

IMPORTANCE OF ZINC COMPOUNDS AND ZINC NANOPARTICLES IN DEVELOPMENT OF PLANTS

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Abstract

Global warming, plant diseases and environmental issues such as excessive use of pesticides and fertilizers have affected the production yield in the agricultural sector. Promoted in the last decade or so, nanotechnology has been offering sustainable solutions to conventional agriculture, having a major impact on improving crop productivity and nutrient supply by increasing and regulating the availability of minerals in the soil. Thus, zinc oxide nanoparticles are widely used in agriculture, due to the multiple roles of zinc in the plant cell, such as the involvement in regulating the metabolism of the proteins, lipids, sugars, and nucleic acids, its enzymatic cofactor activity for some enzymes involved in photosynthesis, or being key element in cellular biomembranes. Although the widespread use of nanoparticles can lead to phytotoxicity phenomena, the research direction in recent years is focused on balancing positive and negative effects. Therefore, the aim of this paper is to update the informations about the applications and the effects of zinc compounds and zinc oxide nanoparticles in agricultural practices.

Key words: agricultural practices, development of plants, nanotechnology, zinc oxide nanoparticles.

INTRODUCTION

Nanotechnology is a continuously developing technology that can lead to a new change in every field of exact sciences (Rico, 2011). This kind of technology is used in association with optics, electronics and medical and material sciences.

Multiple researches in this field have taken a great and unexpected scale in recent years by providing innovative solutions in different scientific disciplines. Nanotechnology offers with nanoparticles which are molecular or atomic aggregates characterized by the size less than 100nm. They are actually a modified form of basic elements derived by their atomic modification, also as molecular properties of the elements (Daniel, 2004).

Nanoparticles have gained significant interest due to their unusual and fascinating properties, with diverse applications, over their bulk counterparts (Kato, 2011).

Agricultural technologies have changed significantly in recent decades. Nanotechnology has a great influence on agriculture. The direction of research in recent years is moving towards nanoparticles because they increase the availability of nutrients in the soil.

Nanoparticles are, in fact, derived from modifying the molecular and atomic properties of basic substances (Moezzi et al., 2012).

Among the nanoparticles used in agriculture, the most common are those based on metal oxides: zinc oxide, cobalt oxide, cadmium oxide, magnesium oxide. Zinc oxide is used in many fields thanks to its specific properties. Many fields, such as the plastics industry, the cosmetics industry, agriculture, use zinc oxide as an additive. Being so used, zinc oxide can reach the environment, where it can accumulate and cause the occurrence of phytotoxicity phenomena. In agriculture, zinc oxide is used in appropriate concentrations to enhance crop production of various plants, zinc having basic functions in plants (Garcia-Lopez et al., 2018). New agricultural technologies are the fundamental basis of the structure of the third world economy, but unfortunately, nowadays, this sector faces various global challenges, such as: climate change, urbanization, sustainable use of resources and environmental problems, environmental accumulation of pesticides, fertilizers (Sabir et al., 2014).

Taking into account that the world's population is constantly growing and the demand for food is increasing, agriculture is a major concern.

There are more than 3.5 billion people who suffer from micronutrient deficiency, so research is directed towards finding solutions by which the intake of micronutrients can be replaced (Graham et al., 2001)

The agricultural application of nanotechnology has as its main goal a better absorption of substances by plants having a great impact on protecting the environment and balancing the economy.

Nanoparticles have a very high potential in terms of increasing productivity in agriculture, especially in the field of nano-fertilizers. Nano-fertilizers are encapsulated mineral nutrients that are more easily absorbed by plants than conventionally used fertilizers. Most of the time the problem with nutrients is not represented by their lack in the soil, but by how the plants can absorb them and how much they are available (Akanbi-Gada et al., 2019).

Tech-Nano has a big role to play in changing conventional farming practices in the idea of enhancing crop productivity. Many of the agrochemicals applied to crops are lost and do not reach the originally proposed target. Nanoparticles are a better and more controllable way to deliver nutrients where needed and reduce side effects (Sabir et al., 2014).

In the last decade, nanoparticles based on metal oxides, such as ZnO or CoO, have been used on a very large scale in many fields. In particular, the physicochemical properties of cesor nanoparticles allow their use in multiple fields.

There are several types of zinc nanoparticles such as ZnS, ZnSe or CdSe/ZnS nanocrystals. However, probably the most used type of nanoparticle is zinc oxide (nano-ZnO). Nano-ZnO is used in many fields of industry, cosmetics, medicine, being characterized by the following attributes: high electrical conductivity, high stability at high temperatures, antimicrobial, antifungal, catalytic and photochemical effects, a high optical absorption in UV, which gives it significant importance in the area of cosmetics (Moezzi et al., 2012).

Being used daily in a wide range of fields, these nanoparticles end up in the environment where they can cause real hazards. It is estimated that 1100 tons of cosmetics and skin care products containing ZnO are produced annually and approximately 25.5% of these end up being "discharged" into the aquatic environment. The

potential toxic effects on plants of nanoparticles include a large number of factors such as: concentration of nanoparticles, their size, surface structure, physicochemical properties, plant species, growth environment, nanoparticle stability (Keller et al., 2010).

THE ROLE OF ZINC IN METABOLISM; CONSEQUENCES OF ITS DEFICIENCY OR EXCESS

Zinc is an fundamental micronutrient for humans and animals and is extensively involved in carbohydrates protein, lipid, nucleic acid metabolism, and gene transcription (McClung et al., 2019). Its role within the human body is extensive in immune function, reproduction, and wound repair. At the microcellular area, it has a role significant effect on the normal functioning of macrophages, neutrophils, natural killer cells, and complement activity (Fallah et al., 2019; Skalny et al., 2018).

Even if it is one of the most abundant trace elements in the human and animal body, zinc cannot be stored in significant amounts and hence requires regular intake or supplementation. Zinc is found in a lot of foods, including meat, fish, legumes, nuts, and other dietary sources, although its absorption varies by the substrate carrying it.

Zinc deficiency is a major health problem worldwide, especially in developing countries. Hence, it is designated by the World Health Organization as a major disease contributing factor (Narváez-Cacedo et al., 2018; Santos et al., 2017). Zinc deficiency can present with growth impairment, some dysfunction, inflammation, gastrointestinal symptoms, or cutaneous involvement (Sanna et al., 2018).

Since it does not undergo reversible valence changes, the role of zinc in redox processes in plants is less important than that of iron or manganese. Being integrated in the structure of some carbohydrates, zinc also plays a role in the respiratory process. It is involved in the activity of enolase, which participates in carbohydrate metabolism and takes part in the process of chlorophyll synthesis (Palacios et al., 2006).

Zinc plays an essential role in stimulating the activity of auxins. In zinc deficiency,

peroxidases accumulate, causing the oxidation of auxins, which implicitly decrease their amount and activity (Akbar et al., 2021). Zinc also is involved in the metabolism of tryptophan. It activates the enzyme systems which catalyzes the biosynthesis (tryptophan synthetase) and degradation (tryptophan peroxidase) of tryptophan, especially the synthesis of heteroauxin. Stimulates protein biosynthesis, P vitamin biosynthesis, fruit and seed development (Broadley et al., 2012).

Zinc is a cofactor and activator for numerous enzymes (dehydrogenases, phosphatases, phosphodiesterases, carboxypeptidases, carbonic anhydrase, enolase). Zinc influences the stability of ribosomes, their tertiary and quaternary structure, the biosynthesis of cytochrome C (Lilburn et al., 2015).

The action of zinc on phosphodiesterases, including the hydrolysis and denaturation of deoxyribonucleic acid can be substituted by magnesium, cobalt and calcium (Auld, 2005).

Copper, zinc, manganese, iron play an fundamental role in antioxidant defense as an integral part of superoxide dismutase (SOD). Copper, manganese, iron, and of course zinc ions are very interesting because they exert a positive effect on the respiratory activity and the growth rate of *Saccharomyces cerevisiae* (Barbulescu et al., 2010).

Zinc is an essential element for glutamyl reductase and for carbonic anhydrase, alkaline phosphatase, thymidine kinase, lactate dehydrogenase, etc. It stimulates the activity of vitamins B and A (Barker et al., 2015).

Zinc contributes to the binding of cell walls by means of pectic substances and to the union of different cell constituents. More recent research shows that zinc stimulates chlorophyll biosynthesis and function, starch biosynthesis and tree fruiting (Samreen et al., 2017).

In humans, zinc is involved in the formation of red blood cells, stimulates and regulates the functioning of the pancreas, pituitary gland, genital glands and prostate. The daily requirement for an adult is 15 mg. Zinc is a stabilizer of the functions of cell membranes and lysosomes. It inhibits osmotic hemolysis of erythrocytes, as well as lipid peroxidation in the liver. Zinc also interacts with the body's accumulation of vitamin E, vitamin B12, vitamin C (Stoican et al., 2021).

Zinc deficiency in plants causes growth reduction, decreasing of the phytohormones content, especially auxins, and the accumulation of some phenolic substances that are toxic and calcium oxalate (Benglsson et al., 2003).

Zinc deficiency lead to fruit fall, to yellow spots formation on the leaves, to shortening of the internodes in cereals, etc. Corn, citrus fruits, tobacco, fruit trees, beans, peas, onions are sensitive to zinc deficiency. Zinc deficiency is manifested by stopping of plant growth as a result of the lack of auxins. The internodes of the plants remain short, the chlorotic leaves become small and arranged in a rosette (Hafeez et al., 2013). Zinc plays an important role in the fruiting process; when zinc is insufficient, the plants grow weakly and do not fruit or when they do, the seeds are small (Constantinescu et al., 1991).

It seems that zinc is necessary for both growth and normal chlorophyll synthesis. It participates in the synthesis of auxin, contributes to the accumulation of tryptophan and improves water exchange (Benglsson et al., 2003).

Food sources richer in zinc include: meat, yeast, cereal seeds, pollen, pumpkin seeds, eggs, milk, beetroot, spinach, cabbage (Salgueiro et al., 2000).

In humans, zinc deficiency causes growth retardation, changes in taste and smell, loss of appetite, skin lesions, eye disorders, delayed sexual maturity, prostate enlargement, etc. In prostate cancer the zinc content drops a lot. A similar action occurs in liver diseases, alcoholic cirrhosis, ulcers. Component of more than 70 metalloenzymes from the group of dehydrogenases, peptidases and proteinases, activator of enzymes such as: enolase, dipeptidases, zinc is present in the entire animal body and, without a doubt, many diseases are the consequence of the low level of activity of one or more enzymes that contain or are influenced by zinc.

In animal organisms, zinc deficiency causes a reduction of vitamin A in the plasma and an inhibition of retinol protein synthesis, important in the process of vision and adaptation to darkness.

Excess zinc has serious consequences for human health. High zinc concentration inhibits iron absorption and transport. Iron, as a part of hemoglobin structure, is of major importance in

the metabolism of mammals. High dietary zinc affects iron metabolism in two ways: by affecting ferritin to incorporate or release iron from ferritin, and by decreasing iron absorption and decreasing the amount of iron stored in ferritin (Roohani et al., 2013).

ZINC UPTAKE AND TRANSLOCATION IN PLANTS

The absorption of the Zn^{2+} ion proceeds initially as a physical process of ion exchange and diffusion. Zinc absorption is strongly reduced in case of low temperatures, in conditions of anaerobiosis and water stagnation. Absorption increases with increasing zinc concentration in the nutrient solution (Hafeez et al., 2013).

It is necessary to fertilize corn, soybean, bean, pea and potato crops with zinc and organic complexes with zinc, because by the annual use of nitrogen and phosphorus fertilizers in large doses, the zinc content of the soil decreases, with negative repercussions on plant growth, due to the decrease in the biosynthesis of tryptophan and auxins (Rico et al., 2011). The absorption of zinc from the soil solution is greatly influenced by the pH.

The acidic reaction of the soil favors the solubility of zinc compounds and the dissociation of the absorbent zinc-clay complex from the soil. Because of this, acidic forest and forest-steppe soils have a higher content of soluble zinc than neutral and alkaline soils (Alloway, 2009).

In the conditions of areas with strong light intensity and increased temperature, the symptoms of insufficient zinc nutrition appear more frequently. In less intense light, zinc assimilates better. At an acidic pH of the culture medium (5.5-6.5), the availability of zinc for plants decreases. Under the conditions of a neutral or basic culture medium, it can be precipitated in insoluble forms, as zinc phosphate. At a pH above 7.8 zinc becomes somewhat more accessible (Butnariu, 1992).

FERTILIZERS BASED ON ZINC ION

Micronutrients are basic substances for the living world. Zinc, copper, iron, magnesium, cadmium,

cobalt are fundamental substances in the case of plants and animals (Gupya & Kalra, 2006).

Only this metal, zinc, is found in all six classes of enzymes: oxidoreductases, transferases, hydrolases, lyases, isomerases, ligases. It is a fundamental element for animals and plants (vegetables and fruits). Zinc is considered to be the fourth most important nutrient limiting crop production (Prasad, 2012; Datcu et al., 2019).

In soil, the amount of total zinc averages between 0.004 and 0.02% of the total atoms in the Earth's crust. It is found mainly in isomorphic forms in augite, hornblende, biotite, magnesite. For normal plant growth, it is necessary that in the soil solution or in the nutrient solution, zinc is found in concentrations of 0.25-3 ppm. In exchangeable form, it is found that Zn^{2+} and $\text{Zn}(\text{OH})^+$ are found in the absorption process in plants (Alloway, 2009).

Heavy soils and those with a neutral or basic reaction have a higher zinc content than sandy and acidic soils. Humus-rich soils are also rich in zinc. The amount of mobile zinc compared to the amount of total zinc represents on average 1.5-7% in mineral soils and 15-60% in acid peat and forest soils. The presence of zinc, as well as manganese, copper or fluorine increases the resistance of plants to the increased concentration of soluble salts in the soil solution. Supplying plants with zinc increases their resistance to drought and frost (Bengtsson et al., 2003).

A concentration higher than 3 ppm zinc in the nutrient solution can be toxic to certain plants, especially in acidic soil conditions. An excess of zinc hinders the assimilation of iron. For many crops, good results are obtained by applying zinc fertilizers to the soil.

The application must be repeated every year and during the same year every 2-3 weeks. Concentrations ranging from 0.015 to 0.3% zinc in the nutrient solution are used (Alloway, 2008).

Traditionally, in agriculture, zinc fertilizers are used as:

- zinc sulfate ($\text{ZnSO}_4 \times 7\text{H}_2\text{O}$) with 22.8% Zn (crystallized salt in the rhombic system, colorless, soluble in water 96.5 mg/100 ml);
- zinc chloride sludge (with a content of 4-6% Zn, zinc chloride particularly soluble in water, 432 mg/100 ml);

- zinc oxide with 78% Zn (white-yellowish, amorphous, hardly soluble in water, 0.16×10^{-3} mg/100 ml);
- zinc carbonate, with 52% Zn (colorless, crystallized in the trigonal system, hardly soluble in water, 10-30 mg/100 ml);
- zinc orthophosphate [$\text{Zn}_3(\text{PO}_4)_2 \times 4\text{H}_2\text{O}$], with 51% Zn (insoluble in water);
- superphosphate enriched with zinc, with a content of 0.8-1% Zn;
- zinc frit (soluble glass), contains 10-12% Zn;
- zinc lignosulfonate, contains 5% Zn;
- zinc polyflavonoids, contain 10% Zn (Balan, 2003).

EASY SYNTHESIS OF ZN NANOPARTICLES

Zinc nanoparticles can easily be synthesized by numerous more or less elaborate techniques, such as green, metallurgical, solid, liquid, and gaseous. In the metallurgical techniques, the Zinc nanoparticles could be achieved by the roasting of a suitable zinc ore through a direct or indirect process (Zelechowska, 2014). Due to development of the methods of obtaining Zinc nanoparticles that enables precise control of the Zinc nanoparticles size that extensive scientific research is possible today.

Taking into account what has been discussed, the chemical techniques are the most reliable, economical, and environmentally friendly and also offer flexibility for controlling the shape and size of prepared nanoparticles (Espitia et al., 2012).

There are a variety of chemical techniques, for example, the mechanochemical process, the precipitation process, the hydrothermal, physical vapor, solvo-thermal, sol-gel, micro-emulsion process and methods. Recent research on colloids and dispersed systems must also be taken into account (Kołodziejczak-Radzimska, 2014).

NEGATIVE OR TOXIC IMPACTS OF ZINC NANOPARTICLES

The toxic effect of Zn nanoparticles is due to their solubility. Zn nanoparticles dissolve in the extracellular region, which in turn increases the intracellular (Zn^{2+}) level. The mechanism for increased intracellular (Zn^{2+}) level and Zn

nanoparticles dissolution in the medium is still unclear (Pandurangan, 2015).

Although the zinc nanoparticles have great commercial importance and are present in various commercial products there is clearly a growing public concern to know about the toxicological and environmental effects of zinc nanoparticles (Sabir, 2014).

To the researchers' dismay, toxicological studies carried out on zinc oxide nanoparticles in the last ten years show that zinc nanoparticles have potential health as well as environmental risks (Franklin et al., 2007).

Zinc nanoparticles can impose serious toxicity to bacteria *Daphnia magna*, freshwater microalga, mice, and even human cells (Sharma, 2008).

Zinc nanoparticles are particularly useful in sunscreens because they have intrinsic ability to filter ultraviolet UVA as well as UVB radiations. Thanks to this special and favorable property, they are offering broader protection than any other sunscreen agent. Must be specified that these nanoparticles have ability to penetrate to the skin and to reach viable cells resulting in the potential toxicity exerted by them (Bengalli et al., 2017).

A comparative analysis of dermal penetration between different animal species was performed, rating them in the order rabbit > rat > pig > monkey > man and it is noted that pig and rat skin are up to 4 and 9-11 times more permeable than human skin, respectively (Wang et al., 2008).

Overall, it is observed after many experiments that penetration through compromised skin was likely to be similar to normal skin but more work still needed to improve the understanding about this important safety issue (Brayner, 2006).

Oxidative stress, cytotoxicity, and mitochondrial dysfunction is explained by taking into account the solubility of ZnO nanoparticles and subsequent increase of intracellular (Zn^{2+}) level. Most of the studies were reported that the ZnO nanoparticle cytotoxicity was due to dissolution of ZnO nanoparticle in the extracellular region (Czyżowska et al., 2020).

Whereas, one study reported that ZnO nanoparticles were taken up by the cell and its dissolution occurred in the intracellular region. Induction of oxidative stress is the major

mechanism of ZnO nanoparticle cytotoxicity. Neurological occur result following the systemic exposure of ZnO nanoparticles (Abbasalipourkabir et al., 2015).

CONCLUSIONS

Because of the unique properties of nanoparticles (NPs), nanotechnology offers enormous value in many kinds of fields. One of the most significant uses of nanotechnology is in the field of plant biogenically utilizing various plant extracts.

Because it doesn't produce hazardous byproduct chemicals, the green synthesis of zinc nanoparticles is far safer and more environmentally friendly than chemical synthesis. When these nanoparticles are applied to crops, their yield and growth are increased. The output of staple crops for food is quite low, despite the fact that the need for food is growing daily. Commercializing metal nanoparticles for environmentally friendly farming is therefore urgently needed.

REFERENCES

- Abbasalipourkabir, R., Moradi, H., Zarei, S., Asadi, S., Salehzadeh, A., Ghafourikhosroshahi, A., & Ziamajidi, N. (2015). Toxicity of zinc oxide nanoparticles on adult male Wistar rats. *Food and Chemical Toxicology*, 84, 154-160.
- Akanbi-Gada, M. A., Ogunkunle, C. O., Vishwakarma, V., Viswanathan, K., & Fatoba, P. O. (2019). Phytotoxicity of nano-zinc oxide to tomato plant (*Solanum lycopersicum* L.): Zn uptake stress enzymes response and influence on non-enzymatic antioxidants in fruits. *Environmental Technology & Innovation*, 14, 100325.
- Akbar, S., Ali, Z., Hussain, S., Mohammad, A., Riaz, Y., Shakeel, A., Ahmad, I., Mussarat, M., Malik, R. N., Khan, K. Y., Sohail, M., & Quraishi, U. M. (2021). Metal accumulation potential, human health risks, and yield attributes of hundred bread wheat genotypes on irrigation with municipal and remediated wastewater. *Environ. Sci. Pollut. Res.*, pp. 1-15, 10.1007/s11356-021-13085-4.
- Alloway, B. J. (2008). Zinc in Soils and Crop Nutrition. *International Zinc Association, Second edition, published by IZA and IFA Brussels, Belgium and Paris, France*.
- Alloway, B. J. (2009). Soil factors associated with zinc deficiency in crops and humans. *Environmental Geochemistry and Health*, 31(5): 537-48.
- Auld, D. S. (2005). Zinc enzymes. In King RB (Ed.) *Encyclopedia of Inorganic Chemistry*. Wiley. Chichester, UK. pp. 5885-5927.
- Balan, V., Dejeu, L., Chira, A., & Ciofu, R. (2003). *Horticultura alternativa si calitatea vietii*, Editura G.N.P. Minischool, Bucuresti.
- Barbulescu, D. I., Rusu, N., Rughinis, R., Popa, O., Stefaniu, A., & Casarica, A. (2010). Obtaining yeast biomass enriched with copper, zinc and manganese. *Romanian Biotechnological Letters*, 153219173229(1): 40-21.
- Barker, A.V., & Eaton T.E. (2015). Zinc. In Barker AV, Pilbeam DJ (Eds.), *Handbook of Plant Nutrition. 2nd ed.* CRC Press. Boca Raton, FL, USA, pp. 537-564.
- Bengalli, R., Gualtieri, M., Capasso, L., Urani, C., & Camatini, M. (2017). Impact of zinc oxide nanoparticles on an *in vitro* model of the human air-blood barrier. *Toxicology Letters*, 279, 22-32.
- Bengtsson, H., Oborn, I., Jonsson, S., Nilsson, I., & Andersson, A. (2003). Field balances of some mineral nutrients and trace elements in organic and conventional dairy farming – A case study at Ojebyn, Sweden. *European Journal of Agronomy*, 20(1-2), 101-116.
- Brayner, R., Ferrari-Iliou, R., Brivois, N., Djediat, S., Benedetti, M., & Fievet, F. (2006). Toxicological impact studies based on *Escherichia coli* bacteria in ultrafine ZnO nanoparticles colloidal medium. *Nano Letters*, 6(4): 866-70.
- Broadley, M., Brown, P., Cakmak, I., Rengel, Z., & Zhao, F. (2012). Function of nutrients: Micronutrients, In Marschner P. (Ed.), *Marschner's Mineral Nutrition of Higher Plants, 3rd ed.* Academic Press, San Diego, CA, USA, pp. 191-248.
- Butnariu, H., Indrea, D., Petrescu, C., Savitchi P., Chilom, P., Ciofu R., Popescu, V., Radu, G. & Stan, N. (1992). *Legumicultura*, SDPRA, Bucuresti.
- Constantinescu, D. G., & Hatieganu, E. (1983). *Biologia moleculară a celulei vegetale*, Editura Medicala, Bucuresti.
- Czyżowska, A., & Barbasz, A. (2020). Cytotoxicity of zinc oxide nanoparticles to innate and adaptive human immune cells. *Journal of Applied Toxicology*, 41(9), 1425-1437.
- Daniel, G. M., & Astruc, D. (2004). Gold nanoparticles: assembly, supramolecular chemistry, quantum-size-related properties, and applications toward biology, catalysis, and nanotechnology. *Chemical Reviews*, 104(1): 293-346.
- Datcu, A. D., Alexa, E., Ianovici, N., & Sala, F. (2019a). Zinc foliar fertilization effect on some gravimetric indices on wheat, *Research Journal of Agricultural Science*, 51(3), 99-105.
- Datcu, A. D., Alexa, E., Ianovici, N., & Sala, F. (2019 b). Zinc fertilization effects on biomass production and some morphometric parameters for wheat. *Research Journal of Agricultural Science*, 51(3), 93-98
- Espitia, P. J. P., Soares, N. D. F. F., Coimbra, J. S. D. R., de Andrade, N. J., Cruz, R. S., & Medeiros, E. A. A. (2012). Zinc oxide nanoparticles: Synthesis, antimicrobial activity and food packaging applications, *Food and Bioprocess Technology*, 5, 1447-1464.
- Fallah, A., Mohammad-Hasani, A., & Colagar, A. H. (2018). Zinc is an Essential Element for Male Fertility: A Review of Zn Roles in Men's Health,

- Germination, Sperm Quality, and Fertilization, *J Reprod Infertil.*, Apr-Jun; 19(2): 69-81.
- Franklin, N. J., Rogers, S. C., Apte, G. E., Batley, G. E., Gadd, E., & Casey, C. S. (2007). Comparative toxicity of nanoparticulate ZnO, bulk ZnO, and ZnCl₂ to a freshwater microalga (*Pseudokirchneriella subcapitata*): the importance of particle. *The Scientific World Journal solubility, Environmental Science & Technology*, 41(24): 8484-90.
- García-Lopez, J. I., Zavala-García, F., Olivares-Saenz, E., Lira-Saldivar, R. H., Barriga-Castro, E. D., Ruiz-Torres, N., Ramos-Cortez, E., Vazquez-Alvarado, R., & Nino-Medina, G. (2018). Zinc Oxide Nanoparticles Boosts Phenolic Compounds and Antioxidant Activity of *Capsicum annuum* L. during Germination, *Agronomy Journal*, 8: 1-13.
- Graham, R. D., Welch, R. M., & Bouis, H. E. (2001) Addressing micronutrient malnutrition through enhancing the nutritional quality of staple foods: Principles, perspectives and knowledge gaps. *Advances in Agronomy*, 70: 77-142.
- Gupya, U. C., & Kalra, Y. P. (2006). Residual Effect of Copper and Zinc from Fertilizers on Plant Concentration, Phytotoxicity, and Crop Yield Response, *Communications in Soil Science and Plant Analysis*, 37: 2505-2511.
- Hafeez, B., Khanif, Y., M., & Saleem, M. (2013). Role of zinc in plant nutrition - A review. *Am. J. Exp. Agric.* 3: 374-391.
- Heinlaan, A., Ivask, I., Blinova, H. C., Dubourguier, C. & Kahru, A. (2008). Toxicity of nanosized and bulk ZnO, CuO and TiO₂ to bacteria *Vibrio fischeri* and crustaceans *Daphnia magna* and *Thamnocephalus platyurus*, *Chemosphere*, 71(7): 1308-16.
- Kato, H. (2011). *In vitro* assays: tracking nanoparticles inside cells, *Nature Nanotechnology*, 6(3): 139-40.
- Keller, A. A., Wang, H. T., Zhou, D. X., Lenihan, H. S., Cherr, G., Cardinale, B. J., Miller, R., & Ji, Z. X. (2010). Stability and aggregation of metal oxide nanoparticles in natural aqueous matrices. *Environmental Science & Technology*, 44: 1962-1967.
- Kołodziejczak-Radzimska, A., & Jesionowski, T. (2014). Zinc oxide – from synthesis to application: a review, *Materials*, 7, 2833-2881.
- Lilburn, M., & McIntyre, D. (2024). An historical overview of zinc in poultry nutrition. *Poultry Science*, 103(12), 104294.
- McClung, J. P. (2019). Iron, Zinc, and Physical Performance. *Biol Trace Elem Res. Mar*; 188(1): 135-139.
- Moezzi, A., McDonagh, A., & Cortie, M. (2012). Zinc oxide particles: Synthesis, properties and applications. *Chemical Engineering Journal*, 185-186: 1-22.
- Narváez-Cacedo, C., Moreano, G., Sandoval, B. A., & Jara-Palacios, M. A. (2018). Zinc Deficiency among Lactating Mothers from a Peri-Urban Community of the Ecuadorian Andean Region: An Initial Approach to the Need of Zinc Supplementation. *Nutrients*, Jul 05; 10(7).
- Palacios, C. (2006). The role of nutrients in bone health, from A to Z. *Crit Rev Food Sci Nutr.*; 46(8):621-8.
- Pandurangan, M., & Kim, D., H. (2015). *In vitro* toxicity of zinc oxide nanoparticles, *Journal of Nanoparticle Research*, 17(3).
- Prasad, T. N. V. K. V., Sudhakar, P., Sreenivasulu, Y., Latha, P., Munaswamy, V., Raja Reddy, K., .Sreeprasad, T. S., Sajanlal P. R., & Pradeep T. (2012). Effect of nanoscale zinc oxide particles on the germination, growth and yield of peanut. *Journal of Plant Nutrition*, 35(6): 905-927.
- Rico, C. M., Majumdar, S. M., Duarte-Gardea, J. R., Peralta-Videa, M., & Gardea-Torresdey, J. R. (2011). Interaction of nanoparticles with edible plants and their possible implications in the food chain. *Journal of Agricultural and Food Chemistry*, 59(8): 3485-98.
- Roohani, N., Hurrell, R., Kelishadi, R., & Schulin, R. (2013). Zinc and its importance for human health: An integrative review, *J. Res. Med. Sci. Feb*; 18(2): 144-157.
- Sabir, S., Muhammad, A., & Sunbal, K. C. (2014). Zinc Oxide Nanoparticles for Revolutionizing Agriculture: Synthesis and Application. *The Scientific World Journal*, 2014: 925494.
- Samreen, T., Shah, H., U., Ullah, S., & Javid, M. (2017). Zinc effect on growth rate, chlorophyll, protein and mineral contents of hydroponically grown mungbeans plant (*Vigna radiata*). *Arab. J. Chem.*, 10: S1802-S1807.
- Sanna, A., Firinu, D., Zavattari, P., & Valera, P. (2018). Zinc status and autoimmunity: a systematic review and meta-analysis. *Nutrients*. Jan 11; 10(1): 68. doi: 10.3390/nu10010068.
- Santos, C. A., Fonseca, J., Lopes, M. T., Carolino, E., & Guerreiro, A. S. (2017). Serum zinc evolution in dysphagic patients that underwent endoscopic gastrostomy for long term enteral feeding. *Asia Pac J Clin Nutr*, Mar; 26(2): 227-233.
- Salgueiro, M. J., Zubillaga, M., Lysionek, A., Sarabia M. I., Caro, R., De Paoli, T., Hager, A., Weill, R. & Boccio, J. (2000). Zinc as an essential micronutrient: a review. *Nutr Res.*, 20: 737-755.
- Sharma, R. K., Shukla, N., Saxena, D., Parmar, M., & Dhawan, D. (2009). DNA damaging potential of zinc oxide nanoparticles in human epidermal cells. *Toxicology Letters*, 185(3): 211-8
- Skalny, A.V., Aschner, M., & Tinkov, A. A. (2021). Zinc, *Adv Food Nutr Res.*, 96:251-310.
- Stoican, E., Mosoiu, C. E., & Israel Roming, F. (2021). Gluten-free products and possibilities of new Formulation for improving textural and nutritional Characteristics – review. *Scientific Bulletin. Series F. Biotechnologies*, XXV(1), 76-86.
- Wang, W., Feng, M., & Wang, L. (2008). Acute toxicological impact of nano and submicro-scaled zinc oxide powder on healthy adult mice. *Journal of Nanoparticle Research*, 10(2):263-276.
- Zelechowska, K. (2014). Methods of ZnO nanoparticles synthesis, *BioTechnologia. J. Biotechnol. Comput. Biol. Bionanotechnol*, 95, 150-159.