



## Review Article

# The Nickel Paradox: Its Ambivalent Role in Poultry Nutrition: A Review of Essentiality and Toxicity

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## ABSTRACT

Nickel is a heavy metal found throughout our surroundings and the crust of Earth. Nickel is frequently employed in several of the latest industrial techniques due to its distinct catalytic, magnetic, and optical capabilities, as well as its biological impacts. Nickel has been revealed to have a dual character for poultry, being both needed and harmful. Nickel is one of the elements in the poultry diet that has not yet been designated as necessary. Nickel functions to promote the assimilation of iron in the small intestine by acting like a cofactor or like a constitutional element in several metallo-proteins (urease, hydrolase). A nickel deficit causes the legs' bones to expand (increase in diameter), joints to enlarge, and bone strength to decrease. However, because too much of it might be fatal, it is only necessary at a certain minimum level. Since nickel comes from both natural and man-made sources, it is widely dispersed throughout the environment. Nickel from various sources enters the food chain when nickel-contaminated foods, such as plants and water, are ingested by animals, which are subsequently consumed by humans. Poultry gets exposed to nickel through various factors, with feed being one of the primary contributors. When chickens are provided with a contaminated diet, nickel begins to bioaccumulate in the meat and eggs, and it is also eliminated in their waste. In addition to having harmful effects on the immune system, elevated levels of nickel may induce carcinogenic and allergic effects. Consuming chicken that has a high nickel level seriously harms human health. Using hyperaccumulating plants to absorb trace minerals present in the land following their storage in parts of flora that can be harvested makes phytoremediation a potential nickel remediation method. The amount of nickel in the diet of poultry must be sufficiently high to meet the birds' needs while being limited assuring the quality of poultry diet, human nutrition products, as well as litter due to environmental concerns. An increased understanding of both the detrimental and essential effects of nickel is crucial.

## Article Information

Received 28 February 2025  
Revised 25 July 2025  
Accepted 30 August 2025  
Available online 14 July 2026  
(early access)  
Published 19 August 2026

## Authors' Contribution

HA, SF and ZM contributed to literature review and writing original draft. SM and GM contributed to supervision and critical revision. NB, QR, SK and FA contributed to revising and editing the original draft. All authors contributed to the conceptualization of the review article and approved the final version of the manuscript.

## Key words

Trace element, Poultry chicken, Poultry feed, Micronutrient

## INTRODUCTION

Heavy metals are classified as metalloids and metals having an atomic density of 4,000 kg/m<sup>3</sup> or more. Heavy metals constitute significant pollutants in our daily food supply, and their pollution poses a grave concern for our ecology. Continuous exposure to these contaminants, even in minimal quantities, may significantly adversely affect living organisms, and the deposition of trace minerals in

the ecosystem is regarded as a biohazard (Aljohani, 2023). Crops cultivated on soil with high levels of metals or irrigated with contaminated water, as well as animals grazing in pastures with elevated levels of heavy metals, are two frequent ways that people are exposed to heavy metals in the food supply. According to Reddy *et al.* (2017), this causes metals to bioaccumulate or biomagnify in animal tissues.

Nickel (Ni) is found in soil, water, and air and is one of the most prevalent transition metals in the crust of the Earth. Ni is extensively employed as a crucial element in many current industrial processes because of its special catalytic, magnetic, optical, and biological effects (Deng *et al.*, 2016). According to Baloš *et al.* (2017), Ni is regarded as both a necessary and harmful element for people, animals, plants, and microbes. Although too much Ni poisons plants and animals, it is known to be a necessary element for many vital biological functions, including the proper development of soil/water microorganisms

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0030-9923/2026/0005-2233 \$ 9.00/0



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and higher living organisms. Hydrogenase, urease, cis-trans isomerase, acetyl coenzyme-A (CoA) synthase, and carbon monoxide (CO) dehydrogenase are among the enzymes that include Ni as a structural element (Begum *et al.*, 2022).

According to Reddy *et al.* (2017), human pollution has the potential to raise the levels of Ni that are already present in food and water. Fossil fuel burning and industrial processes utilizing Ni are two examples of natural and man-made activities that contribute to environmental Ni each year in the range of as low as 150,000 and as high as 180,000 metric tons (Shahzad *et al.*, 2018). The potential health dangers to people and animals are heightened by the pollution that results from the increased use of Ni-containing items. While Ni is vital for many plant and animal life forms, as well as certain bacteria, too much of it may be fatal to humans and other animals. According to prior research, Ni and Ni compounds are carcinogenic, nephrotoxic, hepatotoxic, neurotoxic, genotoxic, immunotoxic, and harmful to the reproductive and respiratory systems (Deng *et al.*, 2016).

The significance of poultry for human consumption is assessed through the FAO (Food and Agriculture Organization of the United Nations), which asserts that human population derives substantial benefits from poultry meat and eggs, as they supply food that is rich in high-quality protein and possesses a low-fat content with an advantageous fatty acid composition. Particularly in poor nations, where people often go without basic nutrition, these meals might be a lifesaver due to their accessibility and low cost (Ravindran, 2013). The general nutritional profile of poultry meat is favorable for people. Because of its low collagen content, low fat level (most of which are unsaturated fatty acids), and high biological value protein, vitamin, and mineral content, this meat is ideal for consumption at any age. The opinion is supported by cross-sectional and prospective epidemiological studies, which demonstrate that eating enough chicken meat can help control weight loss (particularly because of its high protein content) and have a neutral or positive impact on the risk of developing the major degenerative diseases that are common in our society, such as cancer, diabetes, and cardiovascular diseases (Marangoni *et al.*, 2015).

Poultry eggs are a cost-effective and low-calorie source of high-quality protein and critical nutrients, regarded as a complete food vital for well-being. Consumers recognize them as varied and nutritious, providing a balanced array of nutrients necessary for life and development. Besides their nutritional value, they include health-promoting qualities, including preventative and therapeutic potentials (Zaheer, 2015). The nutrition of an animal or its genetic pattern are the two main factors that determine the quality

of products made from animals. The prevalence of heavy metal toxicity in poultry on a global scale is estimated to be between 2.1% and 3.4% (Aljohani, 2023). Despite the relatively low concentration of Ni in the chicken diet, its significance in metabolic processes requires significant importance. An imbalance in mineral content, whether due to a low amount of or an elevated level of specific nutrients may lead to disorders of the immune system and a deterioration regarding bodily functions, in addition to reduced efficiency. But at the same time, Ni elevated concentrations are exceedingly hazardous (Baloš *et al.*, 2017).

Poultry is typically subjected to various forms of heavy metal toxicity as a result of exposure to contaminated water, poultry feed, sewage, industrial effluents, and aerial applications in areas designated for poultry reproduction. Another significant factor contributing to the contamination of meat is its predominant sale in open markets, as well as occasionally along roadways. The raw ingredients, spices, and water used in the packing process may also cause poisoning of meat products as a result of the processing procedure (Khan *et al.*, 2015). Contamination seriously harms the health of chickens and may make its products dangerous for humans (Korish and Attia, 2020). When consumed by people, the sick animals may serve as carriers of several deadly illnesses (Khan *et al.*, 2015).

To reduce the potential for heavy metal contamination, it is crucial to track the levels of heavy metals in poultry products carefully. This is because even at relatively low levels, these metals can be extremely toxic. So, this review aims to assess the essentiality as well as toxicity of Ni in poultry chickens so that an adequate level of Ni is maintained to avoid deficiency symptoms but at the same time, we also have to keep this level at a safe limit. This balance between minimal requirement and toxicity at low concentrations is necessary to be maintained for the proper health of poultry and consumers as well as the environment.

## Ni: ITS PROPERTIES, OCCURRENCE AND APPLICATIONS

Ni is a transition metal with an atomic number of 28, an atomic weight of 58.6934 Da, and a density of 8908 kg/m<sup>3</sup>. It has a melting point of 1455 °C and a boiling temperature of 2913 °C. Ni is a ferromagnetic metal that is hard, ductile, and silvery-white in color. It also has good thermal and electrical conductivity. Its electronic configuration is [Ar] 3d<sup>8</sup>4s<sup>2</sup>. Together with iron, cobalt, palladium, platinum, and five other elements, it is a member of group 10 of the periodic table. It may exist in a range of oxidation levels, from -1 to +4, although the +2

oxidation state, which is represented by  $\text{Ni}^{2+}$ , is the most common in both environmental and biological contexts. Ni ranks as the 24<sup>th</sup> most prevalent element in the Earth's crust, often found in conjunction with oxygen and sulfur as oxides and sulfides, and it is the 5<sup>th</sup> most plentiful element by weight, behind iron, oxygen, magnesium, and silicon. It constitutes around 0.008% of the Earth's crust. The majority of Ni on Earth is unreachable since it is located in the iron-nickel alloy of the Earth's molten outer core, and only 10% Ni of it is situated above the solid inner core and below the mantle and is accessible for living organisms (Schaumlöffel, 2012). Ni may be found in meteorites, soil, and volcanic eruptions in conjunction with other elements. The sea has around eight billion tonnes of Ni (Begum *et al.*, 2022). As a naturally occurring element, Ni may be found in a variety of mineral forms. Ni is a silver-white solid metal in its elemental form while in nature, it is found in association with antimony, arsenic, and sulfur (Schaumlöffel, 2012).

It is highly soluble in dilute oxidizing acids at a pH of less than 6.5. While Ni salts of mild inorganic acids, Ni sulfides, and Ni oxides are weakly soluble in water, Ni salts of strong acids (chloride, nitrate, and sulfate) and organic salts are readily soluble (Denkhaus and Salnikow, 2002). Ni Compounds of significant commercial relevance include Ni chloride, carbonate, nitrate, sulfate, acetate, hydroxide, and oxide. The unique blend of Ni's exceptional physicochemical qualities makes it useful in various applications. Cempel and Nikel (2006) and Henderson *et al.* (2012) found that it is completely recyclable, has excellent ductility, and is resistant to oxidation, corrosion, and very high temperatures. Ni is employed in contemporary metallurgical practices across a diverse array of processes, including the production of alloys, electroplating, the manufacture of Ni-cadmium batteries, and as a catalyst within the chemical and agricultural industries (Beattie *et al.*, 2017). Ni and its byproducts pollute the environment throughout their lifecycle, from production to recycling to final disposal, due to the widespread use of these goods (Genchi *et al.*, 2020).

### ROLE OF Ni AS A MICRONUTRIENT IN POULTRY

Historically, heavy metals like Ni have received insufficient attention from poultry physicians, as evidenced by the scant amount of relevant literature (Begum *et al.*, 2022). Recent advancements in understanding the critical functions of heavy metals in bone metabolism, antioxidant status, homeostatic regulation, product quality, immunity, and the innovative sources of heavy metals have gained attraction in the last decade. There is an increasing trend

in optimizing trace mineral nutrition, taking into account their significance and possible toxicological effects (Nys *et al.*, 2018).

The nutritional needs for microelements are comparatively minimal, with daily recommended levels ranging from micrograms to milligrams. The buildup of these elements in quantities exceeding those necessary for optimal metabolism may result in signs of overdosing. Fluoride, Ni, silicon, tin, and chromium are minerals that are important to a chicken's diet but aren't considered necessary yet (Henry and Miles, 2001). The poultry diet must include sufficient amounts of vital microelements to meet the needs of the chickens while maintaining the protection of feed for animals, as well as meat and eggs for human consumption. Although the toxic nature of Ni was long recognized, its vital functions in poultry nutrition are currently being studied (Baloš *et al.*, 2017).

#### *Biological essentiality of Ni in poultry health*

The needs for Ni in animals are currently unclear. As stated by Puls (1994), the poultry diet must contain an appropriate concentration of Ni maintained in the range of 0.1-3 mg kg<sup>-1</sup> based on dry matter. Conversely, Bersényi *et al.* (2004) recommended that the Ni level should be within the limit of as low as 50 and as high as 100 µg Ni kg<sup>-1</sup> of diet averting the manifestation regarding pathological defects. Plant-based feeds exhibit elevated levels of Ni compared to their animal-based counterparts. Consequently, the majority of poultry diets incorporate significant quantities of this element as plant proteins, including sunflower, soybean, and flaxseed vary in their Ni content from 5.24-7.91 mg kg<sup>-1</sup> based on dry matter, whereas cereals such as maize, barley, and oats contain Ni as low as 0.08 and as high as 1 mg kg<sup>-1</sup> based on dry matter (Baloš *et al.*, 2017).

Ni serves a dual function, participating in the composition of certain metalloenzymes, such as urease and hydrogenase, and as a co-factor that aids in the assimilation of ferric ions in small intestines (Bersényi *et al.*, 2004). Broilers' bone strength and performance were shown to be favorably affected by Ni intake, according to Wilson *et al.* (2001), and it was found to modestly increase daily gain and feed conversion rate according to Bersényi *et al.* (2004). It promotes the release of glucagon, and a decrease in fat accumulation in poultry has been linked to insulin conversion to glucagon, indicating that blood Ni content affects the integrity of poultry meat (Oscar *et al.*, 1995).

#### *Deficiency symptoms of Ni in poultry*

Ni deficiency symptoms appear under various circumstances and are linked to dietary content. A lack of Ni causes oxidative metabolism, aberrant lipid levels, and

altered cellular structure. It also diminishes the specific activity of numerous enzymes that are integral to the metabolism of carbohydrates and amino acids (Wilson *et al.*, 2001). Reduced development, swollen joints, thickened (diameter-wise) leg bones, and decreased bone strength are all symptoms of an artificially caused Ni shortage in chickens. Puls (1994) identified symptoms of Ni deficiency as the diminished yellow coloration of the meat, limb hypertrophy, joint edema, inflammation of the carcass skin, and anemia. The body may also have difficulty absorbing Fe in Ni-deficient conditions. Quantities of zinc, iron, and copper might be decreased in the digestive system of living organisms having Ni deficiency (Begum *et al.*, 2022).

## Ni EXPOSURE IN THE ENVIRONMENT AND ITS TOXICITY

Because it comes from both natural and man-made sources, Ni is widely dispersed throughout the ecosystem (Sinicropi *et al.*, 2010). There is a correlation between the speciation of Ni compounds and the kind and intensity of the reactions they elicit in ecosystems and on the creatures that inhabit them. Ni is harmful to both plants and animals when environmental quantities are high enough. Numerous factors, such as the organism's inherent sensitivity, environmental geochemical conditions, various environmental pressures, as well as pathway of exposure, have been shown to have a significant impact on the concentration of Ni that will result in toxicity (Merrington *et al.*, 2016).

A substance is assimilated, following its subsequent transportation, breakdown, removal, and probable bioaccumulation, and is said to be bioavailable (Peters *et al.*, 2018). The most hazardous and bioavailable type of Ni in the surroundings is the free  $\text{Ni}^{2+}$  ion, according to research (Schlekat *et al.*, 2010). There is a strong correlation between solubility and bioavailability; for example, soluble Ni salts have a high bioavailability, but certain Ni oxides are barely soluble and have a lower bioavailability. When evaluating the possible bioavailability of Ni, it is just as crucial to comprehend the chemical properties of the medium in which the encounter takes place as it is to comprehend the biology of the living creature (Buxton *et al.*, 2019).

## SOURCES OF Ni EXPOSURE AND TOXICITY

### *Natural sources of Ni*

Ni compounds are ubiquitous and may be found at ambient levels in every ecosystem. The naturally occurring sources of land and aquatic Ni encompass soil particles

produced by sediments undergoing degradation, marine salinity, burning of flora, volcanoes as well as the exudates produced by vegetation. Collectively, these sources contribute approximately 16% to the atmospheric Ni load (Buxton *et al.*, 2019). Direct discharge from sediments and rocks results in elevated levels of Ni present across the environment, existing predominantly with bivalency, alongside suspended insoluble particulates (Cempel and Nikel, 2006).

### *Anthropogenic sources of Ni*

Ni pollution in both aquatic and terrestrial environments may be attributed to a variety of activities performed by humans. These include mining, refining, processing alloys, recycling scrap metal, burning fossil fuels, incineration of garbage, emissions from electric power utilities, and emissions from automobiles. The combustion of fossil fuels, including coal, gas, and oil as well as effluents undergoing the treatment process predominantly contribute to excess Ni present in the atmosphere (Sinicropi *et al.*, 2010). Tobacco smoking, cheap jewelry, and stainless steel kitchenware are other environmental sources of Ni. The Ni content of smoke from cigarettes might be found in the form of  $\text{Ni}(\text{CO})_4$ , which can be very harmful to animals; research has shown that one cigarette contains 1.1 to 3.1 g of Ni (Cempel and Nikel, 2006). Oxides, sulfides, soluble compounds, and, to a smaller degree, metal Ni are the forms of Ni that are discharged into the environment by human activities.

Food consumption is another way that contacts with Ni may occur; in fact, large concentrations of this hazardous metal can be found in nuts, cocoa, and chocolate in addition to certain vegetables (tomato, spinach, green beans, asparagus, broccoli, and carrot) (Vasiluk *et al.*, 2019). Ni is also inadvertently incorporated into the diet by way of food manufacturing that employs stainless steel equipment, as well as via bodily interactions (Lavinia *et al.*, 2018).

### *Ni in agricultural system*

Ni penetrates the ecosystem through both anthropogenic and natural means. Following its circulation within the biosphere, only a portion of Ni is assimilated by plant life, which is subsequently ingested by living organisms (Chen *et al.*, 2009; Wilson and Maliszewska-Kordybach, 2000). Soil Ni concentrations range from around 20 mg/kg on average, however, this may fluctuate widely concerning the soil's parent material and ranges from 0.2 to 450 mg kg<sup>-1</sup> (Jin *et al.*, 2006; Oorts *et al.*, 2007).

Ni in the soil is present in various carbon-containing or carbon-deficient forms such as free or dissolved ions within the soil solution and sediments or crystalline



molecules. Soil acidity improves Ni availability, which means that a lower pH makes Ni transfer to plant roots easier (Li *et al.*, 2009). It has been noted that insoluble hydroxides are prevalent in soil solutions with pH values over 6.5 while Ni compounds are found in comparatively larger quantities with pH values below 6.5 (Lock *et al.*, 2007).

The anthropogenic contributions of Ni to soils primarily arise from emissions associated with smelting and refining processes, as well as the disposal of municipal waste or its application as a fertilizer. Soil Ni may be released naturally by weathering and erosion of rocks and sediments. Additionally, plants can have their Ni leached into soils by acid rain (Buxton *et al.*, 2019).

#### *Ni in aquatic system*

Twenty  $\mu\text{g L}^{-1}$  of Ni is the suggested permissible level in drinking water according to the Bureau of Indian Standards. Based on reports, the ocean contains roughly 0.5 to 2 parts per billion (ppb) of Ni, whereas rivers exhibit a concentration of about 0.3 ppb of Ni species. Up to 980  $\mu\text{g L}^{-1}$  of soluble Ni has been detected in groundwater with a pH less than 6.2. Ni concentrations in urban storm runoff water samples are analyzed to possess about as low as below one and as high as 87 g/L (Begum *et al.*, 2022). Ni may be found in the aquatic environment from a variety of natural sources. Environmental evaporation of Ni from sediments, their weathering, and dissolution contribute to environmental Ni that occurs naturally. The organic materials found in aquatic systems, such as detritus, algae, and bacteria, and humic and fulvic acid in the form of dissolved salts may be found on clay particles (Beattie *et al.*, 2017). Because basic bedrock minerals dissolve in rain, surface water may get polluted with it. Following the occurrence of acid rain, Ni exhibits enhanced mobility within the soil, consequently elevating its concentration in groundwater. Anthropogenic sources of Ni in aquatic environments include pollutants resulting from industrial activities such as mining, processing, and refining, as well as industrial wastewater and effluents, including discharge from tailing piles. Additionally, domestic wastewater and discharge from landfills contribute to this contamination (Rauch and Pacyna, 2009).

#### *Ni in food chain*

Ni from all sources enters into the food chain when Ni-contaminated food like plants and water is ingested by animals and animals are ultimately consumed by humans. Due to its mobility, Ni can migrate from soil to plant parts such as seeds and leaves, increasing the likelihood that it will enter the food chain. Cullaj *et al.* (2004) found that when Ni levels in plants accumulate at toxic levels,

it may have serious consequences for both humans and animals. Hyper-accumulator plants possess the capability to sequester elevated concentrations of toxic metals from soil, which may pose risks to human and animal health by infiltrating the food chain. To prevent potential health and environmental hazards, it is important to dispose of the large amounts of polluted and dangerous biomass that accumulate as a result of phytoremediation in an appropriate manner (Mohanty and Patra, 2011). This hazardous biomass comprises lignin, hemicellulose, ash, organic matter, and cellulose characterized by elevated water content in addition to vaporous components. Its calorific significance is contingent upon the specific plant species (Cempel and Nikel, 2006). Plants used for phytoremediation should not only be resistant to diseases but also non-edible and suitable only for use as a renewable energy source (Shahzad *et al.*, 2018).

### TOXICOKINETICS OF Ni IN POULTRY

#### *Absorption of Ni through inhalation*

The introduction of Ni particles and their subsequent absorption by the respiratory system is contingent upon their physical and chemical characteristics. Particles deposit in various parts of the respiratory system depending on parameters including their aerodynamic size (Deng *et al.*, 2016). For instance, merely fifty percent of particles possessing aerodynamic diameters of less than 30  $\mu\text{m}$  are capable of being inhaled by animals. Within this subset, the larger particles, ranging from 5 to 30  $\mu\text{m}$ , tend to deposit in the nasopharyngeal region, whereas the smaller particles, measuring between 1 and 5  $\mu\text{m}$ , penetrate the lower sections of the lung, specifically the trachea and bronchiolar region (Terra *et al.*, 2008). Only the finest particles, measuring less than 1 micrometer, are capable of penetrating the alveolar region of the lungs. After deposition, organisms ability to absorb Ni is impacted through both physical characteristics and elemental composition related to particles, including size and surface area. Soluble Ni compounds are swiftly assimilated by the pulmonary system (Massányi *et al.*, 2000). The ciliary transport system quickly eliminates Ni ions after dissolving Ni particles in mucus. On the other hand, less soluble Ni particles may be phagocytosed into the lung's epithelial cells, where they dissolve gradually and offer a steady supply of Ni ions. The higher carcinogenicity of inhaled sulfidic and oxidic species compared to soluble Ni species may be explained by cellular absorption and molecular processes (Schaumlöffel, 2012).

#### *Absorption of Ni through ingestion*

Because soil and plants have far greater quantities

of Ni than the atmosphere, consuming food may promote Ni more to an animal's body burden than inhalation. However, the absorption of Ni along the alimentary canal is markedly slow as compared to the respiratory system (Kumar and Sharma, 2019). According to Foulkes and McMullen (1986), there is a two-step process that the body goes through to absorb dissolved Ni along the alimentary canal. The first step includes Ni ions to cross the mucosal membrane. The second step is for the mucosal cells to passively transfer Ni in both directions into the body through the circulatory system. Research has shown that the rate of Ni absorption is affected by dietary components. Research indicates that the assimilation of Ni sulfate in the gastrointestinal tract is markedly enhanced when administered in drinking water compared to its administration alongside food. Including protein or fiber in your diet may reduce soluble Ni in the gastrointestinal tract by a factor of two (Yang *et al.*, 2023). It seems that the presence of positively charged ions having charge +2 affects the availability of Ni (Outridge and Scheuhammer, 1993), who also found that Zn and milk competitively inhibit Ni absorption throughout the small intestine might be due to  $\text{Ca}^{2+}$  or protein. According to Ling and Leach (1979), introducing supplementation of iron and copper at the rate of 100 mg per kg considerably decreased the buildup of Ni in the tissues of chicks fed with a food containing supplementation of 500 mg of Ni per kg.

#### *Cellular uptake and tissue distribution of Ni*

Absorbed Ni is disseminated throughout the body via the bloodstream. Serum Ni translocates across cell membranes in animals by binding mostly to albumin, but also to L-histidine and  $\alpha$ -2-macroglobulin. In contrast to the passive method of cellular absorption of Ni from the blood, macrophages and sarcoma1 cells with phagocytic capability have been shown to endocytose Ni particles having  $>5 \mu\text{m}$  in diameter *in vitro* (Schaumlöffel, 2012). The cells phagocytose the crystalline Ni particles. Vacuoles are responsible for enclosing particles after they are phagocytosed leading to acidification and dissolving of Ni consequently elevating the concentration of Ni within the cells.

Studies have shown that complexes and ions of Ni are eliminated by the ciliary action quickly which arises by the dissolution and breakdown of Ni. Conversely, phagocytic cells like epithelial cells and macrophages may kill the insoluble Ni by phagocytosis (Hadyait *et al.*, 2018).

As these particles undergo diffusion within the cellular environment, they gradually undergo dissolution (for instance,  $\text{Ni}_3\text{S}_2$  dissolves through the process of oxidation), thereby facilitating a sustained release of Ni (II) ions (Massányi *et al.*, 2000). Reduced nuclear and

greater cytoplasmic Ni levels are the consequence of salts of Ni which are easily dissolved in aqua medium and shapeless  $\text{Ni}_2\text{S}_3$  being inadequately assimilated, in contrast to crystalline Ni particles. The negative charge is responsible for the ordered arrangement of  $\text{Ni}_2\text{S}_3$  whereas the positive charge causes it to be shapeless (Rehan *et al.*, 2023).

Scientists believe that due to the impermeable and densely packed junctions of the intestinal epithelium, Ni from the open spaces of organ systems moves to the spaces present between the cells through a particular transport mechanism. The jejunum may absorb and secrete Ni by trans-membrane diffusion, according to several investigations; moreover,  $\text{Ca}^{2+}$  channels are capable of moving Ni ions (Begum *et al.*, 2022).

#### *Excretion of Ni*

The primary excretion pathway for assimilated Ni is through urine, irrespective of the exposure route, with an alternative route being defecation. Chicken refuse constitutes the most substantial waste product produced during the poultry production process. Feathers, bedding materials, discarded food, medication, and water are all combined to form chicken litter. The substantial volumes of chicken manure generated each year are heavily distributed over very limited land areas, leading to buildups that might endanger the ecosystem by contaminating surface and groundwater (Irshad *et al.*, 2013).

To minimize adverse effects regarding the ecosystem and living organisms and optimize an advantage related to poultry manure as an organic fertilizer, it is imperative to fill the information gap. Chicken litter may be a rich source of micronutrients due to the presence of heavy metals including Ni, Se, Cu, Zn, Fe, etc. which are necessary for plant development (Rehman *et al.*, 2012). Nevertheless, higher levels present significant health hazards to animals, plants, and the overall integrity of the environment. The recurrent ingestion of feed containing elevated levels of heavy metals may result in the bioaccumulation of these metals within poultry litter, subsequently affecting manure and compost utilized for soil application (Yasmeen *et al.*, 2023).

A certain amount of harmful minerals being a part of chicken feed are expelled in chicken litter via feces and urine, with just 5%-15% being absorbed by the birds. Layer chicken farms are highly polluted as compared to broiler ones as layer litter is more persistent than broiler litter because of the high transition capacity of layers (Kyakuwaire *et al.*, 2019). Research by Kyakuwaire *et al.* (2019) examined the possibility of utilization of poultry manure in agriculture having hazardous impacts on living organisms and the ecosystem and they also sought to

determine if the present state of chicken litter meets the minimal requirements for use as organic fertilizer.

## Ni TOXICITY IN POULTRY

The accessibility of minerals derived from plant-based feed materials, in conjunction with conventional inorganic sources such as oxides, sulfates, or carbonates, is comparatively limited. Conversely, the demand for microelements among contemporary, high-yield strains of poultry grown for meat and egg production is significantly elevated (Saripinar-Aksu *et al.*, 2012). These facts, coupled with a comprehensive interpretation regarding the minerals essentiality in the normal metabolic processes, and the fluctuating profile of micronutrients present in the diet, have caused substantial incorporation of heavy metals in chicken farming commercially. This incorporation often occurs at levels significantly exceeding the birds' nutritional requirements, with a considerable safety margin. Particularly in regions with heavy chicken farming, this might result in an elevated level of microelements in poultry products as well as their buildup in the food chain and the environment (Świątkiewicz *et al.*, 2014).

### *Ni toxicity in solid and liquid poultry feed*

Heavy metals can get into the soil (through manure application), water (employing leaching), living things like plants and animals (via the food chain) (Ukpe and Chokor, 2018), and the air (through suspended particulate matter) if they are used in poultry feeds (Yasmeen *et al.*, 2023). The metals are incorporated into formulated feed as pre-mixers to facilitate the growth of early chickens, the development of their guts, and the production of meat. It began to generate complications when it exceeded the WHO's permissible thresholds. Metals begin to bioaccumulate in chicken meat and eggs when chickens are fed contaminated feed, and they are subsequently passed along to humans. This is the reason why food safety authorities must track the integrity of feed production to prevent the inappropriate introduction of heavy metals during the production process (Kumar and Sharma, 2019; Yang *et al.*, 2023). 0.02 ppm is the value of Ni suggested to be acceptable in solid feed used for poultry and water should not have 2.00 ppm Ni (Alkhalaf *et al.*, 2010; Uluozlu *et al.*, 2009).

Management practices are responsible for substantial variations in the quality of poultry feed. Imran *et al.* (2014) discovered that Ni concentrations were higher in feed gathered from poultry farms than in feed from companies. This may be attributed to the contamination of feed ingredients or the use of low-quality feed ingredients in self-formulated feed. The finisher feeds were determined

to contain the highest mean amount of Ni, followed by the grower and starter feeds, after a comparison of three types of broiler feeds: the starter, grower, and finisher. While comparing commercial chicken feed with locally compounded feed, Suleiman *et al.* (2015) discovered that the Ni supplementation was insufficient, falling short of the nutritional needs of broiler chickens to a potentially harmful level in local feed. In the last few decades, shaving dust, a significant solid residue from the process of tanning, has been employed as a source of proteins in poultry feed manufacturing due to its cost-effectiveness and it is also found to be involved in contributing to heavy metal pollution in poultry (Mottalib *et al.*, 2016). Because heavy metals from the copper containers leach under hot acid treatment conditions and are subsequently adsorbed by dust powder, Mottalib *et al.* (2016) found that the mean concentration (mg/kg) of Ni in shaving dust powder was higher as compared to raw shaving dust. Heavy metals in poultry feed, including Ni, were diluted with other ingredients, so their concentration was significantly lower than in dust powder.

Ni has been confirmed to be translocated from poultry feed to its tissues in previous studies. Shamshad *et al.* (2017) emphasized the transfer of heavy metals throughout the samples and reported that the average level of Ni was  $0.016 \pm 0.02$  mg/kg in feed, build up as  $0.013 \pm 0.05$  mg/kg in the leg,  $0.006 \pm 0.00$  mg/kg in the liver,  $0.006 \pm 0.02$  mg/kg in the heart samples, and transmitted to the eggs at a rate of  $0.007 \pm 0.00$  mg/kg. A research indicated the translocation of Ni from the poultry diet to its bodily tissues in the form of a transfer factor of 0.09-0.3 (Mottalib *et al.*, 2016). They also highlighted the level of Ni in various tissues from the greatest concentration of  $7.41 \text{ mg kg}^{-1}$  in the liver to the least concentration of  $2.22 \text{ mg kg}^{-1}$  in the bone.

Elevated contamination of poultry products and their waste is because of the introduction of heavy metals through their diet. Poultry diet and manure were found to be highly polluted with Ni by Ukpe and Chokor (2018). They determined that the trace minerals in the poultry diet are significantly consistent with their amounts in poultry manure. Because of bioaccumulation and other sources (particularly water intake), the concentration of Ni ions in the examined poultry waste was  $1.89 \text{ g/kg}$ , higher than the concentration in the feed ( $1.71 \text{ g/kg}$ ). Ni concentrations in feed samples were found to be reflected in litter and air, as noted by Yasmeen *et al.* (2023). They compared the feed quality based on the Ni concentration in the litter, and it was determined that the retention and feed quality of brand C may be favorable due to the lesser amount of Ni in the litter compared to groups A and B. Solid feed and water are both responsible for heavy metal pollution in poultry, as determined by Kabeer *et al.* (2021). Because

farms are more polluted than backyards, they found mean Ni concentration in the solid feed and water of poultry farms to be higher.

According to Hashemi *et al.* (2019), commercial laying hens may be consuming heavy metals at an increased rate through their food sources. They identified substantial variations in the feed of various strains of commercial laying hens. LSL hens had the highest Ni content in their feed (4.71 mg/kg FW), followed by Hy-Line hens (2.69 mg/kg FW), Bovans hens (2.50 mg/kg FW), Shaver hens (2.08 mg/kg FW), and Native hens (1.78 mg/kg FW). Ni concentrations were discovered to be greater in feed than in eggs, except in native hens, when the transfer of Ni from feed to eggs was measured. According to research by Jabeen *et al.* (2024), Ni concentration was found to be lower in feed samples compared to egg samples.

#### *Ni toxicity in poultry tissues*

The production cycle for poultry is shorter compared to that of animals raised for red meat, and it is also a better feed converter (Mahmoud and Abdel-Mohsein, 2015). Poultry meat is popular for several reasons, the most important of which are its inexpensive and competitive pricing and its dietary and nutritious qualities in comparison to other meats (Mansour *et al.*, 2009). Around the globe, poultry meat is an essential component of everyday diets. Nevertheless, chicken meat is not always as beneficial as it appears; it can also be impacted by environmental contamination, particularly heavy metals, which have the capability to bioaccumulate and biomagnify, thereby posing a potential threat to humans (Imran *et al.*, 2015). FAO and WHO allowed the Ni level in poultry edible tissues to be up to 0.5 ppm (FAO/WHO, 2000).

The typical heavy metal is not biodegradable, has a lengthy biological half-life, and may accumulate in many bodily systems, causing both short-term and long-term harmful consequences (Radwan and Salama, 2006). Pollutants are not evenly distributed throughout an organism's organs; instead, they build up in certain target organs (Terra *et al.*, 2008). The accumulation of an element in the organs is contingent upon the animal's age and breed, the quantity of the ingested element, and the interval of exposure (Massányi *et al.*, 2000).

Ni or Ni compound toxicity is primarily directed at the respiratory system following inhalation exposure. Deng *et al.* (2016) found that the dietary pathway induces pulmonary oxidative stress and inflammatory responses, which subsequently contribute to histopathological lesions and dysfunction, as a result of NiCl<sub>2</sub> intake. Additionally, Imran *et al.* (2015) identified a higher concentration of Ni in the rib cage than in the neck, which may have an impact on the airways.

It has been demonstrated that metals accumulate in the liver and muscular portion of poultry. Toxin contamination in chicken livers poses a significant threat to human health due to the potential for cytotoxicity and general pathologies following digestion (Rehan *et al.*, 2023). A comparatively high percentage of Ni contamination in poultry was reported by Khan *et al.* (2015). The liver was found to contain the maximum concentration of Ni, followed by the blood and musculature. Imran *et al.* (2015) also observed that Ni was more abundant in the liver of chickens than in the heart and kidney. Upon comparing the bones, they discovered that the leg bone was more contaminated with Ni and in limbs, wings contained a greater amount of Ni than legs. Mahmoud and Abdel-Mohsein (2015) found that breast and leg muscles had a higher Ni contamination rate of 4.78 µg/g (dry weight) than the liver, which had a rate of 4.1 µg/g (dry weight). Compared to the liver, the gizzard was found to be significantly more Ni-polluted by Anjum *et al.* (2022) and Hadyait *et al.* (2018).

Atmospheric contaminants contribute to heavy metal accumulation by poultry meat during its sale on the roads in an open environment (Anjum *et al.*, 2022). Hadyait *et al.* (2018), Karaaslan and Yaman (2018), and Reddy *et al.* (2017) confirmed this by analyzing Ni contamination in chicken meat sold in various marketplaces. Kamaly and Sharkawy (2023) concluded that the carelessness of poultry farm owners is the major reason for the introduction of Ni in poultry meat as they detected Ni to be highest in breast tissues with the range of 0.154-0.228 µg g<sup>-1</sup> followed by leg tissues having 0.143-0.255 µg g<sup>-1</sup> Ni and liver with the 0.112-0.217 µg g<sup>-1</sup> Ni. Ni contamination varied in different geographical regions of Pakistan ultimately affecting its content in poultry as Hyderabad was found to have Ni-contaminated poultry blood and chicken tissues of Thatta were analyzed to have great Ni contaminants (Khan *et al.*, 2015).

Broiler and domestic poultry have varying levels of Ni and this can be attributed to their different feeding habits. Gender differences also influence Ni pollution in poultry. As, female domestic hens and male broilers were determined to be more contaminated with Ni (Rehman *et al.*, 2013). Rehan *et al.* (2023) evaluated layer and broody poultry to be significantly less contaminated with Ni in comparison to broiler ones.

Food items having remarkable quality and high nutrition is a basic right of humans and concern related to it has increased because of awareness about contamination of food (Mansour *et al.*, 2009). Our government must take action and strictly command the quality control organizations to ensure a pollution-free environment for poultry production (Khan *et al.*, 2015).



### *Ni toxicity in poultry eggs*

Food safety is a critical component of the production, management, and ingestion of food (Omari *et al.*, 2018). Eggs from chickens are a great way to get the vitamins, minerals, proteins, and amino acids that people need (Aendo *et al.*, 2019; Fu *et al.*, 2014). Nevertheless, heavy metals from the environment and food may build up in eggs, which might be harmful to people, especially children (Fu *et al.*, 2014). PTEs, such as Ni, may be absorbed by female birds from a variety of environmental sources and then transferred into their tissues and eggs (Aendo *et al.*, 2018). Various sources, including feed, water, litter, housing equipment, and the environment, may contribute to elevated concentrations of metals in chicken products (Codling *et al.*, 2008). According to Ul-Islam *et al.* (2014), several of these metals have the ability to pass through the eggshell and may potentially pose harm to the developing chicken embryos. An indication of the exposure of chickens to metals throughout their lifespan is provided by the estimated amount of heavy metals in their eggs (Saad-Eldin and Raslan, 2018). Poultry eggs must have Ni levels up to 1.65 ppm which is considered safe for consumption (Ul-Islam *et al.*, 2014).

Consumers can enhance their nutritional intake by selecting eggs from ecological sources, which have a higher nutritional value, as there are variations in egg quality among various habitation systems. This may be attributed to variations in feed ingestion and the adjacent environment. The metal concentrations in egg albumen from various environments were examined by Kirov *et al.* (2023). Organic eggs are the healthiest option, according to the results, which showed that backyard chickens had the highest Ni levels at 0.235058 mg/kg, followed by soil/litter hens at 0.1891993 mg/kg, free range hens at 0.136302 mg/kg, caged hens at 0.1227397 mg/kg, and organic hens at 0.094421 mg/kg. This idea is also supported by Saad-Eldin and Raslan (2018) that organic eggs have decreased Ni poisoning. According to Saad-Eldin and Raslan (2018), balady eggs, which are produced from free-range house-fed chickens, had 1.31 ppm Ni, while commercial eggs, which are produced from laying hens fed on commercial ration, had 0.61 ppm Ni. In contrast, organic eggs, which are produced from laying hens fed on an organic-based ration, had a lower Ni content of 0.29 ppm. The consumption of heavy metal-contaminated feed is positively correlated with the increased content of metals in chicken farm eggs. As, Kabeer *et al.* (2021) found that heavy metal content is greater in eggs gathered from chicken farms than in eggs from chickens maintained in backyards, lending credence to the same argument. However, Hashemi *et al.* (2019) found that the highest concentration of these elements was found in eggs from free-range hens. This concentration

exceeded the standard maximum limits due to the fact that the hens are exposed to flora that have been affected by heavy metals. Elements like Ni may migrate across the membrane from albumen to yolk in eggs, as comparing the two halves of an egg showed that the yolk had larger amounts of these elements than the white (Kabeer *et al.*, 2021). Seasonal fluctuations may influence the elemental composition of eggs from free-range hens. Altun *et al.* (2019) found that the amounts of metal elements in the eggs of free-range hens varied statistically with season.

Metal concentrations in eggs are influenced by a variety of variables, including the hens growing phase, the origin of the eggs, and their varying capacities for heavy metal absorption and accumulation (Shaheen *et al.*, 2016; Zhang *et al.*, 2016). Hashemi *et al.* (2019) investigated the substantial differences in Ni concentration among various strains of laying hens. Eggs laid by Native chickens had the greatest Ni content at 2.018 mg/kg FW, followed by eggs laid by LSL hens at 1.42 mg/kg FW, Bovanse hens at 1.4 mg/kg FW, Shaver hens at 0.36 mg/kg FW, and Hy-Line hens at 0.05 mg/kg FW. Differences in levels of metals were also observed in previous investigations among various bird species. According to Yuan *et al.* (2023), the maximum concentration of Ni was found in duck eggs (34.70 µg/kg ww), followed by chicken eggs (31.32 µg/kg ww) and quail eggs (30.38 µg/kg ww).

While the exact mechanism of heavy metal bioaccumulation by laying hens is unknown, several factors affect it, including the physicochemical characteristics of the metal, the location, the season, and the hens age, metabolic cycles, breeding, and feeding habits (Farahani *et al.*, 2015; Okoye *et al.*, 2015). Shamshad *et al.* (2017) emphasized the migration of heavy metals across the samples and reported that the mean concentration of Ni was  $0.016 \pm 0.02$  mg/kg taken in feed, accumulated as  $0.013 \pm 0.05$  mg/kg in the leg,  $0.006 \pm 0.00$  mg/kg in the liver,  $0.006 \pm 0.02$  mg/kg in the heart samples, and transmitted to the eggs at a rate of  $0.007 \pm 0.00$  mg/kg. Compared to raw meat and table eggs, the meat products had greater Ni levels, according to Korish and Attia (2020). The average Ni concentration in the diet of layer hens was approximately 5.42 ppm throughout the entire production process, the progeny of layer hens contained 10.31 ppm of Ni, while it was undetectable in the eggs (Korish and Attia, 2020). Jabeen *et al.* (2024) determined that Ni was the most concentrated metal, with an average concentration of 157.158 mg/kg in feed, as opposed to 151.044 mg/kg in eggs. There is a correlation between the trace elements, but they also show different origins, suggesting that they behave similarly and independently throughout transportation (Izah *et al.*, 2022). Izah *et al.* (2022) identified the association of Ni with other metals.

Using a multivariate method, they concluded that the typical content of Ni in chicken eggs was strongly tied to copper and was not affected by other trace elements.

Eggs, particularly those produced by free-range poultry, are regarded as the optimal samples for the detection of environmental contaminants because chickens inhabit the same climate as humans. It is imperative to enhance the welfare and husbandry practices of animals in the production sector, with an emphasis on ecological standards. It is strongly advised to monitor metal levels in eggs produced by various bird species as well as feeds fed to birds since they are the primary sources of their susceptibility to these metals (Giannenas *et al.*, 2009).

Quercetin supplementation is one of the methods of mitigating the burden and adverse impacts of in-feed heavy metals. The results of Zoidis *et al.* (2021) research on dietary supplementation of *Gallus gallus domesticus* were encouraging, as the elemental composition of eggs changed as a consequence of quercetin supplementation. The author also suggested that the addition of quercetin resulted in an improvement in the incorporation of minerals in the egg compartments of *Gallus gallus domesticus* compared to hens that were fed a basal diet. This finding may suggest that it is feasible to develop eggs that have been optimized to meet the nutritional and health needs of a specific population in the future. The molecular formula of quercetin is  $C_{15}H_{10}O_7$ . Many fruits and vegetables, including apples, onions, and their by-products, contain quercetin, a member of the flavonol subclass of flavonoids (Lee *et al.*, 2020; Ulusoy and Sanlier, 2020). Dietary flavonoids may influence cellular oxidative status and metal homeostasis by interacting with trace minerals and influencing the level of metallothionein. Through their ability to chelate transition metals, flavonoids exhibit antioxidant properties. Protecting against oxidative stress, metal-flavonoid chelates are superior free radical scavengers. Flavonoids also form complex compounds which have great capability to make heavy metals unavailable to body tissues ultimately mitigating heavy metal contamination (Malešev and Kuntić, 2007). Quercetin being a flavonoid performs this by associating with metal particles through chelation. It is available in two forms: with a carbohydrate called glycoside or having carbohydrate absent known as aglycone (Saeed *et al.*, 2017).

#### *Ni toxicity in poultry litter*

The growing public health risks from the increase in intensive poultry farming pollutants have become a major concern for experts (Yasmeen *et al.*, 2023). Poultry litter functions as a profitable marketing tool for the industry because it contains high mineral contents which enable crop fertilization yet contains hazardous heavy metals

within it. Heavy metals in poultry feed at elevated levels per kg produce two outcomes: Their storage in bird tissues and their passage into litter (Rehman *et al.*, 2012). The environmental impact of trace minerals happens when they exceed animal requirements and are eliminated through manure production. Studies monitored the amounts of metals while demonstrating that soil containing poultry litter contained elevated metal concentrations when compared to untreated soil (Yasmeen *et al.*, 2023). Plants that grow in manure-treated soil contain encapsulated trace metals that enter the food chain to negatively impact both human health and the environment. In Pakistan, the agricultural sector is putting all living organisms at great risk by using heavy metal-contaminated chicken manure in place of fertilizers. To use poultry manure as a fertilizer, it should be first treated to eliminate harmful contaminants (Korish and Attia, 2020). 21 mg kg<sup>-1</sup> is the Ni level in poultry waste considered to be safe for usage in agriculture according to VICEPA (Kyakuwaire *et al.*, 2019).

Recent investigations revealed the capability of heavy metal-contaminated poultry feed to contaminate poultry waste with the same heavy metals. A chicken diet is capable of harming our ecosystem by introducing harmful trace elements in chicken manure that lead to heavy metal pollution in agricultural lands as studied by Jackson *et al.* (2003). The level of heavy metals in feed is directly proportional to their level in the manure as they are not significantly different (Ukpe and Chokor, 2018). Rehman *et al.* (2012) investigated the route of heavy metals from their addition through the feed to their deposition in the body and at last their release in the environment and found that less of them were released in the litter while much of them were absorbed in the body. Yasmeen *et al.* (2023) compared the poultry feed of three companies and also the litter of chickens grown on this feed to analyze the effect of feed quality and management practices. The poultry diet of Group C proved to be the best as the low concentration of metals was detected in their corresponding litter and Group A showed a higher concentration of metals in their litter, giving a hint of improper management practices. Layer and broiler chickens were compared for their heavy metal concentrations of litter at different production stages. Layer chickens had Ni concentrations in the order of 11.4 mg/kg, 10.8 mg/kg, and 8.74 mg/kg in the starter, grower, and laying stages respectively. On the other hand, broiler chickens contained Ni in order of 54.3 mg/kg, 46.7 mg/kg, and 23.0 mg/kg in the finisher, starter, and grower stages. At all stages of production, Ni was found to be greater in the manure samples as compared to feed samples (Korish and Attia, 2020). Irshad *et al.* (2013) analyzed the Ni content in manure samples of different animals in order of sheep having the highest contamination followed by chicken,

ostrich, goat, and cow having the least contamination.

Research shows that Ni levels in feed samples directly affect Ni content in poultry fecal matter. The reduction of Ni bioaccumulation in the environment requires both feed-related Ni guidelines and specific management programs for intensive poultry farming.

### TOXIC EFFECTS OF Ni ON POULTRY HEALTH

Scientists have conducted various research studies regarding Ni's harmful effects. High Ni concentrations create health risks that include allergies, together with cancer and non-malignant respiratory diseases and impaired immune system function (Deng *et al.*, 2016). Excessive Ni levels in chicken dietary supplements cause pulmonary hypertension through their accelerating effect on erythropoietin production and subsequent elevations in blood hemoglobin content. Ni triggers two processes: it enhances rapid lipid destruction along with protein decomposition and it activates free radicals while blocking DNA repair mechanisms (Baloš *et al.*, 2017).

According to Ling and Leach (1979), any dietary Ni level above 300 mg/kg substantially harmed poultry growth. The researchers documented cases of anemia together with increased mortality outcomes in chickens that received diets with 1100 mg/kg Ni supplementation. An experimental study on broiler chickens by Bangyuan *et al.* (2013) showed that Ni dietary supplementation resulted in lower glutathione hormone (GSH) levels along with reduced activities of glutathione peroxidase (GSH-Pk), catalase (CAT), and superoxide dismutase (SOD) which in turn led to oxidative stress and anti-oxidation impairment.

### HUMANS ARE AT RISK

4  $\mu\text{g g}^{-1}$  is the safe and acceptable level of Ni in food items consumed by humans (Mahmoud and Abdel-Mohsein, 2015). In 2008, Ni was regrettably designated as the Allergen of the Year (Prueitt *et al.*, 2020). Having chickens with high Ni concentrations has a significant negative impact on human health. According to the findings of several *in vitro* and *in vivo* studies, oxidative stress, inflammation, apoptosis, and lung toxicity are all caused by Ni and Ni oxide nanoparticles (Codling *et al.*, 2008). Ni inhibits the catalytic function of an enzyme by interacting with the active site present on it that contains a particular sequence of protein subunits such as lysine, glutamate, histidine, and cysteine. Alternatively, it may interact with allosteric locations present on any of the enzymatic molecules, thereby exerting an inhibiting or promoting influence on their functioning (Sutunkova *et al.*, 2018).

*et al.*, 2018).

Ni compounds, either soluble or insoluble, are categorized as Group 1 of cancer-causing agents by IARC (International Agency for Research on Cancer), indicating that Ni produces carcinogenic effects in living organisms (Xu *et al.*, 2015). In contrast, both the Ni and Ni compounds have been categorized as Group 2B, suggesting that they are potentially carcinogenic to humans. The research community has not yet determined the exact biological processes through which Ni causes cancer, but several pathways might be responsible for cancer development. The actual carcinogenic form of Ni exists as ionic  $\text{Ni}^{2+}$  because of its strong ability to attach itself to DNA and nuclear proteins (Schaumlöffel, 2012). Ni ion activity leads to heterochromatinization because it initiates chromatin material condensation when it interacts with DNA complexes containing histone proteins. Ni compounds can modify DNA methylation patterns of genes through epigenetic alterations while inducing DNA hyper-ubiquitination of H2A and H2B proteins and DNA hyper-phosphorylation at H3S10 position and DNA hyper-methylation at H3K4 sites. DNA-histone protein complexes that experience Ni compound interaction might lead to cellular alteration and tumor development and ultimately cancer (Cantone *et al.*, 2011).

Ni-induced neurotoxicity mechanisms are poorly understood yet, however, oxidative stress and defective mitochondria account for most damage. Ni exposure creates damage to mitochondria through three mechanisms, which include reductions in mitochondrial ATP content as well as damage to mitochondrial DNA and disruption of mitochondrial membrane potential. Any disruptions within either the electron respiratory chain or the mitochondrial performance will produce increased reactive oxygen species (ROS) (Imran *et al.*, 2015). According to Song *et al.* (2017), antioxidant agents, for example, taurine, melatonin, and L-carnitine possess antioxidant properties and are important in processes of detoxification, energy production, and homeostasis in mitochondria and neurotransmission. They are capable of lowering oxidative stress and ROS production, resultantly inhibiting carcinogenic and neurogenic effects introduced by Ni.

### NICKEL REMEDIATION

To reduce Ni's detrimental impact on ecosystems, it is almost always essential to clean up polluted soils. Ni-decontamination presents significant challenges in terms of both financial expenditure and technical intricacy (Sheoran *et al.*, 2010). Biological, physical, and chemical methods are being employed worldwide for heavy metal

remediation from ecosystems. Solidification, in situ vitrification, washing, flushing, soil incineration, stability of kinetic and electrical systems, excavation, and landfills are examples of typical remediation approaches (Kamran *et al.*, 2016; Ma *et al.*, 2011).

The employment of hyper-accumulating plants to remove harmful trace minerals present in the land and stock them in floral parts that can be harvested makes phytoremediation an attractive heavy metal remediation strategy (Sheoran *et al.*, 2010; Wuana and Okieimen, 2011). Under conditions of heavy metal stress, gene expression facilitates the initiation of adaptive and survival mechanisms in plants through the processes of ion exclusion or chelation/sequestration within the vacuole. The second tactic, which involves compartmentalizing or storing metals in vacuoles and is made possible by the chelation of organic acids, has been employed by hyperaccumulator plants (Krämer, 2010). Therefore, hyperaccumulator or hypertolerant plants often have higher levels of organic acids (citric acid, malic acid, etc.) (Sun *et al.*, 2011). Seventy-five percent of hyperaccumulators consist of species that accumulate Ni (Ghaderian *et al.*, 2007). A variety of plant species are known for their Ni accumulation capabilities, with the genus *Alyssum* from the Brassicaceae family exhibiting the greatest variety of species, which continues to grow over time (Özhatay *et al.*, 2011). Approximately 48 species within the Brassicaceae family can accumulate as much as 3% Ni in their foliage. For example, the hyperaccumulator plants *Thlaspi oxyceras* and *Alyssum caricum* belonging to the family Brassicaceae are capable of accumulating Ni in their leaves at the rate of 13778 mg kg<sup>-1</sup> and 12273 mg kg<sup>-1</sup> accordingly. Nonetheless, the *Alyssum* genus possesses a wider capability of Ni storage as compared to the other hyperaccumulator plants within the group (Altinözlü *et al.*, 2012).

## CONCLUSION

Around the globe, poultry products are among the most widely consumed and reasonably priced sources of protein. Nickel is considered to be biologically essential for poultry health at a minimal level, but its high concentration contributes to lethal effects. Living organisms are exposed to Ni and its harmful effects through numerous natural and man-made causes. Through Ni-contaminated chicken products, the Ni can easily be entered into the food chain and the human body. This contamination also appears in poultry litter affecting the environment. Desi poultry products are recommended due to their provenance from indigenous chicken varieties, which are allowed to forage freely on natural vegetation and invertebrates. Promoting

the dietary intake of desi birds may serve as a temporary solution; so, it is imperative to establish more rigorous regulations to ensure the safety of all chicken products available in the marketplace. The characterization and extraction of Ni present a considerable challenge due to its occurrence in minor amounts within the environment. However, bioaccumulation and agglomeration have direct or indirect effects on human health, making characterization and quantization a crucial endeavor that must be managed. The paramount concern lies in achieving an appropriate equilibrium between the identification of trace minerals essential for poultry and the assessment of their toxic or lethal dosages.

## RECOMMENDATIONS

Future research should concentrate on the metabolic roles of Ni, as well as its forms and how available it is from natural sources. There needs to be more awareness of the dangerous and required concentrations of nickel. It is imperative to perform thorough quality assessments and regular inspections of poultry feed, products, and debris. Although certain poultry products may potentially contain excessive levels of Ni, necessary quality assurance strategies should be implemented within the poultry industry, coupled with the proper training of nutritionists and best management rules, significantly mitigating the hazards induced by Ni overconsumption. To deter farmers from not complying, sanctions should be imposed on those who add Ni over the allowed limits. Furthermore, it is imperative to employ critical measurements for the effective detoxification of Ni from poultry waste.

## DECLARATIONS

### *Generative AI and AI-assisted technology statement*

The authors declare that no generative AI and AI assisted technology was used in the creation of this manuscript.

### *Statement of conflict of interest*

The authors have declared no conflict of interest interest.

## REFERENCES

- Aendo, P., Netvichian, R., Tippayalak, S., Sanguankiat, A., Khuntamoon, T., Songserm, T. and Tulayakul, P., 2018. Health risk contamination of heavy metals in yolk and albumen of duck eggs collected in central and western Thailand. *Biol. Trace Elem. Res.*, **184**: 501-507. <https://doi.org/10.1007/>



- s12011-017-1202-0
- Aendo, P., Thongyuan, S., Songserm, T. and Tulayakul, P., 2019. Carcinogenic and non-carcinogenic risk assessment of heavy metals contamination in duck eggs and meat as a warning scenario in Thailand. *Sci. Total Environ.*, **689**: 215-222. <https://doi.org/10.1016/j.scitotenv.2019.06.414>
- Aljohani, A.S., 2023. Heavy metal toxicity in poultry: A comprehensive review. *Front. Vet. Sci.*, **10**: 1161354. <https://doi.org/10.3389/fvets.2023.1161354>
- Alkhalaf, N.A., Osman, A.K. and Salama, K.A., 2010. Monitoring of aflatoxins and heavy metals in some poultry feeds. *Afr. J. Fd. Sci.*, **4**: 192-199.
- Altinözlü, H., Karagöz, A., Polat, T. and Ünver, İ., 2012. Nickel hyperaccumulation by natural plants in Turkish serpentine soils. *Turk. J. Bot.*, **36**: 269-280. <https://doi.org/10.3906/bot-1101-10>
- Altun, S. K., Paksoy, N., Dinç, H. and Durmaz, H., 2019. Determination of 17 elements in free-range hen eggs with ICP-MS. *Appl. Ecol. environ. Res.*, **17**. [https://doi.org/10.15666/aecer/1704\\_83698380](https://doi.org/10.15666/aecer/1704_83698380)
- Anjum, Z., Tarana, M., Ali, S., Yousaf, F., Rahat, A. and Yousaf, S., 2022. Comparative study on absorption of heavy metal residues in broiler chicken available in the university campus Peshawar, Pakistan. *Sarhad J. Agric.*, **38**: 1533-1539. <https://doi.org/10.17582/journal.sja/2022/38.4.1533.1539>
- Baloš, M. Ž., Ljubojević, D. and Jakšić, S., 2017. The role and importance of vanadium, chromium, and nickel in poultry diet. *World's Poult. Sci. J.*, **73**: 5-16. <https://doi.org/10.1017/S0043933916000842>
- Bangyuan, W., Hengmin, C., Xi, P., Jing, F., Zhicai, Z., Junliang, D. and Jianying, H., 2013. Investigation of the serum oxidative stress in broilers fed on diets supplemented with nickel chloride. *Health*, **5**: 454-459.
- Beattie, H., Keen, C., Coldwell, M., Tan, E., Morton, J., McAlinden, J. and Smith, P., 2017. The use of bio-monitoring to assess exposure in the electroplating industry. *J. Expo. Sci. Environ. Epidemiol.*, **27**: 47-55. <https://doi.org/10.1038/jes.2015.67>
- Begum, W., Rai, S., Banerjee, S., Bhattacharjee, S., Mondal, M. H., Bhattarai, A. and Saha, B., 2022. A comprehensive review on the sources, essentiality, and toxicological profile of nickel. *R. Soc. chem. Adv.*, **12**: 9139-9153. <https://doi.org/10.1039/D2RA00378C>
- Bersényi, A., Fekete, S. G., Szilágyi, M., Berta, E., Zöldág, L. and Glávits, R., 2004. Effects of nickel supply on the fattening performance and several biochemical parameters of broiler chickens and rabbits. *Acta Vet. Hung.*, **52**: 185-197. <https://doi.org/10.1556/avet.52.2004.2.7>
- Buxton, S., Garman, E., Heim, K. E., Lyons-Darden, T., Schlekat, C. E., Taylor, M. D. and Oller, A. R., 2019. Concise review of nickel human health toxicology and ecotoxicology. *Inorganics*, **7**: 89. <https://doi.org/10.3390/inorganics7070089>
- Cantone, L., Nordio, F., Hou, L., Apostoli, P., Bonzini, M., Tarantini, L., Angelici, L., Bollati, V., Zanobetti, A., Schwartz, J., Bertazzi, P. A. and Baccarelli, A., 2011. Inhalable metal-rich air particles and histone H3K4 dimethylation and H3K9 acetylation in a cross-sectional study of steel workers. *Environ. Hlth. Perspect.*, **119**: 964-969. <https://doi.org/10.1289/ehp.1002955>
- Cempel, M. and Nikel, G.J.P.J.S., 2006. Nickel: A review of its sources and environmental toxicology. *Pol. J. environ. Stud.*, **15**: 375-382.
- Chen, C., Huang, D. and Liu, J., 2009. Functions and toxicity of nickel in plants: recent advances and future prospects. *Clean Soil Air Water*, **37**: 304-313. <https://doi.org/10.1002/clen.200800199>
- Codling, E.E., Chaney, R.L. and Mulchi, C.L., 2008. Effects of broiler litter management practices on phosphorus, copper, zinc, manganese, and arsenic concentrations in Maryland coastal plain soils. *Commun. Soil Sci. Pl. Anal.*, **39**: 1193-1205. <https://doi.org/10.1080/00103620801925901>
- Cullaj, A., Hasko, A., McBow, I. and Kongoli, F., 2004. Investigation of the potential of several plants for phytoremediation of nickel contaminated soils and for nickel phytoextraction. *Eur. J. Miner. Process. Environ. Prot.*, **4**: 144-151.
- Deng, J., Guo, H., Cui, H., Fang, J., Zuo, Z., Deng, J., Wang, X. and Zhao, L., 2016. Oxidative stress and inflammatory responses involved in dietary nickel chloride (NiCl<sub>2</sub>)-induced pulmonary toxicity in broiler chickens. *Toxicol. Res.*, **5**: 1421-1433. <https://doi.org/10.1039/C6TX00197A>
- Denkhaus, E. and Salnikow, K., 2002. Nickel essentiality, toxicity, and carcinogenicity. *Crit. Rev. Oncol. Hematol.*, **42**: 35-56. [https://doi.org/10.1016/S1040-8428\(01\)00214-1](https://doi.org/10.1016/S1040-8428(01)00214-1)
- FAO/WHO, 2000. *Report of the 32<sup>nd</sup> session of the codex committee on food additives and contaminants*, Beijing People's Republic of China 20-24 March 2000.
- Farahani, S., Eshghi, N., Abbasi, A., Karimi, F., Shiri Malekabad, E. and Rezaei, M., 2015. Determination of heavy metals in the albumen of hen eggs from the Markazi Province (Iran) using ICP-OES technique. *Toxin Rev.*, **34**: 96-100. <https://doi.org/10.3109/15569543.2015.1040166>

- Foulkes, E.C. and McMullen, D.M., 1986. On the mechanism of nickel absorption in the rat jejunum. *Toxicology*, **38**: 35-42. [https://doi.org/10.1016/0300-483X\(86\)90170-8](https://doi.org/10.1016/0300-483X(86)90170-8)
- Fu, Q.L., Liu, Y., Li, L. and Achal, V., 2014. A survey on the heavy metal contents in Chinese traditional egg products and their potential health risk assessment. *Fd. Addit. Contam. B*, **7**: 99-105. <https://doi.org/10.1080/19393210.2013.853106>
- Genchi, G., Carocci, A., Lauria, G., Sinicropi, M.S. and Catalano, A., 2020. Nickel: Human health and environmental toxicology. *Int. J. environ. Res. Publ. Hlth.*, **17**: 679. <https://doi.org/10.3390/ijerph17030679>
- Ghaderian, S.M., Mohtadi, A., Rahiminejad, M.R. and Baker, A.J.M., 2007. Nickel and other metal uptake and accumulation by species of *Alyssum* (Brassicaceae) from the ultramafics of Iran. *Environ. Pollut.*, **145**: 293-298. <https://doi.org/10.1016/j.envpol.2006.03.016>
- Giannenas, I., Nisianakis, P., Gavril, A., Kontopidis, G. and Kyriazakis, I., 2009. Trace mineral content of conventional, organic, and courtyard eggs analysed by inductively coupled plasma mass spectrometry (ICP-MS). *Fd. Chem.*, **114**: 706-711. <https://doi.org/10.1016/j.foodchem.2008.09.079>
- Hadyait, M.A., Qayyum, A., Bhatti, E.M., Salim, S., Ali, A. and Shahzadi, M., 2018. Estimation of heavy metals in liver, gizzard, breast and thigh muscles of broiler chicken in different area of Lahore by ICP-OES. *Pakistan Sci. Miss. Vet. Res.*, **3**: 10-14.
- Hashemi, M., Sadeghi, A., Saghi, M., Aminzare, M., Raeisi, M., Rezayi, M. and Sany, S.B.T., 2019. Health risk assessment for human exposure to trace metals and arsenic via consumption of hen egg collected from largest poultry industry in Iran. *Biol. Trace Elem. Res.*, **188**: 485-493. <https://doi.org/10.1007/s12011-018-1437-4>
- Henderson, R.G., Durando, J., Oller, A.R., Merkel, D.J., Marone, P.A. and Bates, H.K., 2012. Acute oral toxicity of nickel compounds. *Regul. Toxicol. Pharmacol.*, **62**: 425-432. <https://doi.org/10.1016/j.yrtph.2012.02.002>
- Henry, P.R. and Miles, R.D., 2001. Heavy metals–vanadium in poultry. *Braz. Anim. Sci.*, **2**: 11-26.
- Imran, R., Hamid, A. and Amjad, R., 2015. Estimation of the heavy metal concentration in the poultry meat being produced in Kasur. *J. Biodivers. Environ. Sci.*, **7**: 62-75.
- Imran, R., Hamid, A., Amjad, R., Chaudhry, C., Yaqub, G. and Akhtar, S., 2014. Evaluation of heavy metal concentration in the poultry feeds. *J. Biodivers. environ. Sci.*, **5**: 394-404.
- Irshad, M., Malik, A.H., Shaukat, S., Mushtaq, S. and Ashraf, M., 2013. Characterization of heavy metals in livestock manures. *Pol. J. environ. Stud.*, **22**.
- Izah, S.C., Aigberua, A.O. and Ogwu, M.C., 2022. Trace element composition of *Gallus gallus domesticus* eggs and health risks associated with their consumption in Port Harcourt, Nigeria. *J. Fd. Saf. Hyg.*, **8**: 202-222.
- Jabeen, S., Jamil, I., Parveen, K., Mansab, S., Hussain, M. and Hussain, S., 2024. Quantification of toxic metals in chicken egg and chicken feed via SOM-artificial neural network. *Environ. Monit. Assess.*, **196**: 197. <https://doi.org/10.1007/s10661-024-12375-x>
- Jackson, B.P., Bertsch, P.M., Cabrera, M.L., Camberato, J.J., Seaman, J.C. and Wood, C.W., 2003. Trace element speciation in poultry litter. *J. environ. Qual.*, **32**: 535-540. <https://doi.org/10.2134/jeq2003.5350>
- Jin, C.W., He, Y.F., Tang, C.X., Wu, P. and Zheng, S.J., 2006. Mechanisms of microbially enhanced Fe acquisition in red clover (*Trifolium pratense* L.). *Pl. Cell Environ.*, **29**: 888-897. <https://doi.org/10.1111/j.1365-3040.2005.01468.x>
- Kabeer, M.S., Hameed, I., Kashif, S.U.R., Khan, M., Tahir, A., Anum, F., Khan, S. and Raza, S., 2021. Contamination of heavy metals in poultry eggs: A study presenting relation between heavy metals in feed intake and eggs. *Arch. environ. occup. Hlth.*, **76**: 220-232. <https://doi.org/10.1080/19338244.2020.1799182>
- Kamaly, H.F. and Sharkawy, A.A., 2023. Health risk assessment of metals in chicken meat and liver in Egypt. *Environ. Monit. Assess.*, **195**: 802. <https://doi.org/10.1007/s10661-023-11365-9>
- Kamran, M.A., Eqani, S.A.M.A.S., Bibi, S., Xu, R.K., Monis, M.F.H., Katsoyiannis, A., Bokhari, H. and Chaudhary, H.J., 2016. Bioaccumulation of nickel by *E. sativa* and role of plant growth promoting rhizobacteria (PGPRs) under nickel stress. *Ecotoxicol. environ. Saf.*, **126**: 256-263. <https://doi.org/10.1016/j.ecoenv.2016.01.002>
- Karaaslan, N.M. and Yaman, M., 2018. Assessment and ICP-MS determination of toxic metal content (Cd, Cr, Ni, and Pb) in turkish chicken meat for use as bioindicator for human health. *At Spectrosc.*, **39**: 16-21. <https://doi.org/10.46770/AS.2018.01.002>
- Khan, M.Z., Perween, S.H., Gabol, K., Khan, I.S., Baig, N., Kanwal, R. and Jabeen, T., 2015. Concentrations of heavy metals in liver, meat and blood of poultry chicken *Gallus domesticus* in three selected cities

- of Pakistan. *Can. J. Pure appl. Sci.*, **9**: 3313-3324.
- Kirov, P.M., Karadjov, M., Hristov, H.K. and Alexandrova, R., 2023. Comparative study of metal concentration determination in albumen of hen eggs originating from industrial poultry farms, backyard and free-range hens using ICP-OES technique. *BioRisk*, **20**: 129-138. <https://doi.org/10.3897/biorisk.20.97322>
- Korish, M.A. and Attia, Y.A., 2020. Evaluation of heavy metal content in feed, litter, meat, meat products, liver, and table eggs of chickens. *Animals*, **10**: 727. <https://doi.org/10.3390/ani10040727>
- Krämer, U., 2010. Metal hyperaccumulation in plants. *Annu. Rev. Pl. Biol.*, **61**: 517-534. <https://doi.org/10.1146/annurev-arplant-042809-112156>
- Kumar, S. and Sharma, A., 2019. Cadmium toxicity: Effects on human reproduction and fertility. *Rev. environ. Hlth.*, **34**: 327-338. <https://doi.org/10.1515/reveh-2019-0016>
- Kyakuwaire, M., Olupot, G., Amoding, A., Nkedi-Kizza, P. and Ateenyi B.T., 2019. How safe is chicken litter for land application as an organic fertilizer? A review. *Int. J. environ. Res. Publ. Hlth.*, **16**: 3521. <https://doi.org/10.3390/ijerph16193521>
- Lavinia, B., Florina, R. and Augustin, C., 2018. Is it possible a nickel-free diet? *Acta Med. Marisiensis*, **64**: 5.
- Lee, S.Y., Lee, S.J., Yim, D.G. and Hur, S.J., 2020. Changes in the content and bioavailability of onion quercetin and grape resveratrol during *in vitro* human digestion. *Foods*, **9**: 694. <https://doi.org/10.3390/foods9060694>
- Li, B., Zhang, X., Wang, X. and Ma, Y., 2009. Refining a biotic ligand model for nickel toxicity to barley root elongation in solution culture. *Ecotoxicol. environ. Safe.*, **72**: 1760-1766. <https://doi.org/10.1016/j.ecoenv.2009.05.003>
- Ling, J.R. and Leach Jr, R.M., 1979. Studies on nickel metabolism: Interaction with other mineral elements. *Poult. Sci.*, **58**: 591-596. <https://doi.org/10.3382/ps.0580591>
- Lock, K., Van Eeckhout, H., De Schampelaere, K.A., Criel, P. and Janssen, C.R., 2007. Development of a biotic ligand model (BLM) predicting nickel toxicity to barley (*Hordeum vulgare*). *Chemosphere*, **66**: 1346-1352. <https://doi.org/10.1016/j.chemosphere.2006.07.008>
- Ma, Y., Rajkumar, M., Luo, Y. and Freitas, H., 2011. Inoculation of endophytic bacteria on host and non-host plants-effects on plant growth and Ni uptake. *J. Hazard. Mater.*, **195**: 230-237. <https://doi.org/10.1016/j.jhazmat.2011.08.034>
- Mahmoud, M.A. and Abdel-Mohsein, H.S., 2015. Health risk assessment of heavy metals for Egyptian population via consumption of poultry edibles. *Adv. Anim. Vet. Sci.*, **3**: 58-70. <https://doi.org/10.14737/journal.aavs/2015/3.1.58.70>
- Malešev, D. and Kuntić, V., 2007. Investigation of metal-flavonoid chelates and the determination of flavonoids via metal-flavonoid complexing reactions. *J. Serb. chem. Soc.*, **72**: 921-939. <https://doi.org/10.2298/JSC0710921M>
- Mansour, S.A., Belal, M.H., Abou-Arab, A.A. and Gad, M.F., 2009. Monitoring of pesticides and heavy metals in cucumber fruits produced from different farming systems. *Chemosphere*, **75**: 601-609. <https://doi.org/10.1016/j.chemosphere.2009.01.058>
- Marangoni, F., Corsello, G., Cricelli, C., Ferrara, N., Ghiselli, A., Lucchin, L. and Poli, A., 2015. Role of poultry meat in a balanced diet aimed at maintaining health and wellbeing: An Italian consensus document. *Fd. Nutr. Res.*, **59**: 27606. <https://doi.org/10.3402/fnr.v59.27606>
- Massányi, P., Trandžík, J., Lukáč, N., Strapák, P., Kováčik, J. and Toman, R., 2000. The contamination of bovine semen with cadmium, copper, lead, and zinc and its relation to the quality of spermatozoa used for insemination. *Folia Vet.*, **44**: 150-15.
- Merrington, G., Peters, A. and Schlegel, C.E., 2016. Accounting for metal bioavailability in assessing water quality: A step change? *Environ. Toxicol. Chem.*, **35**: 257-265. <https://doi.org/10.1002/etc.3252>
- Mohanty, M. and Patra, H.K., 2011. Attenuation of chromium toxicity by bioremediation technology. *Rev. environ. Contam. Toxicol.*, **210**: 1-34. [https://doi.org/10.1007/978-1-4419-7615-4\\_1](https://doi.org/10.1007/978-1-4419-7615-4_1)
- Mottalib, M.A., Sultana, A., Somoal, S.H. and Abser, M.N., 2016. Assessment of heavy metals in tannery waste-contaminated poultry feed and their accumulation in different edible parts of chicken. *IOSR J. Environ. Sci. Toxicol. Fd. Technol.*, **10**: 72-78.
- Nys, Y., Schlegel, P., Durosos, S., Jondreville, C. and Narcy, A., 2018. Adapting trace mineral nutrition of birds for optimising the environment and poultry product quality. *World's Poult. Sci. J.*, **74**: 225-238. <https://doi.org/10.1017/S0043933918000016>
- Okoye, P.A.C., Ajiwe, V.I.E., Okeke, O.R., Ujah, I.I., Asalu, U.B. and Okeke, D.O., 2015. Estimation of heavy metal levels in the muscle, gizzard, liver and kidney of broiler, layer and local (cockerel) chickens raised within Awka metropolis and its

- environs, Anambra state, south eastern Nigeria. *J. environ. Prot.*, **6**: 609-613. <https://doi.org/10.4236/jep.2015.66055>
- Omari, R., Frempong, G.K. and Arthur, W., 2018. Public perceptions and worry about food safety hazards and risks in Ghana. *Fd. Contr.*, **93**: 76-82. <https://doi.org/10.1016/j.foodcont.2018.05.026>
- Oorts, K., Ghesquiere, U. and Smolders, E., 2007. Leaching and aging decrease nickel toxicity to soil microbial processes in soils freshly spiked with nickel chloride. *Environ. Toxicol. Chem. Int. J.*, **26**: 1130-1138. <https://doi.org/10.1897/06-533R.1>
- Oscar, T.P., Mitchell, D.M., Engster, H.M., Malone, B.R. and Watson, W.M., 1995. Growth performance, carcass composition, and pigmentation of broilers fed supplemental nickel. *Poult. Sci.*, **74**: 976-982. <https://doi.org/10.3382/ps.0740976>
- Outridge, P.M. and Scheuhammer, A.M., 1993. Bioaccumulation and toxicology of nickel: Implications for wild mammals and birds. *Environ. Rev.*, **1**: 172-197. <https://doi.org/10.1139/a93-013>
- Özhatay, F.N., Kültür, Ş. and Gürdal, M.B., 2011. Check-list of additional taxa to the supplement Flora of Turkey V. *Turk. J. Bot.*, **35**: 589-624. <https://doi.org/10.3906/bot-1101-20>
- Peters, A., Merrington, G., Schlekot, C., De Schamphelaere, K., Stauber, J., Batley, G., Harford, A., Van Dam, R., Pease, C., Mooney, T., Warne, M., Hickey, C., Glazebrook, P., Chapman, J., Smith, R. and Krassoi, R., 2018. Validation of the nickel biotic ligand model for locally relevant species in Australian freshwaters. *Environ. Toxicol. Chem.*, **37**: 2566-2574. <https://doi.org/10.1002/etc.4213>
- Prueitt, R.L., Li, W., Chang, Y.C., Boffetta, P. and Goodman, J.E., 2020. Systematic review of the potential respiratory carcinogenicity of metallic nickel in humans. *Crit. Rev. Toxicol.*, **50**: 605-639. <https://doi.org/10.1080/10408444.2020.1803792>
- Puls, R., 1994. *Mineral levels in animal health: Diagnostic data*. 2<sup>nd</sup> edn. Sherpa International, Canada. pp. 356.
- Radwan, M.A. and Salama, A.K., 2006. Market basket survey for some heavy metals in Egyptian fruits and vegetables. *Fd. Chem. Toxicol.*, **44**: 1273-1278. <https://doi.org/10.1016/j.fct.2006.02.004>
- Rauch, J.N. and Pacyna, J.M., 2009. Earth's global Ag, Al, Cr, Cu, Fe, Ni, Pb, and Zn cycles. *Glob. Biogeochem. Cycles*, **23**. <https://doi.org/10.1029/2008GB003376>
- Ravindran, V., 2013. Poultry feed availability and nutrition in developing countries. *Poult. Dev. Rev.*, **2**: 60-63.
- Reddy, G.B., Babu, A.J., Supriya, R.A., Swetha, C.S., Sravanthi, M. and Rao, T.M., 2017. Estimation of nickel from the poultry organs surrounding Tirupati, Andhra Pradesh, India. *Int. J. Sci. environ. Technol.*, **6**: 1934-1939.
- Rehan, I., Sultana, S., Rehan, K., Almessiere, M.A., Saqib, N.U. and Khan, M.Z., 2023. Estimation and quantification of toxic metals in hugely consumed chicken livers by advanced diagnostic approaches. *Biol. Trace Elem. Res.*, **201**: 377-386. <https://doi.org/10.1007/s12011-022-03147-0>
- Rehman, H.U., Rehman, A. and Ullah, F., 2013. Comparative study of heavy metals in different parts of domestic and broiler chickens. *Int. J. Pharm. Sci. Rev. Res.*, **23**: 151-154.
- Rehman, K.U., Andleeb, S., Mahmood, A., Bukhari, S.M., Naeem, M.M. and Yousaf, K., 2012. Assessment of heavy metals in different tissues of broilers and domestic layers. *Glob. Vet.*, **9**: 32-37.
- Saad-Eldin, W.F. and Raslan, A.A., 2018. Residues of some toxic heavy metals and trace elements in chicken eggs. *Zagazig Vet. J.*, **46**: 8-16. <https://doi.org/10.21608/zvjz.2018.7619>
- Saeed, M., Naveed, M., Arain, M.A., Arif, M., Abd El-Hack, M.E., Alagawany, M., Siyal, F.A., Soomro, R.N. and Sun, C., 2017. Quercetin: Nutritional and beneficial effects in poultry. *World's Poult. Sci. J.*, **73**: 355-364. <https://doi.org/10.1017/S004393391700023X>
- Saripinar-Aksu, D., Aksu, T. and Önel, S.E., 2012. Does inclusion at low levels of organically complexed minerals versus inorganic forms create a weakness in performance or antioxidant defense system in broiler diets? *Int. J. Poult. Sci.*, **11**: 666. <https://doi.org/10.3923/ijps.2012.666.672>
- Schaumlöffel, D., 2012. Nickel species: Analysis and toxic effects. *J. Trace Elem. Med. Biol.*, **26**: 1-6. <https://doi.org/10.1016/j.jtemb.2012.01.002>
- Schlekat, C.E., Van Genderen, E., De Schamphelaere, K.A., Antunes, P.M., Rogevich, E.C. and Stubblefield, W.A., 2010. Cross-species extrapolation of chronic nickel biotic ligand models. *Sci. Total Environ.*, **408**: 6148-6157. <https://doi.org/10.1016/j.scitotenv.2010.09.012>
- Shaheen, N., Ahmed, M.K., Islam, M.S., Habibullah-Al-Mamun, M., Tukun, A.B., Islam, S. and Rahim, M.A.A.T., 2016. Health risk assessment of trace elements via dietary intake of 'non-piscine protein source foodstuffs (meat, milk and egg) in Bangladesh. *Environ. Sci. Pollut. Res.*, **23**: 7794-7806. <https://doi.org/10.1007/s11356-015-6013-2>



- Shahzad, B., Tanveer, M., Rehman, A., Cheema, S.A., Fahad, S., Rehman, S. and Sharma, A., 2018. Nickel; whether toxic or essential for plants and environment. A review. *Pl. Physiol. Biochem.*, **132**: 641-651. <https://doi.org/10.1016/j.plaphy.2018.10.014>
- Shamshad, J., Najeem, J., Naeem, M. and Chaudhry, M.N., 2017. Simultaneous atomic absorption spectroscopic quantization survey of toxic metals in poultry feed and their translocation in various tissues of chicken in Lahore region of Pakistan. *Int. J. Sci. Eng. Res.*, **8**: 791-796.
- Sheoran, V., Sheoran, A.S. and Poonia, P., 2010. Role of hyperaccumulators in phytoextraction of metals from contaminated mining sites: A review. *Crit. Rev. Environ. Sci. Technol.*, **41**: 168-214. <https://doi.org/10.1080/10643380902718418>
- Sinicropi, M.S., Amantea, D., Caruso, A. and Saturnino, C., 2010. Chemical and biological properties of toxic metals and use of chelating agents for the pharmacological treatment of metal poisoning. *Arch. Toxicol.*, **84**: 501-520. <https://doi.org/10.1007/s00204-010-0544-6>
- Song, X., Kenston, S.S.F., Kong, L. and Zhao, J., 2017. Molecular mechanisms of nickel induced neurotoxicity and chemoprevention. *Toxicology*, **392**: 47-54. <https://doi.org/10.1016/j.tox.2017.10.006>
- Suleiman, N., Ibitoye, E.B., Jimoh, A.A. and Sani, Z.A., 2015. Assessment of heavy metals in chicken feeds available in Sokoto, Nigeria. *Sokoto J. Vet. Sci.*, **13**: 17-21. <https://doi.org/10.4314/sokjvs.v13i1.3>
- Sun, R., Zhou, Q. and Wei, S., 2011. Cadmium accumulation in relation to organic acids and nonprotein thiols in leaves of the recently found Cd hyperaccumulator *Rorippa globosa* and the Cd-accumulating plant *Rorippa islandica*. *J. Pl. Growth Regul.*, **30**: 83-91. <https://doi.org/10.1007/s00344-010-9176-6>
- Sutunkova, M.P., Privalova, L.I., Minigalieva, I.A., Gurvich, V.B., Panov, V.G. and Katsnelson, B.A., 2018. The most important inferences from the Ekaterinburg nanotoxicology team's animal experiments assessing adverse health effects of metallic and metal oxide nanoparticles. *Toxicol. Rep.*, **5**: 363-376. <https://doi.org/10.1016/j.toxrep.2018.03.008>
- Świątkiewicz, S., Arczewska-Włosek, A. and Jozefiak, D., 2014. The efficacy of organic minerals in poultry nutrition: review and implications of recent studies. *World's Poult. Sci. J.*, **70**: 475-486. <https://doi.org/10.1017/S0043933914000531>
- Terra, B.F., Araújo, F.G., Calza, C.F., Lopes, R.T. and Teixeira, T.P., 2008. Heavy metal in tissues of three fish species from different trophic levels in a tropical Brazilian river. *Water Air Soil Pollut.*, **187**: 275-284. <https://doi.org/10.1007/s11270-007-9515-9>
- Ukpe, A.R. and Chokor, A.A., 2018. Correlation between concentrations of some heavy metals in poultry feed and waste. *Open Access J. Toxicol.*, **3**: 555609. <https://doi.org/10.19080/OAJT.2018.03.555609>
- Ul-Islam, M.S., Zafar, M. and Ahmed, M., 2014. Determination of heavy metals from table poultry eggs in Peshawar, Pakistan. *J. Pharmacogn. Phytochem.*, **3**: 64-67.
- Uluozlu, O.D., Tuzen, M., Mendil, D. and Soylak, M., 2009. Assessment of trace element contents of chicken products from Turkey. *J. Hazard. Mater.*, **163**: 982-987. <https://doi.org/10.1016/j.jhazmat.2008.07.050>
- Ulusoy, H.G. and Sanlier, N., 2020. A minireview of quercetin: from its metabolism to possible mechanisms of its biological activities. *Crit. Rev. Fd. Sci. Nutr.*, **60**: 3290-3303. <https://doi.org/10.1080/10408398.2019.1683810>
- Vasiluk, L., Sowa, J., Sanborn, P., Ford, F., Dutton, M.D. and Hale, B., 2019. Bioaccessibility estimates by gastric SBRC method to determine relationships to bioavailability of nickel in ultramafic soils. *Sci. Total Environ.*, **673**: 685-693. <https://doi.org/10.1016/j.scitotenv.2019.04.059>
- Wilson, J.H., Wilson, E.J. and Ruszler, P.L., 2001. Dietary nickel improves male broiler (*Gallus domesticus*) bone strength. *Biol. Trace Elem. Res.*, **83**: 239-249. <https://doi.org/10.1385/BTER:83:3:239>
- Wilson, M. and Maliszewska-Kordybach, B., 2000. *Soil quality, sustainable agriculture and environmental security in central and eastern europe*. Volume 69, Springer Science and Business Media. <https://doi.org/10.1007/978-94-011-4181-9>
- Wuana, R.A. and Okieimen, F.E., 2011. Heavy metals in contaminated soils: A review of sources, chemistry, risks and best available strategies for remediation. *Int. Sch. Res. Not.*, **2011**: 402647. <https://doi.org/10.5402/2011/402647>
- Xu, S., He, M., Zhong, M., Li, L., Lu, Y., Zhang, Y., Zhang, L., Yu, Z. and Zhou, Z., 2015. The neuroprotective effects of taurine against nickel by reducing oxidative stress and maintaining mitochondrial function in cortical neurons. *Neurosci. Lett.*, **590**: 52-57. <https://doi.org/10.1016/j.neulet.2015.01.065>

- Yang, J., Feng, P., Ling, Z., Khan, A., Wang, X., Chen, Y., Ali, G., Fang, Y., Salama, E. S., Wang, X., Liu, P. and Li, X., 2023. Nickel exposure induces gut microbiome disorder and serum uric acid elevation. *Environ. Pollut.*, **324**: 121349. <https://doi.org/10.1016/j.envpol.2023.121349>
- Yasmeen, R., Hafeez, F., Ammara, U., Younas, R., Ahmad, S., Ali, Z. and Nasir, Z.A., 2023. Characterization of metals in feed, litter and air of intensive poultry farming facilities. *J. Anim. Hlth. Prod.*, **11**: 375-381. <https://doi.org/10.17582/journal.jahp/2023/11.4.375.381>
- Yuan, L., Xiang, J., Zhang, L., Liao, Q., Yan, X. and Zhang, D., 2023. Determination of trace elements by inductively coupled plasma mass spectrometry (ICP-MS) in poultry eggs from Jiangxi province, China and the corresponding health risk. *Anal. Lett.*, **56**: 2085-2098. <https://doi.org/10.1080/00032719.2022.2154786>
- Zaheer, K., 2015. An updated review on chicken eggs: Production, consumption, management aspects and nutritional benefits to human health. *Fd. Nutr. Sci.*, **6**: 1208. <https://doi.org/10.4236/fns.2015.613127>
- Zhang, G., Chen, A., Zhao, Y., Xu, Z., Chen, G. and Yang, S., 2016. Egg safety standards in China need to be improved. *J. Fd. Prot.*, **79**: 512-518. <https://doi.org/10.4315/0362-028X.JFP-15-308>
- Zoidis, E., Pappas, A.C., Goliomytis, M., Simitzis, P.E., Sotirakoglou, K., Tavrzelou, S., Danezis, G. and Georgiou, C.A., 2021. Quercetin and egg metallome. *Antioxidants*, **10**: 80. <https://doi.org/10.3390/antiox10010080>