Sulfites: Allergen of the Year 2024

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Abstract: **Sodium disulfite, also known as sodium metabisulfite or sodium pyrosulfite, is an inorganic compound, which may cause allergic contact dermatitis. Sulfites act as antioxidants and preservatives; common sources include food/beverages, pharmaceuticals, and personal care products. Importantly, sulfites are not included in most screening patch test series and thus may be missed as a relevant contact allergen. The American Contact Dermatitis Society chose sulfites as the Allergen of the Year for 2024 to raise awareness about this significant allergen.**

INTRODUCTION

Overview of Sulfites

Sodium disulfite (SD), commonly referred to as sodium metabisulfite or sodium pyrosulfite (CAS 7681-57-4), belongs to a group of "sulfiting agents," compounds that contain the sulfite ion $SO3^{2-}$ (Table 1).[1] Importantly, sulfites are completely different from sulfates; these 2 chemical categories do not cross-react. Sulfates contain the sulfate ion ($SO4^{2-}$) and are used in a wide range of applications, including industrial processes, mineral formations, and personal care products (eg, sodium lauryl sulfate). Sulfites occur naturally in water, minerals, soil, rocks, plants, and many foods, especially those involving fermentation.

Sulfites are commonly added to commercial formulations as preservatives (substances that prevent microbial growth) and/or antioxidants (compounds that inhibit oxidation and free radicals, thus extending product shelf life). Sulfites are utilized in multiple industries including food,[2] beverages, drug, cosmetic, and occupational settings.[3] They can also be found in personal skin care products and medications, especially topical antifungals, topical steroids, local anesthetics, and prescription eye drops.[4,5] Common ingestible sources include wine and dried fruits.[4]

The recommended patch test vehicle for sulfites is petrolatum because sulfites dissociate into a complex chemical equilibrium in aqueous solutions, leading to false positive/irritant reactions.[6–8] Ralph et al tested a cohort of 380 patients to 3 strengths of sodium metabisulfite: 0.01%, 0.1%, and 1.0% in petrolatum and found that 1.0% was optimal.[9] Commercial patch test preparations are available from Chemotechnique Diagnostics (sodium metabisulfite 1% pet) and AllergEAZE (sodium disulfite 1% pet).

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PREVALENCE

The first report of contact dermatitis to sulfites was in 1968 and described a 40-year-old pharmaceutical worker with hand dermatitis due to occupational potassium metabisulfite exposure.[10] Many cases followed, as recently summarized in a 2021 study.[11] Since publication of that review, there have been 3 additional cases of contact allergy to sulfites.[12–14] Two described hand dermatitis after occupational exposures;[12,13] one involved decanting lidocaine preserved with sulfites in an operating room nurse and the other involved handling shredded coconut preserved with sulfites in a commercial baker.[12,13] The third case involved dermatitis of the lower back, which subsequently generalized in a patient after lumbar subcutaneous injection with Xylocaine, which was preserved with sulfites.[14]

Because sulfites are not included on most screening patch test series, contact allergy to sulfites is likely under-recognized and under-reported. A recent review of 9 European studies involving a total of 37,909 patients undergoing routine testing to sodium disulfite found a pooled prevalence of 3.1% (range 1.4–7.0%).[11] Since that review, other large European studies have reported prevalences of 1.9% (Spain, $N=1850$[15] and Canada, $N=2323$[16]) and 3.8% (Central Europe, $N=6819$)[17] (Table 2). These figures are similar to North American Contact Dermatitis Group (NACDG) findings of 2.7% ($N=4885$, 2017–2018)[11] and 3.3% ($N=4115$, 2019–2020) in routinely patch tested patients.[18] Prevalence is higher in selected groups of patients;[11] a recent Portuguese study of 65 patients with suspected allergic contact dermatitis (ACD) to topical ophthalmic medications found 10.8% positivity.[15–17,19]

CLINICAL CHARACTERISTICS

Contact Dermatitis

Similar to other contact allergens, clinical presentation correlates with exposure. Eczematous dermatitis of the lips is common in patients with ingested food sources of sulfites. Well-defined

TABLE 1. Sulfiting Agents That May Cross-React with Sodium Disulfite

• Ammonium bisulfite	• Sodium bisulfite
• Ammonium sulfite	• Sodium hydrosulfite
• MEA-sulfite	• Sodium metabisulfite
• Potassium metabisulfite	• Sodium sulfite
• Potassium sulfite	• Sulfites

Allergic Contact Dermatitis Society Contact Allergen Management Program.[1] MEA-sulfite, monoethanolamine sulfite.

erythema has also been observed.[9] A recent study by NACDG found that 28.8% of patch test positive sulfite patients presented with facial dermatitis.[11] The second most common anatomical site of dermatitis in this cohort was hands (20.5%) followed by scattered/generalized distribution (13.6%).[11] These findings are consistent with other studies also documenting the most common anatomical locations of dermatitis in patients with sulfite sensitivity were face[9,11,20,21] and hands.[7,22] These anatomic locations are to be expected, given that frequent sources of sulfites include personal care items, food/beverages, and occupational materials.[11] Cases of systemic contact dermatitis to sulfites have also been documented as a result of oral, rectal, and parental exposure.[23–27] Interestingly, 6 of 124 patients in a European study reported systemic symptoms.[6]

There is no clear association of SD sensitivity with sex. Some studies found a male predominance,[7,8,11,20] whereas other studies reported association with female sex.[9,21,22] However, almost all prior studies in routinely tested dermatitis patients reported an average or median age of 40 years or higher.[7–9,11,20,21] The NACDG documented only 1 case of sulfite induced dermatitis in a 11-year-old female out of 234 pediatric patients tested to SD.[11]

Noncutaneous Adverse Reactions

In addition to allergic contact dermatitis, sulfite exposure may cause Type I hypersensitivity reactions (anaphylaxis, urticaria, gastrointestinal symptoms, and bronchoconstriction), and non-immunologic adverse reactions.[3,11] In the 1970s, several reports of respiratory irritation[28] and anaphylaxis[29] were published. These were followed by cases of sulfite-induced asthma,[30–33] abdominal pain, and diarrhea.[34] By 1985, 250 cases of sulfite-related adverse reactions in the United States were documented, which involved nausea, abdominal pain, diarrhea, urticaria, angioedema, asthma, anaphylactic shock, seizures, and death.[35] These severe reactions to sulfites prompted the US Food and Drug Administration (FDA) to ban sulfite use on fruits and vegetables served raw or presented as fresh to the public[36] and implement regulations regarding declaring sulfites on labels.[37]

CLINICAL RELEVANCE

Experts disagree on the clinical relevance of many patch test reactions to sulfites.[7,8,20,22] It is often difficult to determine the clinical relevance of a positive patch test reaction to sulfites as this requires confirming its presence in exposure sources.[8,9,11] Adding to the complexity is the ongoing discovery of new sources of sulfites in products (eg, gloves). Even with sufficient time, energy, and diligence, clinicians (and patients) are often frustrated. Clinical relevance was found in only 12/50 (24.0%) of patients in Italy[8] and 2/51 (3.9%) patients in Sweden[7] in early studies of routinely tested patients. However, recent studies suggest that sulfites may be more clinically relevant than previously acknowledged.[6,9,11,20]

A central European study[20] reported relevance in 128/321 (39.9%) of patients with positive patch test reactions and a North American study documented current relevance in 86/132 (65.2%).[11] A Belgian study found clinical relevance in 80/124 (64.5%) of cases; the majority of these were secondary to the use of topical antifungal or other medical creams, followed by "rinse-off" and "leave-on" cosmetics, respectively.[6] Smaller studies reported clinical relevance frequencies of 50% (4/8).[38] Ralph et al reported that 71.4% (10/14) sulfite-allergic patients cleared with sulfite avoidance at a 3-month follow-up.

Consumer Exposures

Nonoccupational sources of sulfites include various topical medicaments, including antifungals,[39–42] corticosteroids,[43] ophthalmic solutions,[44,45] hemorrhoidal preparations,[46] local anesthetics,[39,47–49] topical antibiotic preparations,[50] and urinary catheterization gels[51]

TABLE 2. Recent Reports of Routine Patch Testing to Sodium Disulfite

First Author, Year Published, Location	Time Period of Testing	Patch Test Concentration	Total No. of Patients Tested	No. of Positive Reactions (%)
Morin (2020),[16] Canada	2005–2019	2% Pet	2323 Patients tested to a customized AVC series which included sodium metabisulfite.	45 (1.9)
Hernández-Fernández (2021),[15] Spain	2019–2020	1% Pet	1850 Patients tested to a series of emerging allergens to determine potential inclusion into the Spanish standard series.	35 (1.9)
Uter (2022),[17] 12 European Countries (ESSCA)	2019–2020	1% Pet	6819 Patients tested to audit allergens that included sodium metabisulfite.	256 (3.8)

Warshaw et al[11] for details of 9 other studies.
AVC, antimicrobials, vehicles, and cosmetics; ESSCA, European Surveillance System on Contact Allergies; pet, petrolatum.

TABLE 3. Nonoccupational and Occupational Sources of Sulfites

Nonoccupational	Occupational
• Personal care products Shampoo Hair colors and bleaches Hair waving/straightening agents Hairspray Skin lighteners Tanning lotions Antiaging products Facial cleansers Body washes Bath oils/salts Eye creams Make-up (foundation, blush, bronzers, highlighters) Sunscreens Perfume Deodorants • Swimming pool water • Medications Topical antifungals Topical corticosteroids Local anesthetics Ophthalmics Nasal solutions Intravenous solutions • Gloves	• Food and drink (preservation, sterilization, and sugar refining) • Brewing, wine making (sterilization during fermentation) • Photography (developers and fixers) • Textile industry (color stripper) • Leather (tanning, solubilizing agent for tannins, reducing chrome liquors) • Mineral extraction (ore flotation aid) • Effluent treatment (to reduce chromium salts) • Chemical manufacture (sulfosuccinates and sodium formaldehyde bisulfite) • Rubber manufacture (latex anticoagulant) • Health care (contact with medications and gloves) Parenteral solutions (prevent oxidation of adrenaline) • Wood, pulp, and paper industries (soften wood material) • Glass industry (facilitates melting process) • Glove manufacturing (anticoagulant and preservative) • Personal care product production (preservative) • Pharmaceutical manufacturing (preservative)

Adapted from Ralph et al[9] and García-Gavín et al.[6]

(Table 3).[6,9] In an evaluation of ingredient databases, certain product categories were found more likely to contain sulfites. These included hair dyes, bleaching creams, vaginal preparations, prescription topical antifungal and antibacterial agents, and injectable medications.[39] In an ingredient analysis of 264 prescription ophthalmic medications, sodium metabisulfite was found in 3.8% of products (10/264).[5]

In a study of 132 North American patients positive to SD, personal care products and topical medicaments were the most common sources.[11] Within the personal care product category, hair dyes accounted for 44.0% (11/25) of exposures. In a central European study, sources of sulfite contact dermatitis were primarily linked to topical medications, creams, cosmetics, and sunscreens.[20] A search of the American Contact Dermatitis Society's Contact Allergen Management Program database found that sulfites were most frequently declared in hair dye kits (including developer/color treatments; 160/176, 90.1%) and prescription depigmenting agents (9/10, 90.0%).[11] Sulfites in products other than personal care products are likely under-recognized and under-reported because ingredient lists are not readily available.

Occupational Sources

Sulfites are used in the following occupations and industries: brewing, wine making, photographic chemicals, leather manufacturing, textile industry, mineral extraction, pulp/paper industry, chemical manufacturing, rubber production, food preparation, health care, pharmaceutical/personal product production, and water/sewage treatment (Table 3).[3,9,22] Case reports describe allergic contact dermatitis to SD in hairdressers,[52] food and beverage industry workers,[53–56] and photographers.[6,7,9,57] Additional sources of sulfites in occupational and nonoccupational settings are summarized elsewhere.[3,9,22]

Gloves

Sulfites are used in rubber manufacturing, including gloves, for their anticoagulant and preservative properties.[3,58] Recently, Dendooven et al[58] performed semi-quantitative analysis of 35 gloves, including natural rubber latex ($n=6$), nitrile ($n=24$), and polyvinyl chloride (PVC) ($n=5$) gloves. Sulfites were detected in 5 of the 6 natural rubber latex gloves (range 25 to $<100\ L^{-1}$) and 23 of the 24 nitrile gloves (range 10 to $<100\ L^{-1}$). Importantly, sulfites were not detected in any of the 5 PVC gloves. This underscores the potential relevance of glove sources in previously unexplained hand dermatitis in sulfite-sensitive individuals. PVC gloves appear to be a safe alternative for these patients.

Ingestible Sources

Sulfites can naturally occur in foods and beverages as a byproduct of fermentation, or they can be added during processing to stop spoilage and discoloration.[11] When listed on food and beverage labels, sulfites may be denoted as E221–E227 (Table 4).[6,8] Common sources of sulfites in foods and beverages include apricots,

TABLE 4. Commercially Available Sulfites Used in Food and Cosmetics

Compound	Chemical Formula	CAS Number	E Number	Food	Cosmetics
Sodium sulfite	Na_2SO_3	7757-83-7	E221	Yes	Yes
Sodium bisulfite	$NaHSO_3$	7631-90-5	E222	Yes	Yes
Sodium metabisulfite	$Na_2S_2O_5$	7681-57-4	E223	Yes	Yes
Potassium sulfite	K_2SO_3	10117-38-1	E225	Yes	Yes
Potassium bisulfite	$KHSO_3$	7773-03-7	E228	Yes	Yes
Potassium metabisulfite	$K_2S_2O_5$	16731-55-8	E224	Yes	Yes
Calcium sulfite	$CaSO_3$	10257-55-3	E226	Yes	No
Calcium bisulfite	$Ca(HSO_3)_2$	13780-03-5	E227	Yes	No
Ammonium bisulfite	NH_4HSO_3	10192-30-0	—	No	Yes
Ammonium sulfite	$(NH_4)_2SO_3$	7026-44-7	—	No	Yes

Adapted from García-Gavín et al.[6]

avocados, baked products, beer, beet sugar, bottled soft drinks and fruit juice, canned seafood, canned soups, cider, corn sweeteners, dried fruits, food starches, fruit bars, gelatin, grape juice, jams and jellies, lemon and lime juice, maraschino cherries, mushrooms, pickled onions, pickles, potatoes, raisins, salads, sauerkraut (especially juice), sausage meats, shrimp (uncooked), vinegar, and wine.[3,9,22]

High dietary sulfite consumption has been linked to systemic contact dermatitis.[23] Concerns revolving around the addition of sulfites to foods arose in the United States after reports of severe cases of skin and respiratory sensitivities.[59] As noted previously, the 1986 FDA regulation of sulfites banned its use in fresh fruits and vegetables,[59] and packaged foods containing 10 ppm or more of sulfites are required to disclose this on labels.[11] However, food service establishments are exempt from this rule and are not required to inform customers whether sulfites are present in food/beverages.[60] In addition, food available for immediate consumption and delicatessen-type food, bakery goods, and confections distributed directly to customers from the preparation site are exempt from labeling.[11] Thus, for patients with signs and symptoms suggestive of systemic allergy/intolerance, label review is critical but not always available; Table 5 provides a general overview of sulfite levels in foods and beverages.[61]

Sulfites in wine deserve special consideration. The process of sulfurization has been used since the time of the ancient Romans to prevent wine from discoloring and to inhibit the growth of bacteria, yeasts, and molds.[62] Although small quantities of sulfites may naturally form during the fermentation of wine,[63] most

TABLE 5. Sulfite Content of Food and Beverages

High (>100 ppm)	Moderate to High (50–99.9 ppm)	Low to Moderate (10.1–49.9 ppm)	Low (<10 ppm)
• Dried fruit (excluding dark raisins and prunes) • Bottled lemon juice (nonfrozen) • Bottled lime juice (nonfrozen) • Wine • Molasses • Sauerkraut juice • Grape juice (white, white sparkling, pink sparkling, and red sparkling) • Pickled cocktail onions	• Dried potatoes • Wine vinegars • Gravies/sauces • Fruit toppings • Maraschino cherries	• Pectin • Shrimp (fresh) • Corn syrup • Sauerkraut (without juice) • Pickled peppers • Pickles/relishes • Corn starch • Hominy • Frozen potatoes • Maple syrup • Imported jam/jelly • Fresh mushrooms • Imported sausage/meat • Cordial alcohols • Dehydrated vegetables • Corn bread/muffin mix • Canned/jarred clams • Clam chowder • Avocado dip/guacamole • Imported fruit juices • Imported soft drinks • Cider • Cider vinegar	• Crackers • Malt vinegar • Sugar (especially beet sugar) • Gelatin • Canned potatoes • Coconut • Fresh fruit salad • Dry soup mix • Pizza dough (frozen) • Pie dough (frozen) • Grapes • Domestic jams/jellies • Soft drinks • Instant tea • Beer cookies

Metcalfe et al [61]

TABLE 6. Consumer Marketed Sulfite Removing Devices

Device	Cost	Instructions	Studies on Sulfite Reduction	Product Claims
PureWine® The Phoenix®	$69.99 for 1 pouring device and 3 BioPod™ wine purifying cartridges.	Insert BioPod™ cartridge into The Phoenix Base, insert The Phoenix firmly into wine bottle and twist. Tilt bottle vertically to pour. Wait 3–5 seconds for pour.	None found	Removes histamines and sulfites from wine.
PureWine The Wave®	$14.99 for 1 The Wave that treats a 750 mL bottle of wine.	Whole-bottle wine purification. Place The Wave on the mouth of the wine bottle. Wine is filtered as poured through the filter housing.	None found	Removes histamines and sulfites from wine.
PureWine The Wand ™	$24.99 for 8 single use wands, each treats 1 glass of wine.	Place wand in a 6 oz glass of wine for at least 1 minute with intermittent gentle stirring.	None found	Removes histamines and sulfites from wine. After 8 minutes, up to 95% of the histamines and sulfites may be removed.
Drop It® Original Wine Drops	$13.99 for 1 bottle of drops which will treat up to 55 glasses or 9 bottles of wine.	Add up to 4 drops per 5–6 oz glass of wine, swirl for 20 seconds.	None found	Reduces tannins and sulfites in wine.
Üllo Original wine purifier	$79.99 for wine purifier and 4 Selective Sulfite™ full bottle filters. $24.99 for 6 replacement Selective Sulfite™ full bottle filters.	Insert filter into wine purifier reservoir. Place wine purifier over glass. Pour wine slowly into purifier reservoir. Whole bottle requires 2–4 minutes to filter.	None found	30–85% reduction in free sulfites in wine.

winemakers typically add 30–90 ppm of sulfites during the production process to prevent spoilage and improve aging properties.[64] An increasing consumer preference for low sulfite wines has led to new winemaking techniques termed "fermentation management," to decrease sulfite levels.[65] In the United States, wines are required to include a warning statement if they contain sulfite levels higher than 10 ppm[66]; in general, wines labeled as "organic" do not have sulfites added during the production process.[66,67]

In some individuals, a side effect of consumption of sulfites, especially in wine, is headaches.[68] We found no studies correlating noncutaneous systemic side effects (eg, headaches) and positive patch tests to sulfites. Several devices have been developed to decrease sulfite-related side effects including headaches (Table 6), although the effectiveness of these products for management of allergic contact dermatitis is unclear.

In addition to food/beverages, ingestible sources of sulfites include oral medications (eg, tablet and liquid forms of hydromorphone). In the United States, the FDA mandates that sulfites must be listed on prescription drug warning labels (21 CFR 201.22).[11]

SHOULD SULFITES BE INCLUDED ON SCREENING SERIES?

Inclusion of an allergen in a baseline screening series is advocated by some experts when the prevalence of contact allergy to the substance in routinely patch tested populations reaches a threshold of 0.5–1.0% coupled with ubiquitous use and/or high clinical relevance.[69] Based on these criteria, sulfites surpass this threshold consistently across multiple large studies and in various geographic regions. However, many baseline screening series do not include sulfites. In 2017, the NACDG added sodium metabisulfite to their screening series.[39]

After analyzing 2019–2020 patch test reactivity and clinical relevance data of multiple audit allergens in patients throughout Europe, sodium metabisulfite was recently added to the European baseline series.[17] Hernández-Fernández et al performed a prospective study of consecutive patients from the Spanish Contact Dermatitis and Skin Allergy Research Group registry who were patch tested in 2019–2020 to sodium metabisulfite and concluded this allergen should be considered for inclusion during the next revision of the Spanish standard patch test series.[15] Currently, the American Contact Dermatitis Core Series does not include sulfites. We advocate that it be included in the next update.

SUMMARY

Sulfites are under-recognized and ubiquitous allergens. Historically, clinical relevance of sulfite allergy was debated, but recent studies document >50% current relevance. This, coupled with prevalence frequency of >1% support the inclusion of sulfites in baseline screening series. We advocate for sulfite inclusion in the next ACDS Core Allergen Series. Contact dermatitis experts should be aware of this important, often missed, allergen.

REFERENCES

1. Contact Allergy Management Program (CAMP). http://www.acdscamp.org/CrossReactor_List Accessed May 27, 2023.
2. 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.
3. Vally H, Misso NLA, Madan V. Clinical effects of sulphite additives. *Clin Exp Allergy J Br Soc Allergy Clin Immunol*. 2009;39(11):1643–1651.
4. Hinton AN, Goldminz AM. Alcohol-related dermatitis: a review. *Dermat Contact Atopic Occup Drug*. 2020;31(3):185–190.
5. Shaver RL, Warshaw EM. Contact allergens in prescription topical ophthalmic medications. *Dermat Contact Atopic Occup Drug*. 2022;33(2):135–143.
6. García-Gavín J, Parente J, Goossens A. Allergic contact dermatitis caused by sodium metabisulfite: a challenging allergen: a case series and literature review. *Contact Dermatitis*. 2012;67(5):260–269.
7. Kaaman AC, Boman A, Wrangsjö K, et al. Contact allergy to sodium metabisulfite: an occupational problem. *Contact Dermatitis*. 2010;63(2):110–112.
8. Vena GA, Foti C, Angelini G. Sulfite contact allergy. *Contact Dermatitis*. 1994;31(3):172–175.
9. Ralph N, Verma S, Merry S, et al. What is the relevance of contact allergy to sodium metabisulfite and which concentration of the allergen should we use? *Dermat Contact Atopic Occup Drug*. 2015;26(4):162–165.
10. Nater JP. Allergic contact dermatitis caused by potassium metabisulfite. *Dermatologica*. 1968;136(6):477–478.
11. Warshaw EM, Buonomo M, DeKoven JG, et al. Patch testing with sodium disulfite: North American Contact Dermatitis Group experience, 2017 to 2018. *Contact Dermatitis*. 2021;85(3):285–296.
12. Ibanez MA, Levoska MA, Zheng DX, et al. Sodium metabisulfite allergic contact dermatitis from lidocaine exposure in an operating room nurse. *Dermat Contact Atopic Occup Drug*. 2021;32(6):e108–e109.
13. Hamann CR, Baker C, O'Hern K, et al. Occupational allergic contact dermatitis to sodium metabisulfite in shredded coconut. *Contact Dermatitis*. 2022;87(4):385–386.
14. Tan MG, Li HO, Pratt MD. Systemic allergic dermatitis to sodium metabisulfite in local anesthetic solution. *Contact Dermatitis*. 2022;86(2):120–121.
15. Hernández-Fernández CP, Mercader-García P, Silvestre Salvador JF, et al. Candidate allergens for Inclusion in the Spanish Standard Series based on data from the Spanish Contact Dermatitis Registry. *Actas Dermosifiliogr*. Published online May 23, 2021:S0001-7310(21)00192-7.
16. Morin CB, Sasseville D. Expanding patch testing beyond the baseline series: usefulness of customized antimicrobials, vehicles, and cosmetics series. *Dermat Contact Atopic Occup Drug*. 2020;31(6):367–372.
17. Uter W, Wilkinson SM, Aerts O, et al. European patch test results with audit allergens as candidates for inclusion in the European Baseline Series, 2019/20: Joint results of the ESSCAA and the EBSB working groups of the ESCD, and the GEIDACC. *Contact Dermatitis*. 2022;86(5):379–389.
18. DeKoven JG, Warshaw EM, Reeder MJ, et al. North American Contact Dermatitis Group Patch Test Results: 2019–2020. *Dermat Contact Atopic Occup Drug*. 2023;34(2):90–104.
19. Alves PB, Figueiredo AC, et al. A closer look at allergic contact dermatitis caused by topical ophthalmic medications. *Contact Dermatitis*. 2022;87(4):331–335.
20. Häberle M, Geier J, Mahler V. Contact allergy to sulfites: clinical and occupational relevance—new data from the German Contact Dermatitis Research Group and the Information Network of Departments of Dermatology (IVDK). *J Dtsch Dermatol Ges*. 2016;14(9):938–941.
21. Pink A, Banerjee P, White IR. Contact allergy to sodium metabisulphite: a redherring? *Br J Dermatol*. 2011;165(1):71.
22. Madan V, Walker SL, Beck MH. Sodium metabisulfite allergy is common but is it relevant? *Contact Dermatitis*. 2007;57(3):173–176.
23. Cussans A, McFadden J, Ostlere L. Systemic sodium metabisulfite allergy. *Contact Dermatitis*. 2015;73(5):316–317.
24. Borges AS, Valejo Coelho MM, Fernandes C, et al. Systemic allergic dermatitis caused by sodium metabisulfite in rectal enemas. *Contact Dermatitis*. 2018;78(6):429–430.
25. Guha-Niyogi B, Sabroe R, Holden C. An unusual case of a systemic delayed hypersensitivity reaction to sodium metabisulfite. *Contact Dermatitis*. 2018;79(4):246–247.
26. Borgemeester RWK, van Laar T, Schuttelaar MLA. Cutaneous adverse drug reaction after apomorphine infusion, possibly caused by a systemic type IV hypersensitivity reaction to sodium metabisulfite: report of 2 cases. *Contact Dermatitis*. 2018;79(5):316–318.
27. Honda T, Kitoh A, Miyachi Y, et al. Drug eruption following high-calorie infusion: a possible systemic type IV allergic reaction to sulphites. *Acta Derm Venereol*. 2015;95(7):854–855.
28. Kochen J. Sulfur dioxide, a respiratory tract irritant, even if ingested. *Pediatrics*. 1973;52(1):145–146.
29. Prenner BM, Stevens JJ. Anaphylaxis after ingestion of sodium bisulfite. *Ann Allergy*. 1976;37(3):180–182.
30. Freedman BJ. Asthma induced by sulphur dioxide, benzoate and tartrazine contained in orange drinks. *Clin Allergy*. 1977;7(5):407–415.
31. Stevenson DD, Simon RA. Sulfites and asthma. *J Allergy Clin Immunol*. 1984;74(4 Pt 1):469–472.
32. Schwartz HJ, Chester EH. Bronchospastic responses to aerosolized metabisulfite in asthmatic subjects: potential mechanisms and clinical implications. *J Allergy Clin Immunol*. 1984;74(4 Pt 1):511–513.
33. Koepke JW, Christopher KL, Chai H, Selner JC. Dose-dependent bronchospasm from sulfites in isoetharine. *JAMA*. 1984;251(22):2982–2983.
34. Huang AS, Fraser WM. Are sulfite additives really safe? *N Engl J Med*. 1984;311(8):542.
35. Yang WH, Purchase EC. Adverse reactions to sulfites. *Can Med Assoc J*. 1985;133(9):865–867, 880.
36. Vally H, Misso NL. Adverse reactions to the sulphite additives. *Gastroenterol Hepatol Bed Bench*. 2012;5(1):16–23.
37. New Sulfite Regulations. *FDA Drug Bull*. 1986;16(2):17–18.
38. Malik MM, Hegarty MA, Bourke JF. Sodium metabisulfite—a marker for cosmetic allergy? *Contact Dermatitis*. 2007;56(4):241–242.
39. Boyd AH, Warshaw EM. Sulfites: no longer a zebra? *Dermat Contact Atopic Occup Drug*. 2017;28(6):364–366.
40. Raison-Peyron N, Roulet A, Dereure O. Occupational allergic contact dermatitis caused by sulfite in a seafood section worker of a supermarket. *Contact Dermatitis*. 2019;80(6):412–414.
41. Garcia-Bravo B, Mazuecos J, Rodriguez-Pichardo A, et al. Hypersensitivity to ketoconazole preparations: study of 4 cases. *Contact Dermatitis*. 1989;21(5):346–348.
42. Lodi A, Chiarelli G, Mancini LL, et al. Contact allergy to sodium sulfite contained in an antifungal preparation. *Contact Dermatitis*. 1993;29(2):97.
43. Heshmati S, Maibach HI. Active sensitization to sodium metabisulfite in hydrocortisone cream. *Contact Dermatitis*. 1999;41(3):166–167.
44. Seitz CS, Bröcker EB, Trautmann A. Eyelid dermatitis due to sodium metabisulfite. *Contact Dermatitis*. 2006;55(4):249–250.
45. Nagayama H, Hatamochi A, Shinkai H. A case of contact dermatitis due to sodium bisulfite in an ophthalmic solution. *J Dermatol*. 1997;24(10):675–677.
46. Sánchez-Pérez J, Abajo P, Córdoba S, et al. Allergic contact dermatitis from sodium metabisulfite in an antihemorrhoidal cream. *Contact Dermatitis*. 2000;42(3):176–177.
47. Oliphant T, Mitra A, Wilkinson M. Contact allergy to sodium sulfite and its relationship to sodium metabisulfite. *Contact Dermatitis*. 2012;66(3):128–130.
48. Dooms-Goossens A, de Alam AG, Degreef H, et al. Local anesthetic intolerance due to metabisulfite. *Contact Dermatitis*. 1989;20(2):124–126.
49. Riemersma WA, Schuttelaar MLA, Coenraads PJ. Type IV hypersensitivity to sodium metabisulfite in local anaesthetic. *Contact Dermatitis*. 2004;51(3):148.
50. Milpied B, van Wassenhove L, Larousse C, et al. Contact dermatitis from rifamycin. *Contact Dermatitis*. 1986;14(4):252–253.

51. Grosch E, Mahler V. Allergic contact dermatitis caused by a catheter system containing sodium metabisulfite. *Contact Dermatitis*. 2017;76(3): 186–187.
52. Aalto-Korte K, Suuronen K, Alanko K. Sodium metabisulfite—a contact allergen? *Contact Dermatitis*. 2009;60(2):115–117.
53. Epstein E. Sodium bisulfite. *Contact Dermat Newslett*. 1970;7:155.
54. Apetato M, Marques MS. Contact dermatitis caused by sodium metabisulphite. *Contact Dermatitis*. 1986;14(3):194.
55. Lee A, Nixon R. Contact dermatitis from sodium metabisulfite in a baker. *Contact Dermatitis*. 2001;44(2):127–128.
56. Sasseville D, El-Helou T. Occupational allergic contact dermatitis from sodium metabisulfite. *Contact Dermatitis*. 2009;61(4):244–245.
57. Jacobs MC, Rycroft RJ. Contact dermatitis and asthma from sodium metabisulfite in a photographic technician. *Contact Dermatitis*. 1995; 33(1):65–66.
58. Dendooven E, Darrigade AS, Foubert K, et al. The presence of sulfites in "natural rubber latex" and "synthetic" rubber gloves: an experimental pilot study. *Br J Dermatol*. 2020;182(4):1054–1055.
59. D'Amore T, Di Taranto A, Berardi G, et al. Sulfites in meat: Occurrence, activity, toxicity, regulation, and detection. A comprehensive review. *Compr Rev Food Sci Food Saf*. 2020;19(5):2701–2720.
60. Papazian R. Sulfites: safe for most, dangerous for some. *FDA Consum USA*. 1996;30(10):10–14.
61. Metcalfe D, Sampson H, Simon R, et al. *Food Allergy: Adverse Reactions to Foods and Food Additives*. Chichester, West Sussex: John Wiley & Sons; 2014.
62. Wüthrich B. Allergic and intolerance reactions to wine. *Allergol Sel*. 2018; 2(1):80–88.
63. Liu C, Chen R, Su YC. Bactericidal effects of wine on Vibrio parahaemolyticus in oysters. *J Food Prot*. 2006;69(8):1823–1828.
64. Goode J, Harrop S. *Authentic Wine: Toward Natural and Sustainable Winemaking*. University of California Press: Oakland, California; 2011.
65. Zara G, Nardi T. Yeast metabolism and its exploitation in emerging winemaking trends: from sulfite tolerance to sulfite reduction. *Fermentation*. 2021;7(2):57.
66. Costanigro M, Appleby C, Menke SD. The wine headache: Consumer perceptions of sulfites and willingness to pay for non-sulfited wines. *Food Qual Prefer*. 2014;31:81–89.
67. Grogan KA. The value of added sulfur dioxide in French organic wine. *Agric Food Econ*. 2015;3(1):19.
68. Silva M, Gama J, Pinto N, et al. Sulfite concentration and the occurrence of headache in young adults: a prospective study. *Eur J Clin Nutr*. 2019; 73(9):1316–1322.
69. Johansen JD, Aalto-Korte K, Agner T, et al. European Society of Contact Dermatitis guideline for diagnostic patch testing—recommendations on best practice. *Contact Dermatitis*. 2015;73(4):195–221.