SULFITES: AN IMPORTANT FOOD SAFETY ISSUE

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An update on regulatory status and methodologies.

Under the Federal Food, Drug, and Cosmetic Act, sulfites are permitted for use as preservatives in food. Like other ingredients, sulfites must be declared in the ingredient statement when added to a food product. Reports in the literature describe the adverse reactions experienced by sensitive individuals upon consumption of foods that contain sulfites, or that contain unexpectedly large amounts of sulfites. Kochen was one of the first to recognize hypersensitivity to foodborne sulfites.[1] Studies by Taylor, Higley and Bush revealed more about the adverse reactions to sulfites.[2] A report that children suffered asthma attacks after eating pickled onions was published in 1995.[3]

Emergency room admissions confirm that ingestion of sulfites can lead to asthmatic attacks, rashes and abdominal upset. An alert physician observed that six patients, who had been admitted to the emergency room, had consumed the same brand of salsa.[4] Two of the patients had asthma flare-ups, two experienced coughing and tightness of the throat, and two required mechanical ventilation. It was discovered that the offending salsa had a sulfite content of 1800 parts per million (ppm)–well above the level of approximately 700 ppm found in other brands of salsa. One of the patients, fully aware of her sensitivity to sulfites, thought it was safe to eat the salsa because it was improperly labeled as "fresh."

Although the physiological basis for sulfite sensitivity is still poorly understood, clinical observations have established that certain medical conditions are associated with a predisposition to sulfite-hypersensitivity. Approximately 500,000 individuals in the United States are at risk because they are asthma sufferers, who are steroid-dependent or who have airway hypersensitivity.[5]

The U.S. Food and Drug Administration (FDA) Center for Food Safety and Applied Nutrition (CFSAN) has monitored reports of adverse reactions to sulfites since 1980. As of June 1999, CFSAN has received 1,132 consumer complaints describing adverse reactions thought to be due to the ingestion of foods with sulfites. Out of 799 reports with adequate information about the intensities of the reactions, 388 (48.6%) were classified as severe.

Completed studies suggest that sulfite in the form of sulfur dioxide is the agent that causes the physiological response. Mansour, et al, hypothesize that sulfur dioxide causes bronchoconstriction.[6] Peroni and Boner postulate that sulfur dioxide acts on tracheobronchial receptors to induce a cholinergic reflex.[7] Gunnison, et al, found that inhaled sulfur dioxide elicited a stronger reaction in sulfite oxidase-deficient rats than endogenously accumulated sulfites and S-sulfocysteine (a reaction product of sulfite with cystine residues in proteins).[8,9] Under the auspices of the FDA, an ad hoc Panel of the Life Sciences Research Office/Federation of American Societies of Experimental Biology issued a report, *Reexamination of the GRAS Status of Sulfiting Agents,* which concludes that certain individuals may experience an adverse reaction upon consumption of sulfites.[10]

REGULATORY STATUS OF SULFITING AGENTS

The FDA acted in 1986 to reduce the likelihood that sulfite-sensitive individuals would unknowingly consume sulfited foods.[11,12] The use of sulfites on fruits and vegetables that are to be served raw, or presented as fresh to the public, was prohibited. As a consequence, foods such as guacamole, fresh mushrooms and fresh salad bar vegetables may no longer be treated with sulfites. Sulfites added to food must be declared. The only exception is made when sulfites are added indirectly (i.e., through a sulfited ingredient, such as sulfited raisins in a fruit cake) and the sulfite level in the food product (such as the fruit cake) is below 10 ppm. In such cases, sulfite label declaration is required if the sulfite content, determined as SO_2 by a prescribed analytical method, is 10 ppm or higher. Sulfur dioxide used as a fumigant for table grapes is officially defined as a pesticide and is required by the U.S. Environmental Protection Agency (EPA) to be at less than detectable levels (less than 10 ppm). These regulations effectively removed the hidden sulfites from the food supply with a few exceptions. Although sulfites may not be used on fresh salad bar vegetables, not every item on the salad bar is free of sulfite. Pickled foods, such as pepperoncini and other processed foods, may be sulfited. Instant potatoes are processed foods that often contain sulfites.

The use of sulfites to preserve the color of fresh cut potatoes–ultimately to be cooked in restaurants, hospitals and other institutions–has been the subject of divergent regulatory interpretations. These products are, in fact, raw as offered for sale. The sulfite, which can be present at levels as high as 500 or 1000 ppm, ensures that the potatoes will look fresh when delivered hours, or even days, after preparation. FDA plans to repropose a ban for sulfites on fresh, peeled potatoes to be sold unpackaged and unlabeled, such as french fries in restaurants. An earlier FDA rule dealing with sulfites on potatoes was invalidated by the court in 1990 on procedural grounds.

SULFITES AND EFFECTS OF FOOD TECHNOLOGY

A variety of food technological effects

result from the "sulfiting" of food with one or more of the substances shown in Table 1. Sulfiting agents effectively inhibit enzymatic browning in foods and beverages because these agents deactivate the mixed function enzyme, polyphenol oxidase (PPO), which is found in fruits, vegetables and meat.[13] PPO catalyzes the oxidation of phenols to form *o*-quinones which polymerize to form high-molecular weight brown pigments (melanin). Sulfites are also used to bleach brown or black pigments.

Sulfites are used for a myriad of food technological functions that include dough conditioner, antioxidant, antimicrobial and color stabilizer. This range of food technological applications has led to the use of sulfites in a wide variety of foods.[14] This is illustrated by the selected results given in Table 2 of the FDA's surveillance of imported foods. All of the products listed in Table 2 were stopped at entry because they did not have the legally required label declarations. Because sulfites are used extensively in dried fruits (except prunes and black raisins), wines, vinegar, instant potatoes and dried vegetables, food processors would be well advised to have a plan to control sulfites, especially if they obtain their ingredients from outside sources.

Sulfur dioxide	SO_2
Sodium metabisulfite	$Na_2S_2O_5$
Sodium bisulfite	$NaHSO_3$
Sodium sulfite	Na_2SO_3
Potassium metabisulfite	$K_2S_2O_5$
Potassium bisulfite	$KHSO_3$

[a]*The agency is aware that use of other substances such as sodium dithionite may also yield residual sulfite in food products. In such instances, consumers must be alerted through appropriate labeling.*

Table 1. Sulfiting agents[a] for food use.

Food	Sulfites Levels (ppm SO_2)
Dried bamboo shoots	2100
Winter melon candy	1920
Dried apple	750
Ginger	1900
Sweet coconut	375
Dried abalone	11000
Sundried tomatoes	800
Shrimp	600

Table 2. Sulfites in imported products.

Plan to Control Sulfites

Sulfiting agents are highly effective food processing substances and will continue to be used in a wide variety of applications. Food processors who do not add sulfites directly but who use ingredients that may be treated with sulfites, should establish a plan to avoid producing products with more than 10 ppm sulfite. The plan should include a careful review of all of the ingredients that are used. The suppliers of ingredients should be asked to provide certification that the ingredients in question are free of sulfites. In the absence of such certification, the food processor may wish to establish a quality control plan that includes sulfite analysis as a quality control specification.

The Nature of Sulfites in Food

Equation 1 illustrates the dynamic equilibrium that exists between the oxosulfur species with the sulfur in the +4 oxidation state.[15]

$$SO_2 + H_2O \Leftrightarrow SO_2(H_2O) = H_2SO_3 \underset{pK_1\approx 2}{\Leftrightarrow} H^+ + HSO_3^{-1} \underset{pK_2\approx 7}{\Leftrightarrow} 2\,H^+ + SO_3^{-2}$$

The distribution between the different forms is dependent upon the pH of the medium. Bisulfite, HSO_3^{-1}, is a predominant form in food in the intermediate pH range. Sulfur dioxide, the predominate moiety at low pH, is a gas that is used for fumigation. The sodium and potassium salts of metabisulfite and bisulfite, and sodium sulfite are salts that are approved as sulfiting agents. The salts are generally used in aqueous solutions that are used as dips or sprays for foods.

In addition to the inorganic chemistry shown in Equation 1, many other reactions occur in food. For example, the mechanism for dough conditioning probably involves the reaction of sulfites with disulfide bonds as shown (Equation 2).

$$R\text{-}S\text{-}S\text{-}R' + SO_3^{-2} \leftrightarrow R\text{-}S\text{-}SO_3^{-1} + R'\text{-}S^{-1}$$

The cleavage of the disulfide linkages weakens the dough, thereby making the dough more suitable for the production of crackers or pizza crusts. The addition of bisulfite to carbonyl compounds (Equation 3) is another important reaction that

$$HSO_3^{-1} + R_2{>}C{=}O \rightarrow R_2{>}C(\text{-}OH)SO_3^{-1}$$

accounts for some of the food technological effects of sulfites. For example, the formation of the bisulfite addition product of acetaldehyde in wine eliminates a rather harsh flavor note.

Analytical Chemistry

The chemistry of oxosulfur(IV) offers many interesting reactions and physical properties that suggest intriguing possibilities for analysis. It seems that few chemists have been able to resist the temptation to develop an analytical method based upon a favorite technique–whether it involves electrochemistry, fluorescence, chemiluminesence, colorimetry, gas-liquid chromatography or liquid chromatography. It is not surprising, then, that there are at least 11 different methods for sulfite described in the *Official Methods of Analysis of AOAC International, 16th Edition* as shown in Table 3.[16] All of the methods introduced since 1987, as well as AOAC Methods 892.02 and 962.16, take advantage of the fact that the addition of water and strong mineral acid to the food will cause all of the oxosulfur(IV) anions shown in Equation 1 to be converted to sulfur dioxide. The sulfur dioxide can be conveniently removed from the bulk of the food components, captured in a solution and analyzed by a variety of means. The methods may appear to be conceptually different, but in fact, the most important aspect of the analysis, which is the conversion of the various forms of sulfite to sulfur dioxide, is the foundation of all of the procedures. If the various methods do not show good agreement, it is because of the differences in the kinetics with which the compounds, both naturally occurring and sulfite-derived, react to yield sulfur dioxide. For example, Method 987.04 utilizes a quick distillation that does not provide the recovery of sulfur dioxide that will be realized with the Monier-Williams distillation that uses a water-cooled condenser and a 90-minute distillation period. In spite of these difficulties, the isolation of sulfur dioxide has given rise to the tradition of expressing the sulfite content of food in terms of sulfur dioxide by weight. This is an oversimplification of the complex nature of sulfites and sulfite-derived products in food; however, the practice has served well for food technologists and government regulators alike.

Other methods based upon the conversion of all of the sulfite-derived compounds to bisulfite, HSO_3^{-1}, have been developed. For example, formaldehyde

Method Number	Year Adopted	Title
892.02	1892	Sulfurous Acid (Free) in Meats–Titrimetry
961.09	1961	Sulfites in Meats–Qualitative Test
962.16	1962	Sulfurous Acid (Total) in Food–Modified Monier-Williams
963.20	1963	Sulfurous Acid (Total) in Dried Fruit–Colorimetry
975.32	1975	Sulfurous Acid in Food–Qualitative Test
980.17	1980	Preservatives in Ground Beef–Colorimetry
987.04	1987	Sulfites (Total) in Foods–Differential Pulse Polarography
990.28a	1990	Sulfites in Foods–Optimized Monier-Williams
990.29	1990	Sulfites (Total) in Foods and Beverages–Flow Injection Analysis
990.30	1990	Sulfites (Free) in Wine–Flow Injection Analysis
990.31	1990	Sulfites in Foods and Beverage–Ion Exclusion Chromatography

Source: *Official Methods of Analysis–16th Edition,* 1995, AOAC International, Gaithersburg, MD.

Table 3. AOAC International Official Methods for sulfites.

has been used to capture the bisulfite as the very stable hydroxymethylsulfonate (HMS).[17-19] This is illustrated by Equation 3 in terms of R = H. The analytical problem then becomes one of determining the concentration of HMS in the food sample that has been treated with buffered formaldehyde solution. These procedures avoid the problems associated with a distillation; however, they share the problems associated with the sulfur dioxide methods because the sulfite and sulfite-derived compounds must be converted to one of the inorganic forms shown in Equation 1.

The FDA has established, by regulation, that the Optimized Monier-Williams (990.28) will be used for official samples. This method causes difficulties for the following reasons: Naturally occurring compounds in isolated soy protein and Allium and Brassica vegetables will yield sulfur dioxide (false-positives), and the method is very labor-intensive. In the laboratories of the FDA, work is progressing on development of a chromatographic method that will detect the substances that readily yield sulfur dioxide under the Monier-Williams conditions. This method can be used successfully to distinguish between thiosulfate and sulfite–two substances that were found in canned tuna because of the use of sodium dithionite to prepare the hydrolyzed protein used in the product. The method is also showing promise in detecting added sulfite in dried garlic. The availability of this next generation of analytical methodology will accomplish two important objectives. First, it will be possible to directly measure compounds derived from added sulfiting agents, and second, it will resolve sulfite-derived compounds. This information will facilitate the identification of the substances that cause physiological responses in sensitive individuals.

Conclusion

The present state of knowledge suggests that sulfur dioxide is the agent that causes the physiological reaction. In view of this, it appears prudent to continue to use the Monier-Williams because any substance that will yield sulfur dioxide in gastric fluid will also produce sulfur dioxide under the conditions of the Monier-Williams.[20] This cautious approach is prudent until a new procedure is developed that will permit speciation of the sulfite-derived compounds.

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Editor's Note: *Additional information on sulfites may be obtained through CFSAN's website at http://vm.cfsan.fda.gov.*

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