

Contact Allergy to Neem Oil

Anton de Groot, MD, PhD,* Berend A. Jagtman, MD, PhD,† and Marjolijn Woutersen, PhD‡

A case of allergic contact dermatitis from neem oil is presented. Neem oil (synonyms: *Melia azadirachta* seed oil [INCI name], nim oil, margosa oil) is a vegetable (fixed) oil obtained from the seed of the neem tree *Azadirachta indica* by cold pressing. Contact allergy to neem oil has been described previously in only 3 patients. The allergen(s) is/are unknown.

Botanical substances are, usually as extracts, widely used in cosmetics and biopharmaceutical products. Although most consumers perceive products marketed as “botanical,” “herbal,” or “natural” as safe, these products not infrequently cause allergic reactions.^{1,2} We recently presented in this journal a review of propolis, a natural and (largely) botanical product that has caused many cases of sensitization.³ Also popular for home use are essential oils, to which various healing and otherwise positive qualities are attributed. The best known is tea tree oil, allergic reactions to which, especially when it is applied undiluted to damaged skin, are far from rare.⁴ We present a patient with allergic contact dermatitis from *Melia azadirachta* seed oil (INCI name), better known as neem oil (which name will be used in this article for clarity).

CASE REPORT

A 66-year-old white man presented himself with an itchy eruption on the forearms, backs of the hands, and legs. His job was to repair agricultural engines. By doing this, he had developed irritant contact dermatitis of the hands from contact with oil, frequent washing, and mechanical stress to the skin. For 2 months, the patient had been using neem oil (producer: Berivita, www.berivita.com) on his hands, arms, and legs to treat his dry skin (Fig. 1). Within 2 weeks, an itchy rash appeared at the sites of application. The patient was not atopic, nor were his relatives.

At inspection, there were plaques with erythema, papules, and crusts at the back of the hands, forearms, and lower legs. Serologic

tests for specific immunoglobulin E antibodies were negative. Patch tests were performed with the European baseline series, a cosmetic series, a therapeutic series, and the neem oil used by the patient. There were positive reactions to sodium metabisulfite 1% petrolatum (D2–, D3+), ketoconazole cream (D2++, D3++) (which contains sodium sulfite), and neem oil (D2++, D3++). The product contained 99.9% neem oil and 0.1% tocopherol. Later, the patient was tested with tocopherol 10% and 30% in arachis oil and retested with the neem oil, which again gave a positive reaction to the oil (D2++, D3++); there were no reactions to tocopherol. Twenty-three controls were tested with the neem oil product with negative results. The reactions to sodium metabisulfite and ketoconazole cream were of past relevance.

DISCUSSION

The neem tree *Azadirachta indica* A. Juss. (synonyms: *M. azadirachta* L., margosa tree) is a fast-growing evergreen tree from the mahogany family Meliaceae that can reach a height of 15 to 20 m. The tree is indigenous to the dry forests of south and southeast Asia and is widely distributed in India, Nepal, Pakistan, Bangladesh, Sri Lanka, Myanmar, Thailand, Malaysia, Indonesia, and Iran. Its original natural distribution is obscured by widespread cultivation, which also takes place in Africa, Central and Southern America, the Caribbean, and the Philippines.⁵ The neem tree is the holy tree of the Hindus and is a major component in ayurvedic and unani medicine. The leaves, bark, seeds, and roots of neem contain more than a hundred pharmacologically active constituents, which may possess antiseptic, anti-inflammatory, antidiabetic, antibacterial, and antifungal effects. The best known are triterpenes called limonoids, including azadirachtin, nimbin, nimbidin, and nimbolide.⁶

The bitter and astringent bark (neem bark, margosa bark, cortex margosae) is used to treat fever and worms. The leaves of the neem are antiseptic; teas and infusions of leaves are used to alleviate intestinal complaints and to treat skin diseases. The flowers are used as tonic, and seed extracts may be used in treating head lice.

The leaves and other parts of the tree are effective insecticides, repellent, and antifeedant agents in plant protection, for which their ingredient azadirachtin is responsible.⁶ Biological, pharmacological, and medicinal aspects of the (various parts of the) neem tree and its seed oil have been reviewed.^{7–9}

From the *Acdegroot Publishing, Wapserveen; †VieCurie Medisch Centrum, Venlo; and ‡National Institute for Public Health and the Environment Centre for Safety of Substances and Products, Bilthoven, the Netherlands.

Address reprint requests to Anton de Groot, MD, PhD, Acdegroot Publishing, Schipslootweg 5 8351 HV, Wapserveen, the Netherlands. E-mail: antondegroot@planet.nl; www.patchtesting.info.

The authors have no funding or conflicts of interest to declare.

The data in this article are presented here in the framework of CESES (Consumer Exposure Skin Effects and Surveillance), a Dutch Cosmetovigilance system monitoring the adverse effects of cosmetics in the Netherlands. CESES is initiated and executed by the National Institute for Public Health and the Environment and the Netherlands Food and Consumer Product Safety Authority. The project is sponsored by the Dutch Ministry of Health, Welfare and Sports. All authors participate in this project.

DOI: 10.1097/DER.0000000000000309

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Figure 1. The neem oil product used by the patient.

The term “neem oil” usually (as in this article) indicates a vegetable oil (fixed oil), obtained from the seeds of the neem tree by cold pressing. This oil is called *M. azadirachta* seed oil in the INCI nomenclature of both the United States and the European Union (CAS 8002-65-1, 90063-92-6). However, the name “neem oil” may also be used for an essential oil obtained by hydrodistillation (INCI name: *A. indica* seed oil; CAS 8002-65-1, 84696-25-3) and for fatty products obtained from the seeds by solvent extraction (INCI name: *A. indica* seed extract; CAS 84696-25-3, 90063-92-6). Adding to the confusion is that the CAS numbers provided in the United States and European Union nomenclature sometimes differ and that the same CAS numbers may be used for different products. It should be realized that the chemical composition of these various “neem oils” differs considerably. The pharmacologically active substances are present especially in the extracts; essential oils from neem seeds are hardly produced and used.⁶

The vegetable neem oil is a yellow-brown bitter substance with a strong sulfuric and alliaceous (garlic-like) odor. It is used to treat skin diseases, such as psoriasis, eczema, fungal infections, and furuncles, and to relieve intestinal worm infections. The fatty oil is also used as lamp oil and to make soap and is effective as insecticide and in crop protection. In addition, neem oil is used in cosmetics as emollient, but only after the bitter and aromatic substances have been removed, and the oil has become colorless and odorless. Its most important constituents are fatty acids: oleic acid (25%–58%), palmitic acid (17%–34%), stearic acid (7%–24%), linoleic acid (6%–24%), behenic acid (0.2%–1.7%), arachidic acid (1.3%), and palmitoleic acid.⁶ In March 2017, *M. azadirachta* (neem) seed oil

was present in 223 of 64,983 cosmetic products, of which the composition is known in the Environmental Working Group’s Skin Deep Cosmetics Database, USA (<http://www.ewg.org/skindeep/>).

Our patient had used neem oil of the brand BeriVita and had purchased the product on the Internet. From information on the product and the Web site of the producer, it was clear that the neem oil was obtained from the seeds of the neem tree *A. indica* by cold pressing. The product consisted of 99.9% neem oil and 0.1% tocopherol, which was undoubtedly added as antioxidant to prevent the product from becoming rancid.

Contact allergy to neem oils has thus far been reported in 3 patients only.^{10–12} The first had applied undiluted oil on the scalp for treating alopecia areata and developed acute dermatitis of the scalp and face.¹⁰ The second patient was a 56-year-old woman who developed dermatitis on the right breast, spreading to the arm, after applying a mixture of neem oil and tea tree oil on a furuncle on the breast.¹¹ The third patient was a woman aged 30 years who developed acute dermatitis in the neck and behind the ears after having treated psoriasis of her scalp with various phytotherapeutics including neem oil.¹² All 3 patients had a positive patch test to undiluted neem oil, which had been negative in 2 investigations in, respectively, 5 and 8 control subjects.^{11,12} In addition, there is a case report of a man who developed allergic contact dermatitis after treating his psoriasis with Psorigon cream, containing 6 botanical substances including *M. azadirachta*.¹³ Patch tests with this component in 4 concentrations (1%, 2%, 5%, and 10%) were positive. The exact nature of this material (extract, essential oil, vegetable oil) was not mentioned, but considering the other botanical materials, this was likely an extract, not the vegetable neem oil.¹³

We here present the fourth case of contact allergy to neem oil in literature. Contact allergy to tocopherol,¹⁴ which was present in the commercial neem oil product, as the cause of the allergic reaction was excluded by patch testing. Irritancy of the oil was excluded by extensive control tests. The allergen or allergens in neem oil are at this moment unknown.

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