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CASE REPORT
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Eficacy the Use of Combined Goji Berry Cream for Skin Rejuvination and Post-Inflammatory Hyperpigmentation: Two Case Reports

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Abstract:

The antioxidant content in Goji Berries is known to prevent various signaling pathways in inflammation. Recent research is beginning to look at the potential of Goji berries in topical preparations for skin rejuvenation as well as their potential to reduce post-inflammatory hyperpigmentation. Two cases of post-inflammatory hyperpigmentation in a 29-year-old man and a 26-year-old woman were reported. The patients were given Goji berry combination cream therapy once daily for 4 weeks. The efficacy of therapy was assessed based on comparative evaluation of clinical conditions, skin analyzer examination, melanin index and erythema index examination with a mexameter, and Transepidermal Water Loss (TEWL) examination with a tewameter. After therapy, there was a decrease in the number of pores, wrinkles, pigmentation, melanin index value, erythema index, and improvement in TEWL in both patients. The use of a combination cream of Goji berry, niacinamide, vitamin E, ubiquinone, ceramide, and hyaluonic acid for skin rejuvenation and improving post-inflammatory hyperpigmentation due to acne vulgaris can be considered as an effective, comfortable, and safe therapeutic modality for patients.

Keywords: *Goji Berry*; Skin Rejuvination; Post-Inflammatory Hyperpigmentation

Introduction

Skin aging and post-inflammatory hyperpigmentation spots are therapeutic challenges in the cosmetic field. Acne vulgaris is a common skin condition involving inflammation of the pilosebaceous unit due to overproduction of keratin within the hair follicle, overproduction of sebum, and inflammation mediated by Cutibacteriun acnes.[1–3] Acne vulgaris is most often found on the face, in adolescents and young adult males. One of the most common complications of acne vulgaris is post-inflammatory hyperpigmentation.[3,4]

Post-inflammatory hyperpigmentation is generally chronic with the most common etiology being acne vulgaris, where there is overproduction of melanin, abnormal melanin deposition, and damage to basal keratinocytes which causes hyperpigmentation manifestations. Post-inflammatory hyperpigmentation is generally asymptomatic but often causes psychological stress and affects a person's quality of life.[5,6] Although this condition will generally improve, the healing process takes a long time and has the potential to prolong the treatment process.[5] Nowadays, there is increasing research on the management of post-inflammatory hyperpigmentation due to acne vulgaris, because it is related to cosmetic issues that affect the psychological state and overall quality of life of patients.[5,6]

Currently, various therapeutic methods have been reported to be carried out on post-inflammatory hyperpigmentation, ranging from etiological therapy, administration of creams with active ingredients, use of sunscreen, chemical peeling, to laser therapy. The use of creams with active ingredients is the most widely used method in the field of dermatology in dealing with cosmetic problems because it is considered quite effective, safe, comfortable, and has minimal side effects.[5,6]

Goji berry (Lycium barbarum) is a fruit that is reported to have a high composition of bioactive substances that play a role in antioxidants, anti-inflammatories, anti-aging, and many other benefits. This is based on the fact that Goji berries have a high antioxidant content and can stimulate the activity of scavenging free radical molecules, increase the production of antioxidant enzymes (SOD, CAT, GPx), reduce the activity of inflammatory mediators, reduce the production of pro-inflammatory cytokines, and prevent various signaling pathways in inflammation.[7,8] Goji berries are commonly consumed in the form of food and supplements. The use of creams containing Goji berries is a new step in the field of cosmetic dermatology, because it is considered capable of bringing out the potential of both its bioactive substance content and practical use for patients. Based on this background, in this study we report two cases related to the efficacy of a combination cream of Goji berry, Niacinamide, Vitamin E, Ubiquinone, Ceramide, and Hyaluronic Acid on skin rejuvenation and post-inflammatory hyperpigmentation after using the cream for 1 month.

Case Reports

In the first case, a 29-year-old man came with a primary complaint of blackish red spots on the cheek area. The complaint had been felt for the past three years. Previously, the patient often complained of acne growth with an oily face in the past 5-6 years. The complaint improved after the patient went to a dermatologist for three years. However, the acne treatment left blackish red marks on both of the patient's cheeks. Complaints of itching or pain in the lesion were denied. In the past three years, the patient has tried to avoid sweet and fried foods. Currently, the patient claims that she still often has new

acne that is not purulent in small amounts. The patient is currently coming because she wants the acne scars on both cheeks to fade so that her face looks smoother and younger. The patient had never undergone any therapy to reduce acne scars on his face.

The patient works as a health worker. Every day the patient works in the room from 06.00-16.00. The patient's activities during the holidays are only indoor activities. Occasionally, the patient goes to exercise indoors in the morning. The patient never used moisturizer or sunscreen on her face. The patient denied any smoking history. The patient has a history of consuming high protein milk currently.

From the patient's physical examination, the general condition appeared good and vital signs were within normal limits. Dermatological examination of the facial region found erythematous macules with partial hyperpigmentation, clear borders, multiple, irregular edges, varying shapes and sizes, with the presence of quite a lot of blackheads and rolling scar type skin atrophy (Figure 1). In addition, the patient's skin condition is also evaluated using a Skin Analyzer tool. From the results of the examination, the results obtained were pores 7.91 (large); wrinkles 2.07 (thin); pigmentation 5.68 (quite severe); sebum U zone 33 (slight), and sebum T zone 366 (slight) (Figure 2). The patient was then assessed for melanin index and erythema index using the Mexameter, as well as Trans Epidermal Water Loss (TEWL) assessment using the Tewameter. From the examination, the average value of the patient's melanin index before therapy was 268.67 (Graph 1); the average erythema index was 464.33 (Graph 2); and the average TEWL value was 20.6 grams/m/hour (Graph 3).

Based on anamnesis, physical examination, and supporting examinations, the patient was diagnosed with post-inflammatory hyperpigmentation due to acne vulgaris and acne scars. Patients were given therapy in the form of a combination cream containing Goji berry (Lycium Barbarum Fruit Extract 0.5%), Niacinamide 5%, Squalene 2%, Vitamin E, Ubiquinone 1%, Ceramide NP, and Hyaluronic Acid which was used once a day at night for 30 days.

Furthermore, a clinical patient evaluation was carried out (Figure 3) and with skin analyzer documentation, assessment of the melanin index and erythema index using the Mexameter tool, as well as TEWL assessment using the Tewameter tool in the 4th week of therapy. The effectiveness of therapy is assessed based on the level of clinical improvement of three indicators, including: pigmentation, peeling, itching/burning/stinging sensation and swelling of the skin which are evaluated during and 1 week after therapy. No side effects occurred in patients, either during use of the cream or 1 week after use of the cream.

From the results of the examination carried out after therapy with the Skin Analyzer tool, the results obtained were pores 4 (slightly large), wrinkles 1.86 (none), pigmentation 2.04 (normal), sebum U zone 1,100 (normal), and sebum T zone 988 (normal) (Figure 4). Meanwhile, from the results of the examination of the melanin index and erythema index using the Mexameter tool, as well as the examination of the TEWL value using the Tewameter tool, the average value of the melanin index after therapy was 249 (Graph 1); the average value of the erythema index was 377 (Graph 2); and the average value of TEWL was 15.63 grams/m/hour (Graph 3).

Figure 1. Dermatological status of the facial region before therapy (week 1). Hyperpigmented macules appear, with firm borders, multiple, irregular edges, varying in shape and size, with the presence of comedones.

Figure 2. Clinical evaluation with Skin Analyzer before therapy on the face (week 0) The results obtained were pores 7.91 (large); wrinkles 2.07 (thin); pigmentation 5.68 (quite severe); sebum U zone 33 (slight), and sebum T zone 366 (slight).

Figure 3. Dermatological status of the facial region after therapy (week 4). Erythema macules and hyperpigmentation appear to have faded, blackheads and skin atrophy are still visible.

Figure 4. Clinical evaluation with Skin Analyzer after facial therapy (week 4). The results obtained were pores 4 (slightly large), wrinkles 1.86 (none), pigmentation 2.04 (normal), sebum U zone 1,100 (normal), and sebum T zone 988 (normal)

In the second case, a 26-year-old woman came with a chief complaint of blackish red spots on the face area

accompanied by several small pimples. Complaints have been felt since the last 1 year. Initially, the complaint was in the form of small pimples, some of which sometimes contained pus. The patient was given a cream from a dermatologist and venereologist whose composition was unknown for the past year. Acne was said to be getting better but left a blackish red patch on the patient's face area after the acne healed. Complaints of itching and pain were denied. There was no history of injury or inflammation preceding the appearance of the brown spots. Nowadays, patients come because they want the acne scars on their face to fade so they look smoother and brighter.

The patient works as a health worker. Every day, the patient works indoors from 07.00-14.00. The patient's activities during the off-work period are more often done at home. The patient only goes out of the house a few times a month. The patient regularly uses doctor's cream, moisturizer, and SPF 45 sunscreen on her face. The patient washes his face using acne soap from the doctor. The patient's last menstruation was a month ago. Smoking history was denied. The patient often consumes sweet foods and drinks, as well as fried foods.

From the patient's physical examination, the general condition appeared good and vital signs were within normal limits. Dermatological examination of the facial region found erythematous macules with partial hyperpigmentation, clear borders, multiple, irregular edges, varying shapes and sizes, comedones, and the presence of box-scar type atrophic scars (Figure 5). In addition, the patient's skin condition is also evaluated using a Skin Analyzer. From the results of the examination, the results obtained were pores 3.2 (normal); wrinkles 1.6 (thin); pigmentation 1.2 (none); sebum U zone 1,200 (a lot), and sebum T zone 970 (normal) (Figure 6). The patient was then assessed for melanin index and erythema index using the Mexameter, as well as Trans Epidermal Water Loss (TEWL) assessment using the Tewameter. From the examination, the average value of the patient's melanin index before therapy was 231.67 (Fig. 9); the average erythema index was 317.33 (Fig. 10); and the average TEWL value was 12.61 grams/m/hour (Fig. 11).

Based on the anamnesis and physical examination performed, the patient was diagnosed with Post Inflammatory Hyperpigmentation due to Acne Vulgaris. The patient was then treated with a combination cream containing Goji berry (Lycium Barbarum Fruit Extract 0.5%), Niacinamide 5%, Squalene 2%, Vitamin E, Ubiquinone 1%, Ceramide NP, and Hyaluronic Acid which was used once a day at night for 30 days.

Furthermore, a clinical patient evaluation was carried out (Figure 7) and with skin analyzer documentation, melanin index and erythema index assessment using the Mexameter tool, as well as TEWL assessment using the Tewameter tool in the 4th week of treatment. The effectiveness of therapy was assessed based on the level of clinical improvement of three indicators, including: pigmentation, skin peeling, itching/burning/stinging sensation and swelling of the skin which were evaluated during and 1 week after therapy. No side effects occurred in patients, either during use of the cream or 1 week after use of the cream.

From the results of the examination carried out after therapy with the Skin Analyzer tool, the results obtained were pores 3 (normal), wrinkles 1.2 (none), pigmentation 0.8 (none), sebum U zone 1,190 (a lot), and sebum T zone 900 (normal) (Figure 8). Meanwhile, from the results of the examination of the melanin index and erythema index using the Mexameter tool, as well as the examination of the TEWL value using the Tewameter tool, the average value of the melanin index after therapy was 197

(Fig. 9); the average value of the erythema index was 272.67 (Fig. 10); and the average value of TEWL was 8.53 grams/m/hour (Fig. 11).

Figure 5. Dermatological status of the facial region before therapy (week 0). Describe the appearance of hyperpigmented macules, firm borders, multiple, irregular edges, varying shapes and sizes, with comedones and boxscar-type skin atrophy.

Figure 6. Clinical evaluation with Skin Analyzer before therapy on the face (week 0). The results obtained were pores 3.2 (normal); wrinkles 1.6 (thin); pigmentation 1.2 (none); sebum U zone 1,200 (a lot), and sebum T zone 970 (normal)

Figure 7. Dermatological status of the facial region after therapy (week 4). Erythema macules and hyperpigmentation appear to have faded, the face looks brighter, blackheads, some erythematous papules, and skin atrophy are still visible.

Figure 8. Clinical evaluation with Skin Analyzer after facial therapy (week 4). The results obtained were pores 3 (normal), wrinkles 1.2 (none), pigmentation 0.8 (none), sebum U zone 1,190 (a lot), and sebum T zone 900 (normal)

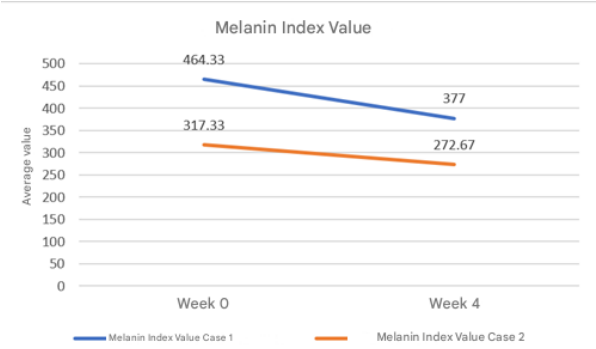

Figure 9. Evaluation of Melanin Index Value before and after treatment with Combination Cream containing Goji berry. A decrease in melanin index value was found in both cases.

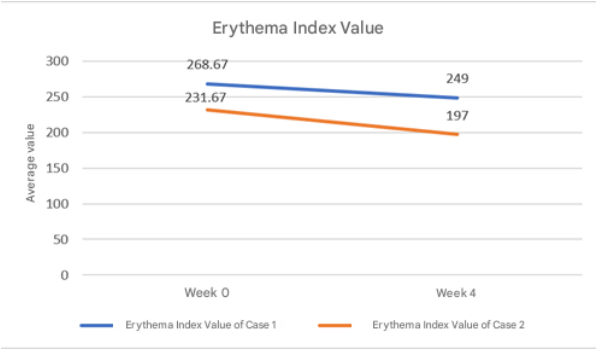

Figure 10. Evaluation of Erythema Index Value before and after treatment with Combination Cream containing Goji berry. A decrease in erythema index value was found in both cases.

Figure 11. Evaluation of TEWL Value before and after treatment with Combination Cream containing Goji berry. A decrease in TEWL value towards normal was found in both cases.

Discussion

Acne vulgaris is a common skin condition involving inflammation of the pilosebaceous unit due to overproduction of keratin in the hair follicle, overproduction of sebum, and inflammation mediated by Cutibacteriun acnes.[1–3] Based on its epidemiology, acne vulgaris is most often found in the facial area in adolescents and young adults, with a prevalence ranging from 35%-90% in adolescents.[1,3] In its pathogenesis, multiple factors interact and cause the formation of primary lesions, namely blackheads with varying degrees of severity from mild acne with few blackheads to severe acne characterized by various inflammatory manifestations that cause hyperpigmentation, scarring, and even psychological impacts.[3]

One of the most common complications of acne vulgaris is post-inflammatory hyperpigmentation. Post-inflammatory hyperpigmentation is an acquired skin disorder that commonly occurs after an inflammatory process or injury to the skin. Post-inflammatory hyperpigmentation is generally chronic and is more common in dark-skinned individuals.[4,5]

Post-inflammatory hyperpigmentation is generally asymptomatic but often causes psychological stress and affects a person's quality of life. On physical examination, this disorder manifests as hyperpigmented macules or patches, regular to irregular in shape, with a distribution consistent with areas of previous inflammation or injury. Epidermal hyperpigmentation is typically tan, brown, or dark brown in color and persists for months to years without treatment but may be resolved as the preceding inflammatory process resolves. Although this condition will generally improve spontaneously, the healing process takes a long time and has the potential to prolong the treatment process.[5,6]

Goji berries (*Lycium barbarum*) are quite popular nowadays because they are reported to have high bioactive content, which is considered to have a positive impact on health.[9] Goji berries are a good source of nutrients, with a composition of 46% carbohydrates, 16% fiber, 13% protein, and 1.5% fat. Goji berries are composed of: sugar (glucose, fructose, sucrose), fatty acids (linoneic acid, oleic acid, palmitic acid, and stearic acid), protein, fiber, multivitamins (riboflavin, thiamine, vitamin C), minerals (potassium, copper, manganese, magnesium, selenium, iron, zinc), and other nutritive bioactive substances, such as phenols, polysaccharides, and carotene, in a balanced composition. Goji berries are currently widely used as food or food supplements throughout the world.[10,11]

Goji berries have many health benefits and biological activities such as antioxidants, anti-inflammatory, antimicrobial, immunity, antidiabetic, neuroprotective, anticancer, prebiotic, antiobesity and many others. The antioxidant activity of Goji berries is associated with the content of polysaccharides, carotenes, flavonoids, AA-2βG (2-O-β-D-glucopyranosyl-L-ascorbic acid). These compositions stimulate antioxidant effects in various ways: radical scavenging activity against ROS by hydrogen atom transfer or electron donation, through metal chelation, or interacting with other antioxidants. Thus, its consumption can help prevent the activity of free radicals in damaging DNA, lipids, and proteins, while increasing the body's antioxidant defenses (such as SOD, CAT, GPx,).[7,8]

In addition, several compositions of Goji berries are related to antiaging, namely betaine, β-carotene, zeaxanthin, AA-2βG, and flavonoids. This composition reduces the activity of inflammatory mediators such as COX-1/COX-2 and iNOS and reduces the inflammatory process that occurs. Goji berries also reduce ROS production and GSSG levels by inhibiting pro-inflammatory cytokines such as IL-1, IL-6, TNF-α, and NF-κB. Goji berries also have a preventive effect on skin damage caused by ultraviolet B (UVB) radiation, which plays a major role in causing skin aging. Betaine has been shown to reduce radiation damage by preventing the formation of UVB-induced wrinkles and collagen damage by inhibiting extracellular signal-regulated kinase (ERK), protein kinase (MEK), and matrix metalloproteinase 9 (MMP-9).[7,8]

To date, there has been no research reporting on the use of Goji berry cream as a treatment for skin rejuvenation and post-inflammatory hyperpigmentation. In this case report, the author evaluated the administration of a combination cream containing Goji berry (Lycium Barbarum Fruit Extract 0.5%), Niacinamide 5%, Squalene 2%, Vitamin E, Ubiquinone 1%, Ceramide NP, and Hyaluronic Acid for skin rejuvenation and cases of post-inflammatory hyperpigmentation preceded by acne vulgaris. The patient underwent clinical documentation of post-inflammatory hyperpigmentation, then an examination was carried out using a skin analyzer, assessment of the melanin index, erythema index, and also TEWL before therapy was given. A combination cream containing Goji berries was applied at night for 30 days to the patient's entire face after the face was cleaned. The patient was advised to stop using night creams with other active ingredients, and to routinely use sunscreen in the morning and afternoon. One week after the administration of the cream, patients were evaluated for side effects that occurred during treatment. Evaluation of the effectiveness of administering combination cream containing Goji berry was assessed based on several parameters by comparing clinical conditions, skin analyzer examination results, melanin

index, erythema index, and TEWL in patients, before and one month after treatment.

Clinically, both patients showed improvements in moisture, pigmentation, and skin looked brighter than before. However, there has been no significant change in skin texture clinically. In addition, the results of the examination using a skin analyzer also showed good improvements in both cases, both in terms of pores, wrinkles, and pigmentation. This is in accordance with the content of substances in Goji berries which act as antioxidants, anti-aging, and anti-inflammatories. Meanwhile, there is an improvement in sebum production towards normal, both in the U and T areas, which is likely an effect of the skin rejuvenation process after using a combination cream containing Goji berries.

In addition to containing Goji berries, this combination cream also contains other active ingredients such as Niacinamide 5%, Squalene 2%, Vitamin E, Ubiquinone 1%, Ceramide NP, and Hyaluronic Acid. Niacinamide or known as Vitamin B3 (Nicotinamide, Nicotinic Acid Amide) is a pyridine-3 carboxylic acid amide form of niacin. Niacinamide is an active form of Vitamin B3 that can inhibit melanogenesis because it can affect the interaction between keratinocytes and melanocytes. The process of melanogenesis is the process of producing melanin through melanocyte cells. The main function of melanocytes is the production of melanin pigment. Niacinamide can reversibly block the transfer of melanosomes from melanocytes to keratinocytes.[12]

Vitamin E is a major lipophilic antioxidant in plasma, membranes, and tissues. Vitamin E is not soluble in water, but can dissolve in oil, acetone, and fat-soluble components that can ward off free radicals and oxygen molecules. The lipophilic nature of vitamin E makes it attractive for application to the skin. In animal models, topical vitamin E was applied to the skin to protect against UV-induced erythema. Topical vitamin E prevents UV-induced carcinogenesis. In addition to photoprotective effects, vitamin E inhibits melanogenesis through tyrosinase inhibition. Vitamin E in the form of emulsion, lotion, hydrophilic cream, hydrophilic ointment because it can increase penetration and absorption. Alpha-tocopherol is used as an anti-inflammatory and antiproliferative at concentrations between 2 and 20%, functions to soften the skin and increase the ability of the stratum corneum to retain moisture, accelerate epithelialization, and contribute to skin protection.[13]

Ubiquinone, better known as Coenzyme Q10 (CoQ10), is a natural antioxidant that plays a vital role in cellular energy production and exhibits significant anti-aging properties for the skin. Ubiquinone is produced naturally by the body; its levels decrease with age and due to external factors, such as UV exposure. Topical application of creams containing Ubiquinone can help fight oxidative stress caused by free radicals, which can accelerate aging and damage skin cells, reduce signs of aging by supporting the skin's ability to produce more collagen and elastin, and help prevent photoaging, which is premature aging of the skin due to sun exposure.[14]

Hyaluronan or hyaluronic acid (HA) is a natural glycosaminoglycan molecule found throughout the body's connective, epithelial, and nerve tissues, and is involved in skin moisture. The skin's natural production of HA decreases with age, contributing to the appearance of wrinkles and loss of skin volume. In dermatology and aesthetics, HA is often used for its hydration and antiaging benefits. This molecule forms a layer on the skin that holds water on the surface, thus slowing evaporation and increasing the elasticity and softness of the skin. So, it is expected that HA administration can maintain skin hydration and maintain skin hydration which plays a role in antiaging.[15]

Other parameters used to assess the effectiveness of therapy are assessment of melanin and erythema index using a mexameter, as well as assessment of TEWL value using a tewameter. In the assessment using the mexameter, a decrease in the melanin and erythema index values was found in both cases. The assessment using the tewameter also showed similar results in the form of a fairly good decrease in TEWL in both cases, with a decrease in TEWL value of <10 g/m2/hour indicating a very healthy skin moisture value. The TEWL value itself is used to assess the occurrence of skin barrier modification through loss of skin fluid. The lower the TEWL value, the healthier the patient's skin barrier.16,17 In addition, no side effects occurred in patients, either during or after using the cream.

Conclusions

Therapeutic modality using Goji berry combination cream given once daily for a month can improve clinical signs of post-inflammatory hyperpigmentation and increase skin rejuvenation. The results of these two case reports show that based on clinical and supporting examinations, improvements were obtained in pores, wrinkles, moisture, and skin pigmentation. Meanwhile, based on the examination of the melanin index and erythema index values using a texameter, a decrease in value was found which indicated improvement in both cases. Similar improvements were found in TEWL measurements using a tewameter. Both patients did not complain of any side effects, either during or after the cream was applied. With the increasing concern and psychological problems arising from post-inflammatory hyperpigmentation due to acne vulgaris and the improvement of skin moisture indicating improvement of skin rejuvenation, the use of Goji berry combination cream can be considered as a safe, comfortable, and quite effective therapeutic modality in improving patient's clinical complaints.

Further studies are needed with additional sample numbers and duration of use to assess the efficacy of topical Goji berry preparations for their anti-aging, anti-inflammatory, and antioxidant benefits for the skin.

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