

Allergic contact dermatitis caused by sodium metabisulfite: a challenging allergen. A case series and literature review

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Summary

Background. Sulfites, preservatives and antioxidants used in the cosmetic, pharmaceutical and food industry are contact allergens whose relevance seems to be difficult to establish.

Objectives. To perform a retrospective study on patients patch tested with a sulfite.

Materials and methods. Between 1990 and 2010, 2763 patients were patch tested with sodium metabisulfite. The reactions were considered to be relevant if there was a clear relationship between the dermatitis and sulfite exposure.

Results. One hundred and twenty-four (4.5%) of 2763 patients patch tested positively to sodium metabisulfite. The most frequent localizations of the lesions were the face (40.3%) and the hands (24.2%). Six patients also reported systemic symptoms. Thirteen cases (10.5%) were occupational, 10 of them presenting with hand eczema. Sodium metabisulfite was the single allergen found in 76 cases (61.3%). The reactions were considered to be relevant in 80 cases (64.5%), of which 11 were occupational.

Conclusions. Allergic contact dermatitis caused by sulfites is frequent and often relevant. One should be aware of possible relevant sources of exposure, particularly in occupational settings such as hairdressing and the food industry, and in pharmaceutical and cosmetic products. Patch testing with sodium metabisulfite, which seems to be the best indicator for sulfite contact allergy, is also useful in cases of immediate reactions to sulfite-containing products.

Key words: allergic contact dermatitis; antioxidants; preservatives; sodium bisulfite; sodium metabisulfite; sodium sulfite; sulfites.

Sulfites are a ubiquitous group of sulfur-based compounds that contain the sulfite ion, SO_3^{2-} , and that are widely used in the cosmetic, pharmaceutical and food industries (1). Sodium sulfite salts, namely sodium sulfite (CAS 7757-83-7), sodium bisulfite (sodium hydrogen sulfite; CAS 7631-90-5), and, particularly, sodium metabisulfite (SMS; sodium pyrosulfite; CAS 7681-57-4), are the most frequently used molecules.

Contact allergy to SMS has been reported several times, but the relevance seems to be difficult to determine (2–4). We report here a large series, and show that contact allergy to SMS may be more frequent and more relevant than previously thought.

Materials and Methods

From 1 January 1990 to 14 October 2010, a total of 2763 among 12 764 patients investigated in Leuven were patch tested with SMS 2%, and later 1%, in petrolatum (Chemotechnique®, Vellinge, Sweden), either because of its presence in the Belgian pharmaceutical and cosmetic series, or when the history had revealed exposure to sulfites. Thirty-nine patients were also tested

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with sodium sulfite 2% pet. (prepared in-house). Patch testing was performed according to the International Contact Dermatitis Research Group criteria (i.e. 2 days of occlusion, readings on D2 and D4, and sometimes also D5 and/or D7, using a score from + to +++). Van der Bend[®] patch test chambers (Van der Bend[®], Brielle, The Netherlands) were applied on the back with Micropore[™] (3M Health Care[®], Borken, Germany), and fixed with Mefix[®] (Mölnlycke Health Care[®], Göteborg, Sweden) as adhesive tape. The reactions were considered to be of past or current relevance only when there was a clear relationship between the dermatitis and exposure to the suspected sulfite-containing products. The significance of the association between SMS-positive responses and other variables was analysed with the chi-square test/Fisher's exact test.

Results

One hundred and twenty-four (4.5%) of 2763 patients patch tested positively to SMS, and none to sodium sulfite (only 39 patients tested). The MOAHLFAs of both the total population studied in this period and of those reacting to SMS are given in Table 1.

Of the 124 patients, 77 (62.1%) were females and 47 (37.9%) were males. The median age was 50 years (variance = 16.6), with a range from 10 to 91 years. All of the patients presented with cutaneous eczematous lesions, except for 1 who reported urticarial lesions after drinking wine and beer. The most frequent localizations of the lesions were: face (40.3%), hands (24.2%), trunk (10.5%), legs (10.5%), and scalp (7.2%). Six patients (including the patients with urticarial lesions) also reported systemic symptoms: 4 of them reported malaise, nausea and dizziness after drinking wine and beer; 1 hairdresser experienced episodes of asthma and rhinitis caused by inhalation of sulfite-containing products at work;

Table 1. MOAHLFAs of the overall group of patients tested from 1 January 1990 to 14 October 2010 (n = 12 746), of the patients tested with sodium metabisulfite (SMS) (n = 2763), and of the sodium metabisulfite-positive patients (n = 124)

	SMS-positive patients (n = 124)	SMS-tested patients (n = 2763)	Overall sample (n = 12 746)
Male (%)	37.4	19.6	34.2
Occupational (%)	10.5	15.7	16.8
Atopy (%)	18	20	21.5
Hand (%)	24.2	29.1	38.3
Leg (%)	10.5	7.6	3.5
Face (%)	40.3	51.3	34.5
Age > 40 years (%)	61.3	54.6	47.6

and, finally, 1 patient suffered from an anaphylactoid reaction following an injection with a sulfite-containing local anaesthetic. None of these patients with systemic symptoms were studied with prick tests.

Thirteen cases (10.5%) were occupational, 10 of them presenting with hand eczema [2 butchers (1 also with facial dermatitis) 2 hairdressers, 1 nurse, 3 photographers, 1 food handler, and 1 pharmaceutical technician], and 3 with facial lesions (2 hairdressers and 1 wine maker).

SMS was the single allergen found in 76 cases (61.3%). Twelve patients presented with one concomitant reaction and 36 with three or more positive test reactions. Interestingly, 95 patients showed a doubtful (n = 9) or clearly negative (n = 86) response on day 2 that became positive on day 4. The positivity ratios on both patch test readings (D2 and D4) were 44.8% [95% confidence interval (CI) 27.7–63] and 52.41% (95% CI 43.6–61.1), respectively.

The reactions were considered to be of present relevance in 72 cases (58%), of past relevance in 8 cases (6.4%), and of unknown relevance in 44 cases (35.5%). Among the occupational cases, 11 of 13 showed present relevance and 2 cases past relevance.

We found a statistically significant association between relevant patch test results and isolated SMS reactivity.

Contact with SMS contained in topical antifungal creams (Nizoral[®] cream; Janssen-Cilag, Berchem, Belgium) was the primary cause of sulfite contact allergy in our series, with a total of 26 cases (21%). Interestingly, 8 of the SMS-positive patients tested with sodium sulfite, the actual ingredient in this cream, reacted negatively to it. This was also the case for 2 additional SMB-positive patients who had contact with sodium sulfite via a cooking fluid from mushrooms and food for animals, respectively. Hair dyes containing sulfites were considered to be responsible for relevant responses in 18 cases (14.5%). A detailed list of products containing sulfites that were related to relevant responses is shown in Table 2.

Discussion

Sulfites occur naturally in some foods and beverages, as a result of fermentation, whereas others are of synthetic origin and are commercially available (Table 3). They are used to control the growth of microorganisms and as bleaching, antioxidant or reducing agents (2, 5). Sodium, potassium and calcium salts are used as food additives and its use is regulated in Europe and must be labelled on the packaging, either by their names or with E-numbers (2, 6). Sodium, potassium and ammonium sulfite salts are

Table 2. Relevant products found in the occupational and non-occupational cases of sulfite-positive patients (n = 80)

	Number of cases	Details	
		Product	n
Non-occupational			
Cosmetics, leave-on	8	Facial cleaner	3
		Body emollient	2
		Not specified	3
Cosmetics, rinse-off	23	Hair dyes	18
		Shampoo	3
		Hand cleaner	1
		Toothpaste	1
Medications	33	Topical antifungal	26
		Topical steroids	1
		Topical anaesthetic	1
		Local anaesthetic	2
		Eye drops	3
Food and/or drinks	4*		
Other	2	Photographic products	1
		Food preserved with sodium metabisulfite (mushrooms/hand eczema)	1
Occupational			
Food	4	Minced meat (butchers)	2
		Food/wine handlers	2
Cosmetics	5	Hair dyes (hairdressers)	4
		Hand cleaner (nurse)	1
Industrial products	4	Photographers	3
		Pharmaceutical technician	1

*Three of these patients also presented with eczematous lesions related to other sulfite-containing products.

approved for use in cosmetics (4). Finally, sulfites are also included in many pharmaceuticals to maintain the stability and potency of some medications (2). A list of common products and foods containing sulfites is shown in Table 4.

Although the apparent safety of the sulfite additives has led to their widespread use, an increasing number of reports associating these substances with adverse reactions began to appear in the 1970s. Even minimal

(oral, parenteral, respiratory, or cutaneous) exposure in subjects with intolerance may provoke various types of reaction, such as asthma, rhinoconjunctivitis, and even anaphylaxis leading to death (4). Malaise, dizziness, confusion, abdominal pain and diarrhoea (4, 7, 8) have also been described. Apart from these manifestations, which are relatively common and well documented, sulfites may also cause cutaneous reactions, which can be classified as follows:

- (1) flushing, urticarial or anaphylactoid reactions following ingestion and/or parenteral exposure, and
- (2) allergic contact dermatitis following skin contact.

Furthermore, these reactions may occur simultaneously, in various combinations, and with various degrees of severity, in some susceptible individuals (4). For example, we have seen 1 hairdresser with hand eczema who also described respiratory symptoms when exposed to sulfite-containing products.

Cutaneous urticarial reactions have been described following ingestion of food containing sulfites (9, 10), exposure to local anaesthetics (11), or exposure to parenteral medicines (12, 13). Immediate reactions have rarely been observed with scratch or prick tests, which seems to exclude Type 1 immediate hypersensitivity in most cases (4). However, late positive patch test reactions in these patients may indicate the potential role of delayed hypersensitivity (4, 11). In our series, we observed similar cases presenting with a delayed reaction to SMS, which may support epicutaneous patch testing to diagnose such patients.

Allergic contact dermatitis caused by sulfites was first reported in 1968, in a patient with hand eczema who worked in a pharmaceutical company and reacted to potassium metabisulfite (14). At present, this molecule is considered to be an unusual but not infrequent sensitizer, and its allergenic mechanisms have been recently described (15). A literature review gave a total of 33 short reports describing contact allergy to SMS

Table 3. List of commercially available sulfites

	Molecular formula	CAS number	E-number	Food	Cosmetics
Sodium sulfite	Na ₂ SO ₃	7757-83-7	E221	Yes	Yes
Sodium bisulfite	NaHSO ₃	7631-90-5	E222	Yes	Yes
Sodium metabisulfite	Na ₂ S ₂ O ₅	7681-57-4	E223	Yes	Yes
Potassium sulfite	K ₂ SO ₃	10117-38-1	E225	Yes	Yes
Potassium bisulfite	KHSO ₃	7773-03-7	E228	Yes	Yes
Potassium metabisulfite	K ₂ S ₂ O 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 ₄ HSO ₃	10192-30-0	—	No	Yes
Ammonium sulfite	(NH ₄) ₂ SO ₃	7026-44-7	—	No	Yes

Table 4. Sources of exposure to sulfites

Cosmetics	Hair colours and bleaches, hair sprays Self-tanning lotions, make-up Skin fading, lighteners, anti-ageing creams, facial cleansers, around-eye creams, sunscreen products Body washes/cleansers Perfumes
Medications	Topical antifungal and corticosteroid products Local anaesthetics (particularly those containing adrenaline) Ophthalmic, nasal and intravenous solutions that contain: Adrenaline, isoprenaline, isoproterenol, isoetharine, phenylephrine, corticosteroids, chlorpromazine, chlorpheniramine, dopamine, propofol, aminoglycoside antibiotics, doxycycline, vitamin B, metoclopramide
Industrial products	Food and beverage industries Leather and textile industries Wood, pulp and paper industries Rubber manufacture Glass industry Mineral extraction Photography products Pharmaceutical industry Cleaning and laundry products Water and sewage treatment Swimming pool water products
Food and drinks	Drinks and liquids: Wine, beer, bottled soft drinks, fruit juice, cordials, cider, vinegar, canned soups Fruits and vegetables: Raisins, dried apricots, fruit bars, avocados, dried potatoes, fresh potatoes, French fries, gravies, sauces, fruit toppings, maraschino cherries, pickled onions, sauerkraut, pickles, maple syrup, jams, jellies, mushrooms, vegetables in cellophane, salads Crustaceans: shrimp (uncooked), canned seafood Meats: delicatessen minced meat, sausages Others: gelatine, food starches, beet sugar, corn sweeteners

(Table 5) and other sulfites (Table 6). We also found seven studies with large series of patch tested patients (Table 7), giving the percentage of positive responses to SMS (six publications) and sodium sulfite (two publications) along with their relevance.

Occupational allergic contact dermatitis caused by sulfites is mainly related to the food, wine and photographic industries. In our series, we describe 13 additional cases, including 4 hairdressers with hand eczema/facial dermatitis caused by SMS, which has been only rarely reported (16).

In our cases, non-occupational contact allergy to sulfites was mainly secondary to the use of Nizoral® antifungal cream, followed by hair dyes.

Traditionally, the relevance of positive patch test reactions to sulfites has been considered to be difficult to establish. In a recently published retrospective study, Kaaman et al. (2) described 1518 consecutive patients (839 females and 679 males) patch tested with 2% SMS pet. Fifty-one patients (3.4%) reacted positively, but the authors could establish the relevance in only 3 occupational cases. They observed a statistically significant predominance of positive patch test reactions in males, and a high frequency of patients with manual

jobs among these, which seems logical, considering that the study was conducted in an occupational and environmental dermatology department. In 1994, an Italian group patch tested 2894 patients with potassium metabisulfite, SMS, and sodium sulfite; 50 (1.7%) reacted positively (45). Only 12 reactions (24%) were considered to be of clinical relevance, 5 of them being occupational. In 1992, Petersen and Menné (46) described 1762 consecutive patients patch tested with sodium sulfite in addition to the standard battery. Although 25 (1.4%) were positive, the authors were unable to determine the clinical relevance in most cases, and therefore did not recommend continued testing.

However, there are also large patch test series concluding that the relevance of sulfites is greater than previously thought. A recent publication of Oliphant et al. described a total of 180 patients patch tested with both SMS and sodium sulfite (44): 8 of 10 positive responses to SMS were considered to be probably relevant. In contrast to our results, the majority of their SMS-positive patients also reacted to sodium sulfite. In 2007, Madan et al. (5) reported a series of 1751 patients patch tested with SMS 1% pet., of whom 71 (4.1%) reacted positively. Thirty-three cases (43.5%) were considered to be relevant,

Table 5. Published short reports concerning allergic contact dermatitis caused by sodium metabisulfite (SMS)

Case number (reference)	Age (years)	Sex	Localization	Occupation	Product	Concentration (%)	Vehicle	Readings	Other relevant positive results
Occupational									
1–4 (2)	NS	NS	NS	Dentist Kitchen worker Photographic processing Laboratory worker	NS	NS	NS	Positive	—
5 (1)	50	F	Hands	Potato slicer	Potatoes	1	pet.	D2 +, D4 +	—
6 (16)	26	F	Face and eyelids	Hairdresser	Hair dyes	2	aqua	D3 ++, D5 IR	—
						0.64	aqua	D3 ++, D5 IR	—
						0.2	aqua	D3 ++, D5 IR	—
						0.064	aqua	D3 ++, D5 IR	—
						0.02	aqua	D3 ++, D5 IR	—
7 (17)	37	M	Airborne	Wine maker	Wine additive	1	pet.	D2 ++, D4 ++	Potassium metabisulfite (D2 ++, D4 ++)
8–15 (5)	NS	NS	NS	Baker Chemical processing Catering (3 patients) Rubber manufacturing Swimming pool worker Brewer (wine)	NS	1	pet.	Positive	—
16 (18)	23	F	Hands	Baker	NS	1	pet.	Positive	Dodecyl gallate 0.25% pet. Positive
17 (19)	37	F	Upper arms/systemic symptoms	Photographic processing laboratory	Colour fixer/black and white film	5	pet.	Positive	—
18,19 (11)	NS	NS	Hands	Photographic processing laboratory (2 patients)	Photographic chemicals	NS	NS	Positive	—
20 (20)	NA	NA	Hands	Baker	—	—	—	—	—
21 (21)	39	M	Hands	Pastry and biscuit factory	Dough containing SMS	2	aqua	D2 +, D4 +	—
						5	aqua	D2 +, D4 +	—
						10	aqua	D2 +, D4 +	—
22 (22)	51	F	Hands	Salad maker	Veg-White® (antioxidant)	10	aqua	D2 ++, D4 +++	Powder Veg-White® (D2 ++, D4 +++)
						20	aqua	D2 ++, D4 +++	—
Non-occupational									
23 (23)	52	F	Face	NR	Shines® bleaching cream	2	aqua	D2 ++, D4 ++	Shines® cream (D3 and D5 positive)
						5	aqua	D2 ++, D4 ++	—
						2	pet.	D2 ++, D4 ++	—
24 (24)	67	F	Face and eyelids	NR	Vistagan-liquifilm® eyedrops	5	pet.	D2 ++, D4 ++	—
						1	pet.	D2 ++, D4 ++	—
25 (25)	NS	NS	Injection site	NR	Local anaesthetic (lidocaine 2% and adrenaline)	2	pet.	D3 ++	Local anaesthetic (lidocaine 2% and adrenaline) (D3 +)

Table 5. Continued

Case number (reference)	Age (years)	Sex	Localization	Occupation	Product	Concentration (%)	Vehicle	Readings	Other relevant positive results
26 (26)	75	F	Face, back, upper arms, and vulva	NR	Trimovate® cream (GlaxoSmith Kline®) (clobetasone butyrate)	0.1 2 5	aqua pet. aqua	Positive Positive Positive	Clobetasone butyrate (positive)
27 (27)	55	M	Perianal, upper limbs, and occipital area	NR	Hubber® haemorrhoidal cream	2	pet.	D2 ++, D4 ++	Hubber® cream, neomycin sulfate, promethazine, propylparaben (D2 ++, D4 ++)
28 (28)	47	M	Perianal	NR	Trimovate® cream (GlaxoSmith Kline®) (clobetasone butyrate)	NS	NS	D2 ++, D4 ++	Trimovate® cream (D2 ++, D4 ++)
29 (29)	26	M	Ear	NR	Trimovate® cream (GlaxoSmith Kline®) (clobetasone butyrate)	NS	NS	D2 +, D4 +	Trimovate® cream (D2 +, D4 +)
30, 31* (29)	NS	NS	NS	NR	Hydrocortisone 1% cream	1	pet.	D2 ++, D4 ++	Hydrocortisone 1% (positive)
32† (30)	NS	NS	NS	NR	Mecloderm® cream	1	pet.	D2 ++, D4 ++	Mecloderm® cream (positive)
33 (31)	31	F	Trunk	NR	Topical drug trial (with mesalanine) for psoriasis	1 2	pet. pet.	D2 ++, D4 ++ D2 +?, D4 ++	Active and placebo cream (D2 ++, D4 ++)
34 (11)	40	F	Face and neck	NR	Neo-lidocaton® (Pharmaton® SA, Belgium) (local anaesthetic)	5	pet.	D2 ++, D4 ++	Sodium bisulfite (D2 ++, D4 ++)
35, 36† (11)	NS	NS	NS	NR	Nizoral® cream (Jonhson & Jonhson)	NS	NS	D2 ++, D4 ++	Neo-lidocaton® (D2 +, D4 +)

F, female; IR, irritant reaction; M, male; NR, not relevant; NS, not stated.

*Active sensitization to sodium metabisulfite in 2 patients using topical corticosteroids that contained this substance.

†Two patients who reacted to sodium metabisulfite contained in Nizoral®, included in our new reported case series.

Table 6. Published short reports concerning allergic contact dermatitis caused by sodium sulfite and other sulfites

Case number (reference)	Age (years)	Sex	Localization	Occupation	Product	Sulfite tested / concentration (%)	Vehicle	Readings	Other relevant positive results
Sodium sulfite									
1 (32)	45	F	Face	NR	Day and night cream	SS 5%	pet.	Positive	Day and night cream (positive) SMS 1% pet. (positive – cross-reaction) Ketoconazole cream (positive) Ketoconazole cream (++++)
2 (33)	NS	NS	NS	NR	Ketoconazole cream	SS 5%	pet.	Positive	
3 (34)	26	M	Face	NR	Ketoconazole cream	SS 2% SS 5%	pet. pet.	D2 +++, D4 +++ D2 +++, D4 +++	
4 (34)	51	M	Face, back, and chest	NR	Ketoconazole cream	SS 2% SS 5%	pet. pet.	D2 ++, D4 ++ D2 ++, D4 ++	Ketoconazole cream (++)
5 (34)	41	F	Face and chest	NR	Ketoconazole cream	SS 2% SS 5%	pet. pet.	D2 +++, D4 +++ D2 +++, D4 +++	Ketoconazole cream (++++)
6 (35)	63	M	Groin	NR	Ketoconazole cream and tablets	SS 0.5% SS 2% SS 0.5% SS 2% SS 5% SS 5%	aqua aqua pet. pet. pet. pet.	D4 ++ D4 ++ D4 ++ D4 ++ D4 ++ D4 ++	Ketoconazole cream and tablets (++)
7 (35)	52	F	Face	NR	Ketoconazole cream	SS 0.5% SS 2% SS 0.5% SS 2% SS 5% SS 5%	aqua aqua pet. pet. pet. pet.	D4 ++ D4 ++ D4 ++ D4 ++ D4 ++ D4 ++	—
8 (36)	25	M	Face	NR	Ketoconazole cream	SS 0.2% SS 2% SS 0.2% SS 2% SS 5%	aqua aqua pet. pet. pet.	D2 +++, D4 +++ D2 +++, D4 +++ D2 +++, D4 +++ D2 +++, D4 +++ D2 +++, D4 +++	Ketoconazole cream (D2 +++, D4 ++++)
Other sulfites									
9 (37)	41	F	Face	NR	Colour bleaching ointment Preguard Wella® (WELLA®, Darmstadt, Germany)	Ammonium bisulfite 2%	pet.	D2 ++, D4 ++	Colour bleaching ointment Preguard Wella® (D2 +++, D4 ++++)
10 (38)	34	M	Face	NR	Ketoconazole cream	SBS 1%	pet.	D2 ++, D4 ++	Ketoconazole cream (D2 +++, D4 ++++)
11 (39)	72	F	Eyelids	NR	Tathion® eye drops	SBS NS	NS	Positive	—
12 (40)	44	F	Face	NR	Bleaching cream	Ammonium bisulfite 0.45% Ammonium bisulfite 0.1%	aqua aqua	D2 +++, D7 + D2 +++, D7 +	SBS 1% aqua, SBS 0.45% aqua, SBS 0.1% aqua (D2 +++, D7 +)

Table 6. Continued

Case number (reference)	Age(years)	Sex	Localization	Occupation	Product	Concentration (%)	Vehicle	Readings	Other relevant positive results
13 (41)	27	F	Hand	Assistant in a dry cleaning establishment	Reagents	Sodium hyposulfite 0.5% Sodium hyposulfite 1%	NS NS	Positive Positive	—
14 (42)	40	M	Airborne	Animal food industry	Pig feed Synkavit®	SBS 0.1% and 1%	pet.	Positive	Synkavit®
15 (43)	40	F	Hand	Pharmaceutical company	Potassium metabisulfite solutions	Potassium metabisulfite 1% Potassium metabisulfite 5%	aqua aqua	D2–, D4++ D2+++, D4+++	—

F, female; M, male; NR, not relevant; NS, not stated; SBS, sodium bisulfite; SMS, sodium metabisulfite; SS, Sodium sulfite.

7 of them (5.6%) being occupational. Moreover, after re-analysis of the 'non-relevant' group, out of 71, the number of relevance cases increased from 33 to 47. As in our series, they also observed a female predominance, but in their study the hands were the most commonly affected primary sites of dermatitis. However, they found a high incidence of facial dermatitis in the 'non-relevant' group, and therefore hypothesized that many of these cases might have been relevant to contact with cosmetics and/or food products. They also observed that, in general, the reactions were more prominent on day 4 than on day 2. They concluded that it was worthwhile including SMS in a baseline series. In the same year, Malik et al. (32) reported another consecutive series of 117 patients patch tested with SMS in Ireland, and found 8 (6.8%) positive responses, with 4 of them being relevant. They also hypothesized that positive responses to SMS represent a marker of contact allergy to other sulfites.

In our series, 64.5% of the 124 positive responses were relevant. As far as we know, this is the largest series ever published giving evidence that: (i) it is worthwhile patch testing with SMS in patients with eczema and a positive history of contact with sulfite-containing products, and (ii) most of the positive responses to SMS are relevant if they are carefully investigated. We are able to refute two of the main arguments that have been traditionally used to justify the supposed low relevance of SMS, namely (i) the ubiquity of sulfites, and (ii) the possibility of false-positive/irritant patch test results. First, all of our relevant cases had a clear history of sulfite exposure. With current labelling standards, it is usually easy to identify which products contain these substances (usually SMS). Second, our patch test results showed a clearly increasing response from D2 to D4. Indeed, the positivity ratios on both D2 and D4 were lower than 80%, the limit above which an allergen is considered to be problematic (47). Furthermore, we used pet. as patch test vehicle, which is recommended to avoid false responses. Indeed, in aqueous solutions, sulfites exist in a complex chemical equilibrium (2, 45). Therefore, our results suggest that the best concentration and vehicle with which to test SMS is 1% pet.

Conclusion

Allergic contact dermatitis caused by sulfites is frequent and often relevant. One should be aware of possible relevant sources of exposure, particularly in occupational settings, such as hairdressing and the food industry, and in pharmaceutical and cosmetic products.

Patch testing with SMS, which seems to be the best indicator for sulfite contact allergy, may also be useful in cases of immediate reactions to sulfite-containing products.

Table 7. Published large patch test series with sulfites

Reference	Number of patients	Sulfite	Patch test sulfite concentration and vehicle	Positive reactions	Relevant cases	Relevance an products involved			Other sulfites tested
						Occupational	Non-occupational	Other sulfites tested	
Oliphant et al. (44)	183	SMS and SS	SMS: 1% pet. SS: 1% pet.	SMS: 10 (5.5%) SS: 7 (3.8%)	SMS: 8 (80%) SS: 3 (42.9%)	None	SMS: 4 topical preparations (Trimovate®) 4 food additives 1 medication SS: 1 food additive 1 hair dye	—	
Kaaman et al. (2)	1518	SMS	2% pet.	51 (3.4%)	3 (5.9%)	1 textile dyer 1 photographer 1 dentist	—	—	
Malik et al. (32)	117	SMS	NS	8 (6.8%)	4 (50%)	—	1 day and night cream* 1 swimming pool 1 false tan 1 hair dye	SS 5% pet. Positive in 1 patient	
Madan et al. (5)	1751	SMS	1% pet.	71 (4.1%)	33 (43.5%)	1 baker (+ Trimodine®) 3 catering 1 chemical processor 1 rubber manufacturing worker (+ Trimodine® and Trimovate®) 1 brewer (+ Trimovate®)	—	—	
Angelini et al. (43)	980	SMS	1% pet.	14 (1.4%)	NS	NS	NS	NS	
Vena et al. (45)	2894	SMS	1% pet.	50 (1.7%)	12 (24%)	1 hairdresser 2 photographers 1 wine producer 1 agronomist 1 carpenter 1 chemical factory worker	5 topical preparations	Potassium metabisulfite 1% pet. and SBS 1% and 5% pet. Both positive in 50 patients. SS 1% pet.	
Petersen and Menné (46)	1762	SS	1% pet.	25 (1.4%)	3 (12%)	—	3 ketoconazole cream	Positive in 1 patient	

NS, not stated; SBS, sodium bisulfite; SMS, sodium metabisulfite; SS, sodium sulfite.

*Reported in Table 6.

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