder, production of (NO) and hyperactivity of smooth muscle of the trachea occurs in the rat due to administration Ag-NPs (45) nm (González *et al.,* 2011).

Administration of Ag-NPs at (25) nm in the mouse by injection at (100-500 mg/kg) induce the oxidative stress. Nanoparticles accumulated in kidneys, lungs and spleen red pulp (Genter *et al.,* 2012, Genter). Au-nanoparticles effects (5-15) nm in diameter were tested on the mouse fibroblasts. Nanoparticles are getting in the fibroblasts cell wherever the smallest (5) nm causes toxic effects on the cells shape and the cytoskeleton function disorder. The cells which exposed to Au-nanoparticles for (72) hours showed disorder in cytoskeleton protein and clathrin heavy chain (Coradeghini *et al.,* 2013). Se-nanoparticles (80-200) nm used for protecting the endotracheal tube against bacterial infection and don't cause any side effects on the fibroblast cell (Ramos and Webster, 2012).

Effects of nanoparticles on Semiaquatic Animals (Amphibia):

The amphibians are having three category caecilians, urodelans and anurans. Gills are used for breathing, the intestine is long with loops because it has a herbivorous diet and has a tail and caudal fin for swimming. The embryo gills of the fishes and the lung tissues are should examine for detection effects of nanoparticles, the heart will be distorted. The tail regresses in anurans but persists in urodelans and sometimes in caecilians. Front and back limbs develop in urodelans and anurans (Van der Ploeg *et al.,* 2014 and Troncarelli *et al.,* 2013). The amphibians are good models for studying effects of nanoparticles on the thyroid gland and pituitary gland. Some of the reports found the nanoparticles causes stress and have a negative effect on thyroid hormones in the laboratory in Rana catesbeiana (Hinther *et al.,* 2010 and Hammond *et al.,* 2013).

The effects of silver nanoparticles, silver nanoparticles aggregates and zinc oxide-nanoparticles on many gene expressions are studies by using qPCR. Results were included studying comparative effects of tissues that exposed to silver nitrate, silver particles measuring several μm and Cd telluride particles measuring several μm. Silver nanoparticles and small aggregates affected the expression of gene related to (T3), with several stress molecules. ZnO-NPs does not cause any side effect. Little levels of sliver nanoparticles cause disrupted in T3 (Hinther *et al.,* 2010).

Titanium oxide nanoparticles effects are tested in the lab in Lithobates catesbeianus that included the gene expression of receptors of the thyroid hormones (thra and thrb) gene, for larval keratin type I (rlkI) gene, stress proteins (hsp30) gene, superoxide dismutase (sod) gene and catalase (cat) gene. The significant changed was found if the models exposed to nanoparticles (20) nm NPs (Hammond *et al.,* 2013 and Shin SH *et al.,* 2007).

Xenopus laevis revealed the toxicity of copper has several forms: CuO-NPs (6) nm, Cu^{++} and aggregates of copper oxide-nanoparticles (100) nm. The cellular toxic effects were depended on the type of the material and stage of the cell cycle. Three types of substances used for mitotic cells for stopped their division with increasing of the apoptotic cells after two days, six-day and seven days. Wherever there are marked decreasing of cell division and the apoptosis increasing (Thit *et al.,* 2013).

The embryo developing in the amphibians revealed weak lethal influence in high concentrations. The embryo doesn't die due to copper, titanium and zinc nanoparticles but causes teratogenic effects in the intestine if the concentrations were more than (50) mg/L. Zinc oxide nanoparticles have severe effects on the intestinal lead to the passing of the nanoparticles to the connective tissue. Titanium oxide-nanoparticles causes hidden physiological effects and teratogenic effects (Bacchetta *et al.,* 2012).

The toxic effects of titanium oxide-nanoparticles are evaluated if it was less than (50) nm, wherever revealed the mortality lesser than 11% in (Rana perezi). The important effects were found on melanin and lactate with high stress. Titanium-selenium-oxide-nanoparticles causes long-time effects on used animals (Salvaterra *et al.,* 2013).

Nanoparticles harmful effects showed that zinc oxide-nanoparticles t (40) nm or more could develop the visual ability. The electroretinograms are used for evaluation of nanoparticles. It showed increased the wavelength if they were exposed to the light. ZnO -nanoparticles is an improvement of visual sensitivity and decrease the time of rhodopsin regeneration (Wahid *et al.,* 2013).

If the earthworms exposed to Au-nanoparticles (10-20) nm, leads to distribution Au-nanoparticles are found in many organs of the frog such as muscle, intestine, spleen, liver, stomach and kidney because the bullfrog ingested fed with earthworms (Unrine *et al.,* 2012 and Ravenzwaay *et al.,* 2009).

Effects of NPs on Aquatic Animals:

Large amounts of nanoparticles are detected in fishes and some the marine organism. Many studies showed that aquatic organisms affect by the nanoparticles. New studies found that nanoparticles are a new pollutant and its effects depended on its size. Many studies founded there are negative effects of nanoparticles on the invertebrates and the fishes. Several animal models were used for evaluation of the effects of the nanoparticles (Matranga and Corsi 2012). Onchorynchus mykiss (trout) and Danio rerio (zebrafish) in bony fish used for evaluation nanoparticles effects.

On Fish:

The salmon's fish are exposed to nanoparticles Ag with $AgNO_3$ reduced with NaBH4. Ag-nanoparticles are deposed in fish gills at (3-220) nm size. However, all the experiment showed Ag nanoparticles accumulation except if the nanoparticles level was less than (1) μg/L. The stress depended on nanoparticles concentration in the gills. Sodium +/potassium + ATPase inhibited based on the depending on the disorder of the osmoregulation. Ag-nanoparticles at (100) μg/L causes necrosis of gill and mortality was 73% (Farmen *et al.,* 2012).

The nanoparticles may be one element or element oxide or more many metals. Furthermore, the chemical properties of nanoparticles silver related with both the aggregation dynamics and the metal ions equilibrium. The acute toxicity of metal nanoparticles silver related to the free ions. Some studies revealed nanoparticles stimuli the causes dyeing of the fishes if the nanoparticles level was varied between (μg/L) to (mg/L) in the around. Some types of fish showed high toxicity by metal-NPs than others. Nanoparticles cause lethal effects like oxidative stress, decreases Na+/K+ ATPase, disruption of tissue elements and breath toxicity (Shaw and Handy, 2011).

The intestine, gills, brain and liver are organ showed pathological changes by nanoparticles and metal salts. Ag-nanoparticles pass the chorion and reach to the egg and embryo. Cu-nanoparticles and ZnO-nanoparticles are more toxic for juveniles and embryos than the corresponding salt because it interferes the metal nanoparticles with corresponding stress (Shaw and Handy, 2011).

Nanoparticles mechanical effects on the fish are studies before the 2000s. The mechanical effects are included metabolism, distribution, absorption and excretion. All the effects are studied and examined in titanium oxide-nanoparticles on many organs such as the gut, adrenal gland, gills and liver. Nanoparticles get in the cell by endocytosis. The kidneys are secret the nanoparticles but at the little amount but the larger amount secret by the bile (Fernández-Cruz *et al.,* 2013).

ZnO-nanoparticles have effects on the hepatocyte of fish and human, wherever it results in high toxicity for the cells (Fernández-Cruz *et al.,* 2013). The comparative study is applied *in vivo* zebrafish and *in vitro* human hepatocytes revealed, that the Ag-nanoparticles silver (120) nm in diameter causes oxidative stress of the liver cells such as increases in INFα, ROS and endoplasmic reticulum and there are increases in Bax and p53 genes. Many differences were found between fish and human liver cells and leading to ER modification. The zebrafish embryos that exposed to Ag-nanoparticles showed malformations (Christen *et al.,* 2013).

The zebrafish reveals Ag-nanoparticles at different sizes (12-28) nm causes neurotoxic effects and interfere with embryo development (Powers *et al.,* 2011). Ag-nanoparticles (1-20) nm has deep effects on the nervous system of zebrafish embryos wherever Ag ions released by Ag-nanoparticles and caused increasing of the malformations. Ag-nanoparticles caused inhibition of the acetylcholine (Myrzakhanova *et al.,* 2013).

Ni-nanoparticles cause the malformations in zebrafish embryos and high mortality. Ni-nanoparticles make the intestine is thin, but Ni solution has no effect. The muscles were affected by Ni-nanoparticles (30, 60, 100) nm. Therefore, Ni-nanoparticles toxicity causes little different from soluble nickel. Ni-nanoparticles (60) nm was toxic on muscles and intestine. Furthermore, Ni (NP, aggregates, or ion) was very important than its size (Ispas *et al.,* 2009). Au-nanoparticles (10) nm was distributed in all tissues of zebrafish embryos. The malformations are occurred due to the spreading of Au-nanoparticles inside the cells during the development. The chemical properties cause the toxicity, Au-nanoparticles have toxicity than Ag-nanoparticles, so, zebrafish embryos used as models in the lab (Browning *et al.,* 2009).

Zebrafish is a good model to make nanoparticles studies, also trout fish used for similar propose. TiO2-nanoparticles and C-nanoparticles were used in studies related to the liver cell in trout. The experiments revealed that nanoparticles were demonstrating ecotoxicological effects. Very amount of elements were causes the toxic effects (Thomas *et al.,* 2011).

Juvenile trouts were administrated many levels of $CuSO_4$ nanoparticles and Cu-nanoparticles. $CuSO_4$-NPs was accumulated in the gills depending on the concentration. However, there is no $CuSO_4$ nanoparticles and Cu-nanoparticles both in muscle, brain, spleen. Cu and Cu-nanoparticles were not toxic and there is a decrease of sodium+/potassium+ ATPase was found in intestine and brain, also Cu-Nanoparticles have toxic effects (Shaw *et al.,* 2012).

TiO2-nanoparticles (20) nm causes many pathological changed in the gills of the exposed onchorynchus mykissm it included gill lamellae thickness and oedema. Metal content in tissue was not affected except for Cu and Zn according to the NPs concentration and more especially in the brain. Na+/K+ ATPase was decreasing in intestine and gills. The thiobarbituric acid level is increased in the brain and the gills. The lipids were showed little change in the liver cell (Federici *et al.,* 2007).

The liver cell affects by Ag-nanoparticles by decrease the metabolism. Au-nanoparticles increased ROS concentration without cell toxic influence (Fouqueray *et al.,* 2013).

TiO2-NPs (25) nm is given for Danio rerio embryos and larvae during the development. At the early stage, the nanoparticles were eaten with food. The fishes were fed with algae exposed to TiO2-nanoparticles; caused hatching was before the mature. The contaminated food by nanoparticles causes changes in the digestive physiology after two weeks of exposure (Fouqueray *et al.,* 2013).

On human:

The human bodies have many immune mechanisms for removing all foreign particles. The immune mechanism is included in two types:

1. The chemical dissolution

2. The physical translocation is included transporting the particles from place to another.

Low-solubility and insoluble particles accumulate in the lung tissues and get out by translocation outside the body. The mucociliary remove the particles that deposited in the respiratory system especially in the tracheobronchial region. Trachea and bronchi membranes are lined by ciliated cells that eliminate the mucus containing the particles during less than one day (Kreyling *et al.,* 2002 and Abu-Elala *et al.,* 2018).

In the lung tissue, the macrophages ingest the insoluble particles by a process called the phagocytosis. The macrophages digest the particles and then remove it by the mucociliary escalator. This mechanism is slow and has a half-life of 700 days in the human being (Oberdörster, 2005). The phagocytosis efficiency is depended on particle size and shape. Many reports revealed aggregated particles in the alveolar tissue not phagocyted by the macrophages (especially the particles have less than (70) nm in diameter (Bergeron and Archambault, 2005). The macrophages have high activity in the particles that have a diameter more than (1-3) micrometre (Tabata and Ikada, 1988).

The nanometric dust often is uptake by the macrophages that causes major aggregative of the particles in the alveolar cells. Many reports revealed that some particles could pass over the epithelium layer to deep interstitial tissue (Borm *et al.,* 2004). It is most common in monkeys and doges more than the rodents (Kreyling and Scheuch, 2000). If it passes the epithelium layer, the particles reach the lymphatic nodules.

There are several of the pathological changes of the cardiovascular and the lungs such as inflammation, asthma, cancer, atherothrombosis, pulmonary fibrosis and chronic obstructive lung disease (Donaldson and Tran, 2002). For that, the particles could cause inflammation. Many studies showed that inflammatory effects of nanoparticles and causes cell stimulation and cell damage (Donaldson *et al.,* 2000), those same effects of titanium oxide, carbon black and polystyrene (Duffin *et al.,* 2002). The particles cause inflammatory effects depending on the type and surface area dose of the particles. The surface area dose-related inflammatory response is linked to transition metals but is found with low-toxicity substances, the particles can form oxidative stress and free radicals (Wilson *et al.,* 2002).

The surface area doses cause inflammation by many pathways such as stress-responsive gene transcription. In the exposed cell to the nanoparticles, the oxidative stress is become high also, stimulation of oxidative stress-responsive transcription agents (AP-1 and NF-κB) (Mroz *et al.,* 2008; Stoeger *et al.,* 2009). Many types of nanoparticles cause inflammatory effects at unknown mechanisms (Lu *et al.,* 2009).

The Nanomedicine provides the possibility of early diagnosis and treatment of the diseases by using nanoparticles sliver. Nanotechnology developed Commercial and its applications reduce human health

hazards without any secondary side effects of NPs. The toxicology is science that study and showed general details of toxic substances related to human health. We do not have complete knowledge about the toxic effects of nanoparticles. The toxicological and pharmacokinetic studies are should make before industrial production. The International Life Sciences Institute Research Foundation, The U.S. Environmental Protection Agency and the Risk Science Institute regulated working teams have experts in the nanotechnology to develop reporting, new toxicity tests for hazard determination of nanoparticles (Oberdörster *et al.,* 2005).

In spite of the benefits of nanotechnology, so we should not neglect the negative possible side effect on human health. There are many studies found a relationship between high morbidity and UFP exposure is compromised person and elderly. Moreover, the new studies found there are impaction variations during the days on particles levels and exposures for a short time as an important agent in cardiac activity. Spreading of the nanotechnology in the world, air pollution could occur.

The nanotechnology will be more active in future, due to the great impact on many applications related to human life such as water purification, contamination removing and cheaper power. Information lack is the major challenge that fronts developing of the nanotechnology that leads to the negative effect those results from nanoparticles exposure. If the general principles of nanotechnology safety are applied as guidelines by government and control and regulating all steps this manufacturing is mandatory to stimuli the nanotechnology for development.

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