

Trend of contact allergy to cosmetic ingredients in Thais over a period of 10 years*

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Summary

Background. Contact allergy to cosmetic ingredients is common. However, there are no recent comprehensive studies on contact allergy to cosmetic ingredients in Asia.

Objectives. To identify positive patch test reactions in patients tested at Siriraj Hospital, Bangkok, Thailand to allergens present in cosmetics.

Methods. A retrospective review of medical records from the outpatient contact dermatitis clinic was conducted from January 1999 to December 2008. Patients with at least one positive patch test reaction to allergens associated with cosmetic ingredients were studied. The results were evaluated using Pearson's χ^2 -test with Yates' continuity correction or Fisher's exact test where appropriate, and a p -value <0.002 was considered to be statistically significant by Bonferroni correction.

Results. There were 1247 cases (239 males and 1008 females; mean age 38.5 years). Fragrance chemicals and preservatives were the most commonly recognized cosmetic allergens. Ammoniated mercury was the only allergen that showed a significantly increased frequency over the 10-year period ($p = 0.0008$).

Conclusions. Our study showed that ammoniated mercury is an emerging cosmetic allergen, showing an increased prevalence in recent years in Thailand. A focus is required on emerging cosmetic allergens and what may account for the upward trend of cosmetic contact dermatitis.

Key words: allergic contact dermatitis; cosmetic allergy; patch testing.

Cosmetics are widely used, and with their large volume of use, allergic contact dermatitis caused by cosmetic ingredients is common. The most common allergens found in cosmetics are fragrance substances and preservatives (1, 2). The rates of contact allergy

to cosmetic ingredients varies over time and with geographical location, owing to differences in the composition of these cosmetic products (3). In Asian countries, people often use cosmetic products made for the domestic markets as well as those cosmetics distributed by multinationals and manufactured according to the regulatory requirements of the United States or Europe.

The aims of this study were to: (i) describe the demographic characteristics of patients patch tested at the Contact Dermatitis Clinic, Siriraj Hospital, Mahidol University, Bangkok, Thailand with an allergic patch test reaction associated with the use of a cosmetic product; (ii) identify the prevalence rate of each of the cosmetic-related allergens; and (iii) investigate trends of cosmetic-related allergy in Thailand over the 10 years from 1999 to 2008.

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Material and Methods

Study population

The Siriraj Institutional Review Board approved this retrospective study of the use of clinical data from patients patch tested by the Contact Dermatitis Clinic, Siriraj Hospital during January 1999 to December 2008. All patients suspected of having allergic contact dermatitis who were referred to our clinic during this 10-year period were patch tested with a baseline series and with additional suspected allergens, depending on the patient's history (including non-cosmetic-related allergens), excluding primin. The cosmetic products brought in by the patients were tested according to the guidelines for cosmetic product patch testing (4). The allergens (Chemotechnique Diagnostics AB, Vellinge Sweden) in aluminium Finn Chambers® (SmartPractice, Phoenix, AZ, USA) were placed on unaffected skin on the upper back for 2 days, and the reactions were read on D2, D3, and D7, according to the guidelines of the International Contact Dermatitis Research Group (5). Patch test results and patient data were collected by chart review.

Statistical analysis

The data were divided into two populations according to the time periods 1999–2003 and 2004–2008. The data were analysed with descriptive statistics. Patients with at least one positive patch test reaction to the allergens associated with cosmetic ingredients were examined. The patch test results for each period of time were compared by using the χ^2 -test with Yates' continuity correction or Fisher's exact test where appropriate. The *p*-value was adjusted by the Bonferroni method for the correction of 23 factors, so a *p*-value <0.002 was considered to be statistically significant. All statistical analyses were carried out with SPSS™ v.18 (SPSS Inc., Chicago, IL, USA).

Results

There were 1247 patients (239 males and 1008 females), with ages ranging from 8 to 84 years (mean age 38.5 ± 13.9 years). Female patients were predominantly affected, and four times more likely than males to present for diagnostic work-up over the decade. There was an increased prevalence of atopic patients, persons with a positive atopic family history, and those with cosmetic allergy history in the study period (Table 1).

The patients were stratified into four age groups: (i) a <20-year-old group, representing those starting to use cosmetics; (ii) a 20–35-year-old group, comprising adults

Table 1. Demographic data of the patients

	1999–2003	2004–2008
No.	570	678
Male/female ratio	117/453	122/555
Age (years), mean $\pm$ SD	38.4 (14.3)	38.8 (13.9)
<20	52 (9.1)	34 (5.0)
20–35	200 (35.1)	269 (39.7)
36–50	198 (34.8)	238 (35.1)
>50	119 (20.9)	137 (20.2)
Atopic history, no. (%)	162 (28.54)	307 (45.4)
Atopic family history, no. (%)	17 (3.0)	200 (29.5)
History of rash caused by cosmetic products allergy, no. (%)	34 (6.0)	113 (16.7)

SD, standard deviation.

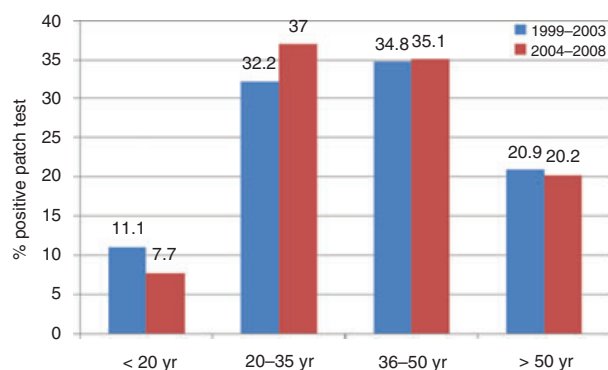


Fig. 1. Relationship between the rate of positive patch test reactions to cosmetic-related allergens and age of patients.

who typically use make-up frequently; (iii) a 36–50-year-old group, comprising the population who employ both make-up cosmetics, anti-aging products, and whitening agents; and (iv) a >50-year-old group, representing the older age demographic. The rate of positive patch test reactions to cosmetic-related allergens increased with age until >50 years (Fig. 1). Both males and females in the 36–50-year-old group showed the highest rate of contact sensitization to cosmetic-related allergens, with a female predominance. Among patients patch tested for suspected allergic contact dermatitis, the prevalence of positive patch test reactions to cosmetic-related allergens was 29%.

The top 10 cosmetic-related allergens for each period are shown in Table 2. Fragrance substances and preservatives were the most commonly recognized cosmetic-related allergens in this decade. Non-formaldehyde-releasing preservatives sensitized approximately four times more than formaldehyde-releasing preservatives in both periods. Antioxidants and nail

Table 2. Positive patch test reactions to cosmetic-related common allergens in each period

Allergen category	Cosmetic-associated allergens	Tested concentration (%)	% positive patch test reactions (ranking)		p-value
			1999–2003	2004–2008	
Fragrance	Fragrance mix I	8	17.7 (3)	17.8 (4)	1.00
	<i>Myroxylon pereirae</i>	25	8.8 (5)	10.3 (9)	0.42
	Fragrance mix II	14	ND	13.6 (8)	NA
	Sesquiterpene lactone mix	0.1	2.5	3.8	0.34
Preservatives	Formaldehyde	1	2.9	3.5	0.70
Formaldehyde-releasers	Diazolidinyl urea	2	3.4	3.6	1.00
	Imidazolidinyl urea	2	1.4	1.7	0.91
	Quaternium-15	1	1.2	1.5	0.80
	DMDM hydantoin	2.0	ND	3.5	NA
Non-formaldehyde-releasing preservatives	Parabens	16	7.2 (6)	9.2	0.248
	Methylchloroisothiazolinone/methylisothiazolinone	0.01	2.3	4.3	0.10
	Methyldibromo glutaronitrile	0.5	3.9 (10)	5.6	0.46
	Sorbic acid	2	2.2	1.6	1.00
	Benzalkonium chloride	0.1	19.3 (1)	18.7 (3)	0.99
	Quinoline mix	6	0.6	1.5	0.31*
	Thiomersal	0.1	10.6 (4)	15.4 (5)	0.33
	Triclosan	2	0	0	NA
	Benzyl alcohol	10	0	2.5	NA
	BHA	2	ND	4.0	NA
	BHT	2	ND	0	NA
	α -Tocopherol	100	ND	2.8	NA
UV absorbers	Benzophenone-3	10	0	1	NA
	PABA	10	1.6	0	NA
	Benzophenone-4	2	1.8	18.8 (2)	0.031*
	Butyl methoxydibenzoylmethane	10	0	6.3	NA
Vehicles, emulsifiers, and other base ingredients	Propylene glycol	5	0	3.0	NA
	Lanolin	30	4.0 (9)	4.1	1.00
	Ethylenediamine dihydrochloride	1	1.0	2.4	0.12
	Cocamidopropyl betaine	1	2.7	15.4 (6)	0.005
	Colophonium	20	7.2 (7)	7.1	1.00
Whitening agents	Hydroquinone	1	3.9	7.0	0.29
	Ammoniated mercury	1	3.8	14.9 (7)	0.0008 [‡]
Hair	p-Phenylenediamine	1	6.5 (8)	9.8 (10)	0.067
	2-Nitro-4-phenylenediamine	1	17.9 (2)	53.8 (1)	0.029*
Nails	Tosylamide/formaldehyde resin	10	ND	1.1	NA

BHA, 2-tert-Butyl-4-methoxyphenol; BHT, 2,6-Ditert-butyl-4-cresol; NA, not analysed; ND, not done; PABA, 4-Aminobenzoic acid; UV, ultraviolet.

*Fisher's exact test.

[‡]Statistical significance by Bonferroni adjustment, $p < 0.002$.

categories have been introduced into our patch test series during the last 5 years. 2-Nitro-4-phenylenediamine was in first place in the common cosmetic allergy ranking (29.3%). Ten of 12 cases were also patch test-positive for p-phenylenediamine.

We introduced cocamidopropyl betaine into our baseline series in 2003, and since then there have been increasing rates of positive patch test reactions to this amphoteric surfactant.

In addition, ammoniated mercury was the only allergen that showed a significantly increased tendency

to cause cosmetic allergies over the 10-year period, according to the Bonferroni correction ($p = 0.0008$; Table 2). Prevalence calculated by age group showed a significant peak of ammoniated mercury sensitization in the age groups 36–50 years ($p = 0.04$) and > 50 years ($p = 0.018$); this was also found in the same age groups for cocamidopropyl betaine sensitization ($p = 0.03$ and $p = 0.02$, respectively). Benzophenone-4 (2-hydroxy-4-methoxybenzophenone-5-sulfonic acid) allergy was found to be significant in patients aged 20–35 years ($p = 0.016$). Furthermore, 2-nitro-4-phenylenediamine

Table 3. Cosmetic product types associated with allergic patch test reactions

Cosmetic category	% of cosmetic products in each category of total number of the products	% positive reactions of the total number of reactions	% positive reactions in each product category
Baby products	5.0	3.5	5.9
Perfumes/fragrances	1.2	7.6	52.4
Hair care products: shampoo,perm solution, spray, gel, hair dyes	4.9	10.4	18.1
Deodorants/antiperspirants	1.1	3.5	27.8
Make-up	29.5	20.1	5.8
Oral hygiene products	7.3	4.9	5.7
Personal cleanliness products: cleansers	7.3	9.0	10.6
Skin care products: moistures, lotions	29.6	27.1	7.8
Sunscreens	10.4	7.6	6.3
Cosmetics, not otherwise specified	3.7	6.3	14.3

allergic reactions significantly increased in people above 50 years of age ($p = 0.003$).

There were a total of 1691 cosmetic products used in patch testing in addition to the baseline allergens. One hundred and forty-four (8.5%) of those products produced allergic patch test reactions. The most common product types associated with the allergic reactions are listed in Table 3. Among all of those positive reactions, skin care products, including moisturizers, body lotions, and aesthetic skin care products, constituted the most common product category showing positive reactions (27.08%). Make-up and hair care products were the second and third most common cosmetic product types producing allergic reactions (20.14% and 10.42%, respectively). Of those cosmetic products that patients brought for testing, perfumes/fragrances showed the highest rate of positivity (52.38%).

Discussion

This study is the only comprehensive study of cosmetic-related contact allergy in Asia during the last 20 years (6, 7). Given the widespread use of cosmetics, it is important to monitor their adverse effects. Our study has shown that allergy to cosmetic ingredients was four times more prevalent in females than in males. This is not surprising, as women usually apply more cosmetics, are more concerned about aesthetic problems, and are more likely to seek medical care even for mild reactions. There were unexpected findings of an increasing prevalence of atopic patients with either personal or family histories of atopic dermatitis or symptoms of allergic rhinitis, allergic conjunctivitis and asthma during the study period. These results, however, do agree with the International Study of Asthma and Allergies in Childhood phase III study, which presented a wide variation in epidemiological data,

including the increasing prevalence of allergy in Asian countries (8).

The number of people with a history of cosmetic allergy has shown an increase during the last 5 years. The prevalence of cosmetic allergy in our study was 29% of patients who were referred for patch testing, as compared with 2.4–36.3% in the same period of time in previous studies (2, 9, 10).

For two decades, the prevalence of allergic contact dermatitis has been rising; the main reason is probably the increase in consumer product use worldwide (11). The prevalence of positive patch test reactions to cosmetic-related allergens increased with age from <20, 20–35 and 36–50 years, and then dropped off at age >50 years. Biehl et al. found that most patients with cosmetic allergy are between the ages of 20 and 55 years (2). This may be attributable to the increasing use of cosmetics and the consequently greater chance of exposure to many ingredients during that period of life.

Fragrance substances and preservatives are among the most common allergens in allergic contact dermatitis caused by cosmetics (2, 9, 12). *p*-Phenylenediamine was introduced in the 1880s, and has been problematic ever since (4). The high sensitization rate of 2-nitro-4-phenylenediamine may result from cross-sensitization with *p*-phenylenediamine. *p*-Phenylenediamine allergy has risen from 6.5% to 9.8% during the decade in our clinic, similar to other parts of the world (13). This rise could be attributed to increased use of hair colouring products (14), occupational exposure in hairdressers (15), the popularity of temporary 'black henna tattoos' containing high concentrations of *p*-phenylenediamine (16), increased use of many chemically related compound that may cross-react with *p*-phenylenediamine (e.g. cyclooxygenase-2 inhibitors, sunscreen agents, and textile dyes) (14), and

the fact that our Asian patients usually tend to have higher rates of *p*-phenylenediamine allergy (17).

Benzalkonium chloride is a quaternary ammonium cationic surfactant and a strong irritant. It is widely used as a preservative in cosmetics, ophthalmic preparations, and skin disinfectants. The rates of positive patch test reactivity were high in this study when benzalkonium chloride 0.1% aqua was used for patch testing. The reactions were probably irritant. Recent reports have shown that benzalkonium chloride is a rare contact allergen (18–20).

Quaternium-15 was the most common cosmetic allergen identified from North American Contact Dermatitis Group (NACDG) reports (9, 21). However, it was not even in our top 10 cosmetic-related allergens. Quaternium-15 is unpopular as an ingredient of cosmetics in Asia, as reported by Minamoto (7).

Cocamidopropyl betaine was included in our baseline series in 2003, and the prevalence of allergy quickly increased, so that it became the second most common cosmetic allergen overall. Our data are consistent with the findings of the NACDG, which reported a prevalence between 3.0% and 7.2% (22). The increasing rates of patch test positivity led to cocamidopropyl betaine being named 'Allergen of the Year' in 2004 (23). However, cocamidopropyl betaine is a problematic patch test preparation, with a low reaction index and a high positivity ratio (24).

The most important cosmetic-related allergen that showed significantly increased rates of patch test positivity during the last 5 years was ammoniated mercury ($p < 0.002$). Ammoniated mercury is an illegal ingredient used to bleach or lighten the skin, which is a common practice among dark-skinned women in Asia and African countries (25–27). Primary sensitization may also result from inoculation with vaccines

containing thiomersal preservatives, antiseptics containing thiomersal, or amalgam dental restorations. Given our positive patch test result for ammoniated mercury, cross-reaction with thiomersal may be a factor. However, the significantly increased rates of ammoniated mercury patch test positivity should be investigated. A recent study also showed that ammoniated mercury was the second most common allergen causing facial dermatitis in Thais (28). Bleaching agents containing ammoniated mercury have been used for >20 years in Thailand. Their popularity increased during the 2000s (27), which corresponds to our study period. The ammoniated mercury sensitization found highest in the patients age >36 years who have melasma, a common problem in this ethnic Asian population.

Our data showed that 8.5% of patients' cosmetic products caused positive patch test reactions; the most common product type comprised skin care products (moisturizers, body lotions, and aesthetic skin care products). Among each cosmetic category, perfumes/fragrances showed the highest rate of patch test positivity. Therefore, perfumes/fragrances should be included for patch testing in patients with suspected cosmetic allergy. The importance of testing patients with their own products when cosmetic allergic contact dermatitis is suspected is well known (29).

The prevalence of allergic reactions to cosmetics may vary by types of cosmetic in use in individual regions, cosmetic product regulations, and time period. Dermatologists should review emerging cosmetic allergens and periodically evaluate the appropriate patch test series for newer allergens. As older cosmetic ingredients are replaced with newer chemicals, these substances also need to be monitored for the development of sensitivity.

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