

Clinical allergy to cocamidopropyl betaine: reactivity to cocamidopropylamine and lack of reactivity to 3-dimethylaminopropylamine

JOHN P. MCFADDEN, JANET S. ROSS, IAN R. WHITE AND DAVID A. BASKETTER¹

St. John's Institute of Dermatology, St Thomas's Hospital, London, UK, ¹SEAC Toxicology Unit, Colworth House, Unilever Research, Sharnbrook, UK

7 patients allergic to cocamidopropyl betaine (CAPB) were detected by positive patch test reactions to Tegobetaine L7TM. These patients were then asked to participate in further testing to its potential impurities, cocamidopropylamine and 3-dimethylaminopropylamine (DMAPA). 4 of the 7 patients were tested to purified CAPB and cocamidopropylamine, with 2 reacting to the purified betaine on allergy patch testing and 3 reacting to cocamidopropylamine 0.1%. At another date, 6 of the 7 were successfully recalled for testing to DMAPA in the presence of sodium lauryl sulfate (SLS) or pure CAPB; 1/6 reacted to DMAPA in water, but only at very high concentrations, at least 3 orders of magnitude higher than that to which skin exposure would occur from use of products containing CAPB. Both SLS and CAPB increased the number of reactions recorded to high levels of DMAPA. However, positive reactions to much lower concentrations of DMAPA (≥ 100 ppm) were found in only 1/6 subjects and then only in the presence of the irritant SLS. 0/6 reacted to pure CAPB alone. Taken together, these results suggest that DMAPA is unlikely to be an important contact allergen in CAPB of appropriate quality. They also confirm that CAPB of suitable purity, where levels of both cocamidopropylamine and DMAPA are minimized, is unlikely to trigger reactions in those ostensibly allergic to the material.

Key words: cocamidopropyl betaine; dimethylaminopropylamine; cocamidopropylamine; allergic contact dermatitis; surfactants; cosmetics. © Munksgaard, 2001.

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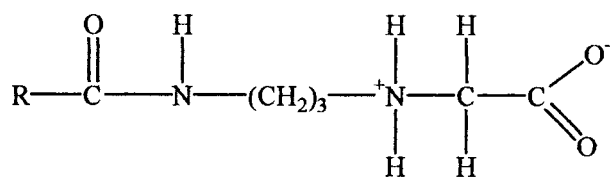
Cocamidopropyl betaine (CAPB) is the most commonly used amphoteric surfactant in the cosmetic industry. It is an infrequent cause of allergic contact dermatitis (1–4). However, there has been some question concerning the nature of the main allergen in allergic contact dermatitis from CAPB (1, 2). Angelini and co-workers have demonstrated that dimethylaminopropylamine (DMAPA) may be an important sensitizing impurity in CAPB (2). In contrast, others have reported that DMAPA is of lesser importance than the other impurity, cocamidopropylamine (1, 4). We report here our experience with investigative testing of CAPB-allergic subjects to the impurities cocamidopropylamine and DMAPA.

Patients, Methods and Results

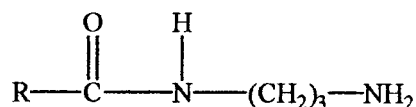
7 cases judged to have clinically relevant dermatitis to CAPB were detected through screening with Tegobetaine L7TM. This had been added to a routine

patch testing series and via this the patients were detected (6 female and 1 male, age range 26–69 years). The precise source of Tegobetaine L7TM was traced in 5 individuals, to a liquid soap (1 individual) and to eye make-up remover (4 individuals).

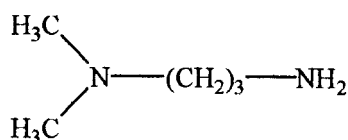
4 of these 7 patients were successfully recalled and tested to 1% aqueous partially purified CAPB (structure presented in Fig. 1) containing <0.5% cocamidopropylamine, and to 0.1% and 0.01% cocamidopropylamine (structure presented in Fig. 1). Allergen was applied to the back using 8 mm Finn Chambers on ScanporTM tape. Reactions were read at 2 and 4 days (D). The results are shown in Table 1. In 1 individual the original positive reaction to Tegobetaine L7TM 1% aq. appeared to be due solely to cocamidopropylamine sensitivity (patient no. 1) and in another (patient no. 2) to CAPB sensitivity. However, in this latter patient reading was only performed at D2, so irritancy cannot be excluded. The remaining 2 patients reacted to both



Cocamidopropyl betaine



Cocamidopropylamine



3-dimethylaminopropylamine

Fig. 1. Chemical structures.

the cocamidopropylamine and the CAPB. Patch tests in 10 controls were negative (data not shown).

6 of the 7 cases were later recalled and tested to DMAPA (structure presented in Fig. 1) with controls. The results are presented in Table 2. Subjects were patch tested to DMAPA from 0 ppm to 10000 ppm on both normal skin and tape-stripped skin (10 strips). In addition, subjects were tested to DMAPA at the same concentrations but in the presence of a weak irritant, a 0.2% aqueous solution of sodium lauryl sulfate (SLS, >99%, Aldrich, Poole, Dorset, UK), or in the presence of 1.0% pure CAPB (Tegobetaine C, Goldschmidt, Germany, <0.3% cocamidopropylamine, <10 ppm DMAPA). Allergens were applied with Finn chambersTM on ScanporTM tape. Reactions were read at D2 and D4. 1 of 6 reacted to DMAPA on

normal or on tape-stripped skin. However, reactivity was not seen at concentrations >1000 ppm (Table 2). With DMAPA in 0.2% SLS, there was reactivity in 3/6 subjects. In 1 subject this was only at concentration of 10000 ppm, in 1 at a DMAPA concentrations down to 1000 ppm and in the 3rd subject at DMAPA concentrations down to 100 ppm. Notably, none of these 6 subjects reacted to the control patch (i.e. 0 ppm DMAPA) containing 1% pure CAPB (the patch therefore containing <50 ppm cocamidopropylamine and <0.1 ppm DMAPA).

Discussion

CAPB is an amphoteric surfactant that is frequently used in cosmetic products, especially shampoos and bath products (3). It may be a relatively important occupational allergen in hairdressers (3). However, the chemical nature of the agent responsible for sensitization has not been unequivocally identified. Angelini et al. (2) found that, of 30 individuals who showed positive patch test reactions to cocamidopropylbetaine, all reacted to 1% DMAPA, there being no such reactions in 50 healthy controls. In contrast, Fowler found of 9 subjects reacting to 1% CAPB, 6 reacted to 0.1% cocamidopropylamine and none to the same concentration (=1000 ppm) DMAPA (1).

This latter report is in broad agreement with our own results, in which 75% of those patch test positive to CAPB also reacted to cocamidopropylamine. We found reactivity to DMAPA in only a minority, and then only at extremely high concentrations, suggesting that in these cases DMAPA is acting either as a weak allergen or perhaps as an irritant. Only 1 subject reacted to a concentration of DMAPA low enough to be related to potential normal skin exposure, and then only in the presence of an irritant.

Thus, we conclude that allergy to CAPB is most commonly due to the sensitizing intermediates (both cocamidopropylamine and DMAPA are strong sensitizers in the guinea pig maximization test – data not shown). However, in our subjects cocamidopropylamine represented the more relevant contact allergen compared to DMAPA.

Table 1. Reactivity to cocamidopropylamine in cocamidopropyl betaine-allergic subjects

Patient no.	Purified betaine 1% aq.		Cocamidopropylamine 0.1%		Cocamidopropylamine 0.01%	
	D2	D4	D2	D4	D2	D4
1	?+	–	+	+	+	?+
2	+	NT	–	NT	–	NT
3	+	+	+	++	–	–
4	?+	+	+	+	–	–

Table 2. Reactivity to dimethylaminopropylamine in cocamidopropyl betaine-allergic subjects

3-DMAPA (ppm)	Patient no. 1	Patient no. 2	Patient no. 3	Patient no. 4	Patient no. 5	Patient no. 6
normal skin						
10000	—	—	—	+	—	—
1000	—	—	—	—	—	—
100	—	—	—	—	—	—
10	—	—	—	—	—	—
0	—	—	?+	—	—	—
tape-stripped skin						
10000	—	—	—	++	—	—
1000	—	—	—	+	—	—
100	—	—	—	—	—	—
10	—	—	—	—	—	—
0	—	—	—	—	—	—
0.2% SLS normal skin						
10000	—	?+	++	++	+	—
1000	—	—	+	—	+	—
100	—	—	—	—	+	—
10	—	—	—	—	—	—
0	—	—	—	—	—	—
1% CAPB normal skin						
10000	+	—	++	++	+	?+
1000	—	—	+	—	+	—
100	?+	—	—	—	—	—
10	—	—	—	—	—	—
0	—	—	—	—	—	—

CAPB itself may less commonly act as an allergen; there is the possibility that cross-reactivity between the betaine and the amine complicates the picture. The recently described reduction in frequency of CAPB reactions on patch test surveillance (4) may in part be due to the use of a more purified CAPB with a low cocamidopropylamine content, both in consumer products and as a screening agent in diagnostic patch testing.

References

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product use test study. *Contact Dermatitis* 1997; 37: 276–281.

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Address:

J. P. McFadden
St. John's Institute of Dermatology
St. Thomas's Hospital
London SE1 7EH
UK