

ORIGINAL ARTICLE

Photopatch testing in a tropical country, Thailand: 20 years' experience

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Abstract

Background: Photoallergic contact dermatitis is one of the important parts of photodermatoses. The investigation of choice is photopatch testing. However, reports with photopatch test results from Asian countries are scarce. The objective of this study was to determine the prevalence of positive photopatch test reactions and to ascertain the common photoallergens among Thai patients during 1998-2018.

Methods: We retrospectively reviewed the records of 339 patients who were clinically suspected of having photoallergic contact dermatitis and had undergone photopatch testing.

Results: A total of 44 photoallergic contact reactions in 38 patients (11.2%) were found. The positive photoallergic reactions were mainly found with organic ultraviolet filters and fragrances.

Conclusions: Organic ultraviolet filter chemicals especially benzophenone-3 and fragrances were found to have a high prevalence of photoallergic contact reactions. Monitoring of the photoallergens employed in photopatch tests should be conducted periodically to provide the best patient care.

KEYWORDS

photoallergic contact dermatitis, photoallergic contact reactions, photopatch test, sunscreen allergy, ultraviolet filters

1 | INTRODUCTION

Photoallergic contact dermatitis (PACD) occurs when exogenous agents (termed photoallergens) contact the skin and are subsequently exposed to ultraviolet (UV) light. After exposure to the radiation, especially UVA, the substances are photochemically converted to new haptens or allergens which can elicit delayed-type hypersensitivity reactions and cause dermatitis on the sun-exposed skin of patients.¹ Photopatch testing is the standard investigation for PACD diagnoses and causative-allergen identification.

Being located in a tropical region near the equator, Thailand is hot and humid (average humidity, 66%-79%) and has a high UV index (average, 10-12). We might expect different photopatch test positivity levels and causative allergens in Thailand than those found in the other climate zones. Moreover, exposure to the culprit photoallergens is often altered over time and geographic areas. Therefore, continuous surveillance of photopatch test reactions in each region is necessary to ensure sound preventive intervention and management.

The prevalence of patients who have dermatitis on photo-exposed areas and for whom PACD is subsequently confirmed by

photopatch testing has been reported to be around 2% to 10% globally.² Most of the related research has been conducted in Europe and the United States. According to previous studies, sunscreens and topical nonsteroidal anti-inflammatory drugs (NSAIDs) are usually the most common causative photoallergens.² However, reports from Asian countries are scarce, and photoallergens might differ within regions and over time. Therefore, the purpose of the current study was to analyse the results of photopatch test reactions and to specify the main photoallergens during the last 2 decades in Thailand.

2 | MATERIALS AND METHODS

2.1 | Study population and photopatch tests

The study was approved by the Siriraj Institutional Review Board (Si337/2019). This retrospective, descriptive study included 339 patients who had undergone photopatch testing during the years 1998–2018. The patients had been referred to the Contact Dermatitis Clinic, Siriraj Hospital, as they had dermatitis on photo-exposed areas and were clinically suspected of having PACD.

Our baseline patch test series had been adapted from the European and International baseline series.³ The set of allergens used for photopatch testing in this study had been continually updated over the 20-year research period, in accordance with scientific publications. Previously known drug photoallergens (such as chlorpromazine, promethazine and NSAIDs) were not patch-tested due to the absence of recent or previous histories of usage of those drugs in our patients. The tests were performed using allergens (Chemotechnique Diagnostics) in aluminium Finn Chambers (SmartPractice).

Two sets of allergens were applied on normal skin on the upper back of patients on day (D) 0. After 48 hours, the first set of allergens was irradiated with UVA 10 J/cm² (UVA 700L; Waldmann), while the other set was left unirradiated.⁴ The reactions were interpreted by dermatologists 20 minutes after the irradiations on D2 and again on D4. The results were reported using the International Contact Dermatitis Research Group grading system, and they were interpreted according to the UK multicentre photopatch study group guidelines.⁵ A positive contact reaction was defined as a reaction that occurred equally on both the irradiated and non-irradiated skin, while a positive photoallergic reaction was a reaction that presented only on the irradiated skin.

2.2 | Statistical analysis

The results of the photopatch tests during the study period were assessed. Analyses were conducted of the patients' demographic and clinical data (comprising age, sex, atopy history, family history of atopy, history of cosmetic and drug allergies, and distribution of skin rash). A history of cosmetic allergy was defined as having a previous presentation of a rash caused by the application of a cosmetic

product. A history of atopic tendency was defined as having at least one of the atopic markers (a history of atopic eczema, asthma or hay fever). Descriptive statistics were presented as frequency and percentage, or as mean $\pm$ standard deviation. Data were analysed using PASW Statistics, version 18.0 (SPSS Inc, Chicago, IL, USA).

3 | RESULTS

Of the 339 enrolled photopatch-tested patients, 38 (11.2%) were photopatch test positive. The vast majority were female, with a male to female ratio of 1 to 4.4. However, the male to female ratio for the positive photoallergic reactions was 1:3.2. The mean age ($\pm$ SD) of all patients was 43.0 ($\pm$ 14.3) years, ranging from 11 to 81 years, while the age of the positive photoallergic reaction patients was slightly higher. Thirteen patients (3.8%) out of all of the patch-tested patients, but only one of the positive photoallergic reaction patients, had outdoor occupations. The three most common eruption sites were the face, arms, and head and neck. A total of 44 photoallergic reactions in 38 patients were observed. The demographic data of the included patients and the positive photoallergic reaction patients are shown in Table 1.

The allergens used in the photopatch tests and the frequencies of the positive photoallergic and positive contact reactions are detailed in Table 2. In the fragrances and plants groups, the common photoallergens were Fragrance mix II, Fragrance mix I and *Myroxylon pereirae* resin. Benzophenone-3 had the highest prevalence of positive photoallergic contact reactions in the sunscreen group.

Five photoaugmented contact reactions were observed in four patients (1.2%). Fragrance mix I was found to be the main cause in 4 out of 315 (1.3%) patients, whereas *Myroxylon pereirae* resin was the culprit in the case of one patient.

4 | DISCUSSION

This study reviewed the photopatch test results of 339 patients over the last 2 decades in Thailand. Regarding the demographic data of the patients in this study, females were tested more frequently than males. This finding correlates with the proportions of the genders of patients referred to our clinic.⁶ Nevertheless, the males demonstrated a higher prevalence of positive photoallergic reactions (9/63, 14.3%) than the females (29/276, 10.5%). This male predominance was similar to the findings of a previous study by a European multicentre photopatch study taskforce.² This particular finding is difficult to explain, but it is possible that the males might have had a higher exposure to the sun through their work or leisure activities than the females.

The predominant sites of the rash in this study—the face, arms, and head and neck—are mainly found on sun-exposed skin. Nevertheless, 5%–8% of our patients presented with an eruption on their trunk and legs. The explanation may be that Thais tend to prefer to wear shorts, sleeveless shirts or no shirts due to the tropical

TABLE 1 Demographic data of all photopatch-tested patients and patients with positive photoallergic reactions

Demographic data	Total patients N = 339	Positive photoallergic reaction patients N = 38
Sex, n (%)		
Male	63 (18.6)	9 (23.7)
Female	276 (81.4)	29 (76.3)
Age (years), mean (SD)	43 (14.3)	45.2 (12.8)
Duration of rash (months), mean (SD)	23.9 (39.5)	24.5 (39.3)
Outdoor occupation, n (%)	13 (3.8)	1 (2.7)
Atopy history, n (%)	111 (32.7)	17 (44.7)
Atopy family history, n (%)	86 (25.4)	11 (28.9)
History of cosmetic allergy, n (%)	60 (17.7)	8 (21.1)
History of drug allergy, n (%)	65 (19.2)	6 (15.8)
Sites of rash, n (%)		
Face	232 (68.4)	25 (65.8)
Arms and forearms	134 (39.5)	12 (31.5)
Head and neck	91 (26.8)	10 (26.3)
Trunk	46 (13.6)	3 (7.9)
Hands	44 (13)	8 (21.1)
Legs	36 (10.6)	2 (5.3)
Feet	9 (2.7)	2 (5.3)

Note: No statistically significant difference in any characteristics between all photopatch-tested patients and positive photoallergic patients.

climate. Moreover, it could be possible from the spreading of allergic rash beyond the site of exposure. The prevalence of positive photoallergic reactions among the patients who worked outdoors (2.7%) was lower than expected, and it was not significantly different to the corresponding rate for the indoor occupation patients. Outdoor occupations in our country, such as a farmer or mason, do not seem to have influenced the incidence of positive photoallergic reactions. The major photoallergens in our study were organic UV filters and fragrances, which are cosmetic ingredients in sunscreen. This finding may relate to the frequent history of cosmetic allergies found among the patients with a positive photoallergic reaction.

The frequency of photoallergic reactions (11.2%) found by our study was lower than we had expected, given the findings of research conducted in other countries.⁷⁻⁹ Living in a tropical area does not seem to predispose individuals to developing a photoallergic reaction. The prevalences of the positive photoallergic reactions and common photoallergens found in various countries are summarised in Figure 1.^{1,2,5,7-21}

In terms of photoallergens, as distinct from studies from Europe and the Americas, the main photoallergens in Asia are primarily

from the fragrance group, such as the fragrance mix and *Myroxylon pereirae* resin, which corresponds with our results. This interesting aspect might occur for many reasons. Differences in the patient demographics or skin-phototypes of diverse population groups might have resulted in the dissimilarity of the photopatch test reactions.⁸ Moreover, the amount of UV that people are exposed to in daily life tends to be higher in Asia. The absence of a globally standardised methodology for photopatch testing might be another explanation for the different test results.²²

Although fragrance can cause either photoallergic or phototoxic reactions. Phototoxic is non-immune, photo-induced process which resulted in direct toxic to keratinocyte.²³ This reaction should have occurred in everyone who received adequate enough amount of substance and light.²⁴ Notwithstanding that phototoxic reactions might not be entirely excluded in cases showing positive photopatch tests to fragrances, our positive numbers were low (<4%) and many control patients (showing no reactions) were included. Moreover, the diminished reactions to fragrances on the irradiated side were not observed. Therefore, in accordance with previous studies,^{16,17,21} some fragrance allergens might provoke true photoallergic reaction which is perhaps underestimated in clinical practice. Additional fragrances allergens might be considered in patients with a suspicious history of fragrances use with photodistributed skin lesions.

Whether UVA dose of 10 J/cm² might lead to phototoxic or false-positive photoallergic reactions in our study especially to fragrance was also concerned. However, our Thai patients have high skin phototype (III-V) and our previous data showed an average minimal erythematous dose (MED) for UVA in Thais is above 30 J/cm².²⁵ Other Asian countries which have resembled skin phototype to our population also performed photopatch test with dose 10 J/cm².^{11,16,17} As a result, dose of 10 J/cm² has not been considered to induce either phototoxic reaction or false-positive photocontact reaction in high skin phototype patients.

As with previous reports, benzophenone-3 demonstrated a high prevalence of positive photoallergic reaction (4.7%); this is because it has been frequently used as a photoprotective agent in sunscreens and personal care products.^{5,11,26,27} However, positive photoallergic reactions to benzophenone-3 in our participants mainly come from sunscreen.

Bis-ethylhexyloxyphenol methoxyphenyl triazine (Tinosorb S) produced a positive photoallergic reaction in this study. Tinosorb S is a new generation, broad-spectrum, organic filter.^{28,29} Its use in the European Union was approved in 2000, and it is currently awaiting the approval of the United States Food and Drug Administration.³⁰ The accessibility of, and exposure to, this UV filter might be less than that for conventional UV filters. Consequently, Tinosorb S has rarely been reported in the literature as causing a photoallergic contact reaction.² Nevertheless, as the usage of this new organic UV filter has been increasing worldwide, it should be continually observed to identify any further reports of contact dermatitis or PACD.³¹

Methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) is a preservative commonly used in cosmetic products, including sunscreen.³² Both MCI/MI and MI have caused an epidemic of allergic

TABLE 2 The prevalences of positive reactions to photoallergens

Allergens	Tested concentration vehicle %	No. tested	Positive photoallergic reaction		Positive contact reactions	
		N	N	(%)	N	(%)
Fragrances and plants						
Fragrance mix II	14% pet	179	7	(3.9)	5	(2.8)
Fragrance mix I	8% pet	315	10	(3.2)	26	(8.3)
Myroxylon pereirae resin	25% pet	308	10	(3.2)	13	(4.2)
Jasmine synthetic	2% pet	90	2	(2.2)	0	(0)
Sesquiterpene lactone mix	0.1% pet	93	1	(1.1)	1	(1.1)
Ylang ylang oil	2% pet	91	1	(1.1)	1	(1.1)
Rose oil Bulgarian	2% pet	89	0	(0)	0	(0)
Preservatives						
Methylchloroisothiazolinone/ methylisothiazolinone	0.02% aq	25	1	(4)	1	(4)
Methylisothiazolinone	0.2% aq	24	0	(0)	2	(8.3)
Triclosan	2% pet	127	0	(0)	1	(0.8)
Miscellaneous						
Colophony	20% pet	40	0	(0)	0	(0)
Sunscreen agents						
Organic chemicals						
Benzophenone-3	10% pet	170	8	(4.7)	3	(1.8)
Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine	10% pet	53	1	(1.9)	0	(0)
4-Methylbenzylidene Camphor	10% pet	67	1	(1.5)	0	(0)
Phenylbenzimidazole Sulphonic Acid	10% pet	117	1	(0.9)	0	(0)
Benzophenone-4	2% pet	127	1	(0.8)	2	(1.6)
Benzophenone-10	10% pet	67	0	(0)	1	(1.5)
Butyl Methoxydibenzoylmethane	10% pet	119	0	(0)	0	(0)
Homosalate	5% pet	66	0	(0)	0	(0)
Ethylhexyl Methoxycinnamate	10% pet	69	0	(0)	0	(0)
Octocrylene	10% pet	53	0	(0)	0	(0)
Ethylhexyl Salicylate	5% pet	43	0	(0)	0	(0)
Organic particulates						
Methylene Bis-Benzotriazolyl Tetramethylbutylphenol	10% pet	52	0	(0)	2	(3.8)
Inorganic particulates						
Titanium dioxide	10% pet	44	0	(0)	0	(0)

Abbreviations: aq, aqua; Pet, petrolatum.

contact dermatitis.³³ However, MCI/MI or MI alone has hardly been reported to cause photoaggravated reactions or photoallergic reactions.^{34,35} MCI/MI and MI were included in our photoallergen set in 2018, but only one case demonstrated a positive photoallergic contact reaction, with confirmation of current clinical relevance from the cosmetic products used by the patient. Further continual observation of isothiazolinones as new photoallergens is needed.

Our limitation was that, over its 20-year research period, the set of photopatch allergens was continuously modified and was not exhaustive. We began our photopatch testing programme in 1998 by utilising the previously reported photoallergens and, since then, we have progressively adjusted our photoallergen set to make it more appropriate for the Thai population. Initially, our photoallergens were mainly comprised of Fragrance mix I and *Myroxylon pereirae*



FIGURE 1 Prevalence of positive photoallergic reactions and common reported photoallergens in various countries

resin. Later, Fragrance mix II, conventional organic UV filter and plant extract were sequentially added to our test. Novel organic UV filter and isothiazolinones were the last groups to be incorporated into the battery. As a result of these evolving changes to the set of allergens used for photopatch testing during the study period, the test numbers for the individual allergens are quite disparate. Moreover, the lack of reading on D7 after irradiation might lead to an underestimation of positive reactions.

In conclusion, benzophenone-3 in sunscreens and other allergens mostly found in cosmetics and household products, such as fragrances, were the common causes of positive photoallergic contact reactions in Thailand. MCI/MI or MI alone and novel organic UV filter might be photoallergens that should be further monitored. We should continually observe and be aware of new photoallergens. The photopatch test battery needs to be updated periodically to provide the best patient care.

CONFLICT OF INTEREST

All authors have neither conflicts of interest nor financial support to declare.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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