

# Contact Dermatitis to Isoconazole Nitrate

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A case of contact dermatitis to isoconazole nitrate (Travogen®) which developed in a 41-year-old male who used it for the treatment of tinea cruris is described. The patient had been treated with multiple creams including Travogen® (isoconazole nitrate), Mycospor® (bifonazole) and Lidex® (0.25% fluocinonide) before the sudden appearance of the eczematous rash on his groin and thigh. The patch test result showed that he was sensitive to multiple imidazole derivatives (isoconazole, bifonazole, ciclopirox) as well as isoconazole nitrate (1% in petrolatum), which suggests allergic contact dermatitis due to isoconazole nitrate. We recommended haloprogin cream for the treatment of tinea cruris. After one year follow up period, the patient was free of skin lesion. (*Ann Dermatol* 1:43–45, 1989)

*Key Words:* Contact dermatitis, Haloprogin, Isoconazole nitrate.

Isoconazole nitrate (1-(2,4-dichloro-β-(2,6-dichlorobenzyloxy)-phenethyl)-imidazole-nitrate) is a newly developed topical imidazole derivative which is widely used as an antifungal agent (Fig. 1). Contact dermatitis to isoconazole nitrate is extremely rare considering the large number of prescriptions filled.<sup>1</sup> However, we recently experienced a case of contact dermatitis to isoconazole nitrate. We suggest that the dermatologist must consider the possibility of contact dermatitis to imidazole derivatives when tinea lesions worsen despite topical treatment with imidazole derivatives.

## REPORT OF A CASE

A 41-year-old male with tinea cruris was seen in our hospital on January 10, 1987. He was treated with a daily application of multiple creams containing Travogen® (isoconazole nitrate), Mycospor® (bifonazole) and Lidex® (0.25% fluocinonide). Three months later, erythematous pruritic skin rashes developed on the groin and both inner thighs. Upon physical examination, erythematous papules and patches were

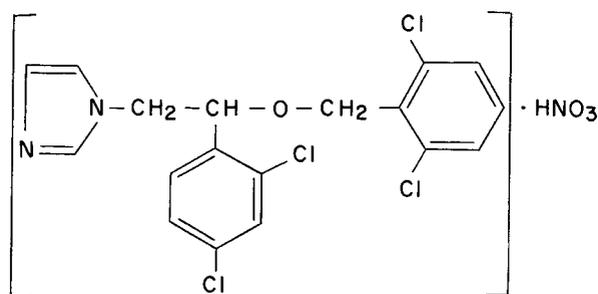


Fig. 1. Chemical structure of Isoconazole nitrate.



Fig. 2. Erythematous papules and patches were seen on the groin, both inner aspects of the thighs and pubic area.

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seen on the groin, both inner aspects of the thighs and pubic area (Fig. 2).

Contact dermatitis to antifungal cream was highly suspected. Therefore, we performed patch tests with several topical antifungal creams, vehicle series (Hollister-Stier) and Lidex<sup>®</sup> cream. Positive results were obtained with Travogen<sup>®</sup> cream(++), Mycospor<sup>®</sup> cream(+) and Batrafen<sup>®</sup> cream(+) on the 4th day (Table 1). Subsequent patch tests with isoconazole nitrate 1% petrolatum and the vehicle of Travogen<sup>®</sup> cream showed only positive reaction to isoconazole nitrate 1% petrolatum on the 2nd and 4th day. Consequently, we discontinued the treatment with Travogen<sup>®</sup> and Mycospor<sup>®</sup> cream and treated the pruritic patches with topical corticosteroid cream. We then recommended Halotex<sup>®</sup> (haloprogin) cream for the treatment of the tinea cruris. After a one year of follow up period, the patient was free of skin lesions.

**Table 1.** Results of Patch testing

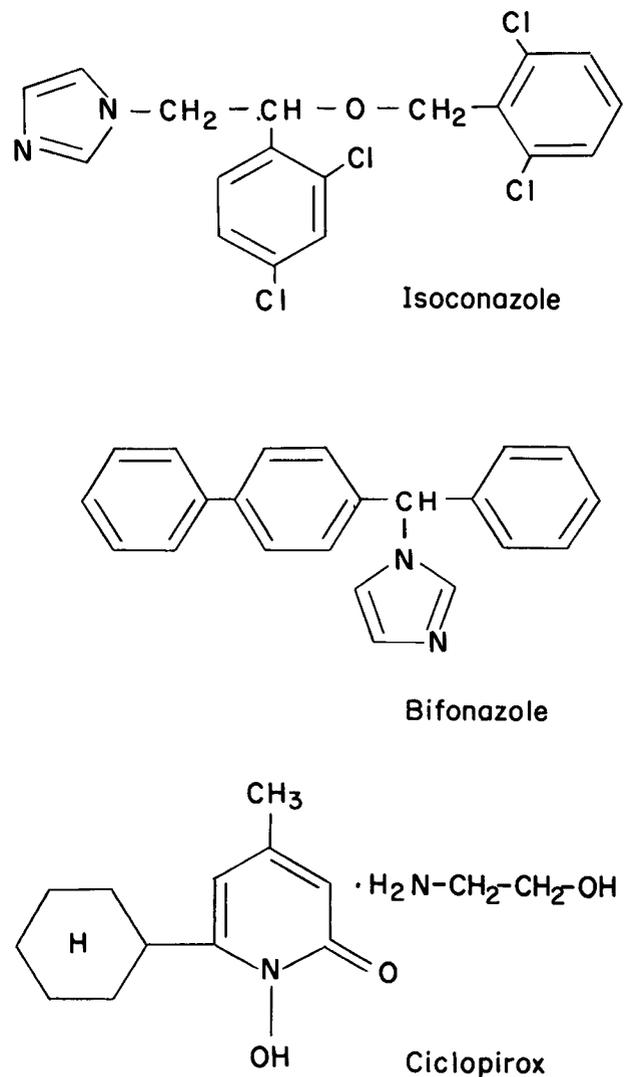
Substance	48h	96h
Vehicle series (Hollister-Stier)	-	-
Travogen <sup>®</sup> (Isoconazole) cream	++	++
Mycospor <sup>®</sup> (Bifonazole) cream	+	+
Nizoral <sup>®</sup> (Ketoconazole) cream	-	-
Trosyd <sup>®</sup> (Tioconazole) cream	-	-
Batrafen <sup>®</sup> (Ciclopirox) cream	?	+
Halotex <sup>®</sup> (Haloprogin) cream	-	-
Lidex <sup>®</sup> (Fluocinonide) cream	-	-
Isoconazole nitrate 1% pet.	++	++
Vehicle of Travogen <sup>®</sup> cream	-	-

## DISCUSSION

Imidazole derivatives are the most widely used and most effective antifungal agents. Their mechanisms include changes in the permeability of cellular membranes and direct enzymatic toxic effects on the metabolism of fungus.<sup>2</sup> Many imidazole derivatives such as bifonazole, clotrimazole, oxiconazole, econazole, isoconazole, miconazole, enilconazole and tioconazole have been developed and are presently available for clinical use. Although widely used throughout the world, contact dermatitis to imidazole derivatives is very rare. Since Van ketel<sup>3</sup> first described contact dermatitis to miconazole in 1974, several cases of contact dermatitis to miconazole,<sup>3,5</sup> clotrimazole,<sup>6,8</sup> econazole,<sup>9</sup> oxiconazole,<sup>10</sup> enilconazole<sup>11</sup>

and isoconazole<sup>1</sup> have been reported.

From the patch test results, it is apparent that the isoconazole nitrate is a contact sensitizer in our patient. It appears that the patient was sensitized with isoconazole nitrate during the treatment of tinea cruris at our hospital because the contact dermatitis developed after continuous treatment for three months. As well as Travogen<sup>®</sup> cream, Mycospor<sup>®</sup> cream and Batrafen<sup>®</sup> cream also showed weak posi-



**Fig. 3.** Chemical structures of Isoconazole, Bifonazole, and Ciclopirox.

tive reaction in our patient. We interpreted the results as an excited skin state because the Travogen® cream showed strong positive reaction and the neighbouring Mycospor® cream and Batrafen® cream showed weak positive reaction. It is conceivable that isoconazole, bifonazole and ciclopirox may have cross reactivity, but it is unlikely because they have different chemical structures (Fig. 3). Raulin and Frosch<sup>12</sup> suggested that isoconazole nitrate, miconazole and clotrimazole may have cross reactivity because they have similar chemical structures. They recommended that bifonazole be the therapeutic alternative for patients sensitive to these drugs since no cross reactivity was observed.

After the lesions of contact dermatitis were subsided with topical corticosteroids, we successfully treated the tinea cruris lesion with haloprogin.

#### REFERENCES

1. Frenzel UH, Gutekunst A: *Contact dermatitis to isoconazole nitrate. Contact Dermatitis 9:74, 1983.*
2. Raab W: *Wertung der Imidazolderivate. Wirkungsweise. Penetration and Absorption. In Mykosobehandlung mit Imidazolpra Paraten, Springer Verlag, Berlin, Heidelberg, New York, 1978, pp 21-23, 48-59, 101-103, Cited from ref. 12.*
3. Van ketel WG: *Allergy to miconazole nitrate (Daktarin).® Contact Dermatitis Newsletter 8:517, 1974.*
4. Foged EK, Hammershby O: *Contact dermatitis due to miconazole nitrate. Contact Dermatitis 8:284, 1982.*
5. Degreef H, Verhoeve L: *Contact dermatitis to miconazole nitrate. Contact Dermatitis 1:269-270, 1975.*
6. Roller JA: *Contact allergy to clotrimazole. Br Med J 2:737, 1978.*
7. Balato N, Lembo G: *Contact dermatitis from clotrimazole. Contact Dermatitis 12:110, 1985.*
8. Kalb RE, Grossmann ME: *Contact dermatitis to clotrimazole. Cutis 36:240-242, 1985.*
9. Valsecchi R, Tornaghi: *Contact dermatitis from econazole. Contact Dermatitis 8:422, 1982.*
10. Raulin C, Frosch PJ: *Contact allergy to oxiconazole. Contact Dermatitis 16:39-40, 1987.*
11. Van Hecke E, De Voss L: *Contact sensitivity to enilconazole. Contact Dermatitis 9:144, 1983.*
12. Raulin C, Frosch PJ: *Contact allergy to imidazole antimycotics. Contact Dermatitis 18:76-80, 1988.*
13. Van Hecke E, Van Brabant S: *Contact sensitivity to imidazole derivatives. Contact Dermatitis 7:348-349, 1981.*