Review

Is Sulphite a Toxicant?

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Posted Date: 11 May 2023

doi: 10.20944/preprints202305.0816.v1

Keywords: Sulphite; food additive; food toxicology.

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Is Sulphite a Toxicant?

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Abstract: Sulphites are the most widely used food additives for their versatile applications in processing; perhaps we are negligence of its shortcomings. On account of various research studies, sulphites induce serious allergic reactions and other health alignments, but still regulatory agents permit its usage. Is it a wiser choice? The purpose of this paper is to clear up ambiguity and provide a clear view on why sulphites are employed in the food industry, why its usage is restricted, and why sulphite is a toxicant.

Keywords: sulphite; food additive; food toxicology

Introduction

Food additives are substances added to food during the stages of production, processing, and storage that serve various purposes. Food additives are primarily employed to extend shelf life, reduce microbial proliferation, and maintain organoleptic properties [1]. Throughout the years, the needs for food additives have been continuously evolving to keep up with the tremendous rate of population expansion and also to alleviate food waste and the hunger crisis. Food additives are diversified into direct and indirect additives; direct additives are those added to food products for technological functions, whereas indirect additives are those present in foods as a repercussion of handling, processing, production, packing, and storage. There are six groups of food additives that have been classified and are numbered by the international numbering system. The six categories of additives are listed in Table 1. Among the various food additives, the use of sulphite, which comes under preservatives, is still controversial for its adverse health and environmental impacts. Sulphites were used in ancient times for their preservation and bleaching properties and to sanitise and disinfect vessels [2]. Sulphites have been extensively used in food processing industry for several decades, for its preservative and antioxidant properties. Sulphur dioxide is produced by burning of sulphur; it is a colourless, non-flammable gas with a strong odour. It was presumably first utilised to preserve fruits, vegetables, and products made from them [3]. Currently, it is used in wide range of foods such as baked goods, beverages, dried fruits and vegetables, meats, pickles, wines. Sulphite inhibits the growth of microbes such as bacteria, yeast and moulds by affecting the normal functioning of the microbes [4]. It can help retain the natural colour of certain fruits, vegetables, and meats by preventing browning and oxidation. SO2 is soluble in water, making it easy to use in various food processing methods. It easily evaporates from solutions when utilised in gaseous form, leaving no residues.

Table 1. Categories of food additives [5].

Category	E number
Colour	100-199
Preservative	200-299
Antioxidant and acidity regulator	300-399
Thickeners, stabilizers, emulsifier	400-499
PH regulator and anticaking agents	500-599

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 11 May 2023 doi:10.20944/preprints202305.0816.v1

Flavour enhancers	600-699

Beside its application in food industries it is also used in pharmaceutical and cosmetic industries. The various types of sulphite used commonly as food additives were shown in Table 2. However, it should be observed that employing sulphur dioxide may have some downsides. Consumption of Sulphite processed foods may induce allergic reactions in some individuals sensitive to it, loss of vitamins and toxicity. In 1986, FDA prohibited the use of sulphites on fruits and vegetables after numerous cases of sulphite-induced asthma [6]. Due to these worsening effects, sulphur dioxide consumption is subject to globally enforceable limit levels.

Table 2. Sulphite used as food additive.

E number	Name
E220	Sulphur dioxide
E221	Sodium sulphite
E222	Sodium hydrogen sulphite
E223	Sodium metabisulphite
E224	Potassium metabisulphite
E226	Calcium sulphite
E227	Calcium hydrogen sulphite
E228	Potassium hydrogen sulphite

Potential Applications of Sulphite as a Food Additive:

The enzymes like phenolase, catalyse, poly phenol oxidase generally present in wide range of fruits and vegetables are major causes of browning due to their reaction with oxygen. SO2 is an excellent and cheap anti browning agent, which inhibit both enzymatic and non enzymatic browning. Studies by [7,8] found that on incubating phenolase with SO2 inhibited its further reactions and prevents enzymatic browning of plant and fruit tissues, this process utilize higher concentration of sulphite but it varies depending upon the substrate [9] .

Table 3. List the food products which contains added sulphur dioxide.

Category	Food Products
Processed fruits	Fruit juices, frozen juices, fruit concentrate, nectar, fruit pulp, dried fruits- fig, grapes, banana, grapes, raspberries, gooseberries, strawberries, cherries, wine, fruit beverage mixes, jam, jellies, syrups.
Processed vegetables	Potatoes, carrots, radish, canned peas, beans, cabbage, pickled vegetables, dried vegetables, Tomato pulp/puree/paste, mushroom.
Drinks	Soft drinks, wine, beer, cordials, cider, tea.
Processed meat and fish	Sausages, frozen fish/ shrimp, poultry, dried fish, lobster.
Bakery products	Bread, biscuits, flours, milling of corn, pie dough, pizza dough, corn starch.

When sulphur dioxide added to food products it binds to the outer membrane of the microbes and limits the amount of dissolved oxygen in extracellular membrane, which is crucial for cell viability, creating an anaerobic condition. Intracellular SO2 inhibits enzyme and binds to ATP, thiamine, amino acids and other components thus affecting the cell growth and function, which

 doi:10.20944/preprints202305.0816.v1

inhibits microbial proliferation [10]. Sulphite added were not oxidized and results in the formation of quinone sulphite complex. The reaction occurs between amino group and carbonyl group leads to the formation of dark coloured polymers which are insoluble in nature, when it occurs in the plant and fruits lead to darkening of the tissues [11]. Sulphite or any metabisulphite are usually added to canned fruits, vegetables and drying fruits including dark raisins and prunes to reduce non enzymatic browning. SO2 is also used in the wet milling of cereals like corn and sorghum. They are steeped in SO2 for 24–40 hours prior to milling to soften the kernels and facilitate the easy removal of germ from the bran and endosperm. During the steeping process, 0.2–0.4 g of SO2 is absorbed per kg [12]. Additionally sulphite, bisulphite, metabisulphites act as conditioner in dough processing and slows down the millard reactions [13].

Adverse Reactions

Symptoms of sulphite allergic reactions can occur within 5 minutes on parenteral exposure and within 15–30 minutes following oral exposure. The mechanism of reaction in asthmatic reactions is not well established yet and remains undetermined, but different studies suggest possible mechanisms. Exposure to sulphites doesn't have an impact on healthy individuals, but may trigger adverse asthmatic symptoms in people suffering from asthma and sensitive to sulphite. Most non-asthmatic individuals can tolerate up to 5 ppm SO_2. It was found that asthmatics had increased bronchomotor reactivity to sulphur dioxide [14]. According to one of these theories[15,16] state that individuals sensitive to sulphite may have defect in production of sulphite oxidase, which aids in maintaining the sulphite produced by some of the sulphur containing amino acid- methionine, taurine, homocysteine and cysteine. Because of these defect the body became unable to efficiently handle the sulphite produced by these amino acids. When those individuals exposed to sulphite found in food leads unstable condition and trigger allergic response. Another study suggests that sulphite react with nitric oxide and its derivatives, and inhibits the nitric oxides ability to reduce the platelet aggregation thus affecting its biological functions [17]. Other theory states that SO2 induce bronchoconstriction when sulphite in the food get converted to SO2 in the stomach and mouth [18]. Other mechanisms yet to be fully understood. Allergic reactions such as hives, itching, and swelling of the face, lips, or tongue. Severe conditions may leads to anaphylaxis. Gastrointestinal issues such as nausea, diarrhea and abdominal pain. Neurological issues such as headaches, dizziness, and seizures. SO2 can cause constriction of blood vessels, which can increase blood pressure and put strain on the cardiovascular system. This can lead to heart disease, stroke, and other cardiovascular issues [19].

Clinical Trial

Sulphur dioxide is readily absorbed into the human body, allergic reactions to SO2 develops at anytime during once life span. Sulphite oxidase is the key enzyme which oxidase sulphite to sulphate which is excreted in urine [20]. Reports states that acute toxicity of free sulphite, the LD50 is in range from 1000-2000 mg/kg and for bound sulphite exceeds 5000 mg/kg [21].

Chronic and sub-chronic toxicity study conducted by [22] in pigs for 15 to 48 weeks. 0.06, 0.16, 0.35, 0.83, and 1.72% are the various concentrations of sodium metabisulphite used. The animals were fed a slurry fortified with thiamine, as SO2 causes thiamine deficiency. Growth retardation was observed at 0.83 and 1.72%. An abnormal increase in the weight of the liver at higher doses and rapid proliferation of fat-containing kupffer cells were observed in the liver. The factors that contribute to such changes in the liver were not accounted for in this study. Pseudomelanosis coli were seen in pigs fed with 0.83 and 1.72% sulphite, and various changes and inflammations in the gastric mucosa of the stomach were found. [23] Further study on the toxicity of SO2 using rats fed sodium metabisulphite for two years for three generations at various proportions (0.125, 0.25, 0.50, 1.0, and 2.0%) and another set with an even higher dosage (0–8%) for 10–56 days. Rats were given food fortified with thiamine to combat thiamine deficiency. Feeding sulphite decreased the level of thiamine in the urine and liver. At higher levels above 2%, growth retardation was seen, similar to the case of pigs. Occult blood in faeces on dosages of 1% and more 2% and more cause anaemia, and

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with 4% and above, splenic haematopoiesis occurred. Weight of the kidney increased and hyperplastic changes in the stomach occurred at 1 and 2% at all three generations, while ulcer and papillomatous elevations were seen at 6 and 8%. This study indicates that SO2 doesn't have a carcinogenic effect. Latter study by [24] confirmed that SO2 does not induce carcinogenicity. On analysis of three groups of mice 50 male and 50 female fed with potassium metabisulphite at various dosage of 0, 1 and 2% in distilled water for two years, no incident of tumour were recorded. But these findings were contradicted with the study of [25], in vitro studies made demonstrates sulphite induces change in nucleic acids which might cause mutagenic effect.

Work conducted by [26] using three groups of wistar rats treated with 0.25, 1, and 4% sodium metabisulphite for 90 days. Sulphite was fed via drinking water. The haematology studies showed a decline in the level of red blood cells, haemoglobin and elevated leukocytes, as well as further enlargement of various organs like the kidney, spleen, stomach, and liver. The study concluded that intake of sodium metabisulphite induces alteration in immune function and haematological, biochemical, and physiological parameters. Subchronic experiments were made on rats fed with sodium metabisulphite at 0, 4, and 6%. Rats were killed after 8 and 12 weeks for analysis. The study reported a variety of histopathological changes, including SO2 induced gastic lesions and the formation of scattered hyperplastic glands in the fundic mucosa [27].

Is it Safe?

Sulphite is generally recognised as safe (GRAS) by the Codex Alimentarius Commission, which is the organisation that regulates the use of various additives. In 1958, the FDA notified sulphite as GRAS. Various international scientific organisations have approved its use. Sulphites must be declared on the label of a packaged food when the concentrations are 10 mg/kg or more. In 1974, the Joint Expert Committee on Food Additive published an ADI of 0-0.7 mg/kg body weight [28].

Retrospective

In the late 1970s and 1980s, the use of sulphites was in high demand among the food industries, which led to many allergic reactions. After receiving reports on adverse health reactions to the use of sulphite, FDA began investigating the GRAS status of sulphite in 1982. The Federation of American Societies for Experimental Biology (FASEB) examined the effects of sulphites and concluded that they may be safe for most people but may have incalculable effects on individuals suffering from asthma [29]. In 1986, the FDA promptly prohibited the use of sulphite in fresh fruits and vegetables. For foods and drinks in which the use of sulphite was not restricted and concentrations exceeding 10 ppm had to be declared on the package label. Despite the restrictions on the usage of sulphites, sulphite sensitivity reports heightened [30]. According to reports published, patients sensitive to metabisulphite develop anaphylaxis after consuming food with metabisulphite and a growing number of reports mention life-threatening reactions to these additives [31]. Food products that contain undeclared amounts of sulphites are in violation of regulations are being subjected to recall. The Centre for Food Safety and Applied Nutrition (CFSAN) maintains a monitoring system for reported incidences of adverse reactions to sulphites. Further, the USDA restricted the use of sulphite on meat because it provides false freshness to meat by restoring the red colour of the meat. The CODEX and FDA list sulphites as one of the top food allergens. The Tax and Trade Bureau (TTB) of the Department of the Treasury specifies regulations for alcoholic beverages and provides guidelines for wine labelling; if wine contains more than 10 mg sulphur dioxide per litre, it needs to be declared on the label [32].

Conclusion

Sulphites as a food additive mark higher applications in the food industry; it is widely used because of its easy availability and low cost. Based on the guidelines of various regulatory agencies, sulphite doesn't cause major reactions when used within the permissible levels; however, sulphite is still associated with some adverse reactions, including asthmatic and other allergic reactions in

individuals sensitive to it. Considering the potential effects, the manufacturer can reduce the use of these additives wherever possible. Sulphite sensitive individuals have to be vigilant while eating out and always look for an allergen warning note and the complete list of ingredients. With rapid industrialization, population expansion, and alteration in the preference of people's diets around the world, the current ADI value and permitted levels of sulphites by regulatory agencies are **whether** sufficient to mitigate the severity remains questionable. The regulatory agents can find an alternative rather than monitoring hazardous sulphites usage. The food we eat is meant to promote health, not anguish. Although these chemicals superficially tend to make processing and end use easier, but in an integral sense, they are evolving as potential toxicants.

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