REVIEW

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Effectiveness and tolerability of bakuchiol (*Psolarea corylifolia*) as a dermal anti-aging modality: A systematic review on skin wellness and harmony

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ABSTRACT

Skin aging is a natural phenomenon caused by a decline in collagen production that leads to skin thinning, dry and pale skin, wrinkles, and sagging. Skin aging may not contribute to the mortality rate. However, people tend to connect their symbol of inner self to external appearance. Therefore, psychosocial effects such as social anxiety, low self-esteem, and low satisfaction in life will affect their personal and social life. Anti-aging procedures focus on the prevention of damage, replacement of tissues, and skin rejuvenation. Bakuchiol (*Psolarea corylifolia*) is a novel anti-aging product with antioxidant, anti-inflammatory, and anti-aging properties that is deemed effective and tolerable in skin rejuvenation. This comprehensive review aims to further examine the effectiveness and tolerability of bakuchiol based on previous studies in order to provide new insights into delaying skin aging. A comprehensive literature search was conducted to assess the effectiveness and tolerability of bakuchiol as a dermal anti-aging modality from search engines, PubMed, Google Scholar, CORE, Science Direct, and Cochrane using search terms ("Bakuchiol" OR "*Psolarea corylifolia*") AND ("Dermal Aging" OR "Skin Aging"). Bakuchiol proved to have anti-inflammatory and antioxidant properties to maintain youthfulness and skin appearance. Regarding tolerability, bakuchiol has fewer side effects compared to other commonly used modalities. Therefore, bakuchiol (*Psolarea corylifolia*) is an effective and tolerable modality in the treatment of aging skin.

Keywords: Bakuchiol, dermal aging, *Psolarea corylifolia*, skin aging.
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INTRODUCTION

Skin aging is a natural phenomenon that occurs due to loss of body mass, poor hydration, and disintegration of the dermis and epidermis junction that cannot be stopped. This phenomenon involves endogenous and exogenous factors with varying mechanisms, such as the glycation process, free radicals, and the cell cycle. Endogenous factors include gene mutation, cellular metabolism, and hormonal factors, while exogenous factors are mostly related to lifestyle, for instance, ultraviolet rays, air pollution, chemicals, smoking, heat, and toxins. These factors and mechanisms lead to various structural and physiological skin, underlying muscles, subcutaneous fat tissue, and bony structures. Two types of skin aging mechanisms overlap with each other. They include ROS generation, DNA damage, and ECM component deterioration that lead to biochemical and biophysical changes such as skin thinning, dry and pale skin, fine wrinkles, and skin sagging as its elasticity decreases. The aging process and ultraviolet rays could reduce collagen production due to a low number of dermal fibroblasts, whereas collagen keeps the skin firm and repairs skin wrinkles as a main component of the extracellular matrix and basement membrane of the skin.[1-6]

These changes surely have psychosocial impacts on individuals, as the external appearance influences personal and social experiences and becomes a symbol of the inner self. Age-related changes in the skin lead to increased social anxiety, lower satisfaction with their lives, avoidance of anxiety-provoking situations, and lower self-esteem in adults.[7] People with better external appearances tend to be more attractive. That factor goes along with better social opportunities, and they are more likely to be married, although this is still understudied.[8] Fortunately, there are ways to delay the aging process for better psychosocial effects on individuals. Anti-aging procedures can prevent or delay the skin aging process at the cellular and molecular levels.[9] They focus on prevention of damage over time, skin rejuvenation, and the ability to replace tissue following injury via different mechanisms of skin aging. Nowadays, people of all ages aim to have a more consistent and younger skin. Therefore, many novel anti-aging products and procedures have arisen, and their market is expanding as the demand is increasing.[7-9]

Bakuchiol, a refined meroterpene phenol present in the seeds of *Psoralea*

corylifolia, may be a potential novel anti-aging product that may contribute to a better skin aging process. This plant-based alternative to retinol has antioxidant, anti-inflammatory, and anti-aging properties, which target several biological pathways. Bakuchiol could upregulate collagen and extracellular matrix formation enzymes and modulate the retinoic acid receptor gene.[10-11] Those pathways lead to increased skin smoothness, clarity, and brightness and decreased wrinkles, sagging, and other skin changes. Even a person with sensitive skin can tolerate bakuchiol application well, as it is safe and traditionally extracted. Their tolerability, photostability, and ability to decelerate skin aging make them a potential property in the development of anti-aging procedures, as the management of skin aging may have become the focus of many dermatologists nowadays.[12] There is a rise in the number of individuals who demand rejuvenating products and procedures that delay the signs of skin aging.[7] Ultraviolet protection, energy-based devices, topical agents, and injectable agents are examples of popular dermal aging management.[13]

Skin aging may not be related to mortality rate, but the skin aging process itself may lead to depression, demoralization, and other psychological impacts, therefore, it plays an important role in contributing to the quality of life index. In this systematic review, we will discuss bakuchiol as an anti-aging agent that targets specific mechanisms of skin aging. Despite the availability of many different promising therapeutic strategies and procedures to combat skin aging, new therapeutic insights to aid medical professionals in developing treatment plans to combat the skin aging process are still needed. Therefore, this systematic review aimed to discuss the potency of bakuchiol for delaying skin aging.

METHOD

In adherence to the PRISMA guidelines, a comprehensive methodology was employed to carry out this systematic review. Before initiating the systematic search, the study protocol was registered and sanctioned in the PROSPERO database (ID: 1133425).

Literature Search

We conducted a comprehensive literature search to assess the effectiveness and tolerability of bakuchiol as a dermal anti-aging modality from search engines, PubMed, Google Scholar, CORE, Science Direct, and Cochrane. The articles were retrieved from 2019 to 2024. The search terms applied are the following: ("Bakuchiol" OR "*Psolarea corylifolia*") AND ("Dermal Aging" OR "Skin Aging"). Literature search was limited to those published in the English language and with full text. In addition, we manually searched for additional possible studies for references.

Study Selection

The inclusion criteria are: (1) primary studies, (2) written in English, (3) full-text is available, and (4) assessed the effectiveness and tolerability of bakuchiol as a dermal anti-aging modality compared to placebo. The exclusion criteria are: (1) case report; (2) commentary; (3) letter to the editor.

Data Extraction

Three authors extracted further information independently about the research that has been included, and the fourth author resolved their differences. The extracted data were as follows: (1) The name of the first author and publication year; (2) Study design; (3) Country of study origin; (4) Subjects; (5) Methods; (6) Outcome; (7) Results.

Type of Outcome Measures

The outcome measures assessed in this systematic review were the effectiveness and tolerability of bakuchiol as a dermal anti-aging modality based on the duration of bakuchiol application.

Quality Assessment

Four independent reviewers assessed the bias risk by applying the Newcastle-Ottawa Scale for intervention studies. The NOS assessed bias from the randomization process, deviations from intended interventions, missing outcome data, measurement of outcome, and selection of reported results. Any disagreements will be resolved through discussion.

RESULTS

Based on the screening of 90 titles and abstracts, a total of 5 studies were included in the present review (Figure 1). The initial database search yielded 160 records. Following the removal of 13 duplicate entries, 147 records remained for further evaluation. During the first screening stage, 57 records were excluded on the basis of study design, as they were identified as non-randomized controlled trials. The remaining 90 records underwent abstract screening, which led to the exclusion of an additional 57 records. 54 of these records did not exclusively address the use of bakuchiol in the context of skin aging, and 3 were published in languages other than English or Indonesian. Subsequently, 33 full-text articles were assessed for eligibility, and 28 of them were excluded because the full text was not accessible. For the final step, 5 studies that met all predefined inclusion criteria were incorporated into the final synthesis (Table 1).

One notable gap about those studies above is of bakuchiol's tolerability, including the sensitive skin groups. An inconsistency regarding the tolerability of bakuchiol was observed, with one study claiming that bakuchiol has a redness effect. There are also no standards to measure the effects caused by bakuchiol as an antiaging property, with studies using 'radiance' and other subjective measurements as the basis for bakuchiol's efficacy. Additionally, some factors, such as oxidative stress, extracellular matrix breakdown, and fibroblast aging, are acknowledged as key mechanisms in skin aging, but there has been no thorough synthesis that directly connects bakuchiol's effects to these processes in clinical settings involving humans. This systematic review addresses these gaps by synthesizing data from clinical trials (2019-2024), highlighting the efficacy and tolerability of bakuchiol, relative to retinol.

Risk of Bias

The risk of bias for randomized studies was evaluated across five domains (Table 2). Draelos et al. (2022) demonstrated low risk of bias across most domains, including the randomization process, deviations from intended interventions, missing

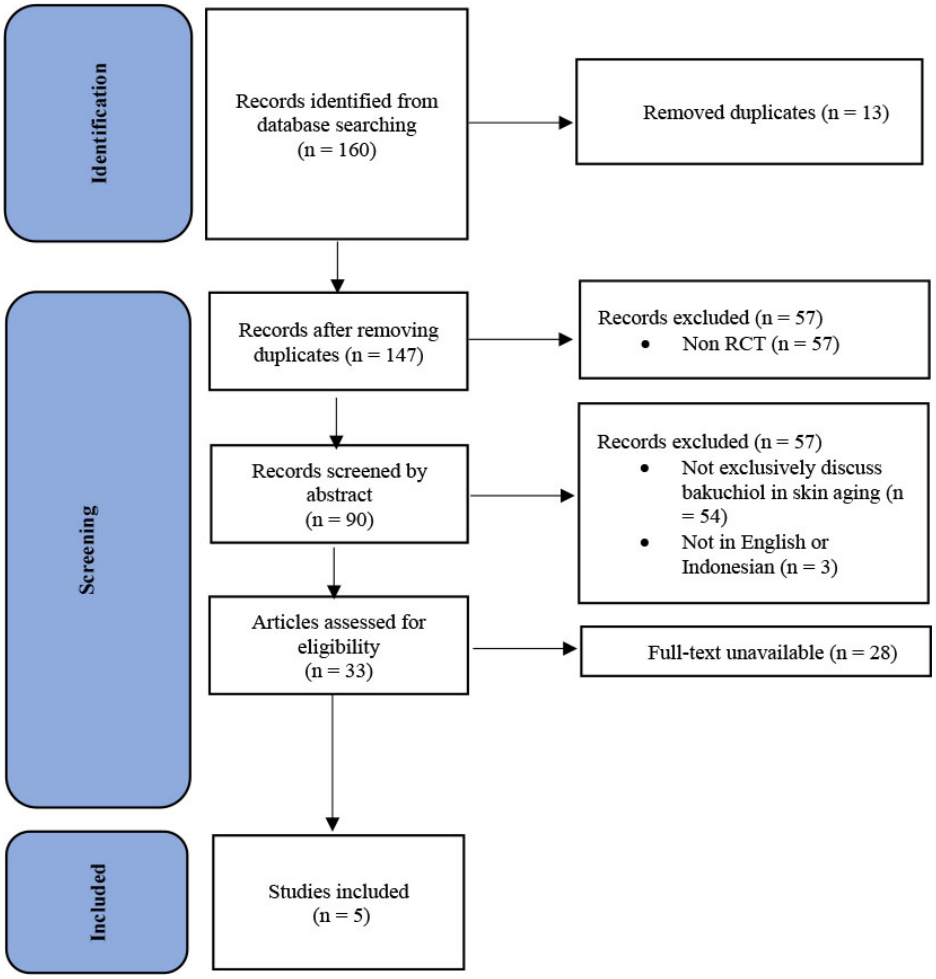

Figure 1. PRISMA Flowchart.

outcome data, and outcome measurement. However, there was concern regarding the selective reporting of results. Goldberg et al. (2019) showed low risk of bias in the randomization process and missing data handling but had concerns regarding deviations from intended interventions and measurement of outcomes. In contrast, Bacqueville et al. (2020) and Bluemke et al. (2022) exhibited low risk of bias across all assessed domains, indicating strong methodological quality. Overall, the included randomized studies were generally of good quality, though selective reporting and outcome measurement biases were noted in some studies.

DISCUSSION

Pathophysiology of Skin Aging

Various factors came into play in skin aging, which can further be categorized into internal and external aging factors. These factors are involved in several theories about the mechanisms of skin aging, such as the theory of cellular senescence, oxidative stress, and chronic inflammation.[19] Extrinsic factors such as ultraviolet rays, smoking, heat, and air pollution all contribute to the production of reactive oxygen species (ROS), which disturb the skin on a molecular and thus cellular level. Whereas intrinsic factors involve endogenous oxidative stress and cellular damage.[20] Both aging processes manifest with wrinkles and the loss of the skin's elasticity, although the severity of each manifestation differs heavily between the two.[21] In addition, in intrinsically aged skin, the skin is thinner and drier, while the extrinsically aged skin is thicker, dyspigmented, with deep wrinkles and decreased laxity.[20,22]

The mechanisms causing the skin to age happen on a molecular level, through the presence of excess oxidative stress. The aging skin itself loses its own cells, which involves the progressive degeneration of the cells and the loss of the cells' regeneration capacity.[23] This is due to the accumulation of damage caused by several factors, one of which mainly includes oxidative stress, both endogenous and exogenous. The aging skin's declining ability to balance the oxidative stress also contributes to the build-up of ROS. Stressors such as DNA damage can force cells into going on a state of irreversible growth arrest, called cellular senescence or the Hayflick effect.[20,23] This effect can upregulate the cell cycle arrest protein, the cells' lysosomal enzymes, and senescence-associated secretory phenotype or SASP, consisting of various inflammatory cytokines, chemokines, proteases, and microRNAs, whilst altering the structure of the nuclear lamina.[24-25] These all contribute to the senescent cells' slower regeneration and disturbance of the skin's structure, which mainly involves the extracellular matrix degradation and collagen breakdown.[20] These inflammations also cause the neutrophils to migrate, producing neutrophil proteases, especially neutrophil elastase, which cause the collagen and elastin fragmentation through upregulating metalloproteinase-1 (MMP-1) activity. This enzyme is responsible for the degradation of the proteoglycan, decorin, a regulator of collagen fibrogenesis.[26] The dermis' fibroblasts are crucial in collagen synthesis, arrangement, and remodeling, contributing to the structure of the extracellular matrix (ECM). With the release of SASPs from senescent fibroblasts, the ECM will experience progressive breakdown and impairment.[27] New study found that metalloproteinases (MMPs) that encourage collagen breakdown, synthesize high molecular weight collagen fragments, which then inhibit new collagen synthesis and extend oxidative stress to the fibroblasts.[28-29] The decrease in collagen will give rise to wrinkling and sagging.[30] These senescent cells are also responsible for initiating cornification, leading to rough skin and age-related pigmentation through the activation of melanocytes.[31-32]

Alongside the accumulation of senescent cells, damage from ROS will also contribute to the degradation of the ECM. Directly, ROS activates the activator protein 1 pathway (AP-1), leading to the

Table 1. Efficacy and Tolerability of Bakuhiol

No	Author	Subject	Duration	Efficacy	Tolerability
1	Draelos, et al. (2020)[14]	60 female subjects aged 40-65 years old with sensitive skin (eczema/ atopic dermatitis, rosacea, and cosmetic intolerance syndrome).	4 weeks (application twice daily).	Increase visual smoothness, tactile smoothness, clarity, radiance, overall appearance, and acts as a global anti-aging.	Minimal tightness, minimal stinging, photostable, not phototoxic, does not require dose escalation.
2	Dhaliwal, et al. (2019)[15]	44 healthy participants.	12 weeks (retinol once daily or bakuchiol twice daily).	- Wrinkles = Reduced compared to baseline (bakuchiol and retinol). - Pigmentation (clinical grading and facial analysis) = Improved (bakuchiol (59%) and retinol (44%)).	- Retinol = More scaling, itching, burning (not significant). - Bakuchiol = Redness.
3	Bacqueville, et al. (2020)[16]	43 women (aged 45 years or older) with naturally aged skin (each skin type (normal, greasy, dry, combination) is represented by a minimum of 20% of participants)	56 days (application twice daily).	- Sagging = Significant decrease of the lower part of the face; more defined contour line, especially on - the jowl part. Firmness = Significant reduction of depth (73%) and volume of skin deformation (78%). Significant skin firmness improvement on - day 56 (95%). Radiance = Significant increase on day 56 (80%).	Judged as "very good" (skin evaluation) and "excellent" (ophthalmologic evaluation).
4	Bluemke, et al. (2022)[17]	34 females with mixed skin types (dry, oily, normal, combination).	12 weeks (bakuchiol or retinoid application twice daily).	Significantly improved youthful appearance.	- Bakuchiol = Well-tolerated overall, especially in participants with sensitive skin. - Retinol = Skin irritation, erythema, dryness, itching, and desquamation in five subjects.
5	Goldberg, et al. (2019)[18]	39 healthy females (aged 40-65 years old) with "crow's feet" wrinkles, moderate skin aging, at least one pigmented spot on the face, following a daily care routine, and regular use of serum products.	3 months (once daily; each evening).	- Wrinkles (Dermatop) = Significant depth reduction. - Firmness (Dynaskin) = Increased. - Pigmentation (CM-700d Spectrocolorimeter) = Reduced uneven - pigmentation. Skin hydration = Increased - for up to 12 hours. Comedogenic = Non-comedogenic.	Well tolerated in all skin types.

upregulation of the MMPs, thus resulting in collagen breakdown.[33] Moreover, it activates the TGF-B/Smad 3 signalling pathway, leading to decreased collagen production.[34] In addition, exposure to UV irradiation will also lead to the upregulation of MMP-1 activity, exhibiting the very same effect of collagen disorganization through decorin.[30] ROS and UV exposure also upregulate elastolytic enzymes, causing elastin to degrade, thus reducing the skin's elasticity.[19,35-37] In skin exposed to UV rays, the oxytalan fibers experience degeneration, increasing the chance of the epidermis detaching from the dermo-epidermal junction, leading to the appearance of wrinkles.[38-39]

Role of Bakuchiol in Aging Skin

Bakuchiol (*Psoralea corylifolia*) is an antimicrobial, anti-inflammatory, anti-osteoporotic, and antitumorigenic compound that exhibits beneficial uses in healthcare. Recently, it has gained significant popularity in the beauty industry as an effective and tolerable analogue of retinol.[40] Normal human body naturally produces free radicals. Free radicals combined with acute overexposure to solar radiation may induce skin changes such as deep furrowing, wrinkle formation, and skin thickening, which is often referred to as "solar scar" or "photoaged

Table 2. Risk of Bias for Intervention Studies

	Bias arising from the randomization process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in the measurement of the outcome	Bias in the selection of the reported result
Draelos et al. (2022)	+	+	+	+	-
Dhaliwal et al. (2019)	+	+	-	-	+
Bacqueville et al. (2020)	+	+	+	+	+
Bluemke et al. (2022)	+	+	+	+	+
Goldberg et al. (2019)	+	+	+	-	+

skin". Other pollutants, allergens, and microbes generate reactive oxygen species (ROS), which results in an imbalance of the oxidation-antioxidation process. Therefore, the anti-inflammatory and antioxidant properties of bakuchiol serve to maintain this balance and thus increase youthfulness and skin appearance.[17,41] Regarding tolerability, bakuchiol proved to have fewer cutaneous side effects compared to retinol, such as less stinging, scaling, irritation, and photosensitivity, especially in sensitive skin. Retinol, on the other hand, strongly depends on its mode of delivery, thus may not be photostable compared to bakuchiol.[15,17]

CONCLUSION

Bakuchiol (*Psolarea corylifolia*) is an effective and tolerable modality in the treatment of aging skin compared to retinol as its analogue. This observational study may serve as a reference. However, due to the limited number of studies, further investigations are required.

CONFLICT OF INTEREST

None.

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None.

AUTHOR CONTRIBUTIONS

Author CFL is the main author in conducting the research method. Authors VE and EFH participated in constructing the research manuscript. Author KKW supervised and gave advice in conducting the research.

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