

Acute irritation thresholds in subjects with Type I – Type VI skin

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It has long been recognized that human skin can be subdivided into simple categories based on their sensitivity to sunlight – from Type I, never tans, always burns, to Type VI, marked constitutive pigmentation. There is also evidence that the more readily sunburnt type of skin is also more susceptible to the effect of irritants. In the present work, the irritancy threshold for sodium lauryl sulfate (SLS) has been assessed using a recently described 4-h acute skin irritation patch test. A total of 110 subjects covering all 6 skin types were examined and their threshold for acute irritancy defined as the lowest concentration of SLS, applied under 4-h occlusion, which would induce a clinically detectable irritant response. The SLS dose response generated using a range of concentrations (0.1%–20%) demonstrated that there was no significant difference between the groups under these test conditions. Even for Type VI skin ($n=25$), the dose-response curve fell within the general pattern. These results reinforce the general applicability of predictions of acute irritant potential made in groups of human volunteers.

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Skin irritants are the major cause of contact dermatitis and, in the process of screening new chemicals, studies must be carried out to determine the potential irritancy of such substances (1). Recently, an approach involving the safe and ethical use of human volunteers for this purpose, the human 4-h patch test, has been described in detail (2–6). Furthermore, the possible variables affecting the method have been investigated (7–9). This work has shown that a key aspect of the assay is the use of a positive control for each test panel, not least because the interindividual variation in the response to irritants is large (8). To evaluate this further, we chose to examine the classic skin types (10) to assess whether their threshold for acute skin irritation differed. To do this, we employed the classic control irritant, sodium lauryl sulfate (SLS), which is also recommended as the positive control for the human 4-h patch test (6).

Materials and Methods

Volunteer subjects

110 volunteer subjects were recruited. They were assessed for their skin pigmentation, history of ability to tan and ease of burning. This allowed

them to be categorized into 1 of 6 skin types (10) (Table 1). Subjects with atopic eczema were excluded, as testing on uninvolved skin in a small number of individuals has suggested a substantially reduced threshold (11).

Patch test method

This has been described in detail earlier (7, 8). Briefly, aqueous SLS solutions, from 0.1%–20%, were dosed (0.1 ml) into 25 mm Hill Top chambers (Hill Top Companies, Cincinnati, Ohio, USA) which were applied to the skin of the upper outer

Table 1. Skin types and categorization of the test subjects

Skin type	Description	No. subjects	Age range (years)
I	always burn, never tan	16	18–75
II	usually burn, sometimes tan	30	20–78
III	usually tan, sometimes burn	16	28–79
IV	always tan, never burn	7	27–74
V	moderate constitutive pigmentation	16	22–65
VI	marked constitutive pigmentation	25	17–77

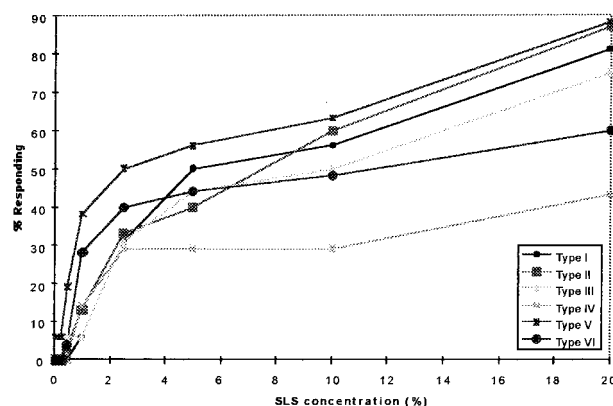


Fig. 1. SLS thresholds in Type I – VI skin.

arm for 4 h. Patch test sites were read on a simple 0, +, ++, +++ scale at 1, 2 and/or 3 days; the primary assessment parameters for the identification of the presence of skin irritation were significant erythema, surface change and /or induration. Any score $\geq +$ on any day was regarded as a positive result. SLS (99%) was obtained from BDH, Poole, UK.

Results

A clear dose response was apparent in the majority of subjects; only 1 individual reacted at SLS concentrations below 0.5%, whilst overall $>75\%$ reacted to 20% SLS. A plot of the dose-response curve for each of the skin-type groups shows there was little difference between them (Fig. 1). The detailed results of the dose-response study and the identification of the skin irritation thresholds in the different skin types are contained in Table 2. There was no overt difference in the SLS skin irritation thresholds across skin Types I – VI, although the figures for Type IV skin are somewhat less precise due to the low numbers.

Discussion

Irritant contact dermatitis is an important clinical problem. Thus, it is essential that those substances which possess significant potential to irritate skin are identified and the risk they present is managed appropriately. Recently, a new approach to the identification of such substances has been described (2–6), which aims to provide high quality information through the use of a 4-h patch test in human volunteers. However, one of the potential drawbacks of such an approach is that data obtained from a limited number of human volunteers (in practice about 30) may not be generally applicable, e.g., across ethnic groups or for different types of skin. It has been reported that there may be ethnic differences in the susceptibility to skin irritation (12, 13). However, these differences may be quite subtle and of little importance in terms of simple identification of acute skin irritation potential (8). What may be more important are inter-individual differences. The impact of atopic status on the response to an acute irritation patch test has already been examined in some detail. Mucosal atopy has little impact, whilst skin atopics are definitely more reactive (9, 14, 15). Sex differences in susceptibility to skin irritation may be quite limited (16). However, none of these parameters, singly or combined, would be sufficient to explain the large range of sensitivity to skin irritation that has been identified (e.g., 8, 17, 18).

Consequently, in this present work, we extended our previous studies (7, 8) to provide an examination of possible differences in skin reactivity between the classic skin types based on their sensitivity to sunlight (10). We had anticipated that there would be a decreasing irritability from Type I to Type VI skin. Such a trend had been indicated in an earlier study, although this work only examined Types I – IV skin in a total of 44 subjects (19). The results of our testing with the 4-h occluded patch suggested that there exists no substantial differences

Table 2. Irritation thresholds to SLS in skin Types I – VI

SLS (%)	Type I		Type II		Type III		Type IV		Type V		Type VI	
	no.	%	no.	%	no.	%	no.	%	no.	%	no.	%
0.1	0	0	0	0	0	0	0	0	1	6	0	0
0.25	0	0	0	0	0	0	0	0	0	6	0	0
0.5	0	0	1	3	1	6	0	0	2	19	1	4
1.0	1	6	3	13	0	6	1	14	3	38	6	28
2.5	4	31	6	33	4	31	1	29	2	50	3	40
5.0	3	50	2	40	2	44	0	29	1	56	1	44
10.0	1	56	6	60	1	50	0	29	1	63	1	48
20.0	4	81	8	87	4	75	1	43	4	88	3	60
–ve	3	100	4	100	4	100	4	100	2	100	10	100

in the proclivity to acute skin irritation in these subsets, although in one case (IV), the group size was relatively small. Indeed, the results indicated that Type IV skin presented a slightly lower level of irritant reactivity at the higher SLS concentrations, but, over lower SLS concentrations (0.1%–2.5%), a similar proportion of the Type VI group reacted in comparison with the other 5 skin types.

It is interesting to consider why our data differ from that reported by Frosch & Wissing (19). Their work characterized the light sensitivity of the volunteers by measuring minimal erythmal dose (MED) and then examined the irritant response to a number of substances applied for 20 h under occlusion. Reactions were scored at only 1 time point. The data showed very large scatter, but there was a clear trend of increasing sensitivity to irritation with lower MED values, including with SLS. The studies reported in the present work examined the acute irritation response to SLS only in the context of the 4-h patch test, but used larger group sizes than the earlier work and also examined Types V and VI skin. These skin types would have even higher MED values and thus, on the basis of the published results, might be anticipated to be even more resistant to irritation. At least under the conditions we employed, this was clearly not the case. Thus, in summary, it can be concluded that data on acute skin irritation potential produced in a modestly sized group of human volunteers does yield data of relevance to the general population.

Note added in Proof

Whilst this paper was in press, one study has shown skin atopic and non-atopic susceptibility to acute skin irritation to be very similar (20).

References

1. EC Annex to Commission Directive 92/69/EEC of 31 July 1992 adapting to technical progress for the seventeenth time Council Directive 67/548/EEC on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances. *Official Journal of the European Communities* 1992; L383A: 35.
2. Basketter D A, Whittle E, Chamberlain M. Identification of irritation and corrosion hazards to skin: an alternative strategy to animal testing. *Food and Chem Toxicol* 1994; 32: 539–542.
3. Basketter D A, Whittle E, Griffiths H A, York M. The identification and classification of skin irritation hazard by human patch test. *Food and Chem Toxicol* 1994; 32: 769–775.
4. York M, Basketter D A, Cuthbert J A, Neilson L. Skin irritation testing in man for hazard assessment – evaluation of four patch systems. *Human and Experimental Toxicology* 1995; 14: 729–734.
5. York M, Griffiths H A, Whittle E, Basketter D A. Evaluation of a human patch test for the identification and classification of skin irritation potential. *Contact Dermatitis* 1996; 34: 204–212.
6. Basketter D A, Chamberlain M, Griffiths H A, York M. The classification of skin irritants by human patch test. *Food and Chemical Toxicology* 1997; 35: 845–852.
7. Judge M R, Griffiths H A, Basketter D A, White I R, Rycroft R J G and McFadden J P (1996) Variation in response of human skin to irritant challenge. *Contact Dermatitis* 1996; 34: 115–117.
8. Basketter D A, Griffiths H A, Wang X M, Wilhelm K-P, McFadden J. Individual, ethnic and seasonal variability in irritant susceptibility of skin: the implications for a predictive human patch test. *Contact Dermatitis* 1996; 35: 208–213.
9. Basketter D A, Blaikie L, Reynolds F. The impact of atopy on a predictive test of acute skin irritation potential. *Contact Dermatitis* 1996; 35: 33–39.
10. Parrish J A, White H A D, Pathak M A. Photomedicine, In: Fitzpatrick T B, Eisen A Z, Wolff K, Freedberg I M, Austen K F (eds): *Dermatology in general medicine*. New York: McGraw-Hill, 1979: 942–994.
11. Nassif A, Chan S C, Storrs F J, Hanifin J M. Abnormal skin irritancy in atopic dermatitis and in atopy without dermatitis. *Archives of Dermatology* 1994; 130: 1402–1407.
12. Berardesca E, Maibach H I. Racial differences in sodium lauryl sulphate induced cutaneous irritation: Black and white. *Contact Dermatitis* 1988; 18: 65–70.
13. Berardesca E, Maibach H I. Sodium lauryl sulphate induced cutaneous irritation. Comparison of white and hispanic subjects. *Contact Dermatitis* 1988; 19: 136–140.
14. Nassif A, Chan S C, Storrs F J, Hanifin J M. Abnormal skin irritancy in atopic dermatitis and in atopy without dermatitis. *Archives of Dermatology* 1994; 130: 1402–1407.
15. Willis C. and Poskitt L. The influence of atopy on susceptibility to irritation. *Allergologie* 1995; 18: 446.
16. Lammintausta K, Maibach H I, Wilson D. Irritant reactivity in males and females. *Contact Dermatitis* 1987; 17: 276–280.
17. Bjornberg A. *Skin reactions to primary irritants in patients with hand eczema*. Thesis, Goteborg, Sweden, 1968.
18. Lammintausta K, Maibach H I, Wilson D. Susceptibility to cumulative and acute irritant dermatitis. *Contact Dermatitis* 1987; 17: 276–280.
19. Frosch P J, Wissing C. Cutaneous sensitivity to ultraviolet light and chemical irritants. *Arch Derm Res* 1982; 272: 269–278.
20. Basketter D A, Miettinen J, Lahti A. Acute irritant reactivity to sodium dodecyl sulphate in atopic and non-atopic. *Contact Dermatitis* 1998; 38: in press.

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