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# Formulation and usage regime approaches to improve retinol tolerance

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## Introduction:

Retinol is well-known to have beneficial effects on the appearance of photoaged skin, with numerous studies showing the ability of retinol to improve parameters including the appearance of lines and wrinkles, mottled pigmentation and measures of elasticity and firmness [1, 2, 3, 4, 5]. However, retinol is often associated with consumer tolerance issues due to retinol-associated irritancy [6], especially at higher concentrations [3].

Despite this, there is a still a demand for high concentration retinol products due to their greater potency, and concentrations as high as 1% can be found on the cosmetic market. There is a need therefore to understand more about the tolerance profiles of high strength retinol products and identify approaches to mitigate the potential for irritation as much as possible.

In this study we aimed to compare the tolerance profiles of two high strength concentrations of retinol, a 0.3% (w/w) formulation and a 1% (w/w) formulation. In a second study, we then further assessed whether formulation design, regime guidance and the addition of a specialised supporting product to the regime could improve the tolerance profile of the highest concentration; 1% retinol.

## Materials & Methods:

We recruited 218 female participants (aged 35 – 70 years old) with facial age-related skin concerns including lines and wrinkles and uneven skin tone/pigmentation to study one; a 6 week at-home tolerance study where one cohort (n=115) tested a 0.3% (w/w) retinol formulation, and a second cohort (n=103) tested an identical 1% (w/w) retinol formulation. Both o/w emulsion products contained retinol in an encapsulation system. Formulations were applied at night-time only, ramping up usage over the study period to eventual nightly use after 4 weeks. Participants were instructed to follow retinol application with their own night-time moisturiser, using this even on evenings when retinol was not applied. All participants applied an SPF day cream each morning of the study.

We followed this up with a second study; an 8-week consumer tolerance study on 208 female participants (aged 35-70) with facial age-related skin concerns, including lines and wrinkles and uneven skin tone/pigmentation. This time applying a re-formulated 1% (w/w) retinol formulation; containing the same encapsulated retinol but with additional soothing and barrier supporting ingredients including bisabolol and niacinamide, followed by the application of a specially designed post-retinol soother product containing further barrier-supporting and soothing ingredients. In this study participants ramped up usage of retinol more slowly over the study period, reaching nightly use on average after 6 weeks, but only as the skin could tolerate. The post retinol soother product was applied nightly throughout the study, even on evenings when retinol was not applied. All participants applied an SPF day cream each morning of the study.

Participants self-reported whether they had any reactions to the retinol formulation and the severity of any reactions they had on a weekly basis, using a classification guide developed by a Dermatologist (Table 1).

*Table 1. The guidelines provided to volunteers to classify their reaction.*

| Skin Reaction Classification Key | |
|---|---|
| 1 - MILD | Tingling, stinging, tightness, blemishes/spots, peeling, dryness without soreness, slight redness, slight feeling of heat/burning. |
| 2 - MODERATE | Red, angry and sore to the touch, blind pimples beneath the surface of the skin, large area of dryness, rash. |
| 3 - SEVERE | Red, angry and sore without touching, eczema-like and persistent. Reactions can include broken skin, blistering, extended rash. |

Participants were grouped according to the most severe reaction reported during the study. Participants not reporting reactions were deemed fully tolerant to the retinol formulation. No reaction and mild reactions were deemed expected and tolerable based on participant feedback and expert Dermatologist and Toxicologist opinion. Therefore, the primary outcome measure was the percentage of participants in the reaction classification of 'tolerant and mild'.

## Results & Discussion:

In study one, in the 0.3% retinol cohort (n=115), 80 participants (69.6%) reported having no reaction and 22 (19.1%) reported having mild reactions, meaning 88.7% of participants were classed as 'tolerant and mild'. In contrast, in the 1% retinol cohort (n=103), 41 participants (39.8%) reported having no reaction and 23 (22.3%) reported having a mild reaction, meaning 62.1% of participants were classed as 'tolerant and mild' (figure 1). In the 0.3% retinol cohort only 11 participants (9.5%) reported moderate or severe reactions, compared with 39 (37.9%) in the 1% cohort. In the 0.3% cohort 2 participants (1.7%) had reactions which were 'unclassified' as no severity information was received.

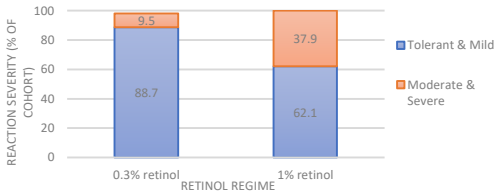


*Figure 1: Tolerance profiles of 0.3% compared to 1% retinol, when tested on a cohort of women over a 6-week period following a specified usage regime. Based on self-reported reaction severity.*

In study two, in the cohort testing a re-formulated 1% retinol product with a post retinol soother product (n=208), 77 participants (37%) reported having no reaction and 76 (36.5%) reported mild reactions, meaning 73.5% were classed as 'tolerant and mild' (figure 2). In this study 55 participants (26.5%) reported moderate or severe reactions.

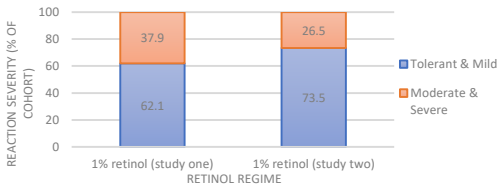


*Figure 2: Tolerance profiles of two different 1% retinol formulations and regimens. In study two retinol was re-formulated with additional soothers and barrier-supporting ingredients, combined with a post-retinol soother product and ramped up more slowly over 8-week vs 6 weeks. Based on self-reported reaction severity.*

## Conclusion:

In this research, we first compared the tolerance profile of 0.3% retinol in formulation with that of 1% retinol and not surprisingly found that more participants in the 0.3% retinol cohort reported no reactions or mild reactions. This suggests 0.3% is better tolerated than 1% retinol, a finding in-keeping with a previous study by Gold et al [3] where a 0.5% retinol formulation was found to be better tolerated than 1% in an 8-week study.

To improve upon this tolerance profile for 1%, a number of strategies were adopted. Firstly, the 1% retinol formulation was re-designed with the inclusion of ingredients that could both help support a stronger skin barrier and soothe the skin; secondly, the retinol product was combined in a nightly usage regime with a cosmetic moisturising barrier enhancer; thirdly, usage ramp up was slowed over the 8-week period. The combination of these approaches improved the tolerance profile of 1% retinol with a reduction in moderate and severe reactions observed.

This study suggests that retinol concentration has arguably the biggest impact on consumer tolerance to retinol, but that a combination of formulation design, the speed of ramp up and supporting products can improve the tolerance of high strength retinol. Although there will still be a proportion of consumers who will be unable to tolerate 1% retinol, indicating those new to retinol should start with lower concentrations.

## References:

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