A perfect duo: bakuchiol and phospholipids

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ABSTRACT

Bakuchiol has recently gained attention as a functional analog and natural alternative to topical retinoids. It was found to have retinol-like functionality sharing some of retinol's anti-ageing, anti-acne, and hyperpigmentation properties, while having fewer adverse cutaneous side effects than retinol.

Unsaturated phospholipids are ideal partners for bakuchiol. They are versatile ingredients offering both technical and physiological benefits to high-end skincare products. As essential constituents of human cell membranes they are highly biocompatible ingredients with proven skin care benefits. In addition, they serve as penetration enhancers for active substances.

Here we show that a combination of bakuchiol and unsaturated phospholipids (tradename BakuLipid®) offers retinol-like activity with superior performance over bakuchiol formulations without phospholipids, perfectly matching consumer expectations that seek more natural, more effective, and better tolerated products. BakuLipid is a combination of two active components – bakuchiol and unsaturated phospholipids for a twofold activity. Plant-based bakuchiol is a skin-friendly retinol alternative. Unsaturated phospholipids are natural penetration enhancers with rejuvenating effects. Combined, they form the perfect active for blemish-free and youthful skin.

Retinol, or vitamin A, is one of the most effective and most popular active ingredients in anti-ageing applications and for the treatment of blemished skin. The cosmetic effects of topically applied retinoids are based on (i) the promotion of keratinocyte proliferation, (ii) the promotion of collagen synthesis, (iii) the improvement of the epidermal barrier function, (iv) the inhibition of collagen degradation, (v) the reduction of transepidermal water loss (TEWL), and (vi) the inhibition of metalloproteinase activity.[1]

As one of oldest active ingredients in use, retinol is well-known to consumers. In our 2023 consumer survey, more than 90% of participants said that retinol is one of the most powerful active ingredients for the treatment of skin blemishes and ageing skin (data not shown).

Yet retinol has its disadvantages: From a formulation perspective, retinoids pose a challenge to researchers because of their proven instability (especially to sunlight), low penetration, and potential for skin irritation. Cutaneous side effects of retinol are common and well documented – consumers often experience side effects like cutaneous erythema, pruritus, peeling, stinging, burning, or sensitivity.[2]

This is reflected in our 2023 consumer survey, where more than 75% of participants said that they are concerned about skin incompatibilities when using retinol (data not shown). Therefore, novel systems are being developed to overcome these limitations.

One example is bakuchiol, a monoterpene derived from the seeds of the small, subtropical medicinal herb *Psoralea corylifolia*, which has gained attention as a functional analog to topical retinoids. Bakuchiol is structurally different to retinol, but induces retinol-like gene expression in human skin.

This includes genes involved in the cellular uptake of endogenous retinol, the activation of retinol in the skin, and the production of extracellular matrix proteins that provide epidermal support and integrity. Thus, bakuchiol induces its own set of chemical pathways, but shares some of retinol's anti-ageing, anti-acne, and hyperpigmentation properties.[3,4,5]

These molecular findings translate to clinical outcomes with improvements in wrinkles, skin blemishes, and hyperpigmentation, with overall fewer adverse cutaneous side effects than retinol. This has been confirmed in several *in vivo* studies using bakuchiol as a retinol replacement. It is therefore not surprising that the number of new product launches with bakuchiol is raising.

According to a Mintel database search, the number of new product launches with bakuchiol in the beauty and personal care category rose exponentially, with only 17 new launches in 2018 versus 275 new launches in 2022. This trend reflects the consumer preference for more natural and skin compatible ingredients.[5]

Still, bakuchiol has its challenges. Bakuchiol is relatively new to cosmetics and bakuchiol formulations are still being optimized. One possible strategy is to improve epidermal penetration to increase the effective concentration in target skin layers or to combine bakuchiol with suitable substances that complement its efficacy.

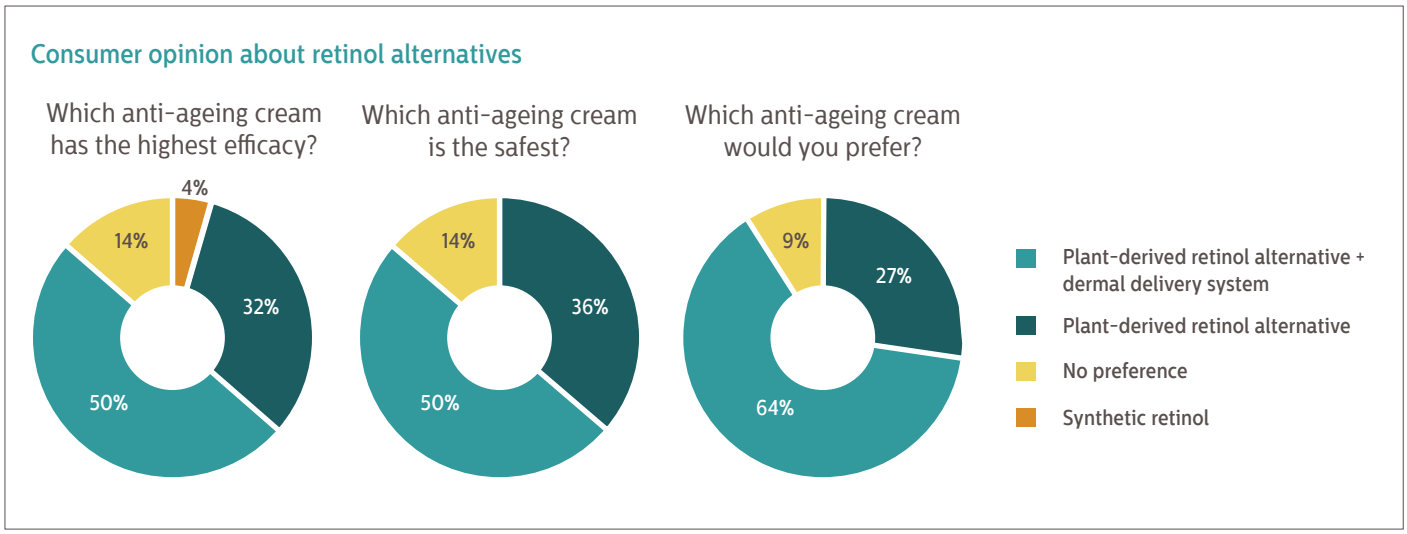

Figure 1: A plant-derived retinol alternative is preferred over synthetic retinol, especially in combination with a dermal penetration enhancer

Phospholipids – ideal partners for bakuchiol

Phospholipids are among the body 's own building blocks and are an essential part of our cell membranes. They are true skin care allrounders – highly biocompatible, completely biodegradable, and irritation-free. Phospholipids complement bakuchiol's function in two ways.

First, they facilitate bakuchiol penetration to target skin layers and second, phospholipids are active ingredients themselves. The structural subclass of unsaturated phospholipids are mediators of skin delivery. They modify the fluidity of the lipid barrier, making it more permeable for cosmetic actives, increasing their bioavailability and efficacy.

At the same time, unsaturated phospholipids are active skin care ingredients that reduce the visible signs of skin ageing by triggering biochemical processes, including enhanced hyaluronic acid production, or diminished extracellular matrix degradation.

Moreover, unsaturated phospholipids are a source of unsaturated fatty acids, such as linoleic acid, which has a positive impact on inflammatory skin disorders, complementing the anti-blemish and anti-ageing activity of other active ingredients. This makes unsaturated phospholipids ideal partners for bakuchiol as they promote bakuchiol's efficacy, and at the same time, complement bakuchiol's activity with skin-caring and anti-ageing benefits.[6,7]

Consumer opinion about retinol alternatives

To understand the consumer's view on retinol and retinol alternatives, we asked 22 female volunteers to rate their preferred anti-ageing ingredient among three different forms: (i) synthetic retinol, (ii) plant-derived retinol alternative or (iii) plant-derived retinol alternative + dermal penetration enhancer, in relation to safety, efficacy, and general preference in cosmetics.

As a result, consumers prefer a plant-derived retinol alternative over synthetic retinol, especially in combination with a dermal penetration enhancer (Figure 1).

Bakuchiol and phospholipids – the perfect team for treating blemished skin

This *in vivo* study examined the effects of bakuchiol with and without the presence of unsaturated phospholipids on blemished facial skin and gathered information about the volunteer's perception of product efficacy.

In a double blind, placebo-controlled, randomized, *in vivo* study, 21 female volunteers with mild to severe blemished skin treated one hemiface with a 4% 'Bakuchiol Phospholipid Cream' and the other side with a 'Bakuchiol Control Cream' containing equimolar amounts of bakuchiol for 42 days. Product efficacy was evaluated by instrumental assessment, clinical expert evaluation, and consumer self-assessment.

As a result, the 'Bakuchiol Phospholipid Cream' significantly reduced sebum levels of blemished skin by 27% after 42 days of treatment, which is 12% better than the 'Bakuchiol Control Cream'. The clinical expert evaluation found that the signs of blemished skin had significantly improved by 52% after 42 days of treatment, which is 20% better than the 'Bakuchiol Control Cream'. The improvement of symptoms is illustrated in Figure 2C showing the hemiface treated with the 'Bakuchiol Phospholipid Cream'.

In the consumer self-assessment, volunteers observed that both the 'Bakuchiol Phospholipid Cream' and the 'Bakuchiol Control Cream' are

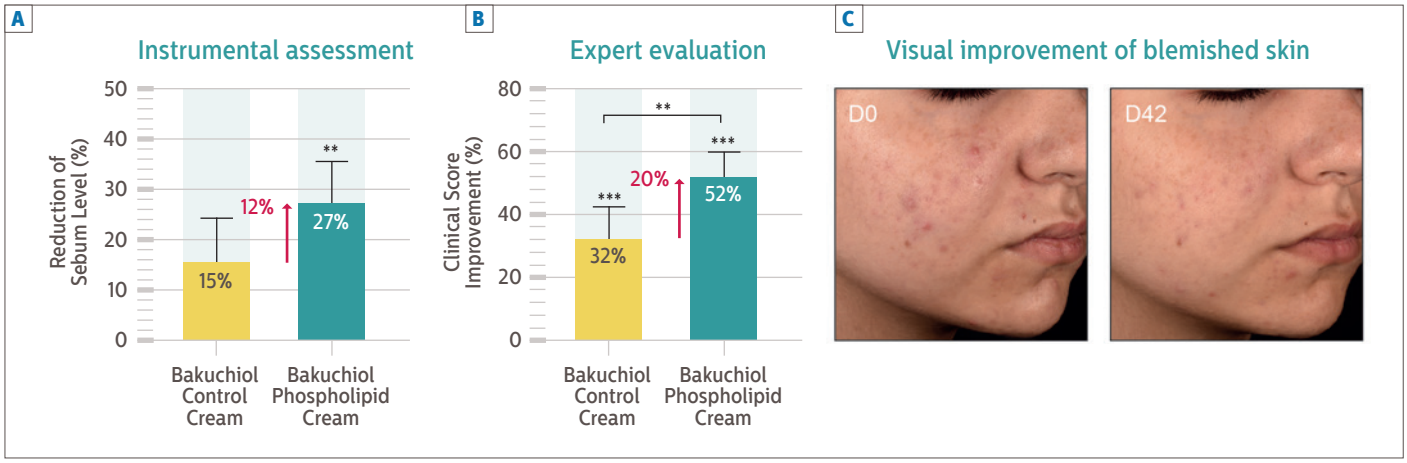

Figure 2: The 'Bakuchiol Phospholipid Cream' reduces sebum levels and facial skin blemishes. A: Sebum levels were recorded with Sebumeter SM 815. B: The clinical expert evaluation was according to the Investigator Global Assessment (IGA)[8]. C: Representative images show the facial half-side treated with the 'Bakuchiol Phospholipid Cream'. Data is presented as percent changes between day 0 and day 42. N = 21; Mean + SEM. Student's t-test D0 versus D42 and between treatments; ** = $p < 0.01$; *** = $p < 0.001$

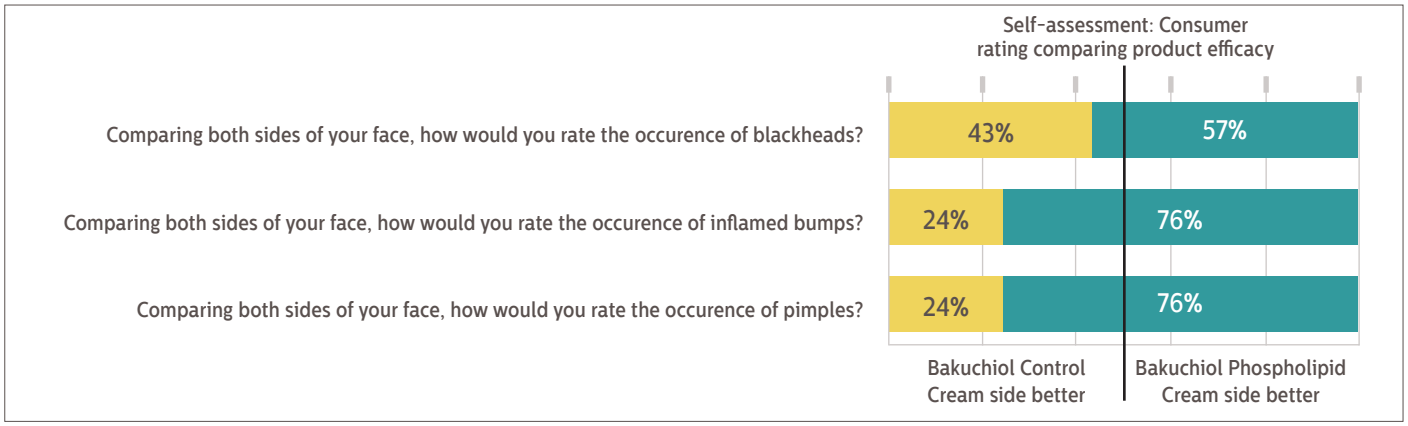

Figure 3: Consumers preferred the 'Bakuchiol Phospholipid Cream' to treat skin blemishes. 21 women applied a 'Bakuchiol Phospholipid Cream' to one hemi-face and a 'Bakuchiol Control Cream' to the other side. After 14 days of treatment, volunteers evaluated both sides for parameters of blemished skin and decided which side they prefer (forced decision). Data is presented as percentage of users that preferred either side

effective in the treatment of skin blemishes, such as blackheads, inflamed bumps, and pimples (data not shown).

However, when directly asked which cream was more effective, most consumers saw better results with the 'Bakuchiol Phospholipid Cream' (Figure 3), confirming the results obtained in the instrumental assessment and in the clinical evaluation.

Bakuchiol and phospholipids – the optimal combination for treating signs of ageing

This *in vivo* study examined the rejuvenating effects of bakuchiol with and without the presence of unsaturated phospholipids on mature facial skin and gathered information about the volunteer's perception of product efficacy.

In a double blind, placebo-controlled, randomized, *in vivo* study, 22 female volunteers treated one hemiface with a 2% 'Bakuchiol Phospholipid Cream' and the other side with a 'Bakuchiol Control Cream' containing equimolar amounts of bakuchiol for 56 days. Product efficacy was evaluated by instrumental assessment and consumer opinion was gathered by a self-assessment questionnaire.

As a result, the 'Bakuchiol Phospholipid Cream' significantly reduced the crow's feet number by 17% after 56 days of treatment, which is 9% better than the control cream. A representative visual illustration shows the improvement of the crow's feet area in the hemiface treated with the 'Bakuchiol Phospholipid Cream' (Figure 4).

In the survey, consumers observed that both the 'Bakuchiol Phospholipid Cream' and the 'Bakuchiol-Control Cream' are effective in treating signs of ageing, such as skin smoothness, evenness, and fine lines (data not shown). However, when directly asked which

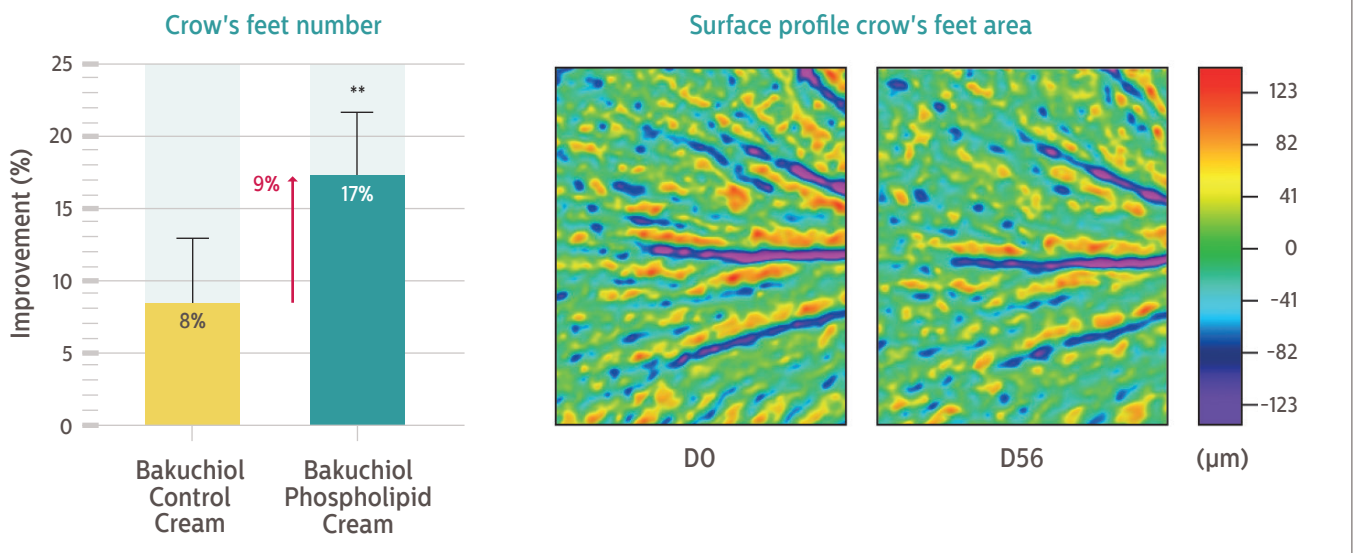

Figure 4: The 'Bakuchiol Phospholipid Cream' improved skin topography. Crow's feet wrinkles were monitored with the AEVA-HE V4 system. Representative images show the surface profile of the facial half-side treated with the 'Bakuchiol Phospholipid Cream'. Data is presented as percent changes D0-D56. N = 22; Mean + SEM. Student's t-test D0 versus D56; ** = p < 0.01

cream is more effective, most consumers see better results with the 'Bakuchiol Phospholipid Cream' (Figure 5).

Conclusion

Consumers see retinol as one of the most powerful active ingredients to treat skin blemishes and signs of ageing. Yet they also know that retinol may cause skin incompatibilities. Natural alternatives to retinol are seen as effective and better tolerated ingredients – they are preferred over retinol. Consumer preference is even more pronounced when the natural active ingredient is combined with a dermal penetration enhancer.

BakuLipid® addresses these consumer preferences and expectations by combining bakuchiol – a plant-derived retinol alternative – with a dermal penetration enhancer based on phospholipids for higher efficacy. At the same time, unsaturated phospholipids provide extra skin care benefits. Therefore, BakuLipid® is an upgraded version of bakuchiol. It is the perfect ingredient for cosmetic anti-ageing concepts that intend to replace retinol with bakuchiol and expect superior activity. **PC**

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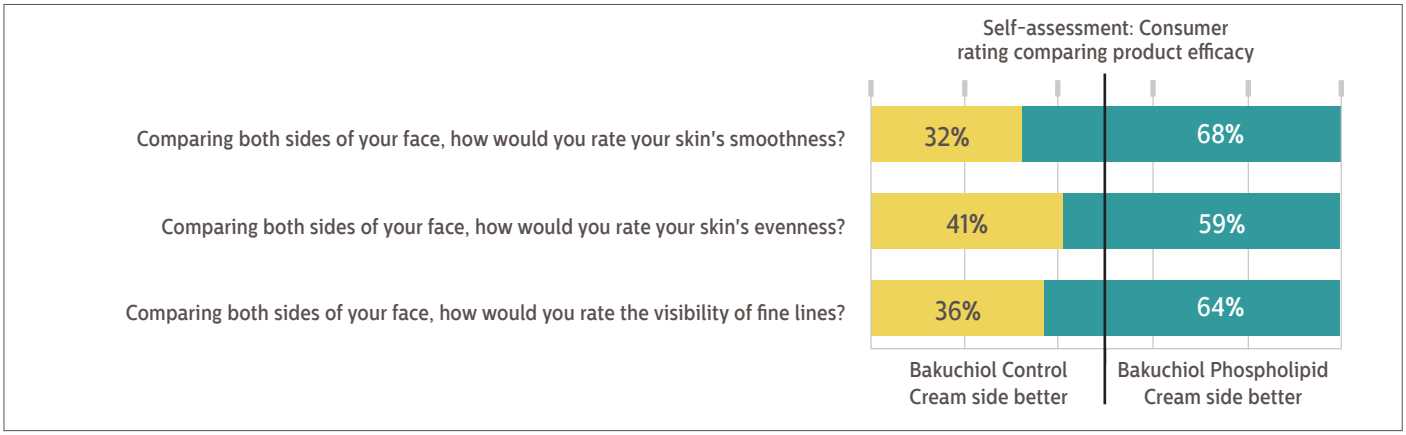

Figure 5: Consumers preferred the 'Bakuchiol Phospholipid Cream' as anti-ageing treatment. 22 women applied a 'Bakuchiol Phospholipid Cream' to one hemi-face and a 'Bakuchiol Control Cream' to the other side. After 56 days of treatment, volunteers evaluated both hemifaces for signs of ageing and decided which side they prefer (forced decision). Data is presented as percentage of users that preferred either side