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Sodium Metabisulfite as a Food Additive: Mechanisms of Action and Health Implications

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Abstract

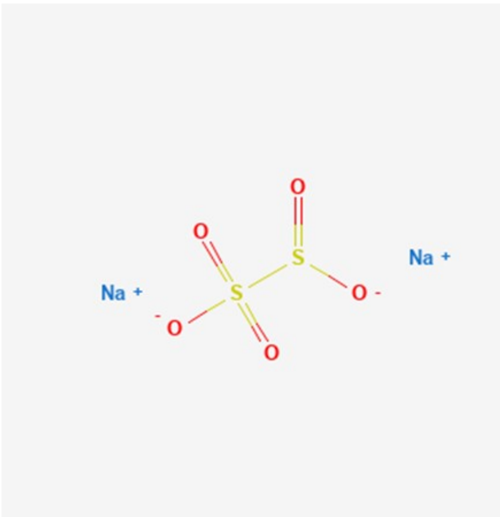
Sodium metabisulfite is a synthetic compound which comes under group of sulfur-based food additives. As a food additive they are used as preservative, antioxidant, dough conditioner, and colour stabilizer. They are used in wide varieties of foods like dried fruits, vegetables, sea foods, juices, and alcoholic beverages. Sulfur dioxide is the active compound which plays a major role as an antimicrobial food additive. Sulfite intake has been related with many adverse health effects such as vitamin deficiency, allergies, gut microbiota dysbiosis. Countries have taken measure to regulate the use of sulfur containing food additives and have legislations that prohibited the use of additive in meats. This review discusses the benefits of sodium metabisulfite, its role in food preservation, with an emphasis on its health risks in animals and humans.

Keywords: Food additive; Preservative; Toxicity; Benefits and Health risks

Introduction

Sulfites are group of compounds that are sulfur based which have the potential to liberate sulfur dioxide, an important active component, that aids in preservation of foods. Usage of sulfites to prevent spoilage of food and to preserve the food color has been in practice since Romans and Greeks in the ancient times. Among the group of sulfites, Sodium metabisulfite (SMB) is very widely used as a food additive. SMB is primarily used as antimicrobial agent, antioxidant, colour or colouring adjunct, dough strengthener, flour treating agent, freezing or cooling agent and oxidising or reducing agent. It is also widely used in the fields of pharmaceuticals and cosmetics [1, 2]. Although they have numerous uses, they are also related to health ailments related to breathing like asthmatic reactions and also degradation of thiamine when used as food additive. Researchers have previously observed that gastrointestinal tract absorbs sulfites and is distributed to different organs [3]. This review paper explores the benefits of Sodium metabisulfite as a food additive, its mode of action, its role in food preservation – such as extending shelf life, preventing discoloration, antimicrobial and antioxidant properties which effectively inhibits the growth of microorganisms in various foods. However, exposure to Sulfite containing compounds like SMB can induce adverse reactions on sensitive individuals. This paper also evaluates its effects on animals with an emphasis on adverse effects on human health and risk groups in order to present a fair assessment that guides safer application of the food additive.

Structure, Physical and chemical properties



Sodium metabisulfite is a synthetic compound with a molecular formula $Na_2S_2O_5$. It has a molecular weight of 190.11 g/mol. The appearance of sodium metabisulfite is a white crystal or powder. It has sulfur odor. When heated to high temperature it may decompose and release oxide fumes of sodium and sulfur which is toxic. It becomes corrosive acid when mixed with water. It freely dissolves in water, glycerol and slightly in alcohol. When sodium metabisulfite is exposed to air and moisture is oxidized to sulfate. When dissolved in water it develops an odor. It decomposes on heating and ultimately forms sodium sulfate with the emission of toxic fumes of sulfur or sulfur dioxide. The aqueous solution of sodium metabisulfite is an acid [4].

$$Na_2S_2O_5 + H_2O \rightarrow 2NaHSO_3$$

Sodium metabisulfite Sodium bisulfite

$$2NaHSO_3 \rightarrow 2SO_2 + H_2O + 2Na^+$$

Some SO_2 is released into the air

$$SO_2 + H_2O \rightarrow H_2SO_3 \rightarrow HSO_3^- \rightarrow H^+$$

Some of the SO_2 will react with H_2O to produce Sulfurous acid which dissociates to give hydrogen ion

Applications of Sodium Metabisulfite in Food Industry

Sodium metabisulfite is used in variety of food products like dried fruits, processed potatoes, Beverages – wine, beers and fruit juices, sea food – shrimp, and snack foods. The table.1 shows the foods which contains sulfites as a food additive.

Table 1: Sulfites in foods [5]

Food category	Examples
Drinks	Bottled soft drinks and Fruit juice, Cordials, Cider, Beer, Wine (including sparkling wine)
Processed fruits	Dried Apricots, Fruit bars, Maraschino Cherries, Canned, Bottled, or Frozen Fruit juices, Commercial preparations of Citrus fruit beverage mixes
Processed vegetables	Canned vegetables (including potatoes), pickled vegetables (including sauerkraut), Dried vegetables, Instant Mashed Potatoes, Frozen Potatoes, Potato Salad
Fish andCrustacean	Canned clams; fresh, frozen, canned, or dried Shrimp; frozen Lobster; Scallops; Dried Cod
Othercommercialfoods	Toppings, Maple syrup, Jams, Jellies, Biscuits, Bread, Pie and Pizza dough, Gelatine, Coconut, Vinegar, Beef stew

Benefits of Sodium Metabisulfite as a Food Additive:

a) Preservation and Antimicrobial Role:

Sodium metabisulfite dissolves in water to produce sulfur dioxide. The activity of SO_2 depends on the pH of the environment, it is favourable when the pH is between 3 and 6. The effect of SO_2 is bacteriostatic against *Acetobacter* species and lactic acid bacteria at low pH and bactericidal at high pH. The antibacterial activity is because of SO_2, it has strong reducing property that helps to reduce the oxygen level below the point in which aerobic organisms thrive or by affecting the disulfide bonds on essential enzymes. Lower the pH higher the toxicity. [6, 7]. Several bacterial genera like *Escherichia coli, Salmonella, Citrobacter freundii, Yersinia enterocolitica, Serratia mercescens, Enterobacter agglomerans, Hafnia alvei, Lactobacillus viridesencs, Pediococcus, Leuconostoc, Oenococcus genera, Acetobacter gene,* malolactic fermentation bacteria, bacterial families like *Listeriaceae, Vibrionaceae, Pesudomonadaceae, Campylobacteraceae* are inhibited by the effect of sulfites ranging from 10 to 240 μg per mL^{-1} [8]. According to Avis *et al.*, [9], Sodium metabisulfite acts by interacting with the cell membrane of *F. sambucinum.* Eradication of cell membrane happens through increased permeability of cell membrane in Fungus.

The sulfur dioxide which is liberated interrupts the cellular constituents. The cell damage is may happen due to the reactions with the sulfhydryl groups that are present in the enzymes, cofactors, vitamins, nucleic acids and lipids. The disulfide bonds are cleaved in proteins which in turn alters the confirmation of the molecules and the enzymes [10].

The antimicrobial role of sulfur dioxide relies on the biological system with which it reacts. It depends on the sulfur dioxide ability to penetrate through the cell membranes of microbes. At low pH this additive can be more potent as an antimicrobial agent. The enzyme activity of protein based on the structure, that is supported by disulfide bond cross links. Some enzymes rely on hydrogen carrier like NAD+, and NADP+ which are inhibited potently by forming inactive adduct with ion of sulfite [11]. Another process that is potently effective in the yeast cells is the breakdown of ATP. Quick fall in the levels of ATP which was noticed in *Saccharomyces cerevisiae*, right before sulfite-mediated microorganism death [12, 13]. Sodium metabisulfite works by inhibiting the synthesis of proteins, energy production, DNA replication, membrane synthesis, and cellular intermediate metabolism [10].

b) Colour preservation and Antioxidant Role:

Sixty-seven percent of Sodium metabisulfite is sulphur dioxide (SO_2), which reacts with water when added to beef to produce between 50% to 55% SO_2. Meat products are usually analysed for SO_2 levels rather than Sodium metabisulfite because residual SO_2 may decrease as a result of different responses. Bacterial presence and storage temperature are two variables that affect how well SO_2 works in meat; higher bacterial counts and warmer temperatures cause SO_2 to degrade more quickly. It works better at lower pH levels and against specific types of bacteria. By reducing the rate at which myoglobin oxidises, SMB can help sausages retain their desired red hue. However, because the free water required for SO_2 generation is frequently bound in the cooked product, its effectiveness decreases after heating [14].

In the seafood business, melanosis, commonly referred to as black spot formation, is a serious post-harvest problem, especially for species of Shrimp like Pacific white Shrimp *(Litopenaeus vannamei*). Polyphenol oxidase (PPO), enzyme oxidises phenolic chemicals into quinones that polymerise into dark pigments, is the cause of this enzymatic browning. Melanosis significantly lowers the shrimp's cosmetic attractiveness and marketability, but it has no effect on the shrimp's safety. By blocking PPO action, sodium metabisulfite (SMS) is frequently used to keep prawns from developing melanosis. Its capacity to dissolve and release sulphur dioxide (SO_2), an antioxidant and antibacterial agent, is the mechanism underlying its efficacy. By attaching itself to PPO's active sites, the SO_2 inhibits its function and stops the enzymatic browning process [15]. The same principle is also used to prevent the browning of fruits and vegetables A [16]. PPO requires cofactor copper ions for enzymatic activity, SMB chelates with these ions which prevents the enzymatic action [17].

The sulfur dioxide has been used as a preservative in wines since ages. The purposes include eliminating brownish colors – bleaching effect, as an antioxidant – reacts with hydrogen peroxide, phenols and aldehydes to make them less effective components, and at last the anti-microbial activity. SO_2 can act in several forms which depends on the pH. In wines as the pH ranges from 3.2 to 3.6, it exists mostly is HSO_3 form. They inhibit polyphenol oxidase enzyme with as little dose as 35mg/L [18]. Sodium metabisulphite is used to change the gluten's strength in doughs. It lowers the shrinking of the dough pieces during baking by making the gluten less elastic and more extensible [19]. It is used as a reductant in baking for economic reasons. It breaks S-S bonds in dough, reducing them to SH groups and lowering the molecular weight of glutenin protein aggregates [6].

Regulations

FDA [20,21] has mentioned, when used in compliance with Good Manufacturing Practice, Sodium metabisulfite is generally recognized as a safe chemical preservative. SMB is primarily used as antimicrobial agent, antioxidant, colour or colouring adjunct, dough strengthener, flour treating agent, freezing or cooling agent and oxidising or reducing agent. The usage of SMB is restricted to use in foods that contain vitamin B1 – thiamine. Sulfites are known to degrade thiamine, hence reduce the nutritional value of the product. For this reason, sodium metabisulfite is prohibited for use in meat products and food that are known to be the source of Thiamine. The processed food should disclose the presence of sodium metabisulfite in concentrations higher than 10ppm/kg for the safety of the consumers.

According to EU, Sodium metabisulfite is governed by E223 of Commission Regulation (EC). For various foods, the permissible range for SMB is from 10 mg/kg to 2000mg/kg. The acceptable daily intake of SMB is 0.7 mg SO_2 per kg body weight. The European Food Safety Authority regularly assess the dietary exposure and usage conditions to adapt as required, especially for the vulnerable populations [22, 23].

The Food Safety and Standards Authority of India (FSSAI) applies to sodium metabisulfite. The maximum permitted quantity of SMB to be used depends on the type of food, which is based on the properties of the food. In carbonated drinks SMB can be used up to 70mg/L. In dried fruits it can be used up to 2000mg/Kg. Wines, beers and alcoholic beverages can have up to

200mg/L. Accurate labelling, allergen warnings and ingredient list are crucial for consumer knowledge [24, 25]

Health Implications and Risk factors

a) Adverse effects on animals:

From the finding of Elmas *et al.,* [26] in albino rats, it was inferred that sodium metabisulfite causes increase of lipid peroxidation in kidney and liver of rats at 520mg/kg/day which is equivalent to 350mg SO_2 daily which represents high sulfite exposure through certain foods, drugs and medical components. They found that the sulfite radicals react with lipids producing lipid peroxides and malondialdehyde. This is also supported by Wairimu *et al.,* [27], where SMB induced MDA, serum nitric oxide, interferon gamma and tumour necrosis factor -*α*.

In a study with mouse tissues, Carvalho *et al.,* [28] observed that SMB induced DNA damage in blood, liver and bone marrow cells. Increase in micronucleus which was also observed in blood and bone marrow at the concentration of 1 and 2g/kg. The DNA damage is induced due to radical mediated reaction. These sulfite radicals may interact with molecular oxygen which results in sulfite peroxyl and sulfate radical, that in turn reacts with lipids which ultimately ends in lipid peroxidation. They may also undergo non-enzymatic reaction where they interact with disulfide bonds, with results in glutathione S sulfonate, that shows increased levels of glutathione levels intracellularly. Protein damage, membrane damage, phospholipid oxidation, single-strand and double-strand DNA breaks, and damaged nucleic acid bases are examples of oxidative stressors. Kayraldiz & Topaktas [29] also concluded the genotoxic effects of SMB. Kocaman *et al.,* [30] observed treating with sulfites caused lowering the nuclear division index (NDI), mitotic index (MI), and replication index (RI) in human cells in a dose-dependent manner, MB demonstrated a lethal effect. The substance also caused Chromosomal aberration and reduced MI in rat bone marrow cells which shows signs of cytotoxicity and genotoxicity.

Lai *et al.,* [31], studied the SMB effect on HL-1 cardiomyocytes and NSC- 34 neurons. In western blotting results it was found that voltage gated sodium channels (I_{Na}) were stimulated the current voltage shifted to negative potential and I_{Na} steady state inactivation curve shifted to a more positive potential. It showed increased expression of sodium channel in cells treated with SMB. It was observed that SMB changes the cellular excitability and excitotoxicity in excitable cells. In study conducted with rats 25mg/kg/day of SMB, there was a 20% and 16% decrease in total volume and neuron number in the deep cerebellar nuclei in the group of rats treated with SMB [32].

a) Adverse effects on Humans:

The sulfite which is present in the food as food additive is oxidized rapidly to sulfate and excreted in urine. The sulfite metabolism takes place in the liver, using the enzyme sulfite oxidase an amount which is finite will enter the systemic circulation, approximately 10% of the dose which is ingested is sent out of the body in unaltered form through urine [33].

Higher than tolerable doses of sulfites have known to cause polyneuritis, bleaching of incisors, visceral organ atrophy, bone marrow atrophy and renal tubular caste, limited growth and spectacle eyes. The effect of sulfite on thiamine which is destructive is found to be the reason for the toxicity [34].

As strong nucleophilic molecule sulfite tends to interact with different biomolecule by substituting on the positions of electrophile which has the potential to cause multitude reactions that can cause cell damage. In living cells, such molecules have been known to inhibit important enzymes which are entailed in the production of ATP and NADH, and that ultimately results in cell death. In mammals the oxidation of sulfite is performed by the enzyme sulfite oxidase which is chiefly present in liver and kidney cells. The amount of metabolization per day depends on enzyme production, environmental condition and genetics of the individual. It has been noted that exposure to sulfite is known to induce allergic reactions, dermatitis, flushing, hypotension, pain in abdomen, diarrhoea. anaphylaxis and asthmatic reactions. It has been previously reported that mast cells and basophils are sensitive to sulphite and trigger degranulation of histamine without depending on calcium or IgE crosslinking. Exposure to sulfites as food additives which can cause increased level of sulfite in plasma which might be a factor for anaphylaxis, in persons who are sulfite-sensitive [35].

Notably, in gastrointestinal tract Irwin *et al.,* [36] reported that sodium sulfite, showed bactericidal effects on beneficial gut bacterial species like *Lactobacillus casei, L. rhamnosus, L. plantarum and Streptococcus thermophilus* within 2 hours of exposure. The allergic reactions could be because of the release of lipopolysaccharides or peptidoglycan which is liberated when the bacteria are lysed. Obesity has been correlated to chronic inflammation because of a different mechanism of pathogens [37]. People who are obese have high number of bacteria which are gram negative in their guts which contributes to high secretion of lipopolysaccharides from the cells which are dying. There are also studies which shows high inhibition of leptin in murine adipocytes, that are lipopolysaccharide treated [33]. Different vitamin B production has been linked to the gut microbial population and in fermented foods. Deficiency of thiamine is factor which is recorded in patient who are affected by obesity, diabetes, and alcoholics. Thiamine is importantly present in meats, whole grains, egg, fish and legumes. For this purpose, it has been restricted to use thiamine in meat products [38]. According to Kerns *et al*., [39], in the metabolism of glucose, thiamine plays a major role as cofactor. The deficiency of thiamine has known to severe cardiovascular and complications in neurological mechanism of the body. The sulfite which is added as a preservative in alcohols and convenient foods may also lead to deficiency of thiamine which is obtained through foods and also by inhibiting the growth of bacteria [36].

Obesity has been correlated to chronic inflammation because of a different mechanism of pathogens. People who are obese have high number of bacteria which are gram negative in their guts which contributes to high secretion of lipopolysaccharides from the cells which are dying.

Sulfites are known to induce reactive oxygen species (ROS) by direct production in order to prime the cell to respond to the tripeptides of bacterial fMLP. The ROS production is induced through protein kinase C and Ca^{2+} calmodulin pathways. This is important as these act as very essential antimicrobial agents against pathogens. But these ROS are also known to cause tissue injury and the change the physiological functions of different organs which includes lungs when there is no regulation on production [40].

There is existing literature about sulfites in wines induce asthma in asthmatic patients. In high sulfite wine, responses were very rapid and showed fall in Forced expiratory volume under 5 minutes which is consistent with previous studies. This likely happens due to neural mechanism. When the responses are severe, the arm of nervous system that involves the pathways like non-adrenergic non cholinergic might be involved, which is proved by the evidences of tachykinins and bradykinin, along with these prostaglandins and leukotrienes are also involved [41].

The risk group is identified as Asthmatic people, who are highly sensitive to sulfites, where SO_2 irritates their airways. An estimated 3% to 10% of people who are asthmatic experience these symptoms [42- 44]. There were also many asthma reactions or skin reactions among asthmatic patients, when treated with bronchodilator medications which contained sulfites [45-47]. Asthmatics who are steroid dependent and people with hyperresponsive airway are at greater risk of developing adverse reactions to foods which contain sulfite [48]. There are evidences which suggest that respiratory sensitivity to sulfites can be more common among children [49 – 52].

Conclusion

The use of food additive has become imperative in the society, with increased use of convenient food there is growing need for food additive. To maintain the food for retaining its original state such as texture, colour, odour and flavour, it is necessary to add food additive. Food with high moisture content do not keep well when stored and microbes are one the major causes of food spoilage. The role of sulfur containing food additives are an important component as a preservative. As the usage increases, they should be regulated and regularly assessed and scrutinized by regulatory bodies to prevent over usage. To summarize precisely, SMB is known for its preservative property which effectively controls the growth of microbes which in turn increases the shelf life of the food, which makes the use of Sulfite containing food additives inevitable in the food industry. The antioxidant properties of SMB contribute to maintain colour and enhance flavour in food improving the general quality and appeal to the consumers. SMB, however, maybe harmful to health in particular for those who are sensitive. Adverse reactions such as allergies, gastrointestinal distress, respiratory problems. It has also been previously reported that exposure to sulfite can also cause symptoms like dermatitis, urticaria, flushing, hypotension, diarrhoea, possibly fatal anaphylactic and asthmatic reactions. Sodium metabisulfite has applications which is beneficial but also has health impacts that can cause serious effects. Consumer awareness, changes in the trend of nutrition consumption especially in processed food can pave way for alternative to chemically synthesized additives like sodium metabisulfite and other sulfiting agents.

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