

Patch-Test Reactions to Formaldehydes, Bioban, and Other Formaldehyde Releasers

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Background: Contact allergy to formaldehyde, Bioban, and other formaldehyde releasers and cross-reactivity between them have been reported in the literature; however, not many studies have data on this cross-reactivity.

Objective: To study (1) the rates of allergy to formaldehyde and to Bioban and other formaldehyde releasers and (2) the rates of cross-reactivity between them.

Methods: We present a retrospective chart analysis of patch-test results for all patients referred for allergic contact dermatitis testing at the Milton S. Hershey Medical Center from June 2004 to September 2005. Anyone allergic to formaldehyde, Bioban, or other formaldehyde releasers was included. Cross-reactivity between the agents was then analyzed.

Results: The charts of 210 patients were analyzed. Of these patients, 24 (11%) were allergic to formaldehyde, Bioban, or other formaldehyde-releasing agents. Seventeen (8.1%) of the patients were allergic to formaldehyde, 15 (7.1%) were allergic to Bioban, and 20 (9.5%) were allergic to other formaldehyde-releasing agents. Eleven (65%) of the 17 formaldehyde-allergic patients were also allergic to Bioban. Of the 20 patients allergic to formaldehyde-releasing agents, 14 (70%) were also allergic to one of the three Bioban products tested. Of the 15 patients allergic to Bioban, 11 (73%) were allergic to formaldehyde, 14 (93%) were allergic to formaldehyde-releasing agents, and 11 (73%) were allergic to both formaldehyde and formaldehyde-releasing agents.

Conclusion: A high cross-reactivity rate between formaldehyde, Bioban, and other formaldehyde-releasing agents was found.

THE VARIOUS BIOBAN PRODUCTS (Dow Chemical, Midland, MI) are broad-spectrum bactericidal and fungicidal agents used in metalworking fluids, paints, inks, emulsions, slurries, nonfood contact adhesives, and surfactants and also in consumer, household, and institutional products.¹ Bioban P-1487 is a mixture of 4-(2-nitrobutyl)-morpholine and 4,4'-(2-ethyl-2-nitrotrimethylene) dimorpholine; the structure of Bioban CS-1246 is 1-aza-3,7-dioxo-5-ethylbicyclo (3.3.0) octane; and the structure of Bioban CS-1135 is 4,4-dimethyl-oxazolidine (Fig 1).¹ The mechanism of the biocidal activity of Bioban CS-1246 is believed to be the generation of formaldehyde secondary to hydrolytic degradation.² Bioban CS-1135 can liberate one formaldehyde molecule, and Bioban CS-1246 can liberate two formaldehyde molecules.³ Typical concentrations of Bioban CS-1246, CS-1135, and P-1487 for various applications are 400 to 2,000 ppm, 400 to 5,000 ppm, and 100 to 1,000 ppm, respectively.¹ The brochures for these products all carry a

warning about skin exposure,¹ and contact allergy to Bioban has been reported in the literature.¹⁻¹² Formaldehyde is a very common preservative and contact allergen. Formaldehyde releasers are preservatives that release formaldehyde. The aim of this study was to assess the prevalence of formaldehyde, Bioban, and other

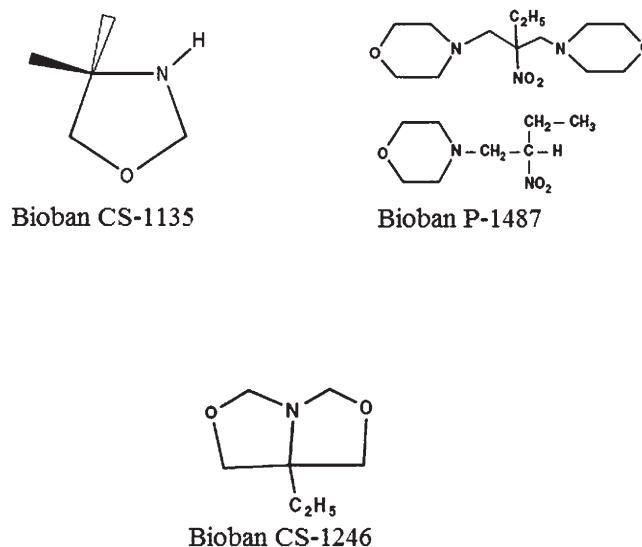


Figure 1. Molecular structures of Bioban CS-1135, Bioban P-1487, and Bioban CS-1246.

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Table 1. Interpretation and Scoring of Patch-Test Results

Code	Interpretation
1	Weak (nonvesicular) reaction, palpable erythema, infiltration possible, papules (+)
2	Strong (edematous or vesicular) reaction (++)
3	Extreme (spreading, bullous, ulcerative) reaction (+++)
4	Macular erythema only (+/- reaction)
5	Irritant morphology
6	Negative reaction (-)

formaldehyde releasers as well as cross-reactivity between the three substances.

Methods

Patch testing with Bioban CS-1246 1.0% in petrolatum (pet), Bioban CS-1135 1.0% pet, and Bioban P-1487 0.5% pet started at Milton S. Hershey Medical Center in June 2004. Since then, all patients referred for patch testing were tested with formaldehyde, the three Bioban agents, and other formaldehyde-releasing agents (including imidazoli-

Table 2. Patch-Test Results of Patients Allergic to Formaldehyde, Bioban, or Other Formaldehyde Releasers

Pat. No.	Age	Sex	Occupation	A	B	C	D	E	F	G	H	I	J	K	L	M
1	57	m	Massage therapist	-	++	++	+	-	+	-	-	-	+	+/-	-	-
2	73	f	(Unemployed)	+	-	+	+/-	-	-	-	+	+	+	+	+	-
3	61	f	Hospital environmental health	+	-	-	-	-	-	-	-	-	-	-	-	-
4	49	m	Welder	-	+	-	-	-	-	-	-	-	-	-	-	-
5	45	f	(Unemployed)	-	+	+	-	-	-	-	-	-	-	-	+/-	-
6	63	m	(Retired)	-	++	++	+	+	-	-	+	+	++	+	+	-
7	77	f	(Unemployed)	-	+	+	-	-	-	-	+	-	-	-	+	-
8	42	m	Management analyst	-	++	+/-	-	-	-	-	-	-	-	-	-	-
9	46	m	Grinding- machine operator	-	+	+	+	+/-	-	-	-	+	-	+	+	-
10	55	f	Nurse	+/-	+/-	+	-	-	-	-	-	-	-	+	+	-
11	61	m	Shipping/ receiving clerk	-	+	+	-	-	-	-	-	-	-	++	++	-
12	52	m	Machine operator (misc.)	+	++	-	-	+	-	-	++	++	+	+	+	-
13	52	m	Truck mechanic	-	-	+	-	-	-	-	-	-	-	+	+	-
14	65	m	(Retired)	-	-	-	-	-	-	-	+	+	-	-	-	-
15	82	f	(Unemployed)	+/-	+	+	+	-	+	-	-	+/-	-	-	-	-
16	68	f	(Unemployed)	-	+	+	-	-	-	-	-	-	-	+	+	-
17	62	m	(Unemployed)	+	+	+	+	-	+	-	-	+	+	+	+	-
18	78	f	(Retired)	+	+	-	+	-	+	-	-	+	+	+	-	-
19	44	f	(Unemployed)	-	++	+	+	+	-	-	-	-	+	+	+	-
20	53	f	Social worker	-	-	-	-	-	-	-	-	-	-	-	-	++
21	22	f	Health technician	-	+	-	-	-	-	-	-	-	-	-	-	-
22	43	m	Advertising/sales	+	-	-	-	-	-	-	-	-	-	-	-	-
23	50	m	Industrial machine repairer	-	++	++	-	-	-	-	-	-	-	++	++	-
24	24	f	Nurse	-	+	+	-	-	-	-	-	-	-	+	+	-

A = imidazolidinylurea 2% aqueous (aq); B = formaldehyde 1% aq; C = quaternium-15 2% in petrolatum (pet); D = diazolidinylurea 1% pet; E = 1,3-dimethylol-5,5-dimethyl (DMDM) hydantoin 1% pet; F = imidazolidinylurea 2% pet; G = 2-bromo-2-nitropropane 1,3-diol 0.5% pet; H = DMDM hydantoin 1% aq; I = diazolidinylurea 1% aq; J = ethyleneurea/melamine formaldehyde 5% pet; K = Bioban CS-1246 1.0% pet; L = Bioban CS-1135 1.0% pet; M = Bioban P-1487 0.5% pet; misc. = miscellaneous; Pat. = patient; +/- = macular erythema; + = papular erythema; ++ = vesicular; +++ = bullous/spreading.

dinylurea 2% aqueous (aq), quaternium-15 2% pet, diazolidinylurea 1% pet, 1,3-dimethylol-5,5-dimethyl (DMDM) hydantoin 1% pet, imidazolidinylurea 2% pet, 2-bromo-2-nitropropane 1,3-diol 0.5% pet, DMDM hydantoin 1% aq, diazolidinylurea 1% aq, and ethyleneurea/melamine formaldehyde 5% pet). Patch-test results of patients referred to rule out allergic contact dermatitis from June 2004 to September 2005 were analyzed. The analysis included any patients who had positive reactions to the following: imidazolidinylurea 2% aq, formaldehyde 1% aq, quaternium-15 2% pet, diazolidinylurea 1% pet, DMDM hydantoin 1% pet, imidazolidinylurea 2% pet, 2-bromo-2-nitropropane 1,3-diol 0.5% pet, DMDM hydantoin 1% aq, diazolidinylurea 1% aq, ethyleneurea/melamine formaldehyde 5% pet, Bioban CS-1246 1.0% pet, Bioban CS-1135 1.0% pet, and Bioban P-1487 0.5% pet. Tests were conducted with the Finn Chamber system (Epitest Ltd Oy, Tuusula, Finland) and Scanpor tape (Norgesplaster A/S, Vennessla, Norway) and with the North American Contact Dermatitis Group Standard Allergen Tray and the Bioban agents.¹¹ The method of testing involved taping the allergen to the patient's back on day 1 and interpreting the results on day 3 and on day 4 or 5. The Finn Chambers were occluded for 48 hours. Interpretations were scored with a number

system (Table 1). Chemotechnique Diagnostics was the supplier of all patch-test preparations.

Results

A total of 210 patch tests were conducted between June 2004 and September 2005. Twenty-four patients (11.4%) were allergic to formaldehyde, Bioban, or the other formaldehyde-releasing agents listed above. Of these 24 patients, 17 (8.1% of the total) were allergic to formaldehyde, 15 (7.1%) were allergic to Bioban, and 20 (9.5%) were allergic to the other formaldehyde-releasing agents. Eleven (64.8%) of the 17 formaldehyde-allergic patients were also allergic to Bioban. Of the 20 patients who were allergic to the other formaldehyde-releasing agents, 14 (70%) were allergic to Bioban. Of the 15 patients who were allergic to Bioban, 11 (73%) were allergic to formaldehyde, 14 (93%) were allergic to formaldehyde-releasing agents, and 11 (73%) were allergic to both formaldehyde and formaldehyde-releasing agents. The majority of the reactions were classified as + reactions or as palpable erythema (data on these patients are presented in Table 2).

Table 3 presents the percentages of patients allergic to each preservative and compares them with the correspond-

Table 3. Comparison of Study Patient Allergies to Formaldehyde, Bioban, and Formaldehyde Releasers

Allergen	% of Patients with Positive Reactions				
	Authors' Study (N = 210)	Jacobs et al ⁹ (N = 5,167)	De Groot et al ⁸ (N = 627)	Brinkmeier et al ^{3*} (N = 408)	Gruvberger et al ¹⁰ (N = 1,102)
Imidazolidinylurea 2% aq	2.9	—	—	—	—
Formaldehyde 1% aq	8.1	2.36	3.30	—	—
Quaternium-15 2% pet	7.1	1.82	0.50	—	—
Diazolidinylurea 1% pet	3.3	—	—	—	—
DMDM hydantoin 1% pet	1.4	—	—	—	—
Imidazolidinylurea 2% pet	1.9	0.99	0.50	—	—
2-Bromo-2-nitropropane 1,3-diol 0.5% pet	0.0	0.62	—	—	—
DMDM hydantoin 1% aq	2.4	—	—	—	—
Diazolidinylurea 1% aq	3.3	0.97	—	—	—
Ethyleneurea/melamine formaldehyde 5% pet	3.3	—	—	—	—
Bioban CS-1246 1.0% pet	6.2	—	—	1.96	—
Bioban CS-1135 1.0% pet	6.2	—	—	1.47	—
Bioban P-1487 0.5% pet	0.5	—	—	2.21	1.09

aq = aqueous; DMDM = 1,3-dimethylol-5,5-dimethyl; N = total number of patients; pet = petrolatum.

*A prospective study on metalworkers.

Table 4. Association between Formaldehyde, Bioban, and Other Formaldehyde Releasers*

	<i>Formaldehyde</i>	<i>Bioban</i>	<i>Other Formaldehyde Releasers</i>
Formaldehyde	3 (18%)	11 (73%)	14 (70%)
Bioban	11 (65%)	1 (7%)	14 (70%)
Other formaldehyde releasers	14 (82%)	14 (93%)	3 (15%)
Total positive for allergy	17	15	20

Adapted from Jacobs MC et al.⁹

*Percentages add up to > 100% because some patients were allergic to all three types of allergens.

ing percentages found in other studies. The association between formaldehyde, Bioban, and other formaldehyde releasers is presented in Table 4; for example, a total of 17 patients were allergic to formaldehyde, of which 3 (18%) were allergic to only formaldehyde, 11 (65%) were allergic to both formaldehyde and Bioban, and 14 (82%) were allergic to other formaldehyde releasers.

Discussion

In general, our percentages of positive test results were higher than those found in the literature (see Table 3). Our highest percentage of positive results was for formaldehyde, which was also the case in other studies. The majority of reactions in our series of patients were macular erythema or + reactions, which also agrees with previous reports.³

We found a strong association between Bioban, formaldehyde, and other formaldehyde releasers in our series of patients who were referred for contact dermatitis. In particular, of patients who tested positive for Bioban, 81% were positive for formaldehyde and 88% were positive for other formaldehyde releasers. Only 4 patients (patients 9, 12, 13, and 23) who were allergic to Bioban worked in industries that likely used Bioban. However, our data are incomplete because 7 patients who were allergic to Bioban were either retired or unemployed, so we do not know if they had previous work-related exposure to Bioban.

Overall, our patient population was relatively small compared to those of other studies because we had just started patch-testing with Bioban in the previous year. In the future, it would be helpful to analyze our data after a few more years of testing and also to bring people who had positive results back for retesting (Brinkmeier and colleagues found that only 2 of 10 patients had positive

results during their retest³). We then could also ascertain patients' previous employment to see if there is any link between their occupations and their allergies.

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