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A REVIEW

Zinc fertilizer : Potent public health intervention under COVID-19

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SUMMARY

Corona virus disease 2019 (COVID-19) caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) represents the biggest current health challenge for the society. At the moment, the therapeutic strategies to deal with this disease are only supportive. It is well evident that zinc (Zn) possesses a variety of direct and indirect antiviral properties, which are realized through different studies during the course of time. Administration of Zn supplement has a potential to enhance antiviral immunity, both innate and humoral, and to restore depleted immune cell function or to improve normal immune cell function, particular in immune-compromised or elderly patients.In recent years, the increasing zinc (Zn) deficiency problem has garnered attention and appears to be the most serious micronutrient deficiency along with vitamin A deficiency. The concentration of Zn in cereal crops is inherently very low and growing cereals on potentially Zn-deficient soils further decreases grain Zn concentrations. It is, therefore, not surprising that high Zn deficiency in humans occurs predominantly on areas where soils are deficient in plant-available Zn. Biofortification (enrichment) of crops with Zn and breeding new cereal genotypes for high grain Zn concentration is the most realistic and cost-effective strategy to address this problem. However, this strategy is a long-term one, and the size of plant-available Zn pools in soils may greatly affect the capacity of Zn-efficient (biofortified) cultivars to take up Zn and accumulate it in grains. Therefore, application of Zn-containing fertilizers represents a quick and effective approach to biofortify cereal grains with Zn. It is obvious that enrichment of widely applied fertilizers with Zn and/or foliar application of Zn fertilizers appear to be a high priority with the strongest potential to alleviate Zn deficiency-related problems in India. A Government action and policy plan for enrichment of selected major fertilizers with Zn is required urgently.

Key Words : Coronavirus disease 2019 (COVID-19), Zinc, Deficiency, Fertilizers, Biofortification, Policy

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Zinc inadequacy, both in human and plants, have now become a serious issue among the nutritionists, medicinal researchers and agronomists. The world is currently in the middle of COVID-19 pandemic caused by a novel coronavirus, *i.e.,* SARS-CoV-2. The damage from COVID-19 had been significant in terms of morbidity and mortality. Millions of people had been infected and died worldwide since its inception (Worldometers, 2021). It is very well known that micro-nutrients play a greater role in maintaining good health. At present, many of the required micronutrients are representing deficiencies in both human and plants out of which, zincdeficiency is quite prevalent ranging from about 5-50 % of the population (Wessells and Brown, 2012). Prevalence of Zn deficiency is associated with increased susceptibility to diseases, mental capacity, complications, high morbidity and mortality in mothers and neonates [NIH Office of Dietary Supplements, ODS, 2020]. Given its role in the overall human health and wellbeing, efforts are being made the problem through fortification of foods throughout the world (Maares and Haase, 2020). The countries from the high-income group that consumes a more diverse micronutrient-rich diet tend to have Zinc deficiency below 5-10 per cent (Gupta *et al.*, 2020) even then, these had been the countries also worst affected by COVID-19 (Worldometers, 2020). Zinc is proven to be effective at slowing down the multiplication rate that similar viruses such as SARS and common cold replicate in the body.

Zinc is considered the fifth most important yield-limiting nutrient (following N, P, K, and S) in India's upland crops, and in lowland crops like rice, it is second only next to N. About 40% of soil samples analyzed for available Zn in India was found to be deficient (Fig. 1). There are multiple reasons for the increasing incidences of Zn deficiency in India, including large quantity of Zn exploitations due to high crop yields and intensive cropping systems, lesser application of organic manures, use of high analysis fertilizers, increased use of phosphatic fertilizers resulting in P-induced Zn deficiency and the use of poor-quality irrigation water with high calcium carbonate content.The critical level of Zn in Indian soils is 0.6 ppm and there is a growing concern that it should be increased to 1.2 ppm, or higher, as the intensity of crop production increases. Zinc deficiency varied among states with a minimum of 9.6% in Uttarakhand to as high as 75.3% in Rajasthan (Shukla and Tiwari, 2016.). Zinc sulfate, ammoniated zinc and chelated zinc are good fertilizer options. Zinc can be also applied into soils after fortification of commonly applied NPK fertilizers. One-percent zinc-containing NPK and urea fertilizers are available in many countries. Sulfates are the most commonly applied inorganic zinc fertilizer. Zinc sulfate is a granular product that may be banded or broadcast. There are two forms of zinc sulfate: (1) Zinc monohydrate with 36% zinc, More commonly used due to availability, higher zinc content per pound and lower water content resulting in lower transportation costs. (2) Zinc heptahydrate with 22% zinc.

Zinc ammonia complexes are typically found in starter fertilizers. They work well in liquid blends made from ammonium phosphate. Specific ammoniated zinc solutions can also be mixed with UAN or aqua ammonia solutions. Chelated zinc is another liquid product. It is the most common soil-applied organic source of zinc. It can be banded, broadcast or foliar-applied with application rates up to one fifth less than inorganic sources. It is the least likely of the options to be fixed in high pH, calcareous soils. Chelated zinc is also the most expensive option.

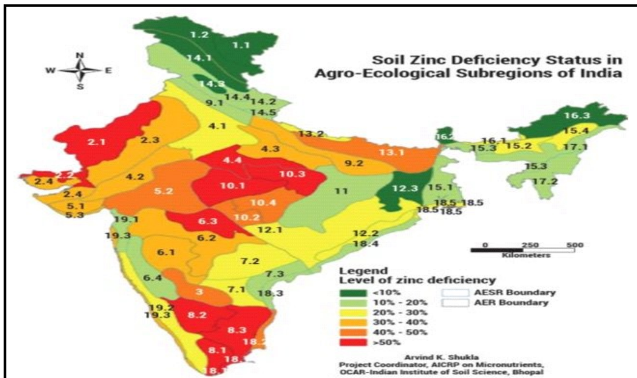

Fig. 1: Soil zinc deficiency status in India (Shukla and Tiwari, 2016)

Zinc deficiencies are normally corrected by soil applications. However, foliar sprays are usually used on higher value fruit trees and grape vines and for treating annual field crops. Other methods include seed treatments and root-dipping of transplant seedlings (e.g. in rice production). Fertigation is a relatively new application method in which both Zn fertilizers and NPK fertilizers are added together to irrigation water to improve uniform distribution, homogeneous mixing and greater availability and reduced risk of damage to plants, especially in semi-arid and arid areas. Zinc fertilizers are also often used to fortify other fertilizers including blended NPK fertilizers. In this application, it is common to see fortification rates in the order of 0.5% to 1.0% zinc by mass. Remobilization of Zn from leaf tissue to grain is dependent on the availability of Zn and is only crucial when its bioavailability was low.This goes back to the solubility of the product. Zn fertilizers are primarily taken up by the roots as Zn^{++} cation from the soil solution. Therefore, higher the solubility, higher the initial availability of the product to the plant. Both sulfates and chelates are very water soluble, but again, chelates are not prone to soil fixations in higher pH soils. Where farmers are applying zinc fertilizers on a regular basis (either to the soil or as foliar sprays), regular soil or plant analysis should be carried out to determine whether sufficient residues of zinc have accumulated in the soil or not; thus, zinc applications could be discontinued for one or more years. This saves cost of zinc fertilizer application and helps to ensure that zinc does not accumulate to undesirably high levels. Local expert advice should be sought on all aspects of the management of the zinc status of soils as part of a balance approach to fertilization. In this paper, we provide a review on effect of zinc on crops, human requirement, consequences and causes of zinc deficiency and prevention strategies of zinc deficiency.

Crop response to zinc fertilizers:

Zinc (Zn) is a critical micronutrient for proper growth and development of plants. Although we do not fully understand zinc's specific role, it is certain that zinc is involved in the production of chlorophyll, protein and various enzymes involved in metabolic reactions for proper growth. Crops that are most prone to zinc deficiency are grain sorghum, soybeans and corn. Wheat, sugar beets and edible beans can also show a positive response to zinc fertilizer when it is deficient in the soil. Crop response to Zn has been observed in most crops in almost all types of soils and agro-climatic conditions. While the response was found to be higher in grain crops like rice and maize, fruit and vegetable crops also responded well to applied Zn. Singh (2008) summarized the range of crop response to Zn based on over 15,000 on-station field trials in India as: Cereals: 420 to 550 kg/ha (16 to 23%) Pulses: 170 to 460 kg/ha (7.3 to 28%) Oilseeds: 110 to 360 kg/ha (11 to 40%) Fodders: 90 to 4620 kg/ha (5 to 34%). Shukla and Tiwari (2016) also studied the response of Zn application on cereals (rice, wheat, and maize), pulses (chickpea), oilseeds (soybean), fiber crops (cotton) and vegetable (cabbage) based on a large number of experiments and on-farms trials in different states of India. Zinc application resulted in a 9 to 12% increase in rice yield at different locations. A similar range of responses were also observed for chickpea, cotton, maize, soybean, wheat, and cabbage at different locations (Table 1).

Field experiments on rice and wheat in India showed that application of Zn-enriched urea (upto 3% Zn) significantly enhanced both grain Zn concentration and grain yield in rice and wheat (Shivay *et al.,* 2008). Application of Zn not only increases the crop yield, but also improves its quality. For potato, it increased ascorbic acid in tubers, reduced phenol content and enhanced reducing sugars, sucrose and total sugar. Zinc was also found to increase the phenol and tannin content of leaves, kernels and seed coat of cotton. A study (Myers *et al.,* 2014) highlighted reduction in nutritional quality of grains due to climate change impact. Results support that appropriate Zn application could improve wheat growth under drought stress (Yavas and Unay, 2016). Therefore, adequate Zn application in crops would be necessary to

Table 1 : Response of different crops to Zn application

Crop	Location	On-farm trials	Grain yield, t/ha		% Response Zn 5 / Zn 10
			Zn 0	Zn 5 / Zn 10*	
Rice	Assam	43	35.1	35.6	12
Rice	Jharkhand	46	33.8	34.0	9.3
Rice	West Bengal	46	34.8	35.3	10
Chickpea	Maharashtra	45	31.0	31.1	9.4
Cotton	Maharashtra	25	31.3	31.5	9.8
Maize	Maharashtra	45	32.6	32.9	10
Soybean	Maharashtra	36	31.1	31.2	8.8
Wheat	Maharashtra	16	33.9	34.2	8.8
Cabbage	Tamil Nadu	42	39.5	42.5	7.3

*Zn application of 5 or 10 kg/ha. Source: Shukla and Tiwari, 2016 alleviate climate change impacts on crop yield and nutritional quality.

Zinc in human health:

Zn appears to be a multipurpose element, necessary for health and well-being. It is undoubtedly one of the most essential micro-nutrient thatplays an important role in human physiology, cell-mediated immune functions, oxidative stress and as an intracellular signaling molecule. it is an anti-inflammatory agent and its biochemistry is involved in epigenetic processes, gut microbial composition and medicinal targets (Chasapis *et al.*, 2020). Zn is an important trace element in human health and its deficiency can lead to retarded growth, anorexia, smell and taste failure,infections, impaired brain function, poor mental development and other symptoms in humans (Chasapis *et al*., 2012). It is an essential antioxidant mineral for preventing formation and reactive response of free radicals, which are unstable atoms that contain one or more unpaired electrons that can damage cells, leading to the progression of chronic and degenerative diseases (Pae *et al.*, 2012.). Zn plays a crucial role in proper cellular function, including differentiation, cell division, cell growth, cellular transport, endocrine and immune system, transcription, protein synthesis, RNA and DNA synthesis and DNA replication (Ackland and Michalczyk, 2016). It is found in many tissues, with the majority in the testes, muscle, liver, bones and brain (Glutsch *et al.,* 2019).

Zinc is essential for good health and immune competence. In the absence of reliable methods to assess the Zn status of a population, the deficiency or inadequacy in a population is estimated by combining the dietary intake by a population as per FAO's Food Balance Sheet and the estimated prevalence of stunting [NIH Office of Dietary Supplements (ODS), 2020]. So, more evident-gathering of follow-up exercises for the closer scrutiny of the COVID-19 patients' medical records, including the micronutrient supplementation and food consumption details is advisable to ascertain the role of Zinc deficiency in COVID-19 pandemic and potentially find an early solution to COVID-19 (Singh, 2008).

Factors affecting zinc avalability:

Although genotypic factors are important in determining either tolerance or susceptibility of a crop cultivar to zinc deficiency, it is soil factors which are responsible for low available zinc supply. In general, soilfactors most commonly associated with zinc deficiency problems in plants mainly due to the factors like neutral to alkaline in reaction, especially where the pH is above 7.4, high calcium carbonate content in topsoil or in subsoil exposed by removal of the topsoil during field leveling or by erosion, coarse texture (sandy soil) with a low organic matter status, permanently or intermittently waterlogged soil,wet and cold soil conditions that cause slow roots development, slow release of the Zn from organic matter, high available phosphate status, high bicarbonate or magnesium concentrations in soil or irrigation water and acid soil of low zinc status developed on highly weathered parent material.Presence of calcium carbonate decreases the availability of zinc due to higher soil pH. Saline soils contain high concentrations of soluble salts which restrict the types of crops which can be grown and reduces the availability of zinc (Dogra *et al.*, 2015). The poor availability of zinc caused by water logging can be due to a relatively high pH, zinc being present as the insoluble sulphide (ZnS) and elevated concentrations of ferrous, bicarbonate and phosphate ions (Doberman, *et al.,* 2000). High soil phosphate levels are one of the most common causes of zinc deficiency in crops by cations added with phosphate salts can inhibit zinc absorption from solution, H^+ ions generated by phosphate salts inhibit zinc absorption from solution and phosphorus enhances the adsorption of zinc into soil constituents. Nitrogen appears to affect the zinc status of crops by both promoting plant growth and by changing the pH of the root environment. In many soils, nitrogen is the chief factor limiting growth and yield and therefore, not surprisingly, improvements in yield have been found through positive interactions by applying nitrogen and zinc fertilizers (Gonzalez *et al.,* 2019). Several macronutrient elements including calcium, magnesium, potassium and sodium are known to inhibit the absorption of zinc by plant. Interactions of zinc with other micronutrients such as with copper, iron, manganese and boron influence their concentration in plants due to, zinc-copper interactions occur due to copper and zinc sharing a common site for root absorption or copper nutrition affects the redistribution of zinc within plants, iron-zinc interactions study resulted increasing zinc supplies to plants have been observed to increase the iron status, to decrease it and to have no effect on it (Loneragan and Webb, 1993). In contrary to the previous report, Zn application had adverse effect on Fe concentration and Fe uptake in plants (Imtiaz *et al*., 2003). By understanding soil conditions and how the crop will respond to zinc fertilizer, farmer/researchers will be able to apply the proper product at the proper time. There are options for correcting a zinc deficiency. This starts with a proper soil test. A correct analysis of field conditions and crop to be grown, cost of product and application methods will help farmers/researchers determine the best zinc source for their crop.

Zinc biofortification:

The word "biofortification" refers to enhancing bio available micronutrient content of food crops through genetic selection via plant breeding. It is a promising strategy to address nutrition security and was initiated with five criteria, *viz*., crop productivity (*i.e*., yield) must be maintained or increased to ensure farmer acceptance, the enhanced micronutrient level must have significant impact on human health, the enhanced micronutrient trait must be relatively stable across various edaphic environments and climatic zones, the bioavailability of micronutrients in enriched lines must be tested in humans to ensure that they improve the micronutrient status of people preparing and eating them in traditional ways within normal household environments and consumer acceptance must be tested (taste and cooking quality must be acceptable to household members) to ensure maximum impact on nutritional health (Rao *et al.*, 2020).

Although a few independent groups have initiated research on biofortification since 2000 in India, the programs kick-started after Harvest Plus programme implementation in India during 2007. Department of Biotechnology (DBT) and Indian Council of Agricultural Research (ICAR) of Government of India have also initiated support to biofortification projects leading to the consorted national and international research efforts toward the development of biofortified rice varieties. With the negative impact of zinc deficiency on human metabolism, especially in countries with rice as a major staple food, development of zinc-biofortified varieties has become one of the important objectives of crop improvement programmes. The success of biofortification relies on the existence of diversity for the target trait in the germplasm of crop, successful recombination of the target trait with yield and identification of suitable recombinants with yield and target trait through multilocation evaluation. To phenotype the zinc content of rice grains across thousands of germplasm lines or mapping populations, X-ray fluorescence spectroscopy (XRF) was found to be promising because of its high throughput, cost-effectiveness and rapid analyses over atomic absorption spectrometry and inductively coupled plasma mass spectrometry (Rao *et al.*, 2020). Harvest Plus has supported rice biofortification research of several laboratories in India through sponsoring XRF equipment and providing preliminary biofortified rice breeding lines.

ICAR–Indian Institute of Rice Research (IIRR) is a national institute that facilitates rice varietal release through All India Coordinated Rice Improvement Project (AICRIP) (*http://www.icar-iirr.org/*); IIRR is also translating the benefits of the research on zinc biofortification of rice to society through release of biofortified rice varieties through AICRIP and coordination of a Consortia Research Platform on biofortification of the cereals.

Factors ditermine use of zinc:

Soil nutrient degradation has been a significant problem for India, following years of imbalanced heavy chemical fertilizer use. Distortionary, direct subsidies have kept the relative price of urea low and have made other macro- and micronutrients much more expensive (Liu *et al.*, 2014). Farmers, for that matter, have lacked awareness about soil quality and crop requirements that would prevent soil depletion (Coleand Sharma, 2017). Although subsidies can provide an initial push to adopt new agricultural technologies and practices, however, on other side, its improper use may impose the financial burdenon the country like India. Large proportion of farmers were unaware of zinc and its benefits, even though nearly 47% of the farmers reported that they could identify zinc deficiency in their soil (Gupta *et al.*, 2020). There are many issues due to which farmers are not using of zinc fertilizers some of which are depicted in Fig. 1.

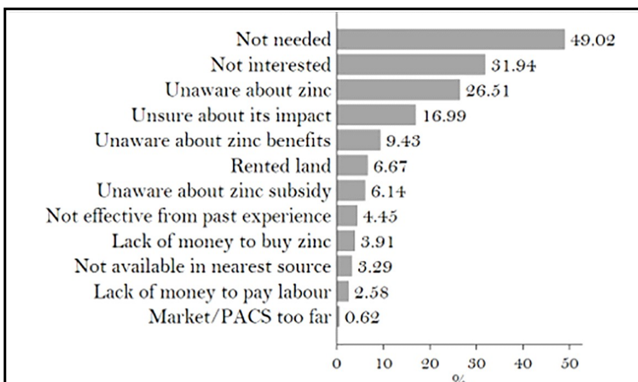

Fig. 2: Reasons for non-usage of zinc

Source: Gupta *et al*. 2020

There is a strong argument that charging a positive price for a commodity is necessary to ensure its effective use (Easterly 2006). For consumers, the price becomes the index of quality for new or unfamiliar products (Ashraf *et al.,* 2013) as is the case with zinc for many farmers. Products that are free or low-priced may signal low quality, at least to new users and may lead to low uptake if there is even a small amount of transaction cost involved in obtaining the "free" input. This could be one of the reasons why farmers are not using zinc in their fields even when it is free and the probability of a farmer using it has a small but significant negative association with the distance to the fertilizer outlet. The demand for a subsidized product is liable to drop drastically when its price is raised even slightly above zero (Shampanier *et al.,*2007). Although the exercise of eliciting the true willingness to pay for zinc could be misleading due to a tendency to anchor valuations around the subsidized price (zero), in an incentive compatible experimental auction, Fishman and others found similar values of the willingness to pay for zinc among paddy growers in the state of Bihar (Fishman *et al.*, 2016).

For promotion of zinc fertilizers:

The prime reason for nutrient imbalance in the country is heavy subsidies on urea. In the 1970s, urea subsidy used to be 10-20 per cent of the cost of production; it is now at 75 per cent. This has led to excessive use of urea in agriculture over the other chemical fertilisers. In fact, the share of urea consumption among all nitrogenous fertilisers is the highest 80 per cent in India, compared with 23 per cent in the United States and Europe, 54 per cent in Brazil and 46 per cent in China (Sardana, S, A. Union Budget 2020-2021). This shows there is an urgent need to shift its focus from urea alone to producing and promoting a balanced spectrum of NPK fertilisers as well as micro-nutrients such as zinc, which are dwindling in the Indian soil at an alarming rate.The government must also bring reforms in its policies to promote the balanced use of fertilisers. To begin with, it must introduce a measure of decontrol in the urea sector. Decontrolling urea will promote balanced fertiliser use, improved soil health and will reduce subsidy burden. It is heartening to note that neem coated urea is a success story in India. However, it is very unfortunate that zinc, a widespread deficiency of which is causing malnutrition in humans and its fortification with urea was grossly ignored, though Zincated-Urea was approved in Fertiliser Control Order (FCO) by Centre way back in the 1990s. But, it is not being produced or marketed in India due to some minor price disparity.At present, about 32 million tonnes of urea is being consumed in India, whereas there is not a single grain of zincated-urea used (Das, 2020). It is, therefore, strongly recommended to focus must be diverted towards considering widespread zinc deficiency in soils/crops and measures should be adopted to deal with this alarming situation. During the launch of GST - a historic tax reform in India implemented since independence and the price on fertilizer was reduced from 12 per cent to 5 per cent, which has proved beneficial for farmers.However, this reduced tax rate is restricted to N, P, K fertilizers only and the secondary and micronutrient fertilizers are left out. The GST rate on micronutrients is 12 per cent and higher. This taxation system is discriminatory and discourages the farmers in practising balanced plant nutrition and using micronutrients like zinc fertilizers. The GST rates, therefore, should be made at par for all the fertilizers mentioned in FCO. The government should take cognizance of these recommendations to address the widespread zinc deficiency in crops and also provide benefit to the farmers. Zinc deficiency has drawn the attention of the government and policy makers in India who have realized the need to create awareness on the critical role of zinc in fertilizers. Under the NBS Scheme, the government has provided additional subsidy of INR 500 per tonnefor fortification of urea with Zn (Zincated Urea), however, this is also not adequate enough to meet the cost of Zn and its fortification in urea. The Zincated-Urea policy needs to be reformed and prioritized, considering the widespread Zn deficiency in soils, crops and humans.Though ZnO is not included as a fertilizer in FCO, its liquid form, ZnO suspension concentrate with 39.5% Zn is approved in FCO. In addition, ZnO solution is also recommended by the State Governments for root dipping and seed coating before crop transplantation. ZnO is also a preferred raw material for fortification of bulk fertilizers. Moreover, due to lack of availability of quality Zn ash, the production of Zn-fertilizers is getting impacted. The inclusion of ZnO dry powder in FCO as fertilizer, preferably for the acidic soils, would serve as a viable option for the farmers to choose from the product basket.

Conclusion :

Zn possess several antiviral effects which are realized through the generating both innate and acquired (humoral) immune responses. Multiple antiviral effects of Zn have been demonstrated in a variety of viral species, including several nidoviruses, and SARS-CoV-2 belongs to the same group of virus *i.e.* nidoviruses. It suggests that Zn supplementation may be of benefit for prophylaxis and treatment of COVID-19. However, zinc deficiency in crops and humans is a critical issue and a global challenge. The sustainable solution is to apply an adequate and balanced quantity of Zn in crop production, so that the soil health, food and nutritional security are ensured. This could be achieved by ensuring the availability of new and innovative Zn fertilizer products for higher use efficiency, timely access to quality Zn fertilizers, increased stakeholder awareness on Zn requirement in the soil-plant-animal-human continuum and a supportive and conducive policy environment for encouraging the balanced fertilizer use by the farmers in India.

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