

# Combined Contact and Photocontact Allergic Dermatitis to Etofenamate in Flogoprofen Gel

Javier Sánchez-Pérez, Tatiana Sanz Sánchez, and Amaro García-Díez

**We report a case of combined contact and photocontact allergic dermatitis to etofenamate in Flogoprofen gel (Chiesi Wasserman, Barcelona, Spain). Patch test results were positive at the nonirradiated site, but there was a stronger reaction at the irradiated site with etofenamate 0.05% in petrolatum (pet.) at d2 and d4. The use frequent of topical agents containing etofenamate and sun exposure can result in a predisposition to contact photoallergy. Clinical findings caused by etofenamate are uncommon. Allergic contact dermatitis is the most common cutaneous reaction reported. In American studies observed, no reactions were observed to etofenamate in subjects with photosensitivity because it was not included in the series of antigens used in testing.**

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NONSTEROIDAL ANTI-INFLAMMATORY drugs are available for topical treatment of musculoskeletal disorders, soft tissue trauma, and some inflammatory skin diseases. Etofenamate is a lipophilic, topical, nonsteroidal anti-inflammatory drug that is derived from antranilic acid. Its chemistry structure corresponds to 2-(2-hydroxyethoxy)-ethyl-N-( $\alpha,\alpha,\alpha$ -trifluoro-m-tolyl)-anthranilate, which causes inhibition of prostaglandine-synthetase. Cutaneous side effects of etofenamate are uncommon. These side effects include contact urticaria,<sup>1</sup> allergic contact dermatitis,<sup>2-4</sup> exfoliative dermatitis,<sup>5</sup> and photoallergic contact dermatitis.<sup>6</sup> Positive reactions to etofenamate in patients attending the patch test clinic were reported in 2 out of 371 consecutive patients, and the reaction of 1 patient was clinically relevant.<sup>7</sup> Members of Group Italian Research Dermatitis Contact Allergy (GIRDCA) diagnosed allergic contact dermatitis to etofenamate in 1 of 102 patients.<sup>8</sup> Concurrence of contact and photocontact allergic dermatitis has not been observed, but was present in this case report.

## Case Report

A 67-year-old woman reported the application of Flogoprofen gel (etofenamate 5%) (Chiesi Wasserman, Barcelona, Spain) on her right ankle in an attempt to treat arthralgias for 1 month. She developed itching erythematous, bilateral, asymmetric plaques on her ankles and legs, 4 days before presenting, after exposure to the sun. Before she consulted us, there were cutaneous lesions enlarged in size and number grouped on the right ankle, joint edema, and pain. The lesions cleared 15 days after stopping Flogoprofen gel and treatment with oral and topical corticosteroids.

*From the Department of Dermatology, Hospital Universitario de la Princesa, Universidad Autónoma, Madrid, Spain.*

*Address reprint requests to Javier Sánchez Pérez, MD, Department of Dermatology, Hospital Universitario de la Princesa, C) Diego de León, 62, 28006 Madrid.*

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Patch and photopatch tests were performed with Spanish standard allergens, anti-inflammatory series, Flogoprofen gel, and its components applied in duplicate to the back on either side of the midline. One day after the test application, one set was uncovered and irradiated with 10 J/cm<sup>2</sup> of ultraviolet + A (UVA). At d2 and d4 both the irradiated and covered sites were evaluated. Later, patch and photopatch tests with etofenamate and 96% etilic alcohol were performed with a lower concentration. As shown in Table 1, patch test results were positive to etofenamate 0.05% in petrolatum (pet.) (+/+), 0.5% pet. (+++), and 5% pet. (+++), and irritant reaction to 96% etilic alcohol. Photopatch testing revealed a positive reaction (+++) to etofenamate 0.05% pet. Patch testing with etofenamate 5% pet. elicited a negative result in 25 controls, and photopatch testing with etofenamate 0.05% pet. elicited a negative result in 10 controls. Six weeks after the beginning of the skin test, we observed blurred, limited, hypocromic macules at the sides of patch and photopatch tests with Flogoprofen gel and etofenamate 5% pet.

## Discussion

Our case represents a combined contact and photocontact allergic dermatitis to etofenamate in Flogoprofen gel that has been confirmed by positive reaction at the nonirradiated site, with a stronger reaction at the irradiated site to etofenamate 0.05% pet. at d2 and d4. The patient presented hypocromic lesions at the edges of patch and photopatch test areas with Flogoprofen gel and etofenamate 5%; these lesions might have arisen from intense inflammatory reaction. The testing performed on controls was necessary to rule out a simple phototoxic response on testing.

Most of the cutaneous side effects of topical anti-inflammatory drugs appear in countries with extensive use of these drugs, such as Europe and, most especially, the Mediterranean region.<sup>1-8</sup> We have found one reported case of photoallergic contact dermatitis to etofenamate with negative patch test results and positive photopatch test

**Table 1.** Patch and Photopatch Tests Results in the Case Report

	<i>No Irradiation</i>		<i>10 J/cm<sup>2</sup></i>	
	d2	d4	d2	d4
Alergenos del GEIDC				
Mercaptobenzotiazol	+	+	+	+
Flogoprofen gel a.i.	+++	+++	+++	+++
Etofenamate 0.05% pet.	+ / + +	+ / + +	+++	+++
Etofenamate 0.5% pet.	+++	+++	+++	+++
Etofenamate 5% pet.	+++	+++	+++	+++
Ethanol 96% 90% aq.	—	—	—	—
Ethanol 96% 50% aq.	—	—	—	—
Ethanol 96% 10% aq.	—	—	—	—
Ethanol 96% a.i.	IR	IR	IR	IR
Others excipients of				
Flogoprofen® gel	—	—	—	—

results with etofenamate 2% pet. in Flogoprofen spray.<sup>6</sup> Contact sensitization by use of topical nonsteroidal anti-inflammatory drugs was caused mainly by active substance, although excipients must not be underestimated.<sup>8</sup> In our case, we have shown an irritation to 96% etilic alcohol, the concentration of which in Flogoprofen gel was 50%. It could lead to sensitization and later appearance of cutaneous lesions to etofenamate. In American studies,<sup>9-11</sup> no reactions to etofenamate were observed in subjects with photosensitivity because it was not included in the series of antigens used in testing. In these studies, sunscreens, fragrances, antimicrobial, and therapeutic agents (chlorpromazine, promethazine) were the most common clinically

relevant photoallergens. These chemicals are also well known contact allergens without UV light exposure,<sup>12</sup> according to the standardized photopatch test procedure of the German, Austrian, and Swiss Group.

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