Assessment of the capability of formulations on effectively mitigating the erythema triggered by niacinamide in 24-h occlusive human patch test

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Introduction:

In recent decades, niacinamide applied topically is proven to be effective in improving many skin conditions[2]. Although, it was proven to be capable of anti-inflammatory, which reduced the skin's redness considered as an indication. There is still a chance that consumers might experience the irritation introduced by niacinamide, shown as the symptom erythema, especially in the Asian population[3]. The intolerance would impact consumers' willingness to use it. Thus, developing a formulation that could ensure efficacy and safety is critical. Owing to the specific physiological activities, hexyldecanol, active substances combination (gallic acid, α-arbutin and Hydroxyethylpiperazine ethane sulfonic acid) are chosen as the potential candidates in mitigating the niacinamide-induced irritation.

Accordingly, the present study was designed to determine whether these ingredients in different schemes have the potential for mitigating niacinamide-induced irritation. Single occlusive human patch test has been developed for accessing the skin irritancy/mildness potential of cosmetics and cosmeceutical products and has been widely recognized [11]. In this study, 24-h occlusive human patch tests developed for assessing niacinamide-induced irritation through erythematous reaction was exceeded as a short-term screening protocol for the optimized formula.

Materials & Methods:

Materials:
Positive control: 4% niacinamide (purchased from supplier A)

There were five different schemes:
niacinamide supplier A:
- 4% niacinamide + 1% hexyldecanol
- 4% niacinamide + 2% hexyldecanol
- 4% niacinamide + 0.1% HEPES+0.01% gallic acid+0.5% α-arbutin
- 4% niacinamide + 1% hexyldecanol + 0.1% HEPES+0.01% gallic acid+0.5% α-arbutinl

niacinamide supplier B:
- 4% niacinamide + 1% hexyldecanol + 0.1% HEPES+0.01% gallic acid+0.5% α-arbutinl

All the schemes were added into the identical cream vehicle.

Subjects:
Twenty-eight healthy Chinese volunteers, five men and twenty-three women, aged 23-41 years (mean±SD, 29±5), were enrolled in 24-h occlusive human patch tests for schemes screening
Thirty healthy Chinese volunteers, nine men and twenty-one women, aged 20-51 years (mean±SD, 31±8), participated in the human patch test designed to verify the safety and tolerance of the least irritation formula chosen from the former human patch tests
- free of skin or systemic diseases
- not apply any topical preparations on the test areas within 30 days before the test started
- no moles, scars, and some other blemishes
- female subjects not pregnant or breasting feeding
- written informed consent was obtained from all subjects
- approved by the local ethical committee

Occlusive Human Patch Test:
Single 24-h occlusive human patch test was utilised in this study for both scheme screening and final formula verification. A blank Finn Chamber was also applied to each subject as blank control.

The investigator assessments, after the patch removed for 0.5h, 24h and 48h, were measured and evaluated. All the visual gradings were scored under the guidance of the terminology established by the International Contact Dermatitis Research Group (ICDRG).

Statistics:
Irritation scores (visual grading score) for each treatment were graded as described above, ranging from 0 to 4. Moreover, in each grading scale classification, the skin adverse reactions of subjects were counted at all the observation points.

Results & Discussion:

Occlusive human patch tests for schemes screening

- Only the grade 1 irritation score was observed in all three patch tests, indicating that the niacinamide shows a low potential in triggering severe irritation.
- 26 out of 28 subjects suffered from the erythematous reaction at 4% niacinamide treatment (table 1).
- Active substances (0.1% HEPES+0.01% gallic acid+0.5% α-arbutinl) alone did not show a significant soothing effect on niacinamide irritation since 23 subjects experienced erythema at the 4% niacinamide + active substances test site.
- 1% hexyldecanol was verified to be capable of intimidating the niacinamide-induced irritation effectively. However, the percentage of erythema reactions were still relatively high. There was still 46% (13 out of 28) of subjects who experienced a mild niacinamide-induced erythema reaction.
- A combination of 1% hexyldecanol with active substances showed the best soothing effect among all schemes, of which adverse reactions were only 5 (niacinamide supplier A) and 3 (niacinamide supplier B).

Table 1. visual grading results for the first and second 24-h human patch test (n=28)

Treatment Schemes	Niacinamide Supplier	The sum of the number of subjects who suffer erythema reactions in each visual scale class during the whole patch test period				
		0	1	2	3	4
4% niacinamide	A	2	26	0	0	0
4% niacinamide + active substances		5	23	0	0	0
4% niacinamide + 1% hexyldecanol		15	13	0	0	0
4% niacinamide + 2% hexyldecanol		17	11	0	0	0
4% niacinamide + 1% hexyldecanol+ active substances		23	5	0	0	0
4% niacinamide + 1% hexyldecanol+ active substances	B	25	3	0	0	0

Verification test for ensuring the formula's attenuating effect

- The formula 4% niacinamide + 1% hexyldecanol + 0.1% HEPES+0.01% gallic acid+0.5% α-arbutinl from niacinamide supplier B was chosen as the final formula owing to the minimal adverse reaction, and there was no erythema reaction observed in the verification 24-h occlusive human patch test (table 2).

Table 2. visual grading results for the verification 24-h human patch test (n=30)

Treatment Schemes	Niacinamide Supplier	The sum of the number of subjects who suffer erythema reactions in each visual scale class during the whole patch test period				
		0	1	2	3	4
4% niacinamide + 1% hexyldecanol+ active substances	B	30	0	0	0	0

Conclusions:

In this study, the formula, 4% niacinamide (purchased from supplier B) + 1% hexyldecanol + 0.1% HEPES+0.01% gallic acid+0.5% α-arbutinl, was proven to be the most effective in mitigating the erythema triggered by niacinamide among all schemes through a 24-h occlusive human patch test. In addition, this formula offers a solution that can avoid the potential irritation of nicotinamide efficiently.

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