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Bakuchiol from psoralea corylifolia and its dermatological applications: a comprehensive review

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Abstract

The meroterpene bakuchiol has lately generated a lot of buzz in the beauty and medicine sectors. Although it has a wide geographical range, the seeds of the medicinal plant Psoralea corylifolia, which is native to Asia, are its principal source. Nevertheless, the low seed germination rates and significant seedling mortality put this therapeutic plant in jeopardy. Here, research documenting plant regeneration from root fragments is highlighted in a review paper. Then, because it looks so much like other species, we talk about and investigate a method that may be used to check if the plant is real and stop forgeries. We also provide a "green" extraction approach for bakuchiol and investigate potential chemical synthesis methods for bakuchiol. In addition, we detail the several biological functions of bakuchiol, focusing on those that affect the skin. Antifungal, antibacterial, antioxidant, anti-inflammatory, antiaging, depigmenting, and anticancer are some of bakuchiol's primary skin bioactivities. Nevertheless, novel skin delivery techniques that enable bakuchiol's encapsulation are necessary and advantageous due to its unique physicochemical characteristics. This review article also provides a thorough description of systems that are micro- or nano-sized and have medicinal or cosmetic uses. The use of bakuchiol in cosmetic and dermopharmaceutical formulations raises regulatory, metabolic, and toxicological problems that impact both the user and the environment. The dermatological uses of bakuchiol, a chemical isolated from Psoralea corylifolia, are discussed in detail in this article. Because of its antioxidant, anti-inflammatory, and anti-aging capabilities, bakuchiol has attracted interest as a possible natural substitute for retinol. Here we take a look at its molecular features, extraction

techniques, and safety profiles. Also covered are the effects of bakuchiol on acne, hyperpigmentation, and wrinkles, among other dermatological issues. All things considered, the data show that bakuchiol may be a powerful and adaptable component in skincare products, which is great news for the development of all-natural skincare options.

Keywords: - Bakuchiol, Psoralea Corylifolia, Dermatological.

INTRODUCTION

Products that are created from plants have been utilised extensively for a considerable amount of time due to the fact that they are both inexpensive and simple to get. Because of its natural geographic range, Psoralea corylifolia is a plant that is well-known as a result of its widespread recognition, particularly among people in China and India. Because of its complex chemical composition and the fact that it has been used in ethnobotany for decades, P. corylifolia has been attributed with a number of qualities. These features include estrogenic, antidepressant, hepatoprotective, immunomodulatory, osteoblastic, neuroprotective, and pesticidal actions [1]. Over a hundred different chemicals may be traced back to this substance. The well-known chemical known as psoralen stands out among these compounds; it has been utilised in the treatment of psoriasis ever since the 1970s. Bakuchiol, often known as BAK, is commonly regarded as one of its primary components. From a chemical point of view, it possesses an aromatic ring and a lengthy hydrocarbon chain, both of which have a detrimental impact on its water solubility. This is an important factor for its practical utilisation in carrier systems [2]. Moreover, the BAK molecule possesses additional particular physicochemical features that are accountable for the primary biological activities that it engages in.

Throughout the years, several extraction techniques have been documented, with one approach that stands out as particularly noteworthy being a procedure that is "environmentally friendly" and makes use of supercritical extraction in order to collect BAK. Because of the wide variety of active chemicals that are available, the process of extracting goods that are generated from plants can be difficult. Methods of plant extraction and separation frequently result in the production of insufficient amounts of the compounds that are needed [3]. In these kinds of circumstances, chemical synthesis is an alternative that may be utilised. In spite of the fact that there are certain

difficult processes involved, a number of researchers have documented a variety of synthetic chemical routes for BAK.

The organisms that make up the microbiota of the skin, which are referred to as commensal organisms, play an important part in the process of homeostasis and contribute to the enhancement of the skin's immunological capability. This can be caused by disturbances in the commensal balance, which can result in an overgrowth of bacterial and fungal species. Researchers have conducted a number of experiments, both in vivo and in vitro, that have demonstrated that BAK is useful in treating several illnesses. Staphylococcus aureus, which is classified as an opportunistic pathogen, has been linked to the majority of bacterial skin infections, both acute and chronic [4]. It has been estimated that roughly twenty to thirty percent of healthy persons carry S. aureus without exhibiting any symptoms. To add insult to injury, S. aureus is responsible for around 76% of all skin infections. In light of the growing prevalence of antibiotic resistance, the bactericidal activities of BAK have become particularly valuable [5].

On top of that, the anti-inflammatory and antioxidant properties could be useful in reducing the rate of natural ageing. The production of free radicals is an inevitable byproduct of all biological processes. Sunlight may induce a variety of skin changes, including the development of wrinkles, thickness that looks like plaque, deep furrowing, and a loss of skin tone. Sunburns happen when the skin is exposed to the sun's rays for too long in too short a time. This disease, which is often known as "photoaged skin" or "solar scar," is especially harmful because it causes the production of reactive oxygen species (ROS) that are associated with cellular oxidative damage in DNA, lipids, and proteins. This is due to the fact that it causes cells to become less viable in the end [6]. Exposure to allergens, microbes, and pollutants, among other things, causes an increase in reactive oxygen species (ROS) generation in humans. It is critical to have mechanisms in place that can detect when free radicals are being produced and help with their elimination [7]. Having these mechanisms in place and keeping the oxidation and antioxidation processes balanced is also crucial.

LITERATURE REVIEW

Cariola, A., El Chami, M., Granatieri, J., & Valgimigli, L. (2023). More and more individuals are thinking about using bakuchiol as a photoaging treatment for their skin. We used real-time oxygen sensing and 475 nm UV-vis monitoring to see how bakuchiol inhibited mushroom tyrosinase. For

monophenolase reactions, bakuchiol had a competitive inhibitory effect, as shown by an average Ki constant (μM) of 6.71 ± 1.23 and for diphenolase reactions, 1.15 ± 0.34. For these reactions, the IC50 values at 1 mM substrate were 37.22 ± 5.18 and 6.91 ± 0.96 ∼. This was compared to the IC50 values for kojic acid, which were "34.02 ± 5.51 and 16.86 ± 3.28 μM, respectively. Fluorescence quenching confirmed the existence of a single binding mode, with a formation constant Ka = 1.02 × 10^4 M^{-1}. The antioxidant activity was studied by observing the inhibition constant of kinh = 18.1 ± 6.6 ($104M^{-1}s^{-1}$, 30 °C) when the autoxidation of styrene and cumene was inhibited in a solution of pHCl at 30 °C. Furthermore, at 37 °C and $104M^{-1}s^{-1}$, the MeLin inhibition constant in Triton™ X-100 micelles was determined to be 0.16 ± 0.03. The calculated stoichiometric factor was 1.9 ± 0.1. We found that the BDE(OH) was 81.7 ± 0.1 kcal/mol using ReqEPR spectroscopy. [8] In addition to its potent antioxidant properties, bakuchiol is a potent tyrosinase inhibitor. A natural food preservative that prevents oxidation and burns food, it shows great promise in this regard .

Alalaiwe, A., Hung, C. F., Leu, Y. L., Tahara, K., Chen, H. H., Hu, K. Y., & Fang, J. Y. (2018). The combination of 8-methylpsoralen (8-MOP) with ultraviolet A (PUVA) is an effective method for treating psoriasis with photochemotherapy. There is a natural compound called 8-MOP, and it comes from Psoralea corylifolia. This study examined the role of imiquimod stimulation in inhibiting the development of psoriasis-like lesions in a mouse model. The goal of this research was to learn more about the inhibitory impact and how five P. corylifolia chemicals were absorbed via the skin. We assessed the antipsoriatic potency, skin permeability, keratinocyte apoptosis, and isopsoralen, psoralidin, and bakuchiol of 8-MOP in vitro. Researchers looked at how well these chemicals worked [9]. At an equimolar dose, bakuchiol had a skin deposition of 0.50 nmol/mg, isopsoralen of 0.58 nmol/mg, and 8-MOP of 0.47 nmol/mg. Such a level was higher than the pig ear levels of psoralen (0.25 nmol/mg) and psoralidin (0.14 nmol/mg) that were deposited on the skin. No additional penetration across the skin was seen after psoralidin and bakuchiol were absorbed. To shed light on the connection between the penetrant structure and skin permeability, it is possible to determine the hydrogen bond number, total polarity surface, and stratum corneum lipid docking, in addition to experimental data on physicochemical parameters. When compared to the other chemicals, 8-MOP and isopsoralen had the most powerful antiproliferative action against keratinocytes. Topical application of PUVA utilising 8-MOP and isopsoralen effectively reduced transepidermal water loss from 55 to 33 and 38 g/m2/h, respectively, in imiquimod-

induced plaque [10] . In contrast to imiquimod's 117 μm epidermal thickening, 8-MOP and isopsoralen decreased it to 62 μm and 26 μm, respectively. While 8-MOP and other compounds did not affect IL-6 expression in psoriasiform skin, isopsoralen did. It is possible to consider isopsoralen as a potential option for PUVA therapy.

Khushboo, P. S., Jadhav, V. M., Kadam, V. J., & Sathe, N. S. (2010). Through the course of thousands of years, plants have served as the foundation for a wide variety of traditional medicines all across the world, and they continue to offer innovative treatments to the human race. Ever since the dawn of human civilization, plants have been one of the most important sources of medicinal substances. The recent resurrection of plant remedies can be attributed to a number of causes, including the efficacy of plant medicines and the lower risk of adverse effects when compared to medical treatments that are now available [11]. Psoralea corylifolia, more generally referred to as babchi, is a well-liked herb that has been utilised for a considerable amount of time in traditional Ayurvedic and Chinese medicine due to the miraculous capabilities it possesses in treating a variety of skin conditions. In addition, pharmacological research is being conducted on this plant to investigate its chemoprotective, antioxidant, antibacterial, and antiinflammatory effects. With regard to its ethnobotany, pharmacognostic features, traditional applications, chemical ingredients, and a synopsis of its numerous pharmacologic actions and clinical impacts, this study makes an effort to highlight the material that is currently accessible on P. corylifolia. Additional topics, such as toxicity and safety considerations, are also included in this discussion. The creation of interest in babchi will be facilitated by this, and it may also be of assistance in the development of novel formulations that have more medicinal and commercial value [12].

Attri, S., Singh, A., Rashid, F., Singh, S., Mohana, P., Alshehri, S., ... & Arora, S. (2023). One of the most common kinds of cancers in the world are skin cancers that do not include melanoma. The most frequent skin ailment in India is subcutaneous squamous cell carcinoma (SCC), and the likelihood of developing this illness grows significantly as sun exposure accumulates. Although there are several options for treating squamous cell carcinoma (SCC), it is important to find safe and effective ways to deal with recurrence and metastasis. This is why we set out to examine Bakuchiol's (Bak) effects; this plant has a long history of usage in traditional medicine for skin ailments in a variety of countries, but its exact mode of action has remained a mystery. Using the human squamous carcinoma (A431) cell line as a model, we studied Bak's effects on proliferation, apoptosis, and inflammation [13].Bak was isolated from Psoralea corylifolia and subsequently

characterised by NMR, HRMS, and FTIR. This allowed for the characterization of the pure component. The bioefficacy of these compounds was examined using a battery of in vitro experiments conducted on the A431 cell line. We used real-time quantitative polymerase chain reaction (RT-qPCR) to analyse the expression levels of inflammatory markers (TLR 9, IFN β, IL 23, JAK 3, and STAT 3) and get molecular insights.Bak therapy inhibited A431 cell proliferation in a dose-dependent fashion, according to the results [14]. Initially, apoptotic markers were identified in cell samples analysed by scanning electron microscopy, fluorescence, and phase-contrast imaging. Exactly how cells die was the motivation for this procedure. Also, a flow cytometer was used to study the cell cycle, and what was found was that cells treated with Bak had more reactive oxygen species (ROS), less matrix metalloproteinase (MMP), and were arrested at the G0/G1 phase, which made the induction of apoptosis even more effective. Furthermore, the therapeutic importance of Bak was further supported by the findings of RT-qPCR research, which showed that A431 cell inflammatory marker expression was reduced following Bak administration. The molecular docking study provided more evidence that Bak has an ideal scaffold that can meet the pharmacophoric criteria for inhibiting JAK3 kinase [15].

METHODS

The literature was subjected to a comprehensive evaluation that was carried out. It was determined to implement a thorough approach.

Preferred reporting items for systematic reviews and meta-analyses, or PRISMA, is the protocol that should be followed .

RESULT

Following the completion of the literature search, a total of six research publications were acquired. These studies were able to describe the impact that bakuchiol has on the ageing process of the skin and were able to fulfil the inclusion criteria. In the table that follows, each of the six articles that were chosen is stated (Table 1) [16].

Through their research, Draelos and colleagues demonstrated that the incorporation of bakuchiol into face moisturisers and cleansers has the ability to enhance the smoothness and wrinkles of the skin, as well as its clarity, brightness, general look, and moisture levels ($p<0.001$).8. In general, people with sensitive skin have a very positive reaction to the product.8. This is consistent with

the findings of research carried out by Dhaliwal et al. and Chaudhuri and Bojanowski in a different study. In all of these studies, the researchers attempted to compare bakuchiol with retinol, a substance that is well-known for its favourable impact on preventing or improving the signs of skin ageing.3, 9 According to the findings of both investigations, bakuchiol has an impact that is comparable to that of retinol in terms of decreasing wrinkles and fine lines [17].

Additionally, Dhaliwal et al. reported that bakuchiol has the ability to reduce hyperpigmentation of the skin. Chaudhuri and Bojanowski reported that bakuchiol improves elasticity, firmness, and overall decrease in indications of photodamage.3, 9 To investigate the impact that melatonin, bakuchiol, and ascorbyl tetraisopalmitate have on the ageing process of the skin, Goldberg, Robinson, and Granger conducted a different research in which they employed a triple combination of components. On two different occasions, in 2018 and 2020, they employed a mix of creams that was quite similar to one another.ten, eleven Wrinkles, skin hydration, transepidermal water loss (TEWL), oily skin, and non-comedogenic skin were the subjects of the first research, which utilised a large sample size of 103 individuals. These individuals were divided into five experimental groups, and each group was subjected to personal testing in terms of the following characteristics [18].

There was a significant reduction in the appearance of wrinkles and redness, as well as an increase in the stiffness of the skin ($P < 0.01$), as well as an improvement in the overall quality of the skin and the complexion. A considerable decrease in TEWL was seen, but the levels of hydration were increased. Excellent approval across the board, including from those with oily skin.ten The later research, which was conducted in the year 2020, likewise revealed comparable findings, but with a lower sample size of twenty-four individuals. The enhancement of the skin texture, pigmentation, erythema, skin tone, complexion, fine lines, and wrinkles was shown to be statistically significant ($P < 0.05$)11

The most recent research that utilised combination compounds was conducted by Bacqueville and colleagues. However, the chemicals that were utilised were a combination of bakuchiol and vanilla tahitensis extract (VTE). According to the findings of his research, the extract of the combination of these two substances has the potential to considerably improve the degree to which the skin is firm and radiant [19].

DISCUSSION

As a multidimensional biological process, ageing is impacted by both internal and extrinsic variables that collectively contribute to the ageing of the skin. The discussion portion of the study review dives into the complicated nature of ageing as a multiple biological process. An inherent and spontaneous process that takes place spontaneously over the course of time is referred to as intrinsic ageing. This type of ageing is also sometimes referred to as chronological or biological ageing. This process takes place over time and involves the progressive degradation of organ design and functioning, which ultimately leads to a reduction in flexibility and resistance against a variety of stresses. Extrinsic ageing, on the other hand, is frequently connected with photoaging. This kind of ageing is controlled by external variables such as exposure to sunshine, smoking, and eating habits, all of which contribute to the structural and functional deterioration of the skin. The selected publications that were reviewed in the study review included clinical studies that particularly examined the tolerance and efficacy of products that included bakuchiol, which is a chemical that is derived from Psoralea corylifolia, on sensitive skin. The purpose of these clinical research was to evaluate the feasibility and effectiveness of integrating bakuchiol into skincare routines, with a particular emphasis on persons who have skin types that are sensitive. The findings of these clinical trials gave useful insights into the effects of goods containing bakuchiol, offering light on the potential advantages that these products may have for persons who have skin sensitivities who would benefit from them.

Comparing the efficacy of retinol, a well-known chemical that is recognised for its good effects on preventing or ameliorating skin ageing, with that of bakuchiol, the research was conducted to determine which compound was more successful. According to the findings of the comparison study, retinol and bakuchiol both have comparable efficacy in terms of decreasing the appearance of wrinkles and fine lines. The significance of this discovery lies in the fact that retinol, which is highly recognised and frequently utilised in the beauty industry due to its anti-aging qualities, is present. Because of the similarities in efficacy between retinol and bakuchiol, it is possible that bakuchiol might serve as a viable alternative with comparable advantages, while also providing a choice that is perhaps more bearable for persons who are prone to skin irritation. The discussion section sheds insight on the complex processes that occur during the ageing process, with particular emphasis on the interaction between internal and extrinsic variables. Additionally, it highlights the results of scientific trials that evaluated products containing bakuchiol, specifically focusing on the efficacy and tolerance of these products by those with sensitive skin. A comparison with retinol

provides more evidence that bakuchiol has the potential to serve as an alternative in the field of skincare, having effects comparable to those of retinol in terms of decreasing wrinkles and fine lines. Individually and collectively, these findings contribute to a better understanding of the function that bakuchiol plays in skincare and the potential benefits that it may have in treating indications of ageing.

The biological process of ageing is a complicated but unavoidable one that occurs over the course of time. It is unavoidable and is something that happens on its own. The ageing process often results in the deterioration of organ architecture and functioning, which in turn leads to a reduction in flexibility and resilience to various forms of stress. Photoaging, also known as extrinsic ageing, is associated with variables such as smoking, hunger, and sun exposure, all of which contribute to the breakdown of the structure and functioning of the skin [20]. Intrinsic ageing, on the other hand, is a process that occurs naturally and mechanically. It is also referred to as chronological ageing, spontaneous ageing, and biological ageing.a 13 The skin ages as a result of a number of factors that have an effect on it and lead it to lose some of its functions.14, 15 The typical manifestations of ageing skin include the emergence of wrinkles, uneven pigmentation, dryness, and textural irregularities, as well as thinning skin, loss of elasticity, and the appearance of creases.

Table 1. Articles Selected

No	Origin	Design	Purpose	Sample	Result	No
1.	America[8]	Clinical trial	Finding out how sensitive skin reacts to bakuchiol-containing cleansers and moisturisers, as well as their effectiveness and barrier impact	60 ladies, ranging in age from 40 to 65, who suffer from wrinkles, sensitive skin, and skin discoloratio n	Clinical assessment	Global anti-aging, general brightness, clarity, and smoothness all noticeably improved. Those with sensitive skin will find that it is highly tolerable. A significant rise in skin moisture was revealed by cheek

						corneometry readings.
2.	America[3]	Results from a randomised, controlled trial	Analysing the effects of retinol and bakuchiol on skin ageing, as well as their respective side effects	Forty-four individuals used either retinol cream 0.5% daily or bakuchiol cream 0.5% twice daily.	Face photography, questioner	There were no statistically significant differences in the effects of retinol and Bakuchiol on the reduction of wrinkles and hyperpigmentation.
3.	America[9]	Clinical trial, blind study	Analysing the differences and similarities between retinol and bakuchiol in skincare	17 women aged 40-65 with aging skin	Clinical assessment	There was a marked decrease in the appearance of photodamage, as well as an improvement in the skin's elasticity, firmness, and fine lines and wrinkles.
1.	America[8]	Clinical trial	Finding out how sensitive skin reacts to bakuchiol-containing cleansers and	60 ladies, ranging in age from 40 to 65, who suffer from wrinkles,	Clinical assessment	Global anti-aging, general brightness, clarity, and smoothness all noticeably improved. Those with sensitive skin

			moisturisers, as well as their effectiveness and barrier impact	sensitive skin, and skin discoloration		will find that it is highly tolerable. A significant rise in skin moisture was revealed by cheek corneometry readings.

Collagen, which is largely synthesised and released by fibroblasts, is considered to be one of the most important structural proteins utilised by human skin [21]. Collagen promotes firmness in the skin and aids in the healing of age-related skin thinning.15–16th The extracellular matrix of the skin (collagen types I and III) and the basement membrane (collagen type IV) both include a significant amount of collagen as important components. There is a decrease in the quantity and quality of dermal fibroblasts, which leads to a decrease in the generation of new collagen [22]. This is a consequence of the ageing process and UV light.

The results of the first study conducted by Dreaelos and colleagues in the United States are presented in Table 1. This investigation demonstrated that the bakuchiol appliance has a substantial impact on the indications of skin ageing, including smoothness, clarity, brightness, and overall look [23]. Researchers from the Indian Institute of Chemical Technology (IICT) were the first to successfully isolate bakuchiol [(1E, 3S)-3-ethenyl-3, 7-dimethyl-1, 6octadien-1-yl] phenol from the seeds of Psoralea corylifolia L. Medik [24]. According to traditional Chinese and Indian medicine, this plant, which belongs to the family Fabaceae, has been utilised in many therapies. For its antioxidant, antibacterial, anti-aging, anti-inflammatory, anti-cancer, antidepressant, and hypoglycemic effects, bakuchiol has garnered a lot of attention [25].

Conclusion

According to the extensive scientific evaluation, bakuchiol, which is extracted from Psoralea corylifolia, has demonstrated encouraging results in reversing or reducing a number of skin ageing symptoms. The reviewed research provide credence to the idea that bakuchiol can alleviate common skin issues such dryness, hyperpigmentation, fine lines, and wrinkles, as well as loss of elasticity. With results like these, bakuchiol is starting to look like a serious rival in the skincare industry, with potential advantages on par with more well-known compounds like retinol. The

review highlights the fact that bakuchiol has few adverse effects, suggesting that it might be a better option for people with sensitive skin. Given that several skincare components tend to cause discomfort, this trait is very important. Bakuchiol has shown promise as an anti-aging treatment, and its positive safety profile and effectiveness make it a promising candidate for a wider spectrum of people. Although the results show promise, the review calls for more targeted studies to fully understand bakuchiol's effects when taken alone. It is advised to conduct a more targeted investigation of bakuchiol as an independent skincare agent, while the current investigations do provide light on its potential in conjunction with other substances and its effectiveness when compared to retinol. Additional study on bakuchiol's mechanisms, best uses, and possible interactions with other skincare products might lead to a more detailed understanding of these topics. The review highlights bakuchiol as an ingredient in effective skincare that shows promise and is well-tolerated. It encourages more research to determine its full therapeutic potential when used alone. These results provide hope for the future of skincare products that use bakuchiol, which might give people an effective and safe alternative to current anti-aging skincare products. From what we can tell from the research, bakuchiol helps keep skin looking young by minimising or avoiding the appearance of fine lines and wrinkles, elasticity and firmness loss, dullness, uneven hyperpigmentation, dryness, and other indications of ageing. Furthermore, bakuchiol's adverse effects are minimal. Still, bakuchiol is still used in combination with other drugs in certain publications, which means that overlapping effects might still be a possibility. Therefore, future studies should aim to be more targeted.

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