

Update on sulfite sensitivity

Simon RA. Update on sulfite sensitivity.
Allergy 1998; 53 (Suppl 46): 78-79. © Munksgaard 1998.

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Sulfiting agents have a long history of use in foods. These agents include sulfur dioxide (SO_2) and any of several inorganic sulfite salts that may liberate SO_2 under their conditions of use. These include sodium and potassium metabisulfites ($\text{Na}_2\text{S}_2\text{O}_5$, $\text{K}_2\text{S}_2\text{O}_5$), sodium and potassium bisulfites (NaHSO_3 , KHSO_3), and sodium and potassium sulfites (Na_2SO_3 , K_2SO_3). In the early 1980s, we first reported that the ingestion of sulfites could produce severe and even life-threatening asthmatic reaction in sensitive subjects (1). These data have been confirmed by others, and the overall prevalence of sulfite sensitivity in the adult asthmatic population appears to be approximately 5% (2-4). The prevalence seems to be higher in the steroid-dependent asthmatic patients (5).

Three different mechanisms have been proposed to explain reactions to sulfite. The first involves the inhalation of sulfur dioxide. Sulfur dioxide is formed and becomes available for inhalation as solutions with sulfites are made acidic in warm temperatures. Delohery et al. (6) noted that certain sulfite-sensitive asthmatics reacted to an acidic metabisulfite solution when it was administered as a mouthwash or swallowed, but not when it was instilled through a nasogastric tube. We have shown other sulfite-sensitive asthmatics who react to sulfites contained in capsules and then swallowed (1).

It has been believed that sulfur dioxide produces bronchoconstriction through cholinergic reflex mechanisms. In fact, we have shown that the inhalation of atropine or the ingestion of doxepin (an antihistamine with anticholinergic properties) can protect sulfite-sensitive individuals from reactions to ingested sulfite (7). Guinea pig studies

suggest that this involves capsaicin-sensitive sensory nerves and the signal transduction of the neuropeptide NKA (8, 9). Similarly, in guinea pigs, it was concluded that sulfite induced bronchoconstriction in bowel stimulation of bradykinin β_2 -receptors (10).

While the inhalation of SO_2 clearly explains most of the asthmatic responses to sulfites, there is evidence that suggests a possible IgE-mediated reaction. There are reports of sulfite-sensitive anaphylaxis (11, 12) in which patients have been shown to have positive sulfite skin tests. Additionally, some sulfite-sensitive asthmatics have also been shown to have positive skin tests (13).

Finally, we have seen sulfite-sensitive asthmatics who have less sulfite oxidase activity in skin fibroblasts than normal controls (14).

Uses of sulfites in foods

Sulfites provide a number of useful attributes when applied to food. This includes inhibition of enzymatic browning (especially in fresh fruits and vegetables, shrimp, and raw potatoes) and inhibition of nonenzymatic browning, especially in dried fruits and dehydrated vegetables (15). Sulfites have antimicrobial activity in wine, dough-conditioning activity in frozen pie and pizza crusts, and bleaching effects in maraschino cherries. The use of sulfites in fresh fruits and vegetables has been banned by the US Food and Drug Administration (FDA) since 1985.

The levels of sulfites contained in foods varies greatly from under 10 parts per million (ppm) in frozen doughs, corn syrup, and jellies, to up to 60 ppm in fresh shrimp, pickles, and fresh mushrooms,

to up to 100 ppm in dried potatoes, wine vinegar, and maraschino cherries. The highest levels of sulfites (even up to 1000 ppm) can be found in dried fruit; lemon, lime, grape, and sauerkraut juice; and certain store-bought fresh sauces.

Sulfites readily react to food constituents, and an equilibrium exists between free and bound sulfites. Some of the binding is dissociable and can serve as reservoirs of free sulfite in food, while irreversible reactions also occur and tend to remove sulfite permanently from the pool of free sulfite. The likelihood of a particular food's provoking a reaction depends upon the ratio of free to bound sulfite (16). For example, lettuce has few components to which sulfite can react; therefore, most of the sulfite in lettuce remains in the free inorganic state. This is why lettuce (salad bars) seems to provoke sulfite-sensitive reactions most frequently (17). In contrast, sulfites added to shrimp and potatoes tend to be bound and are not as likely to produce reactions in those sulfite-sensitive subjects who react to the inhalation of sulfur dioxide (18).

Diagnosis of sulfite sensitivity

While a careful history is important in determining who may be sulfite-sensitive, it is not sufficient to make the diagnosis. Skin testing, with either prick puncture or intradermal technique, can discern only the few patients who may have IgE-mediated sulfite sensitivity. Therefore, various diagnostic challenge protocols have been developed to diagnose sulfite sensitivity. For most ingested sensitivities, challenges are performed with the substance contained in opaque capsules. However, if the pathogenesis of the sensitivity has to do with inhaled sulfur dioxide, capsule challenges may lead to false-negative results. However, since all asthmatics are sensitive to inhaled sulfur dioxide (unlike nonasthmatics), acid solutions admitted by sulfite may produce false-positive challenges, if the dosage is too high.

Since the FDA banned the use of sulfites in foods served fresh in the USA in 1985, we have only occasionally had to perform sulfite challenges in asthmatic subjects (except for research purposes). In those cases, we performed solution challenges up to 100 mg/ml of sulfite (19).

For subjects with a history suggesting sulfite-induced urticaria or anaphylaxis, we use capsule challenges up to a maximum dose of 200 mg (19). However, it should be noted that in a recent study of 75 subjects with chronic idiopathic urticaria and angioedema, we found none to be sensitive to sulfite (or other common food additives) in rigorous challenges that were blinded and pla-

cebo-controlled, and used objective criteria for positive reaction (15, 20).

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