# The Potential Health Issues of Nanoscale Additives in Food Industry

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**Abstract.** Nanotechnology is widely used in medicine, electronics and food industries. Among them, in the food industry, nanotechnology is mainly used in the fields of food packaging and food additives. Many foods now contain food additives, and nanotechnology has become an important part of it. However, it is not known whether these nanoparticles are actually beneficial to the environment and the body. There is proof that they also negatively impact human health by looking up and examining online scientific papers and experimental data. This paper introduces metal particles like silver and gold nanoparticles used as food additives which protects food and applies coloring, Moreover, inorganic substances with nutritional benefits like titanium dioxide and zinc oxide were utilized as food dyes, then discusses the nanoscale additives' negative effects on human body like toxicity or cell death, following the damage to human body for instances gut and liver damage, DNA and cell damage, inflammation of the liver, kidney and spleen.

**Keywords:** Nanoscale additives, metal particles, inorganic compounds, health issues.

## 1. Introduction

Nanoparticles (NPs) are particles between 1 and 100 nanometers in diameter. Nanomaterials constitute an extensively enlarged scientific and technological research area because of the myriad novel applications that these physical, chemical, or biological features. Nanomaterials make quality household items such as stain removers, air purifiers and filters, as well as specialized paint and sealing products which are really close to people's life. One of the most important applications is in food packaging and food additives, which leads to widespread exposure to nanoparticles, especially food additives that allow nanoparticles to enter the body.

However, there is evidence that nanoparticles such as metal particles and inorganic compound particles contained in food additives can have an effect on the human body. Metal nanoparticles such as silver ions can be used to preserve food, while gold particles can be used as food coloring and food coating. Silver particles can cause gut and liver damage, as well as being toxic to the body leading to weight loss, while gold particles can cause DNA and cell damage. There are also some commonly used inorganic compounds, among which the most commonly used are titanium dioxide and zinc oxide. Titanium dioxide helps to define the color clean and protects the foods from UV degradation. Zinc oxide is used to provide increased nutritional value to the body. Titanium dioxide can cause inflammation of the liver and spleen, while zinc oxide usually produces cytotoxicity to the human body and then causes liver and kidney damage to the body. Other materials such as silicon dioxide are widely used as thickeners and anti-caking agents and flavoring agents in food. Silica also releases associated cytotoxicity.

## 2. Metal nanoparticles' (silver and gold) potential hazard to human body

Silver and gold nanoparticles are metals which are always used in the fields like medication, diagnostics, and electronic devices etc. However, those metal nanoparticles are not as safe as previously believed, and their negative side effects in food additives are usually neglected.

### 2.1. Silver nanoparticles (AgNPs)

AgNPs are one of the most prevalent metal nanoparticles additives in daily life, but the toxicity of silver nanoparticles is still controversial. They typically cause more pro-inflammatory reactions and oxidative stress through generating reactive oxygen species (ROS) [1].

Recent analysis of the nanoparticle fraction in E174 revealed that up to 23% of the material was composed of silver nanoparticles. According to a study, E174 caused cytotoxicity and raised ROS generation by roughly 60% in both healthy and cancerous cells from the human colon. [2]. Kim et al. completed an analysis on rats and treated silver nanoparticles by mouths for 90 days, and showed weight loss in male rats after 28 days of orally treated with the silver nanoparticle additives and alkaline phosphatase activity changes and cholesterolemia [2]. This phenomenon suggests that the exposure to silver nanoparticles more than 125 mg/kg might cause slight liver damage [3].

Generally, the M cells in isolated gastrointestinal lymphoid tissues and Peyer's patches can absorb the nanoparticles into the digestive tract. However, some study shows that the absorption of silver nanoparticles might cause inflammation of the intestine, and some of the silver nanoparticles may not be absorbed by the human body. According to a study, ingested silver nanoparticles appeared to be dispersed throughout all of the organs looked at, with the gut and stomach receiving the most attention. Death, losing weight, lessening of activity, changed levels of neurotransmitters, and reduced liver enzyme activity, enlarged hearts, and immunological effects have all been reported in dose-dependent toxicity studies. Additionally, there is proof that suggests the effects of silver nanoparticles are caused by the surface of the particles that release the silver nanoparticles.

The liver receives the ingested silver and excretes it in bile. Many experimental mice have been detected with weight loss. Shahare et al. show that silver nanoparticles damage the microvilli of the intestine and cause a decrease in absorption capacity [4].

AgNPs administered orally can be distributed to organs. The gut and liver are most often affected. Poisoning from the silver released from the silver nanoparticles' surfaces has the possibility of resulting in losing weight. [1].

### 2.2. Gold nanoparticles (AuNPs)

AuNPs can be used as food color and coating, and specifically, they are also used in food additives E175. However, the toxicity of gold nanoparticles is one of the most important things to be tested since they are related to the human body.

In accordance with a study, gold nanoparticles do not trigger cytotoxicity in cells and lower the level of potential hazardous reactive oxygen species. However, the nanoparticle precursors, cation-active cetyltrimethylammonium bromide (CTAB) and the gold salt $HAuCl_4$, are toxic to cells at concentrations of approximately 10 nM. Therefore, an essential stage in any in vivo experiment will be the effective purification of the gold nanorods [5]. Rotello et al. examined the toxicity of 2 nm cationic and anionic surface-functionalized gold nanoparticles in various cell types. Due to electrostatic interactions between negatively charged cell membranes and cationic nanoparticles, The statistics show that cationic particles are often more dangerous than anionic ones at far lower concentrations.

Gold nanoparticles are associated with oxidative status imbalance in vitro. A recent study shows that exposure of hepatocytes to gold nanoparticles leads to a dose-dependent increase in ROS production, with the higher doses of AuNPs producing more damage. This result indicates the appearance of cellular mortality. Thus, gold nanoparticles are capable of causing initial oxidative damage and cells try to control the excessive production of ROS probably due to the increase in antioxidant activity [6]. Gold nanoparticles produce DNA damage, which is responsible for genotoxicity. Gold nanoparticles have a strong affinity for DNA, and their inhibitory properties on DNA replication are stronger than those of other nanoparticles [7]. Many studies have focused on DNA damage caused by gold nanoparticles.

The size of gold nanoparticles are the factors that caused the cell death. According to a study, gold nanoparticles of 1.2 nm size cause apoptosis while those of 1.4 nm size cause necrosis in the cells.

## 3. Effects of inorganic compounds as the food additives

Inorganic compounds like titanium dioxide and zinc oxide are also the prevalent food additives in people's daily life. Titanium dioxide, also known as E171, helps to define the colour clean and also protects the foods from UV degradation. They are typically used in candy, coffee creamer, or cake decorating etc. Zinc oxides are often used as nutrient additives to increase the nutrient values of foods.

### 3.1. Titanium dioxide

An absorption study found that oral administration of 23 or 46 mg titanium dioxide capsules in humans resulted in a 5- to 10-fold increase in blood titanium dioxide levels. Following oral administration of titanium dioxide nanoparticles to laboratory mice, the particles collected in the tissues of the liver, spleen, kidney, and lungs and were accompanied by myocardial ischemia, liver and kidney histopathological changes together with serum changes [8].

In another study, the experimental mice were also administered titanium dioxide anatase for 30 days at doses ranging from 60 to 250 mg/kg. At a concentration of 125 mg/kg, titanium dioxide nanoparticles caused weight loss, reduced the activity of leukocytes, platelets, erythrocytes, hemoglobin, reticulocytes, lymphocytes, and interleukin 2. In addition, the levels of numerous liver enzymes and cholesterol fluctuated during therapy, suggesting that the harm to the immune system and hemostasis may be the cause of the liver function deterioration [9].

Mice given 5 to 50 mg/kg titanium dioxide orally every two days showed apoptosis of hepatocytes and increased accumulation of liver reactive oxygen species, followed by decreased expression of many crucial genes involved in stress reactions and detoxification [9]. Those researchers conducted a similar study that showed that titanium dioxide accumulates in the liver and induces histopathological changes [9].

Strong evidence exists that gastrointestinal absorption of titanium dioxide for bioconcentration, bioaccumulation, and biomagnification can occur in mammals. The organs with the largest bioconcentrations of titanium dioxide include the spleen, liver, and kidney, according to the findings. Titanium dioxide's effects on various animal organs' histopathology and physiology depend on the dose. According to the results of experiments, the liver and spleen are the major organs that titanium toxicity when consumed targets.

Changing biochemical parameters causes inflammation of the liver and spleen. At the same time, the photosensitivity of these nanoparticles makes them mediators of ROS, resulting in an imbalance between oxidation and antioxidation, leading to oxidative stress and liver damage. Prolonged inflammation in the liver leads to activation of HSC cells, and multiple signaling pathways contribute to extracellular matrix (ECM) deposition, leading to liver fibrosis [10].

### 3.2. Zinc oxide

In an in vivo toxicology experiment, GPT and ALP levels in experimental mice were found to be higher, which were attributed to liver dysfunction. The results showed that the intravenous route of administration was more toxic than the injectable route, as the administration of zinc oxide nanoparticles to mice via the intravenous route caused a relative decrease in body weight and severe pathological inflammation. The target organs from zinc oxide nanoparticles may include the liver, kidney, lung, spleen, and pancreas, according to the pathological findings. Therefore, the toxicity of nanomaterials such as zinc oxide is closely related in addition to their physiological characteristics and the chosen route of administration [11].

The generation of reactive oxygen species and release of zinc ions by zinc oxide nanoparticles is associated with their toxicity, suggesting that under physiological conditions, solubility has a significant impact on toxicity. Compared with nanoparticles that are also food additives such as silica and titania, the toxicity of zinc oxide is relatively high, which may be related to the higher toxicity of zinc.

Additionally, the zinc oxide nanoparticles' cytotoxicity may result from interactions with food and biomatrices. According to Precupas et al., decreased structural stability of BSA was correlated with increased enthalpy of adsorption of interacting BSA on nanoparticles, which also led to biological changes such cell death and DNA strand fractures [12]. According to Da Silva et al., zinc oxide nanoparticles reduce lactate dehydrogenase activity because of the concentration-dependent adsorption of LDH, and this interaction between the organism and the nanoparticles is most likely what controls their cytotoxicity and in vitro biological response. [13].

The hydrodynamic diameter of nanoparticles of zinc oxide was reduced by food-grade albumin from eggs, which led to higher concentrations of zinc oxide nanoparticles with enhanced ROS generation, membrane damage, and cell growth inhibition. This study further demonstrated that the enhanced cytotoxicity was caused by human gastrointestinal Caco-2 cells absorbing more zinc oxide nanoparticles into their cells. The greater cellular absorption of zinc oxide nanoparticles in the presence of dietary albumin was blamed for the increased cytotoxicity [14].

Thus, the physical chemistry of zinc oxide nanoparticles is also impacted by the interactions induced. The nature of the cytotoxicity of zinc oxide nanoparticles is also a key factor influencing cytotoxicity between zinc oxide nanoparticles and the matrix. Experimental results by Cao et al. found that vitamin C made cells more poisonous. of zinc oxide nanoparticles compared to zinc oxide nanoparticles alone. There was also evidence of combination synergistic toxicity with repeated oral dosing, in terms of liver and kidney damage in mice.

### 3.3. Other inorganic compounds

Other materials like nano silica are utilized extensively as an anti-caking agent in flour-based baking mixtures. Silicon dioxide, also known as synthetic amorphous silica, is widely used as a thickener and anti-caking agent in foodstuffs and as a flavouring agent. However, nano silica also contains risks to the human body.

Recently, silicon dioxide and ferric oxide nanoparticles have been shown to interfere with tubulin polymerization. The possibility of NPs interacting with the mitotic spindle during cytokinesis is evidence in favor of a no-life effect.

Additionally, it has been demonstrated that exposure to silicon dioxide (15 nm) causes cytotoxicity that is linked to the activation of apoptosis, chromosomal damage, and the greatest concentration of the pro-inflammatory cytokine IL-8. Additionally, the harmful effects may also be influenced by ROS generation [15].

## 4. Discussion

Food additives have become an indispensable technology in today's society, with nanotechnology being even more emerging and widely used. Then there are still a large number of these nanomaterials that can cause harm to humans and many people are unaware of them. Although some of their use has been banned or limited, this is still a challenge to the chemical discipline. First, many nanomaterials have not been proven to be non-toxic and non-harmful to humans, and this requires more effort from chemistry labs. Secondly, chemists need a lot of theoretical proof and experimental studies to change or neutralize these existing toxic nanomaterials in the body so that they become harmless or do not react with organs or other nutrients in the body. However, there are still many nanomaterials that have not yet been discovered or experimentally proven to be used as food additives. However, nanomaterials and nanotechnology are emerging technologies that will be selected and studied by more and more chemists. It is believed that in the near future, an increasing number of safer nanomaterials will be proven to be used as food additives and provide nutritional value to the human body.

## 5. Conclusion

The toxicity of nanoparticles can cause non-negligible damage to human lungs, kidneys, spleen, DNA and cells. Changing biochemical indicators causes liver and spleen inflammation. At the same time, the photosensitivity of these nanoparticles makes them mediators of ROS, leading to an imbalance of oxidative and antioxidant properties, causing oxidative stress and liver damage. Prolonged inflammation in the liver leads to HSC cell activation, and multiple signaling pathways promote extracellular matrix (ECM) deposition, leading to liver fibrosis. There are still many nanomaterials that have not yet been discovered or experimentally proven to be useful as food additives. It is believed that in the near future, more nanomaterials will be proven to be used as food additives to provide nutritional value to the human body while avoiding health issues.

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