

Allergic Contact Dermatitis from Dimethyl Fumarate after Contact with a Chinese Sofa

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Background: Dimethyl fumarate has been successfully used in the treatment of psoriasis in the past. Despite its clinical use, cutaneous contact with this molecule may cause contact dermatitis.

Objective: We report a case in which skin exposure to a synthetic fabric sofa containing dimethyl fumarate made by a Chinese furniture manufacturer resulted in a severe, pruritic, papulovesicular, eczematous dermatitis to the sites of contact with the sofa.

Methods: The patient was patch-tested with serial dilutions of dimethyl fumarate.

Results: Patch testing results revealed strong positive reactions to dimethyl fumarate at different concentrations.

Conclusion: Dimethyl fumarate is a potent contact sensitizer and is commonly found in sachets inside furniture and footwear boxes.

Contexte: Le fumarate de diméthyle a été utilisé avec succès, dans le passé, dans le traitement du psoriasis. Malgré cet usage clinique, les contacts cutanés avec la molécule peuvent causer une dermatite de contact.

Objectif: Nous faisons état ici d'un cas d'exposition de la peau à du fumarate de diméthyle présent dans le tissu synthétique d'un sofa fabriqué en Chine, qui a entraîné un eczéma grave, prurigineux, et papulovésiculaire aux sièges de contact avec le sofa.

Méthode: Le patient a été soumis à des tests épicutanés, avec dilutions successives du fumarate de diméthyle.

Résultats: Les résultats des tests épicutanés ont révélé une forte réaction positive au fumarate de diméthyle, à différentes concentrations.

Conclusion: Le fumarate de diméthyle est un puissant sensibilisant de contact, qu'on trouve souvent dans les sachets placés dans les meubles et dans les boîtes à chaussures.

FURNITURE ALLERGIC CONTACT DERMATITIS (ACD) has been well documented. This type of ACD most often presents on the posterior thighs and forearms, which are the main sites of furniture contact. Perspiration and friction may facilitate this process. Components in textiles, mainly textile dyes and textile formaldehyde resin finishes, have been identified as causing ACD. Examples of offending textile dyes include specific azo dyes and anthraquinone dyes used mainly on synthetic manufactured fibers applied by the disperse or direct application method. There are reported cases involving textile formaldehyde resin finishes that impart antiwrinkle properties to the fabric as well as isocyanates, used in the

production of thermoplastic polyurethane foam, which is commonly used in furniture cushioning.¹ Leather furniture may also induce ACD. Cases have been reported from compounds produced in the tanning process, such as hexavalent chromium,² and antifungal agents, such as a pyridine derivative in polyvinyl chloride leather.³

Since 2006, outbreaks of severe furniture ACD have been described in Europe. Initial reports from Finland and the United Kingdom indicated that the dermatitis was pruritic and usually limited to the areas of the body in contact with offending sofas through clothing. This ACD was typically resistant to treatment with potent topical corticosteroids,^{4,5} and many patients required systemic treatment with corticosteroids or even azathioprine, methotrexate, cyclosporine, or psoralen plus ultraviolet A (PUVA) to control severe dermatitis.⁶ Notably, many patients required hospitalization.^{5,6} Exacerbations of pre-existing asthma, wheezing and sneezing, were also endured by several patients, particularly when on or near the offending sofas.⁶ Symptoms tended to resolve after the responsible sofa was avoided and discarded.⁴⁻⁶

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DOI 10.2310/7750.2011.11059

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Subsequent chemical analyses and patch-testing studies identified the responsible contact sensitizer as dimethyl fumarate (DMF) (Figure 1), which was isolated from the sofas at a concentration up to 470 µg/kg and triggered positive reactions down to a level of 1 ppm.⁴ Implicated sofas and chairs were found to be produced in a factory in the south of China. Subsequently, the European Directive (2009/251/EC) in March 2009 banned all products containing DMF from the European market.

DMF, a lipophilic methyl ester of fumaric acid, is a biocide used in consumer products to prevent mold and fungal growth during storage and transportation. It is commonly placed in sachets inside furniture and footwear boxes, subsequently permeating the products.

To date, thousands of cases have been described in Europe; however, there have been no formal reports in North America. Here we describe a case identified in Canada in 2008.

Case Report

A 37-year-old male electrician was referred for suspected contact dermatitis related to exposure to his sofa. This patient did have an atopic diathesis, with a history of asthma, hay fever, and allergies to cats, dust, and pollens. He reported no past history of any eczematous disease.

This patient developed a delayed eczematous dermatitis after purchasing a Carter sage green microfiber dual recliner sofa, which was labelled Cart-SG-RS and manufactured by a Chinese furniture company (Link-wise Furniture Company Ltd, Guangdong, China). Specifically, he acquired a pruritic, papulovesicular, eczematous dermatitis involving his volar forearms, posterior thighs, and calves. He reported noticing this eruption approximately 14 days after he exposed himself to the sofa, and he did not have a problem when he avoided the sofa. Furthermore, the problem resolved altogether after the sofa was returned to the store.

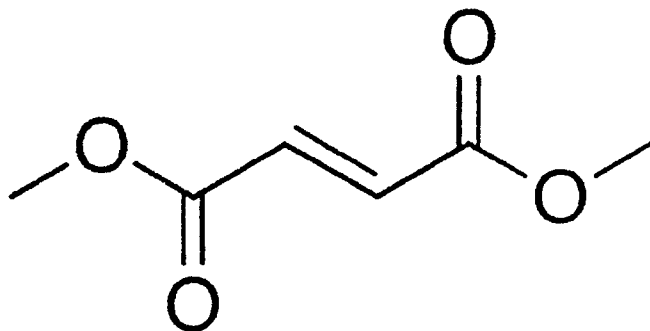


Figure 1. Chemical structure of dimethyl fumarate.

Prior to his presentation for patch testing, he presented to the emergency department, was diagnosed with cellulitis, and was treated with intravenous cefazolin through a peripherally inserted central catheter (PICC) line.

Patch testing was performed with the Finn Chambers system (Epitest Ltd, Oy, Tuusula, Finland) and Scanpor tape (Actavis Norway AS, Norgesplaster, Vennesla, Norway). The contact allergens tested included the North American Contact Dermatitis Group (NACDG) Standard Screening Series (Chemotechnique Diagnostics AB, Malmö, Sweden), the entire Chemotechnique Textile Series (Chemotechnique Diagnostics AB), the Allergeaze Textile Dye Series (Allergeaze, Calgary, AB), and both sides (lining side and external side) of a 1.0 × 1.0 cm water-soaked piece of the sage green microfiber sofa. The patches remained in place for 48 hours, and the test sites were evaluated at 48 and 96 hours. At 96 hours, positive 1+ reactions to both the lining side and the external side of the microfiber sofa were observed (Figure 2). All other patch testing produced negative reactions.

Approximately 1 month later, a second set of patch testing was completed with dilutions of 0.1% and 0.01% DMF (Alfa Aesar, Ward Hill, MA) in petrolatum (dilutions performed in clinic). Results at 96 hours were not obtained as the patient failed to return for the 96-hour reading. However, readings at 48 hours revealed strong positive 2+ reactions to both DMF 0.1% petrolatum and DMF 0.01% petrolatum (Figure 3).

Discussion

To date, the outbreaks of furniture ACD in Europe from Chinese sofas have been well documented and studied. International cooperation and networking were central to revealing the scope of this “sofa dermatitis” epidemic and to alert dermatologists to be vigilant for additional patients.⁶ In 2008, three independent groups discovered the cause of this dermatitis.^{4,5,7,8} Foulds identified the responsible sensitizer to be the antifungal sachets located deep inside the sofas.⁸ In this study, initially five leather colors and foam and fiber interiors were tested, although only weak positive reactions to wet fiber were obtained. However, when the agent from the antifungal sachets located inside the sofas was evaluated, positive patch tests resulted in all patients, and negative reactions were found in controls. The study also achieved sensitization with one application of this agent.

In a complementary study, Rantanen isolated DMF as the specific contact sensitizer, which was measured in the

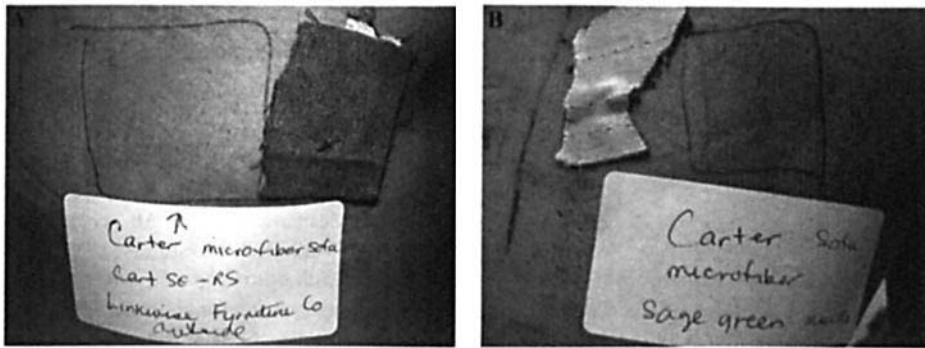


Figure 2. External side (A) and lining side (B) of the microfiber sofa.

accountable sofas at a concentration up to 470 $\mu\text{g}/\text{kg}$.⁴ In that study, furniture samples were analyzed by gas chromatography–mass spectrometry, and isolated compounds were identified with a mass spectrum library. Patients were patch-tested and found to have positive reactions to DMF down to a concentration of 0.0001% (or 1 ppm).

Unequivocal confirmation of DMF as the potent sensitizer was realized by the third group with chemical analyses that involved patch testing thin-layer chromatograms (TLCs) prepared from an extract of sofa material.⁹ Subsequent gas chromatography–mass spectrometry analyses of the positive TLC spot revealed nine chemicals, including DMF. On patch testing the patients to each of these nine chemicals, DMF 0.01% petrolatum produced positive reactions in all patients, whereas the other chemicals yielded negative reactions. In addition, gas chromatography–mass spectrometry analysis identified DMF as the principal content of the antifungal sachets.

This study unambiguously demonstrated that DMF was the sensitizing allergen.

Discussion regarding the mechanism of sensitization and consequent dermatitis from the antifungal sachets arose. Notably, the varied distribution of the dermatitis resulted from the haphazard distribution of the DMF-containing sachets within the sofas.⁶ Perspiration and friction facilitated sensitization in the affected patients. Foulds' study found that affected patients were more likely to present in warm months and have higher body mass indexes.⁸ The report suggested that the sensitizer (DMF) permeated from the sachet into the sofa fiber and then into the leather from the pressure of sitting. This resulted in sensitization and subsequent development of dermatitis within 4 to 6 weeks.

In addition to triggering sofa dermatitis, DMF was also identified as a sensitizer causing shoe contact dermatitis. In this study by Giménez-Arnau and colleagues, all eight adult patients were patch test positive to DMF $\leq 0.1\%$ petrolatum, and chemical analysis of shoes found DMF in all shoes evaluated.¹⁰ For the majority of shoes, it was felt that the DMF had impregnated the product from the antimold sachets; however, one shoe was found to have DMF integrated into the shoe's structural material.

Despite the recent reports of DMF acting as a potent contact sensitizer, oral DMF has been used in the treatment of many cutaneous diseases. It has been used in the treatment of psoriasis by inhibiting T-cell activity¹¹ and may be used to treat resistant alopecia areata.¹² DMF has also been used to treat disseminated granuloma annulare,¹³ cutaneous sarcoidosis,¹⁴ and necrobiosis lipoidica.¹⁵ Finally, reports that DMF may reduce melanoma growth and metastasis through antiproliferative and proapoptotic activity have been published.¹⁶

In addition, DMF has been recognized to have other medical uses. It has been used to treat systemic sarcoidosis,¹⁴ multiple sclerosis,¹⁷ autoimmune myocarditis,¹⁸ autoimmune encephalomyelitis,¹⁹ and noninfectious uveitis.²⁰

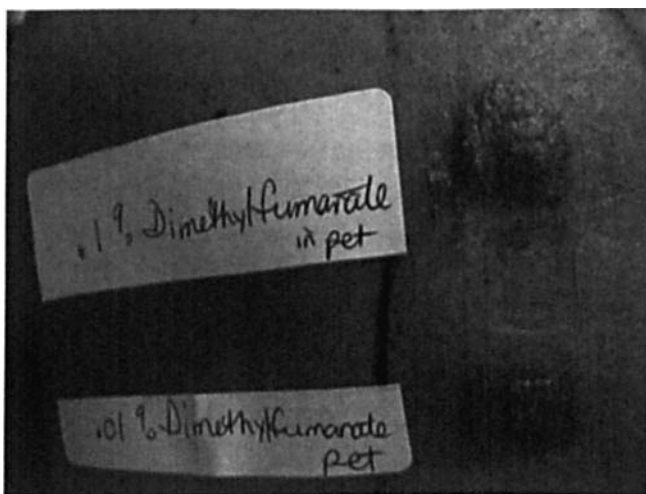


Figure 3. Readings at 48 hours show strong positive reactions to both dimethyl fumarate 0.1% petrolatum and dimethyl fumarate 0.01% petrolatum.

and may have a cardioprotective role in and may reduce the size of myocardial infarcts.²¹ Theoretically, there is the possibility that systemic therapy with DMF may cause systemic ACD after a threshold blood level is reached. However, there have been no reports to date of such a side effect from this systemic therapy.

We have described the first case in North America of ACD induced by DMF, which was traced to a sofa manufactured by Linkwise Furniture Company. Specifically, this patient's sofa was a microfiber sofa, not leather, as in other reports. Microfibers are synthetic fibers made from polyester, polyamide, or other polymers. In this case, the patient had strong positive 2+ reactions to DMF concentrations of 0.1% and 0.01%. It is noteworthy that patch testing with the NACDG series was negative, including methyl methacrylate and ethyl acrylate, as it has been proposed that some acrylates may cross-react with DMF. Specifically methyl acrylate and ethyl acrylate were found to be positive in 20 and 35% of DMF-hypersensitive patients, respectively.²²

Currently, DMF is not banned in Canada, and Health Canada is investigating this contact sensitizer. It is important to emphasize the importance of identifying consumers in Canada suffering from contact dermatitis triggered by DMF in their furniture or shoes. In their review on DMF, Bruze and Zimerson recommended patch testing with DMF when furniture, textiles, or shoes are thought to cause the dermatitis, when the dermatitis has an unusual presentation, and when the diagnosis is elusive with ordinary examinations.²²

Acknowledgment

Financial disclosure of authors and reviewers: None reported.

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