Gastroenterology and Hepatology From Bed to Bench


**REVIEW ARTICLE**

# Adverse reactions to the sulphite additives

**Hassan Vally[1, 2], Neil LA Misso[3]**

[1]*Senior Lecturer, School of Public Health and Human Biosciences, La Trobe University, Melbourne, VIC 3086, Australia.*

[2] *Visiting Fellow, National Centre for Epidemiology and Population Health, ANU College of Medicine and Health Sciences, The Australian National University, Canberra ACT 0200, Australia.*

[3]*Adjunct Associate Professor, Lung Institute of Western Australia (Inc.), Centre for Asthma, Allergy and Respiratory Research, The University of Western Australia, Perth, Australia.*

## ABSTRACT

Sulphites are widely used as preservative and antioxidant additives in the food and pharmaceutical industries. Exposure to sulphites has been reported to induce a range of adverse clinical effects in sensitive individuals, ranging from dermatitis, urticaria, flushing, hypotension, abdominal pain and diarrhoea to life-threatening anaphylactic and asthmatic reactions. Exposure to the sulphites arises mainly from the consumption of foods and drinks that contain these additives; however exposure may also occur through the use of pharmaceutical products, as well as in occupational settings. Most studies report a prevalence of sulphite sensitivity of 3 to 10% among asthmatic subjects who ingest these additives. However, the severity of these reactions varies, and steroid-dependent asthmatics, those with marked airway hyperresponsiveness, and children with chronic asthma, appear to be at greater risk. Although a number of potential mechanisms have been proposed, the precise mechanisms underlying sulphite sensitivity remain unclear.

**Keywords**: Asthma, Food additive, Sulphites.

**(**Please site as: **Vally H, Misso NLA. Adverse reactions to the sulphite additives. Gastroenterol Hepatol Bed Bench 2012;5(1):16-23).**

## Introduction

Sulphites and sulphiting agents, such as sodium and potassium sulphite, metabisulphite, bisulphites and sulphur dioxide ($SO_2$), are ubiquitous compounds with a variety of commercial uses. In fact, $SO_2$ has been used since ancient times as a purifier and disinfectant. Burning sulphur was used by the ancient Greeks to fumigate houses, and by the ancient Romans to sanitize wine vessels (1). The sulphite additives are now used widely in the food industry – predominantly as anti-browning agents, antioxidants and preservatives (2, 3). Sulphites are also used extensively in the pharmaceutical industry (4) and have a number of industrial uses.

Whilst the apparent safety of the sulphite additives lead to their widespread use, reports began to emerge during the 1970s that sulphite exposure was associated with adverse reactions (5, 6). These included the triggering of anaphylactic reactions, as well as the elicitation of a wide range of symptoms, including dermatitis, urticaria, flushing, hypotension, abdominal pain and diarrhoea, although the vast majority of reports described the triggering of bronchconstriction in asthmatic patients (7, 8). Sulphite-induced asthmatic symptoms range from mild in some individuals, to very severe in others, and in some individuals these reactions can be life threatening (9).

*Received*: 22 November 2011 *Accepted*: 8 December 2011
**Reprint or Correspondence**: Hassan Vally, PhD. School of Public Health and Human Biosciences, La Trobe University, Melbourne, VIC 3086, Australia
**E-mail**: H.Vally@latrobe.edu.au

**Table 1.** Major types of food that may contain sulphite additives*

| |
|---|
| **Drinks** |
| Bottled soft drinks and fruit juice, cordials, cider, beer, wine (including sparkling wine) |
| **Other liquids** |
| Commercial preparations of lemon and lime juice, vinegar, grape juice |
| **Fruits** |
| Dried apricots, fruit bars |
| **Commercial foods** |
| Dried potatoes, gravies, sauces and fruit toppings, maraschino cherries, pickled onions, sauerkraut, pickles, maple syrup, jams, jellies, biscuits, bread, pie and pizza dough |
| **Salads and fruit salads** |
| **Crustaceans** |
| **Meats** |
| Delicatessen meats, mince meat, sausages |
| **Other foods** |
| Gelatin, coconut |

*Detailed information regarding foods containing sulphite additives can be found on the *Australasian Society of Clinical Immunology and Allergy* website (http://www.allergy.org.au/content/view/128/1/)

## Exposure to the sulphite additives

For the majority of people, exposure to sulphites occurs as a result of consumption of foods and drinks to which sulphites have been added, primarily for the purpose of preservation (Table 1). In addition to their preservative activity, sulphites are used to prevent the browning of foods, as bleaching agents, as dough conditioning agents, to prevent excess alkalinity of foods, as food processing aids, colour stabilizers and antioxidants (2, 3). Thus, in addition to being cheap and convenient, the sulphites are extremely versatile, and their addition to many foods serves more than one purpose.

Foods containing sulphites include dried fruits, dried vegetables, pickled onions and bottled soft drinks and cordials (8, 10). The addition of sulphite additives to beer and wine is permitted in most countries, and although the use of sulphites in fresh salads, fruit salads, mincemeat or sausage meat, is illegal in many countries, it may occur illegally. In addition to food, exposure to sulphites can occur through the use of cosmetics and medicines (Table 2). Cosmetics containing sulphites include hair colours and bleaches, creams, and perfumes (11). Medicines containing sulphites include eye drops, topical medications, and parenteral medications such as adrenaline, phenylephrine, corticosteroids and local anaesthetics (4,12). The sulphites also have a number of industrial uses, including in the photographic and textile industries, and consequently, occupational exposures to these additives may also occur (13,14).

**Table 2.** Medical and cosmetic uses of sulphites

| |
|---|
| **Cosmetics:** hair colours and bleaches, home permanent solutions, skin fading/lighteners, false tan lotions, anti-ageing creams and moisturisers, facial cleansers, around-eye creams, body washes/cleansers, hair sprays, perfumes, blush, bronzers/highlighters |
| **Medications:** Topical anti-fungal and corticosteroid creams and ointments (e.g. Trimovate®, Timodine®, Aureocort®, Aureomycin®, Nizoral®, Nystatin®, Lustra®, Psoradrate®), adrenaline, isoprenaline, isoproterenol, isoetharine, phenylephrine, dexamethasone and injectable corticosteroids, dopamine, local anaesthetics, propofol, aminoglycoside antibiotics, metoclopramide, doxycycline and vitamin B complex |

## Sensitivity to the sulphite additives

$SO_2$, as well as being one of the family of sulphite additives that is 'ingested' in foods, is

also an air pollutant. Thus, one of the first recorded adverse reactions triggered by sulphites dates back to the eruption of Mt Vesuvius in 79 AD, when Pliny the Elder, whose airways were "constitutionally weak and narrow and often inflamed", collapsed and died after inhaling the sulphurous gases emanating from the volcano (15). Whilst most non-asthmatic individuals can tolerate up to 5 ppm $SO_2$, there is evidence that a large number of asthmatics are hypersensitive to this gas (16,17). It is not entirely clear why this may be the case, but it may be that in these individuals $SO_2$ irritates airways that are already 'twitchy'. In contrast to hyperresponsiveness to $SO_2$ gas, sulphite sensitivity predominantly refers to the triggering of adverse symptoms following ingestion, or parenteral or topical exposure to these additives. While sensitivity to the sulphites can present in a number of ways, it is the triggering of adverse respiratory symptoms (predominantly amongst asthmatics) that seems to occur most frequently. It has been estimated that 3–10% of asthmatics experience such symptoms (7, 18, 19).

One of the earliest reports suggesting that ingestion of sulphites could cause irritation of the respiratory tract was published in 1973 (5). Since then numerous case reports and reviews have been published on the phenomenon of respiratory hypersensitivity to ingested sulphites. The first case of anaphylaxis following ingestion of sodium metabisulphite in a restaurant salad was reported in 1976 (6), and the following year $SO_2$ in orange drinks was reported to induce asthma (15). In the early 1980s there were numerous reports suggesting that ingestion of sulphites by susceptible individuals was the cause of severe adverse reactions. Although many of these were asthmatic responses (19-21), urticaria and angioedema (22), abdominal pain and diarrhoea (23), as well as anaphylaxis (24, 25) were reported. In 1985, Yang and Purchase (26) reported that there had been more than 250 cases of sulphite-related adverse reactions, including six deaths, in the United States, while in Canada, 10 sulphite-related adverse reactions and one death, thought to be sulphite related, had been reported.

As a consequence of these reported adverse reactions, the US Food and Drug Administration (FDA) acted in 1986 to prohibit the use of sulphites on fruits and vegetables that were to be served raw or presented as fresh to the public. For foods and drinks in which the use of sulphite was permitted, sulphite concentrations >10 ppm had to be declared on the label (27). Despite the introduction of these regulations, there continued to be sporadic reports of serious adverse effects following unintended ingestion of sulphites. The potentially severe nature of sulphite sensitivities is highlighted by a number of reports of life-threatening reactions to these additives (28-30).

In the early 1980s there were also a number of reports of asthma exacerbations and/or generalized skin reactions among asthmatic patients treated with bronchodilator medications containing sulphite (24, 31-33). One report highlighted the case of a patient who was hypersensitive to metabisulphite and developed anaphylaxis following ingestion of metabisulphite-treated food (34). This patient had a prolonged clinical course, requiring two visits to the emergency department and three weeks of corticosteroid therapy, suggesting that the relapse and delayed recovery may have been related to continued exposure to sulphites during treatment. Some older, rarely used bronchodilator solutions such as isoproterenol and isoetharine contain sulphites at concentrations sufficient to cause bronchoconstriction in most asthmatic patients, even in the absence of a history of sulphite sensitivity (35). With the availability of selective $\beta_2$-agonists such as albuterol that do not contain sulphites, these older bronchodilator solutions need not be used to treat asthmatic patients.

The presence of sulphites in some other pharmaceutical products is also reason for

concern. There are published reports of anaphylactic or asthmatic reactions associated with the use of sulphite-containing local anaesthetics, as well as gentamicin, metoclopramide, doxycycline and vitamin B complex (12). The generic form of the anaesthetic agent, propofol, contains sodium metabisulphite and has the potential to cause adverse effects, particularly in the paediatric population (36). Treatment of anaphylaxis in patients who are sensitive to sulphite also poses a conundrum in that administration of adrenaline is regarded as the primary treatment for anaphylaxis, and yet all commercially available preparations of adrenaline contain metabisulphite (37). However, even in patients with serious sulphite sensitivity, the benefit from adrenaline is considered to outweigh the risk of sulphite exposure associated with use of adrenaline in an emergency (38).

Asthmatic responses have also been reported following exposure to sulphites in occupational settings. Valero et al. (39) reported the case of a patient who experienced episodes of bronchospasm that required hospitalization after handling sodium bisulphite at work. Metabisulphite-induced occupational asthma has also been reported in a photographic technician (14) and a radiographer (40). Occupational asthma has been reported in a worker who sprinkled dry metabisulphite powder onto potatoes (41) and three cases of occupational asthma related to metabisulphite exposure were reported in France (42). The use of sodium metabisulphite in the fish and prawn-processing industry, with associated exposures to high concentrations of $SO_2$, has been identified as an under-recognised cause of occupational airways disease (43). An increased incidence of asthma and increased asthma-related mortality have also been reported in sulphite pulp mill workers, probably as a consequence of repeated exposures to peak concentrations of $SO_2$ (44, 45).

Over the past three decades a number of challenge studies have been performed in an attempt to confirm sulphite sensitivity and estimate its prevalence in subjects with suggestive histories. The interpretation of these studies is difficult, as the criteria for the selection of subjects have varied and may have been biased towards those with a history of sensitivity or more severe asthma. In addition, the dose and physical form of sulphite used in challenge protocols has varied widely, as have the criteria considered indicative of a positive response (1, 7, 46-48). As a consequence there is some uncertainty as to the true prevalence of sulphite sensitivity amongst asthmatic patients, although the literature consistently reports a prevalence of between 3 and 10% (1, 7, 19, 47, 49). Steroid-dependent asthmatics and those with marked airway hyperresponsiveness appear to be at greater risk of adverse reactions to sulphite-containing foods (8). Although there was an early suggestion that as many as 30% of reported cases of sulphite sensitivity occur in individuals with no known history of asthma (50), later reviews of the literature suggested that adverse reactions to sulphites were extremely rare in non-asthmatic subjects (1, 8). There are some indications that respiratory sensitivity to sulphites may be more common amongst women (7, 51) and children (52-54).

Although the literature regarding the prevalence of skin reactions to the sulphites is somewhat limited, studies suggest that somewhere between 1 and 5% of those patch tested may demonstrate skin sensitivities to these additives (55-57).

Reports in the literature describe adverse dermatological responses following exposure to cosmetics, such as facial cosmetic creams (58), hair dyes (59) and false tanning lotion (57).

In addition, topical medications, such as antifungal (55) and haemorrhoid creams (60) and eye drops (61) have been associated with the elicitation of skin symptoms. Similarly, a wide range of occupational exposures have also been linked with adverse skin reactions to the sulphites (13, 14, 62-66).

## Potential mechanisms of sensitivities to the sulphite additives

Given the wide variations in symptoms, in the severity of reactions, and in the sensitivities of individuals to different forms of sulphite, it is unlikely that any single mechanism can explain all reactions to the sulphite additives.

A number of potential mechanisms that might explain asthmatic reactions to the sulphites have been postulated, although the mode of exposure is a confounding factor (7,8). Nebulized bisulphite solutions, acidified metabisulphite solutions, encapsulated metabisulphite and sulphite containing food or drinks may or may not provoke reactions in the same individual, and the types of reactions and concentrations of sulphite that provoke reactions may vary widely with different forms of exposure. Inhalation of $SO_2$, generated from ingested sulphites in the warm acidic environments of the mouth and stomach, may cause respiratory symptoms. Although nebulized metabisulphite was also thought to cause bronchoconstriction through generation of $SO_2$ in the airways (48), airway responsiveness to acidic metabisulphite solutions and $SO_2$ were not significantly related (67).

Some studies have suggested that sulphites may stimulate the parasympathetic system, with bronchoconstriction being mediated by a cholinergic pathway (7). The enzyme sulphite oxidase oxidizes sulphite to sulphate, and it was suggested that inadequate activity of this enzyme may result in excessive accumulation of sulphite, resulting in cholinergic mediated bronchoconstriction in some individuals (68). The release of histamine and other mediators as a consequence of mast cell degranulation through IgE or non-IgE mediated mechanisms has also been suggested as a possible mechanism in some individuals (69). There is some evidence supporting a role for prostaglandins in sulphite induced asthma (70), and the inhibition of bronchoconstriction by leukotriene receptor antagonists, in asthmatic subjects exposed to $SO_2$, suggests a possible role for leukotrienes (71, 72).

## Conclusion

Many individuals are sensitive to sulphite additives and may experience a range of symptoms, including dermatological, gastrointestinal and respiratory symptoms. Nevertheless, reactions manifesting in the respiratory tract account for the majority of cases of sulphite sensitivity. The true prevalence of asthmatic responses to the sulphites remains uncertain, although it is generally agreed that between 3 and 10% of adult asthmatics may exhibit adverse reactions to the sulphite additives, with a number of these individuals experiencing life-threatening reactions. It is important to note that a number of individuals experience an array of symptoms following exposure to the suphites; thus, skin, intestinal and respiratory reactions may occur simultaneously, and in various combinations and severities.

In addition to triggering episodic and acute symptoms, sulphite additives clearly play a role in the chronic symptoms experienced by some individuals. Sensitive individuals who regularly use cosmetics or topical medications containing sulphites have been reported to exhibit chronic skin symptoms, especially on the hands, perineum and face. Similarly, occupational exposures to the sulphites have been reported to cause persistent skin symptoms. Although the possibility that exposure to sulphites may contribute to chronic asthma has not been widely explored, it is possible that unrecognized regular exposure to the sulphite additives may contribute to the chronic asthma symptoms experienced by some sensitive individuals.

In conclusion, sensitivity to the sulphite additives is a very real problem that significantly

affects the health of many individuals, particularly asthmatics. The possibility of sulphite sensitivity should be considered when individuals demonstrate adverse reactions to a range of exposures, with no obvious pattern, particularly when these individuals experience a worsening of asthma symptoms following the consumption of foods such as dried fruits and wines, or adverse skin reactions following the use of cosmetics or medicated creams.

## Acknowledgements

The authors would like to thank Dr. Vishal Madan for his input regarding skin sensitivities to the sulphite additives.

## References

1. Bush RK, Taylor SL, Busse W. A critical evaluation of clinical trials in reactions to sulfites. J Allergy Clin Immunol 1986; 78:191-202.

2. Roberts A, McWeeny D. The use of sulfur dioxide in the food industry. A review. J Fd Technol 1972; 7:221-38.

3. Taylor SL, Higley NA, Bush RK. Sulfites in foods: uses, analytical methods, residues, fate, exposure assessment, metabolism, toxicity, and hypersensitivity. Adv Food Res 1986; 30:1-76.

4. Challen RG. Sulphite content of Australian pharmaceutical products. Med J Aust 1990; 152:196-98.

5. Kochen J. Sulfur dioxide, a respiratory tract irritant, even if ingested. Pediatrics 1973; 52:145-46.

6. Prenner BM, Stevens JJ. Anaphylaxis after ingestion of sodium bisulfite. Ann Allergy 1976; 37:180-82.

7. Gunnison AF, Jacobsen DW. Sulfite hypersensitivity. A critical review. CRC Crit Rev Toxicol 1987; 17:185-214.

8. Lester MR. Sulfite sensitivity: significance in human health. J Am Coll Nutr 1995; 14:229-32.

9. Jamieson DM, Guill MF, Wray BB, May JR. Metabisulfite sensitivity: case report and literature review. Ann Allergy 1985; 54:115-21.

10. Grotheer G, Marshall M, Simonne A. Sulfites: Separating Fact from Fiction: Institute of Food and Agricultural Sciences, University of Florida, 2005.

11. Environmental Working Group. Skin Deep Cosmetic Safety Database. Available at http://www.ewg.org/skindeep, accessed 29 November 2011.

12. Smolinske SC. Review of parenteral sulfite reactions. J Toxicol Clin Toxicol 1992; 30:597-606.

13. Apetato M, Marques MS. Contact dermatitis caused by sodium metabisulphite. Contact Dermatitis 1986; 14:194.

14. Jacobs MC, Rycroft RJ. Contact dermatitis and asthma from sodium metabisulfite in a photographic technician. Contact Dermatitis 1995; 33:65-66.

15. Freedman BJ. Asthma induced by sulphur dioxide, benzoate and tartrazine contained in orange drinks. Clin Allergy 1977; 7:407-15.

16. Boushey HA. Bronchial hyperreactivity to sulfur dioxide: physiologic and political implications. J Allergy Clin Immunol 1982; 69:335-38.

17. Nowak D, Jorres R, Berger J, Claussen M, Magnussen H. Airway responsiveness to sulfur dioxide in an adult population sample. Am J Respir Crit Care Med 1997; 156:1151-56.

18. Bush RK, Zoratti E, Taylor SL. Diagnosis of sulfite and aspirin sensitivity. Clin Rev Allergy 1990; 8:159-78.

19. Stevenson DD, Simon RA. Sulfites and asthma. J Allergy Clin Immunol 1984; 74:469-72.

20. Schwartz HJ, Chester EH. Bronchospastic responses to aerosolized metabisulfite in asthmatic subjects: potential mechanisms and clinical implications. J Allergy Clin Immunol 1984; 74:511-13.

21. Koepke JW, Christopher KL, Chai H, Selner JC. Dose-dependent bronchospasm from sulfites in isoetharine. JAMA 1984; 251:2982-83.

22. Habenicht HA, Preuss L, Lovell RG. Sensitivity to ingested metabisulfites: cause of bronchospasm and urticaria. Immunol Allergy Practice 1983; 5:243.

23. Huang AS, Fraser WM. Are sulfite additives really safe? N Engl J Med 1984; 311:542.

24. Twarog FJ, Leung DY. Anaphylaxis to a component of isoetharine (sodium bisulfite). JAMA 1982; 248:2030-31.

25. Schwartz HJ. Sensitivity to ingested metabisulfite: variations in clinical presentation. J Allergy Clin Immunol 1983; 71:487-89.

26. Yang WH, Purchase EC. Adverse reactions to sulfites. CMAJ 1985; 133:865-7.

27. Food and Drug Administration. New sulfite regulations. FDA Drug Bull 1986; 16:17-18.

28. Wuthrich B, Huwyler T. [Asthma due to disulfites]. Schweiz Med Wochenschr 1989; 119:1177-84.

29. Tsevat J, Gross GN, Dowling GP. Fatal asthma after ingestion of sulfite-containing wine. Ann Intern Med 1987; 107:263.

30. Nagy SM, Teuber SS, Loscutoff SM, Murphy PJ. Clustered outbreak of adverse reactions to a salsa containing high levels of sulfites. J Food Prot 1995; 58:95-97.

31. Baker GJ, Collett P, Allen DH. Bronchospasm induced by metabisulphite-containing foods and drugs. Med J Aust 1981; 2:614-17.

32. Koepke JW, Selner JC, Dunhill AL. Presence of sulfur dioxide in commonly used bronchodilator solutions. J Allergy Clin Immunol 1983; 72:504-8.

33. Sher TH, Schwartz HJ. Bisulfite sensitivity manifesting as an allergic reaction to aerosol therapy. Ann Allergy 1985; 54:224-26.

34. Riggs BS, Harchelroad FP Jr, Poole C. Allergic reaction to sulfiting agents. Ann Emerg Med 1986; 15:77-79.

35. Asmus MJ, Sherman J, Hendeles L. Bronchoconstrictor additives in bronchodilator solutions. J Allergy Clin Immunol 1999; 104:S53-60.

36. Langevin PB. Propofol containing sulfite-potential for injury. Chest 1999; 116:1140-41.

37. Roth JV, Shields A. A dilemma: How does one treat anaphylaxis in the sulfite allergic patient since epinephrine contains sodium metabisulfite? Anesth Analg 2004; 98: 1499.

38. Australasian Society of Clinical Immunology and Allergy. Sulfite allergy. Available from: http://www.allergy.org.au/content/view/128/1. [Accessed 15 December 2011]

39. Valero AL, Bescos M, Amat P, Malet A. [Bronchial asthma caused by occupational sulfite exposure]. Allergol Immunopathol (Madr) 1993; 21:221-24.

40. Merget R, Korn M. Metabisulphite-induced occupational asthma in a radiographer. Eur Respir J 2005; 25:386-88.

41. Malo JL, Cartier A, Desjardins A. Occupational asthma caused by dry metabisulphite. Thorax 1995; 50:585-86.

42. Agard C, Nicolet-Akhavan F, Bouillard J, Sandron D. [Occupational asthma to metabisulfites. Three cases]. Rev Mal Respir 1998; 15:537-40.

43. Atkinson DA, Sim TC, Grant JA. Sodium metabisulfite and $SO_2$ release: an under-recognized hazard among shrimp fishermen. Ann Allergy 1993; 71:563-66.

44. Andersson E, Nilsson T, Persson B, Wingren G, Toren K. Mortality from asthma and cancer among sulfite mill workers. Scand J Work Environ Health 1998; 24:12-17.

45. Andersson E, Knutsson A, Hagberg S, Nilsson T, Karlsson B, Alfredsson L, Toren K. Incidence of asthma among workers exposed to sulphur dioxide and other irritant gases. Eur Respir J 2006; 27:720-25.

46. Stevenson DD, Simon RA. Sensitivity to ingested metabisulfites in asthmatic subjects. J Allergy Clin Immunol 1981; 68:26-32.

47. McClellan MD, Wanger JS, Cherniack RM. Attenuation of the metabisulfite-induced bronchoconstrictive response by pretreatment with cromolyn. Chest 1990; 97:826-30.

48. Wright W, Zhang YG, Salome CM, Woolcock AJ. Effect of inhaled preservatives on asthmatic subjects. I. Sodium metabisulfite. Am Rev Respir Dis 1990; 141:1400-4.

49. Prieto L, Juyol M, Paricio A, Martinez MA, Palop J, Castro J. Oral challenge test with sodium metabisulfite in steroid-dependent asthmatic patients. Allergol Immunopathol (Madr) 1988; 16:393-96.

50. Nolan AL. The sulfite controversy. Food Eng 1983; 84-85:89-90.

51. Simon RA. Sulfite challenge for the diagnosis of sensitivity. Allergy Proc 1989; 10:357-62.

52. Towns SJ, Mellis CM. Role of acetyl salicylic acid and sodium metabisulfite in chronic childhood asthma. Pediatrics 1984; 73:631-37.

53. Steinman HA, Le Roux M, Potter PC. Sulphur dioxide sensitivity in South African asthmatic children. S Afr Med J 1993; 83:387-90.

54. Sanz J, Martorell A, Torro I, Carlos Cerda J, Alvarez V. Intolerance to sodium metabisulfite in

children with steroid-dependent asthma. J Investig Allergol Clin Immunol 1992; 2:36-38.

55. Petersen CS, Menne T. Consecutive patch testing with sodium sulfite in eczema patients. Contact Dermatitis 1992; 27:344-45.

56. Vena GA, Foti C, Angelini G. Sulfite contact allergy. Contact Dermatitis 1994; 31:172-75.

57. Madan V, Walker SL, Beck MH. Sodium metabisulfite allergy is common but is it relevant? Contact Dermatitis 2007; 57:173-76.

58. Malik MM, Hegarty MA, Bourke JF. Sodium metabisulfite--a marker for cosmetic allergy? Contact Dermatitis 2007; 56:241-42.

59. Schorr WF. Multiple injuries from permanents. Presented at Cosmetic Symposium, American Academy of Dermatology. 3 December 1983, Chicago, IL.

60. Sanchez-Perez J, Abajo P, Cordoba S, Garcia-Diez A. Allergic contact dermatitis from sodium metabisulfite in an antihemorrhoidal cream. Contact Dermatitis 2000; 42:176-77.

61. Nagayama H, Hatamochi A, Shinkai H. A case of contact dermatitis due to sodium bisulfite in an ophthalmic solution. J Dermatol 1997; 24:675-77.

62. Nater JP. Allergic contact dermatitis caused by potassium metabisulfite. Dermatologica 1968; 136:477-78.

63. Camarasa JG, Barnadas M. Occupational dermatosis by vitamin K3 sodium bisulphite. Contact Dermatitis 1982; 8:268.

64. Epstein E. Sodium bisulfite. Contact Dematitis Newsletter 1970; 7:155.

65. Lee A, Nixon R. Contact dermatitis from sodium metabisulfite in a baker. Contact Dermatitis 2001; 44:127-28.

66. Dooms-Goossens A, de Alam AG, Degreef H, Kochuyt A. Local anesthetic intolerance due to metabisulfite. Contact Dermatitis 1989; 20:124-26.

67. Field PI, McClean M, Simmul R, Berend N. Comparison of sulphur dioxide and metabisulphite airway reactivity in subjects with asthma. Thorax 1994; 49:250-56.

68. Anibarro B, Caballero T, Garcia-Ara C, Diaz-Pena JM, Ojeda JA. Asthma with sulfite intolerance in children: a blocking study with cyanocobalamin. J Allergy Clin Immunol 1992; 90:103-9.

69. Dixon CM, Ind PW. Inhaled sodium metabisulphite induced bronchoconstriction: inhibition by nedocromil sodium and sodium cromoglycate. Br J Clin Pharmacol 1990; 30:371-76.

70. Wang M, Wisniewski A, Pavord I, Knox A, Tattersfield A. Comparison of three inhaled non-steroidal anti-inflammatory drugs on the airway response to sodium metabisulphite and adenosine 5'-monophosphate challenge in asthma. Thorax 1996; 51:799-804.

71. Lazarus SC, Wong HH, Watts MJ, Boushey HA, Lavins BJ, Minkwitz MC. The leukotriene receptor antagonist zafirlukast inhibits sulfur dioxide-induced bronchoconstriction in patients with asthma. Am J Respir Crit Care Med 1997; 156:1725-30.

72. Gong H, Jr., Linn WS, Terrell SL, Anderson KR, Clark KW. Anti-inflammatory and lung function effects of montelukast in asthmatic volunteers exposed to sulfur dioxide. Chest 2001; 119:402-8.