Review

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Does Nitrate and Nitrite Additive Make Food Super Toxic?

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Does Nitrate and Nitrite Additive Make Food Super Toxic?

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Abstract: Nitrate and nitrite are the most extensively used food additives in the food industry for their multifunctional properties, and they have been in the spotlight for decades for its controversial back effects. The conversion of nitrate and nitrite to various nitroso compounds, specifically N-nitrosamine raises the question of the integrity of these additives. Nitrosamine is a well-known carcinogen and mutagen. A large number of studies demonstrate the carcinogenic effects of these salts. Are these findings credible? Nonetheless, the regulatory agencies approve its usage; is it biased? Are we feeding on the carcinogens in processed foods? The current work provides an insight into the basic and toxicological findings of the food additives -nitrate and nitrite.

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Introduction

Food is inextricably linked to human existence; in fact food makes life on earth possible. The demand for food has steadily risen over the years, and the demand reduces food safety. Quality and availability are frequently unassured. To make food whole, nutritious, safe, and available for a long time, preservation techniques were developed. Food preservation techniques extend the shelf life of food products by destroying microbes that spoil food and also preventing the outbreak of serious food borne illnesses. There are several methods of preservative techniques that have been discovered and employed for decades. Heating, cooling, drying, smoking, salting, and curing are the most conventional techniques used since ancient times. These methods have their own merits and limitations. To sustain rapid urbanisation, robotization, and technical advancements, the mandatory need for processed or convenient food is surging. Preservatives are required in the production of all processed foods. Preservatives are classified as food additives by the regulatory agencies. Food additives are substances added to food during processing, production, storage, or even packaging for various reasons [1]. Preservatives used currently might originate from either natural or synthetic sources. Plants, animals, and microbes are a few of natural sources. The most popular natural preservatives include salt, sugar, honey, spices, vinegar, and oils. Preservatives have the ability to serve as antimicrobials, antioxidants, or both. Preservatives are virtually always present in all goods. Wine, cider, alcoholic drinks, cheese, jams, preserves, dried fruits, and canned vegetables all include antimicrobial preservatives [2]. Antioxidant preservatives are commonly employed in minimally processed foods to prevent enzymatic browning of fruits and vegetables. There was not much aversion to natural preservatives, but concern rose often with the synthetic ones. Natural preservatives have many constraints, including availability, climatic impacts, and supply. Synthetic preservatives are often used for their major functional purposes, as they won't impart the primary organoleptic characteristics of food. The list of synthetic preservatives permitted is shown in Table 1 [3]. These artificial preservatives are completely safe when used in the amount stated. The usage of preservatives and the quantities utilised vary by nation; countries that lack a strong and severe food safety administration fail to protect their consumers' health.

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Table 1. List of permitted synthetic preservatives.

Synthetic Preservatives	E number
Sorbic acid includes sodium, potassium and calcium sorbate	E 200-203
Benzoic acid and benzoate	E 210-213
Suphur dioxide and suphite	E 220-228
Nitrite and nitrate	E 249-252
Propionic acid and proprionates	E 280-283
Ascorbic acid and ascorbates	E 300-302
Butylated hydroxyanisole (BHA) & butylated hydroxytoluene (BHT)	E 320-321

Consumers have been concerned about the safety of some preservatives. One such threatening additive includes nitrite and nitrate, which are curing agents. For several decades, the controversies surrounding nitrate and human health have been a matter of discussion among many health communities. Nitrate and nitrite salts are used in cured meats for preservative purposes and also to impart a red colour to meat and enhance flavour. Nitrite acts as a functional component in inhibiting pathogens like Clostridium botulinum [4], a major food borne toxicant, and also inhibiting lipid peroxidation.

Table 2. List of approved Nitrite & nitrate.

Nitrite & nitrate	E number
sodium and potassium salts of nitrite	E 249-250
nitrate	E 251-252

Apart from clostridium nitrite in combination with salt inhibits the growth of other microbes such as Staphylococcus aureus, Bacillus cereus, and Clostridium perfringens. These curing salts also react with myoglobin in meat tissues and provide a characteristic reddish pink colour to the meat. Further it reduces lipid oxidation, thus reducing the rancid flavour and promotes cured flavour to the meat [5]. Despite their numerous benefits, the nitroso compounds produced from nitrate and nitrate salts possess serious carcinogenic effects. When nitrite reacts with amines produced from compounds in food under acidic conditions, further acceleration by higher temperatures results in the formation of N-nitroso compounds [6]. Even the nitrites employed in the foods react with the precursors and forms nitroso compounds in the gastrointestinal tract [7]. Further nitrites react with amines to form nitrosamines, which are linked with colon, gastric, oesophageal carcinogenicity [8]. Most dreadful effects are irreversible conversion of haemoglobin to methemoglobin occurs in the bloodstream, which affects the capacity of haemoglobin in the exchange of oxygen [9]. Particularly children, pregnant women and aged people are more vulnerable to methemoglobin. Nitrate at a concentration above 330 mg/ kg of the body weight is considered to be lethal [10]. As a customer it is critically to watch the amount of added nitrates and nitrite salts in each of the food which they consume. The chief purpose of this work is to provide a clear insight on the applications of nitrate and nitrite in food industries, regulatory restrictions and its intended harmful effects on the human body.

Sources of Nitrate and nitrites:

Nitrates and nitrite are present in wide ranges of fruits and vegetables which forms the natural sources. Sausages, cured meats, bacons and processed foods forms added sources of artificial nitrite salts. Spinach, lettuce, celery, beetroots have higher concentration of nitrite. Broccoli, banana, cucumber, cabbages, pumpkin and potato contain nitrites at concentration ranges from 100 to 450 mg/kg. Carrot and onion have less concentration of nitrate. Several studies [11] [12] found that

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various food processing techniques like heating, pickling, acidification, brining, pasteurization and storage reduces the concentration of nitrate. A major threatening source of nitrate and nitrite is from drinking water as an environmental contaminant, usually the level was negligible, with the usage of synthetic commercial fertilizers, sewage disposal, tends to increase the concentration of these salt levels in the ground water. On this scenario nitrate level in drinking water exceeds 50 mg/L [13]. Added salts are present in processed meat, cheese and cheese products, canned sterile meat products, dried meat, dried cured meat, fermented comminuted meat products.

Regulatory Restrictions:

The Joint Expert Committee on Food Additives (JECFA), have set the acceptable daily intake level for nitrate and nitrites, for nitrate 3.7 mg/kg body weight per day and for nitrites are 0.06-0.07 mg/kg bw/day. Various standard setting agencies after scrutiny fixed the amount of the salts for specific products. Presently the allowed concentration of nitrites in processed meat was 150 mg/kg and in sterilized meat product it is limited to 100 mg/kg. It has to be noted that sodium nitrate is allowed only in cooked meat products, and allowed up to 150 mg/kg. In dairy products like processed cheese the nitrite is used up to 100 mg/kg. Works of [14] reports the average residue of nitrate and nitrite in processed meat was about 180 mg/kg and 60 mg/kg in unprocessed meat products. WHO states that concentration in drinking water should not exceeds 3 mg/L. The United States Environmental Protection Agency sets the limit of 10 mg/L for nitrate and 1 mg/L for Nitrite [15]. Canadian Food Inspection Agency provides guidelines for drinking water and sets limit of 45 mg/L for nitrate and 3 mg/L for nitrite [16]. Food standard Australia New Zealand has set limit up to 500 mg/kg of nitrate and nitrite for slow dried cured meats and fermented, uncooked, unprocessed comminuted meat products.50 mg/kg for cheese and cheese products [17].

Metabolism:

Nitrate and nitrite in the diet are partially excreted and circulating within the human body [18]. Ingested nitrate is rapidly absorbed in the small intestine and subsequently mix with the body fluids and mainly stored in the salivary fluids, serum and urine [19]. The L-arginine/NO-synthase pathway generates the endogenous nitrate and nitrite [20]. It has been found 25% of the ingested nitrate is found in the saliva [21]. Nitrate in the diet and in the saliva is partially oxidized to nitrite and then to nitrogen dioxide in the nitrate-nitrite-NO pathway. Bacteria present in the mouth catalysed by nitrate reductase enzyme reduce 5 to 7% of dietary nitrate and 25% of the salivary nitrate to nitrite [22] [23]. It was also found that even mammalian tissues reduce nitrate and nitrite to bioactive nitrogen oxides [24]. The NO formation varies depend on various factors such as pH, redox status and oxygen tension. Ingested nitrate and nitrite in the stomach are metabolised by various enzymatic and non enzymatic pathways and forms NO and most of this reactions are highly enhanced under hypoxic conditions. De oxy haemoglobin, Myoglobin, Respiratory chain enzymes, Vitamin C, Xanthine oxidase, NO synthase, Aldehyde oxidase, Polyphenols, protons, are the compounds which reacts with nitrate. Formed NO is rapidly absorbed in the small intestine and reaches blood and plasma. On oxidation the NO in blood and plasma end up forming nitrate and nitrite. The complete mechanism forms an unbreakable loop in the body. Excess of nitrate are excreted in the urine and remaining nitrate are stored in the salivary glands and secreted in saliva [25], where the oral bacteria again reduce it to nitrite and the cycle continues. Nitrites are highly unstable under the acidic condition of the stomach, which then decompose to nitrite and NO. In the gastrointestinal tract it reacts with amines and amides to form N nitroso compounds which are well known mutagen, carcinogen and tetratogenic [26]. Primary amines reacts with nitrate and forms unstable nitrosamines which further degrades to alcohol and nitrogen, whereas secondary amines reacts with nitrate to forms carcinogenic nitrosamine [27].

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Toxicological findings:

Nitrate and nitrite are often linked with carcinogenic effects, because of N nitroso compounds. Research studies conducted by [28] including 101 056 adults, they were exposed to nitrate and nitrite in food additives for every 24 hrs. On the end of the study 3311 individuals were diagnosed with cancer, mostly breast cancer in individuals who consumed potassium nitrate in specific. Another key finding includes the occurrence of higher risk of prostate cancer who consumed sodium nitrite and the study concluded that no carcinogenic risk were associated with natural sources of nitrate and nitrite from the diet. Even though natural sources of nitrate are not carcinogenic the fruits and vegetables specifically the tubers tend to increase the plasma nitrate and nitrite 9 folds, causing drop in blood pressure[29], even several studies confirmed the blood pressure lowering effects [30] [31] [32]. Studies by [33] found humans exposed to N-nitroso compounds are more susceptible to incident of cancer. Nitrosodimethylamine a potential carcinogenic derivate of N-nitroso compound, study identified the nitroso and derivates are linked with risk of gastrointestinal cancers specifically of rectal cancer. When the nitrosamine formed react with various harmful metabolizing enzymes results in formation of diazonium ions, which is primary key component of genotoxic effect of nitrosamine. Animal studies conducted on injection of dimethylnitrosamine in female mice induce both lung and liver tumors, a key finding of this research states that methyltransferase offers protection from nitrosamine induced tumours [34]. Few more studies found a shocking revelation that exposure to nitrates can also develops the risk of diabetes mellitus in early childhood [35] [36], even the outcomes of these researches are plausible more intensive research has to be made. Even more studies demonstrate the transfer of nitrate, nitrite and nitrosamine compounds from mother to foetus having negative effect on growth and have the potentiality to cause death or abortion of the foetus [37]. One of the most recent studies [38] conducted to demonstrate the toxicity of sodium nitrite using 48 pregnant female mice, sodium nitrite treated mice shows maternal toxicity including reduction of body weight and death of the foetus. The foetus showed growth retardation and malformation. Also the test mice showed signs of dizziness, diarrhea, dyspnea, nausea, and abdominal cramp. [39] Studies finds that nitrates have the ability to penetrate the placenta blood barrier and passing into the foetus in the womb. Research by [40] conducted on male rats and mice shows reproductive toxicity on exposure to sodium nitrite, the research found an increase in the weight of testis; in contrast the weight of the epididymis was greatly reduced. Also reduction in sperm counts in all experimental animals, 20-60% in mice and 20-50% in rats. Another potential fatal disorder of nitrate is the formation of methemoglobin leads to the condition of Methemoglobinemia. Methemoglobin is formed when nitrate react with ferrous ions in the haemoglobin and oxidize it to ferric form and methemoglobin takes form of haemoglobin and circulates in the body [41]. Methemoglobin doesn't have much ability as haemoglobin to carry oxygen and leads to cyanosis. It's totally normal when 2% of methemoglobin circulates as haemoglobin but it became more harmful when the level exceeds 10% [42]. Recent scientific research studies indicates the association of nitrates and nitrite salts with various health effects including increased abnormal heart rate, head ache, nausea, drowsiness, abdominal cramps and lethargy [43].

Conclusion:

Nitrate and nitrite remain controversial matters from the turn of the century. Summing up, it can be clearly seen that nitrate and nitrite food additives have a wide devastating effect on human health. They are extremely carcinogenic, teratogenic, and mutagenic to humans, which should be the major public concern. Aside from being a carcinogen, there are several contradictory health outcomes. Banning the usage of nitrate-based additives in food is debatable since nitrate and nitrite are even found in natural sources, but consciously restricting them in daily life lies in the hands of consumers. The legal restriction limit of these additives in food fixed by the regulatory agencies was decades old, which may have suited that period of time, but currently in the world of technological advancements at their peak, which paves the way for modern agriculture, advanced food processing technologies, and live stock rearing, the amount of nitrate and nitrite present in the natural sources has escalated, along with the added synthetic source of food additives peaks the level to several folds.

Research states natural sources may not have detrimental effects, but in excess and in combination with synthetic sources, they may impart drastic effects, but there is no scientific holding for any of these plausible statements. Continuous monitoring and a strict regulatory system are much needed to protect consumer's health. Due to potential effects, nitrate and nitrite usage in the food processing industries should be limited, and the consumer should be aware of what they are feeding on.

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