

Short Communication

Occupational contact dermatitis due to biotin precursor

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Key words: biotin precursor; (3aS, 6aR) hexahydro-1,3-dibenzyl-6-hydroxyfurano[3,4-d]imidazol-2,4-dione; occupational; contact allergy; pharmaceutical industry. © Munksgaard, 1998.

A 45-year-old man presented with complaints of itchy reddish eruptions on his face and hands of 1-year duration. He had worked for 1½ years at a plant where a precursor of biotin was produced. His 3rd child suffered from atopic dermatitis but there was no other relevant history. Laboratory examination indicated a slight eosinophilia (5.4% of 8500/mm³ WBC) and elevated Ig-E (1000 u/ml) and RAST scores to cedar pollen, mit-

es, house dust and candida. (3aS,6aR) Hexahydro-1,3-dibenzyl - 6 - hydroxyfurano [3,4-d] imidazol - 2,4 - dione (sample 3), a precursor of biotin made from 1,3-dibenzyl-2-oxo-imidazolidine-4,5-dicarboxylic acid (sample 1) using (8α,9R)-cinchonan-9-ol (sample 2), an optical resolving agent, was being produced at his place of work (Fig. 1).

Patch tests were carried out with these 3 materials

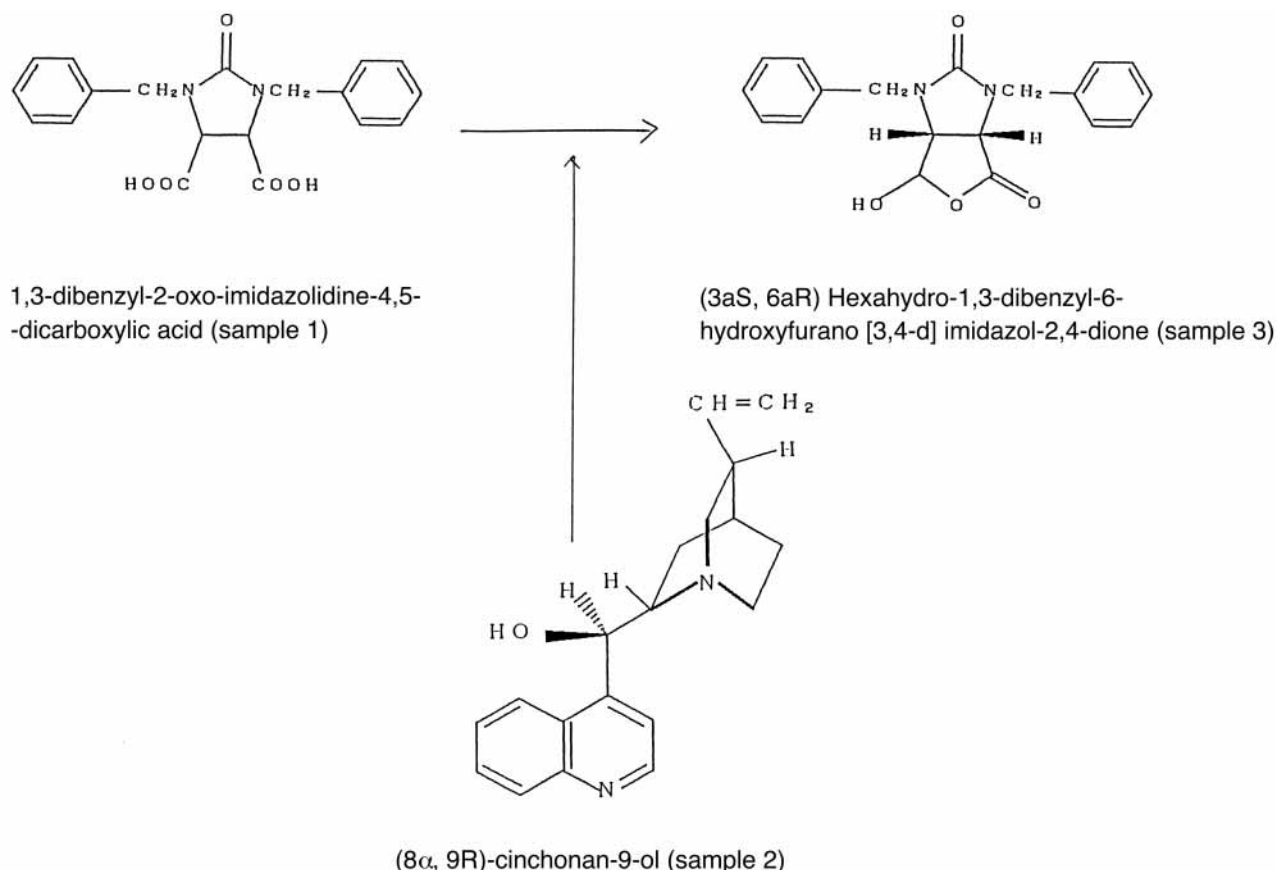


Fig. 1. Production process of the biotin precursor.

Table 1. Patch test results

Materials	% veh.	Patient				Control subjects (N=18)					
		1 st patch testing		2nd patch testing		D2			D3		
		D2	D3	D2	D3	–	?+	≥+	–	?+	≥+
1,3-dibenzyl-2-oxo-imidazolidine-4,5-dicarboxylic acid (sample 1)	0.1 pet.	–	–	NT	NT		NT			NT	
	0.5 pet.	–	–	NT	NT		NT			NT	
	1 pet.	–	–	NT	NT		NT			NT	
	5 pet.	–	–	–	–		NT			NT	
	10 pet.	–	–	NT	NT		NT			NT	
(8 α ,9R)-cinchonon-9-ol (sample 2)	0.1 pet.	–	?+	NT	NT		NT			NT	
	0.5 pet.	?+	+	NT	NT		NT			NT	
	1 pet.	+	+	NT	NT	18	0	0	18	0	0
	5 pet.	++	++	?+	?+	18	0	0	18	0	0
	10 pet.	++	++	NT	NT	17	1	0	18	0	0
(3aS,6aR)hexahydro-1,3-dibenzyl-6-hydroxyfurano [3,4-d]imidazol-2,4-dione (sample 3)	0.1 pet.	++	++	NT	NT		NT			NT	
	0.5 pet.	++	++	NT	NT		NT			NT	
	1 pet.	++	++	NT	NT	18	0	0	18	0	0
	5 pet.	++	++	+	++	17	1	0	18	0	0
	10 pet.	++	++	NT	NT	18	0	0	18	0	0
control (pet).	as is	–	–	–	–	18	0	0	18	0	0

from the place of work, at a purity exceeding 99.9%. The chemical structures were confirmed by infrared absorption spectrometry. Positive reactions to samples 3 and 2 and a negative reaction to sample 1 were noted (Table 1). Further testing (5% pet.) indicated a positive reaction to sample 3 and a negative reaction to sample 1, though not definitely to sample 2. Patch tests in 18 control subjects showed negative reactions in all cases to samples 2 and 3 by the D3 reading. With change of workplace, his dermatitis did not recur. The precursor of biotin has been produced since 1975 at the site, but only the present patient was affected.

Comment

To our knowledge, this is the 1st case of allergic contact dermatitis due to (3aS,6aR) hexahydro-1,3-dibenzyl-6-

hydroxyfurano[3,4-d]imidazol-2,4-dione (sample 3). The present patient showed a positive reaction to sample 3, but not to sample 1. The chemical structure of the closed circle in sample 3 from the -COOH of sample 1 would thus appear to be the determinant structure for sensitization. The patient showed a positive reaction to sample 2 in the 1st patch tests, but a doubtful reaction in the 2nd confirming test. Reaction to sample 2 would thus appear to be either a weak allergic reaction or a false-positive reaction elicited by a strong positive reaction to sample 3. Additional patch tests should be conducted to confirm this.