

Epidermal Skin Barrier and Skin Care in Rosacea: A Narrative Review

*Serap Maden**

Near East University, Faculty of Medicine, Department of Dermatology, Nicosia, Cyprus

*Corresponding author:

Serap Maden

Near East University, Faculty of Medicine, Department of Dermatology, Nicosia 99138, Cyprus;

Tel: +90 5391062693

Email: serap.maden@neu.edu.tr

Received : March 22, 2024

Published : April 19, 2024

ABSTRACT

Rosacea is a chronic skin disease that primarily affects the face and can have a negative influence on the emotional, psychological and quality of life of patients. Due to the chronic and relapsing nature of the disease, as well as its complex pathogenesis, dermatologists often opt for combined therapies when treating patients. Owing to the impaired epidermal barrier function and the sensitive and easily irritated characteristics of their facial skin, patients diagnosed with rosacea are advised to practice gentle skin care, with a focus on gentle cleansing and moisturizing, and the use of sunscreen. It is often recommended by dermatologists that patients affected by rosacea make lifestyle modifications and use proper skin care in addition to medical treatment. Additionally, patients can receive education from their dermatologist and develop effective home care routines for skin care. This review focuses on the importance of skin care in the context of restoring the epidermal barrier for managing rosacea, with the aim of enhancing treatment outcomes and better addressing patient aspirations.

Keywords: Rosacea; Epidermal barrier; Skin care

INTRODUCTION

Rosacea is a chronic and inflammatory skin condition that causes relapsing flares. The clinical presentation of rosacea is characterized by skin sensitivity, flushing, centrofacial erythema, papules, pustules and hyperplasia of the sebaceous glands [1]. Rosacea has four subtypes: subtype 1, erythematotelangiectatic; subtype 2, papulopustular; subtype 3, phymatous; and subtype 4, ocular [2]. The subtypes of rosacea may overlap in some patients who are affected [1].

The diagnosis of rosacea is based on major criteria and secondary signs and symptoms. The diagnostic phenotype is characterized by persistent centrofacial erythema and phymatous changes. The major criteria include flushing, papules, and pustules, telangiectasia, and ocular findings such as lid margin telangiectasia, interpalpebral conjunctival

injection, corneal spade-shaped infiltrates, scleritis, and sclerokeratitis. The presence of two or more of these criteria may be considered diagnostic. Secondary signs and symptoms, such as a burning and/or stinging sensation of the skin, skin dryness, edema, and ocular manifestations, may appear with one or more diagnostic or major phenotypes [3,4].

The pathogenesis of rosacea has a complex and multifactorial process that involves various factors, including immunological, genetic, microbiological, ultraviolet radiation (UV), neurovascular, dietary, psychological stress, and sleep factors [5]. Treatment options include medical and instrumental treatments (laser and light therapies), cosmetic treatments, and behavioral changes. Medical and instrumental treatments can target permanent vascular changes, while betablockers and botulinum toxin can target flushing. Antibiotics, nonspecific antioxidants, and anti-inflammatory molecules can target the innate immune system. Analgesics and antidepressants can target the neurovascular component. Antiparasitic drugs can target *Demodex*. Controlling intestinal bacterial overgrowth can target the microbiome. Cosmetics and certain systemic drugs can target skin barrier impairment. Isotretinoin and surgery can target sebaceous glands. Behavioral changes, such as reducing alcohol and/or coffee consumption and consistently using sunscreen for UV exposure, can target environmental factors [6].

Patients with rosacea often experience symptoms of sensitive skin, which may be linked to impaired epidermal barrier function. Maintaining skin hydration is important for the integrity of the epidermal barrier, and using moisturizer can improve both the barrier function and reduce subjective signs of facial skin irritation [7]. Appropriate skin care plays an important role in maintaining remission and relieving the symptoms of rosacea. Moisturizers are crucial in treating rosacea, particularly in reducing flushing and erythema, as rosacea skin experiences higher trans epidermal water loss (TEWL) [8]. Adhering to skin care advice and using non-irritating skin care products can significantly prevent rosacea aggravation and improve the patient's quality of life [9].

MATERIALS AND METHODS

A retrospective literature review was conducted by searching PubMed and Google Scholar databases using keywords such as 'rosacea', 'epidermal barrier', and 'skin care'. The search was performed until March 2024. This review included the studies that evaluated the methods for managing skin care in patients

with rosacea.

RESULTS

Epidermal Barrier Dysfunction in Rosacea

In patients with rosacea, epidermal dysfunction is one of the causes of increased TEWL from the skin [10]. Epidermal barrier dysfunction can present as burning, stinging, dryness, and edema in clinical practice, which are secondary criteria of rosacea [11]. Epidermal inflammation and higher concentrations of cathelicidins lead to disruption of lipid synthesis and stratum corneum formation, which affects the barrier function and, consequently, facilitates the typical symptoms of rosacea including itching, burning and stinging [12]. Kallikrein-5 activity might be a contributing factor to pathogenesis, as it is a protease that increases at alkaline pH levels, commonly found in rosacea skin. This activity has been linked to epidermal barrier dysfunction in rosacea patients [10]. In injured or irritated skin, the expression of kallikrein, including types 5 and 7, tends to decrease. In rosacea, the pattern of the innate immune response is changed, with upregulation of the toll-like receptor 2, resulting in increased levels of kallikrein 5 from keratinocytes [12]. Furthermore, *Demodex* mites have the potential to compromise the skin barrier, resulting in breaches in the skin that may trigger hypersensitivity in individuals with rosacea [10]. The inflammatory response compromises barrier function, and in addition to vasodilation, there is an increase in TEWL, resulting in a decrease in epidermal hydration, which is a stimulus for inflammation [12]. Along with increased TEWL and moisture loss, the innate immune system has been affected, resulting in elevated levels of antimicrobial peptides, such as cathelicidin, which initiates epidermal barrier dysfunction and causes further TEWL [12].

Skin Care in Rosacea

Proper skin care should involve gentle cleansing, effective moisturization, and the use of soothing ingredients, UV protection, and the application of pigments to help conceal redness [13].

Moisturizers and Cleansing Agents in Rosacea

Moisturizers are crucial for creating an optimal condition for the skin's barrier to repair itself [14]. Moisturizers should be alcohol-free, non-greasy, and water-based [15]. Silicone-based moisturizers are the most recommended due to their

aesthetic appeal, non-warming effect on the skin, and lack of support for organism growth. It is not advisable to employ moisturizers that contain high lipid formulations derived from plant or animal materials that may stimulate bacterial growth. Specifically, it is best to avoid coconut, olive, hemp, argan, and sunflower oils for rosacea patients due to the potential for heat buildup and exacerbation of the complexion [14,15].

In the treatment of rosacea, it is important to consider epidermal barrier dysfunction, which can be clinically expressed as dry or scaly skin. Individuals may experience irritable skin with a burning or stinging sensation when using cosmetic products, particularly those that have the potential to impair the skin barrier, such as exfoliants, soaps and tonics [12]. The addition of physiologic moisturizers and cleansers to standard skin care regimens may improve treatment outcomes in cases of mild to moderate disease [11]. The use of moisturizing products that increase moisture levels reduces the breakdown of stratum corneum proteins and the depletion of epidermal lipids, which contribute physiological elements to the restoration of the skin barrier, and do not include substances with known irritant potential, therefore helping to inhibit the inflammatory process - and thus the symptoms [12].

Proper skin care is essential for individuals with rosacea. However, certain skin care products, such as those containing formaldehyde, can act as *Demodex*-derived proteases and trigger the inflammasome NACHT, LRR, and PYD domain-containing protein-3, exacerbating the lesions. Furthermore, these products can also activate the transient receptor potential ankyrin-1 pathway, which can act as a triggering factor for rosacea. To treat this condition, anti-inflammatory drugs, antibiotics, and brimonidine may be necessary. It is important to avoid the use of these products [9].

A clinical trial evaluated the efficacy of a skin care regimen consisting of micellar water, serum, and cream for sensitive and redness-prone skin in rosacea patients. The trial quantified improvements in facial erythema, rosacea-associated symptoms, and quality of life. A reduction of 16% in skin redness was observed, while rosacea-associated symptoms decreased by 57.1%. Additionally, the quality of life of affected patients in the intervention group improved by 54.5% [16]. A study with 42 participants showed that a skincare routine consisting of wash foam, daily sunscreen cream, and night cream improved skin hydration and skin barrier function. Over 90% of the participants reported that the routine was effective

and pleasant, and they expressed their intention to continue using the products [17].

Due to the increased irritability and vascular reactivity of the skin in patients with rosacea, it is important to use a gentle skin cleansing process [18]. The cleansing requirements of the rosacea patient include elimination of excessive sebum, environmental debris, desquamated corneocytes, undesirable microorganisms [14]. Lukewarm water should be used to avoid any vascular reactions. Additionally, it is important to avoid intense rubbing during drying of the face, peeling products, blood-flow-promoting facemasks, and tonics that contain alcohol or other blood-flow-stimulating or astringent ingredients [18]. Skin cleansing formulations should be soap-free and should not contain astringents, toners, camphor, menthol or acetone. Moisturizers for rosacea should include humectants and occlusives to restore epidermal lipids, retain moisture and repair barrier function. Anti-aging products with cell-stimulating ingredients and products that include astringents, toners, camphor, menthol, alcohol or acetone should be avoided in patients with rosacea [15].

A study of 999 cases of rosacea and 1010 controls found a positive correlation between rosacea occurrence and frequent cleansing and excessive use of cleansing products [19]. Excessive skin cleansing can disrupt the skin's barrier function, potentially triggering the development of rosacea. It is important to avoid this and repair any damage to the skin barrier with proper skincare [20,21].

Inappropriate topical preparations can aggravate rosacea, but correct skin care can help repair the skin barrier and manage symptoms and inflammation [12]. Patient education is crucial to ensure that the individual comprehends the situation and establishes realistic expectations for the treatment in terms of degree of recovery and response. In the non-pharmacologic treatment of rosacea, it is important to counsel the patient on trigger factors and skin care routine such as moisturizing, cleansing, and sun protection [22].

UV Protection in Rosacea

Rosacea patients need broad-spectrum UV protection with a sunscreen with a sun protection factor (SPF) of 30+ to provide protection against UV-B and UV-A radiation. To avoid triggering flushing in individuals with rosacea, it is recommended to avoid facial warmth. For sunscreen-containing moisturizers, it is best to choose those that contain inorganic sunscreens

like titanium dioxide and zinc oxide, which reflect UV radiation energy instead of releasing heat [14]. Blockage of UV light is very important; sunscreens reduce the production of LL-37 and the subsequent production of reactive oxygen species that can induce rosacea [8]. Skin care advice typically includes avoiding triggers, using sunscreen with a SPF of 30 or higher, applying moisturizers for dry skin and drying products for oily skin, and gently cleansing the entire face. Following these steps consistently is important for maintaining healthy skin [9].

Photoprotection is an essential part of skin care. UV radiation can negatively impact skin barrier function, induce skin inflammation and aggravate rosacea [23]. For optimal results, it is recommended that patients with rosacea use moisturizers containing both dimethicone and zinc oxide, which also include sunscreen [14]. Inorganic UV filters, such as titanium dioxide and zinc oxide, also referred to as physical filters, have a lower allergenic potential and are thus preferred for sensitive skin conditions. It is important to avoid applying sunscreen over inflamed skin to prevent systemic absorption and photosensitization. There is still a need for sunscreens that can be safely used across inflamed skin [23].

A study evaluated the effectiveness and tolerability of a tinted daily SPF-30 facial moisturizer on 33 females with mild to moderate rosacea and nontransient erythema. The moisturizer was found to improve the appearance of skin redness and feelings of dryness and tightness/tension in rosacea-prone patients [24].

Camouflage in Rosacea

Rosacea patients often struggle with the misconception that their condition is linked to alcoholism, as well as sensitivity to temperature changes. Many patients seek corrective medical makeup that is both effective and safe. Two significant advances have led to the creation of efficacious formulations tailored to the rosacea skin type. Galenic research has allowed the production of textures that provide coverage while remaining sufficiently fluid to spread well and be easily removed. Additionally, color-wheel-based correction can be used to neutralize redness by adding green pigments to creams or sticks [25].

Botanical Ingredients in Cosmeceuticals that Aid in the Restoration of the Epidermal Barrier

Colloidal oatmeal

Colloidal oatmeal (*Avenasativa*) can relieve itching and irritation through its ability to soothe and prevent inflamed skin. It has a number of bioactive components, such as: polysaccharides, proteins, lipids, saponins, enzymes, flavonoids, vitamins, and avenanthramides (polyphenols). The fine particles are distributed on the skin to form a protective, occlusive barrier that slows the loss of moisture and provides hydration to help improve the epidermal barrier. Additionally, oatmeal saponins aid in dissolving dirt, oil, and sebaceous secretions, which can help to balance the skin's pH. Oats possess significant antioxidant, UV absorbing, and anti-inflammatory effects due to ferulic, caffeic, and coumaric acids, as well as flavonoids and alpha-tocopherol (vitamin E) [26].

Avenanthramides are phenolic compounds found in oat grains that possess anti-inflammatory and antipruritic properties. They achieve this by reducing the production of NF-kappa B in keratinocytes and decreasing the production of proinflammatory cytokines such as interleukin-8. Additionally, avenanthramides inhibit prostaglandin synthesis. Many studies have supported the use of colloidal oatmeal in managing inflammatory dermatoses, such as atopic dermatitis, due to its anti-inflammatory, hydrating, and antipruritic properties. Colloidal oatmeal also may be a useful ingredient in cleansing or moisturizing products used in rosacea [26].

Green tea

Green tea (*Camellia sinensis*) contains polyphenols, including epicatechin, epicatechin-3-gallate, epigallocatechin, and eigallocatechin-3-gallate, which have anti-inflammatory properties [14]. Studies have shown that topical application of green tea has anti-inflammatory effects, and that green tea extract containing epigallocatechin-3-gallate can reduce UV-B-induced inflammation [27]. Additionally, green tea may decrease the signs of rosacea directly by reducing the amount and visibility of telangiectasias and minimizing skin barrier disruption [26].

Aloe vera

The compounds found in aloe vera (*Aloe vera*) include aloin, aloe emodin, aletinic acid, choline, and choline salicylate. The topical application of aloe vera has been shown to have beneficial effects on the skin, including reducing inflammation, decreasing bacterial colonization, and

enhancing wound healing. These effects may be relevant to the treatment of rosacea [14]. In addition, aloe vera contains mucopolysaccharides, amino acids, and zinc, which can help maintain skin integrity, retain moisture, reduce erythema, and prevent skin ulcers [28].

To achieve a cosmeceutical effect for rosacea patients, the concentration of aloe vera in any moisturizer must be at least 10%. The anti-inflammatory activity of aloe vera may be attributed to its ability to inhibit cyclooxygenase as part of the arachidonic acid pathway through the choline salicylate component of aloe vera [14].

Licorice extract

Licorice extracts from *Glycyrrhiza inflata* and *Glycyrrhiza glabra* contain licochalcone A (Lic A) and glabridin, respectively. Both compounds have been shown to possess anti-inflammatory and anti-irritant properties. Licorice has also been found to reduce inflammation, soothe irritation, promote mucous secretion, and stimulate adrenal gland activity [26]. Specifically, Lic A has been shown to possess anti-inflammatory properties.

This is demonstrated by its ability to inhibit the release of prostaglandin E2 (PGE 2) from keratinocytes in response to UVB-induced erythema, as well as the lipopolysaccharide-induced release of PGE 2 by adult dermal fibroblasts [14]. It has been found that the use of skin care products containing Lic A can help reduce the severity of erythema, improve TEWL, and enhance epidermal hydration in patients with pre-rosacea and rosacea subtype I [13]. Lic A is a commonly used active agent in products for rosacea that helps to reduce redness [14].

Niacinamide

The topical application of niacinamide reduces TEWL and improves the moisture content of the horny layer, stabilizing epidermal barrier function. Niacinamide stimulates protein synthesis such as keratin, promotes ceramide synthesis, enhances keratinocyte differentiation, and increases intracellular nicotinamide adenine dinucleotide phosphate concentrations. Topical use of niacinamide may improve surface texture, decrease rhytides, suppress photocarcinogenesis, and have anti-inflammatory effects in rosacea [26] (Table 1).

Table 1: Botanical Ingredients for Epidermal Barrier Restoration [13,14,26-28].

Botanical ingredient	Active agent	The functional effect on skin
Colloidal oatmeal <i>Avena sativa</i>	Polysaccharides, proteins, lipids, saponins, enzymes, flavonoids, vitamins, avenanthramides	-Provides hydration and improves the epidermal barrier -Balances pH of the skin
Green tea <i>Camellia sinensis</i>	Polyphenols (epicatechin, epicatechin-3-gallate, epigallocatechin, epigallocatechin-3-gallate)	-Reduces UV-B-induced inflammation -Reduces the amount and visibility of telangiectasias -Minimizes skin barrier disruption
Aloe vera <i>Aloe vera</i>	Aloin, aloe emodin, aletinic acid, choline, choline salicylate	- Reduces inflammation -Decreases bacterial colonization -Enhances wound healing -Maintains skin integrity -Retains moisture -Reduces erythema
Licorice <i>Glycyrrhiza inflata Glycyrrhiza glabra</i>	Licochalcone A, Glabridin	-Inhibits UV-B-induced erythema -Reduces the severity of erythema -Improves TEWL -Enhances epidermal hydration
Niacinamide <i>Vitamin B3</i>	Niacinamide	-Reduces TEWL -Improves the moisture content of the horny layer -Stabilizes epidermal barrier function -Provides anti-inflammatory effects

Botanical ingredients and active agents are utilized in cosmeceuticals to restore the epidermal barrier in patients with rosacea. UV-B, ultraviolet radiation-B; TEWL, trans epidermal water loss.

DISCUSSION

Rosacea is a multi-system dermatosis with inflammatory, neural and vascular components, in which environmental factors can have a positive or negative impact [12]. The pathophysiology of rosacea is complex and multifactorial, requiring an appropriate care regimen. Therefore, a threefold treatment approach is most likely to be successful. The triad of rosacea care involves considering all of the patient's needs, rather than solely focusing on specific symptoms of the disease. This includes patient education, skin care, and treatment. It is important to avoid only addressing individual symptoms. For instance, patients with erythematotelangiectatic rosacea may benefit from techniques such as relaxation training, cognitive or behavioral therapy, biofeedback, and medication, including antidepressants and beta blockers, to manage psychological factors [22]. Skin care can improve symptom management and quality of life for patients with rosacea [8]. Preserving the skin barrier is crucial for individuals with rosacea, as they belong to a group of people with sensitive skin who may experience negative reactions when exposed to mild irritants or substances that produce unpleasant sensory stimuli [14]. Improving barrier functioning can dramatically reduce symptoms by decreasing inflammation and reducing interaction with irritants. For patients with rosacea, these two factors are fundamental to improving their symptoms [12].

CONCLUSION

When considering medical or device treatment methods for rosacea, it is crucial that dermatologists inform patients about the nature of the disease, the importance of avoiding possible triggers, and the significance of skin care and lifestyle modifications. Patients diagnosed with rosacea should practice gentle skin care, focusing on mild cleansing and moisturizing, and using sunscreens. It is recommended to consider using products that are less likely to cause skin irritation. The ingredients utilized in cosmeceuticals are subject to constant evolution. Further research may lead to the development of new products that could improve the quality of life for individuals with rosacea.

REFERENCES

1. Tan J, Almeida LM, Bewley A, Cribier B, Dlova NC, Gallo R, et al. (2017). Updating the diagnosis, classification and assessment of rosacea: recommendations from the global ROSacea CONsensus (ROSCO) panel. *Br J Dermatol.* 176(2):431-438.
2. Gallo RL, Granstein RD, Kang S, Mannis M, Steinhoff M, Tan J, et al. (2018). Standard Classification and Pathophysiology of Rosacea: The 2017 Update by the National Rosacea Society Expert Committee. *J Am Acad Dermatol.* 78(1):148-155.
3. Schaller M, Almeida LMC, Bewley A, Cribier B, Del Rosso J, Dlova NC, et al. (2020). Recommendations for rosacea diagnosis, classification and management: update from the global ROSacea CONsensus 2019 panel. *Br J Dermatol.* 182(5):1269-1276.
4. Tan J, Berg M, Gallo RL, Del Rosso JQ. (2018). Applying the phenotype approach for rosacea to practice and research. *Br J Dermatol.* 179 (3):741-746.
5. Maden S. (2023). Rosacea: An Overview of Its Etiological Factors, Pathogenesis, Classification and Therapy Options. *Dermato.* 3(4):241-262.
6. Cribier, B. (2022). Rosacea: Treatment targets based on new physiopathology data. *Ann. Dermatol. Venereol.* 149(2):99-107.
7. Del Rosso JQ. (2009). The use of moisturizers as an integral component of topical therapy for rosacea: clinical results based on the Assessment of Skin Characteristics Study. *Cutis.* 84(2):72-76.
8. Abokwidir M, Feldman SR. (2016). Rosacea Management. *Skin Appendage Disord.* 2(1-2):26-34.
9. Buddenkotte J, Steinhoff M. (2018). Recent advances in understanding and managing rosacea. *F1000Res.* 7:F1000 Faculty Rev-1885.
10. Woo YR, Lim JH, Cho DH, Park HJ. (2016). Rosacea: Molecular Mechanisms and Management of a Chronic Cutaneous Inflammatory Condition. *Int J Mol Sci.* 17(9):1562.

11. Marson J, Bhatia N, Graber E, Harper J, Lio P, Tlougan B, et al. (2022). Supplement Article: The Role of Epidermal Barrier Dysfunction and Cutaneous Microbiome Dysbiosis in the Pathogenesis and Management of Acne Vulgaris and Rosacea. *J Drugs Dermatol*. 21(9):SF3502915-SF35029114.
12. Addor FA. (2016). Skin barrier in rosacea. *Anais Brasileiros de Dermatologia*. 91(1):59-63.
13. Schoelermann AM, Weber TM, Arrowitz C, Rizer RL, Qian K, et al. (2016). Skin compatibility and efficacy of a cosmetic skin care regimen with licochalcone A and 4-t-butylcyclohexanol in patients with rosacea subtype I. *J Eur Acad Dermatol Venereol.*;30 (1):21-27.
14. Draelos ZD. (2017). Cosmeceuticals for rosacea. *Clin Dermatol*. 35(2):213-217.
15. Goh CL, Wu Y, Welsh B, Abad-Casintahan MF, Tseng CJ, Sharad J, et al. (2023). Expert consensus on holistic skin care routine: Focus on acne, rosacea, atopic dermatitis, and sensitive skin syndrome. *J Cosmet Dermatol*. 22(1):45-54.
16. Guertler A, Jøntvedt NM, Clanner-Engelshofen BM, Cappello C, Sager A, et al. (2020). Efficacy and safety results of micellar water, cream and serum for rosacea in comparison to a control group. *J Cosmet Dermatol*. 19: 2627–2633.
17. Santoro, F., Lachmann, N. (2019). An Open-Label, Intra-Individual Study to Evaluate a Regimen of Three Cosmetic Products Combined with Medical Treatment of Rosacea: Cutaneous Tolerability and Effect on Hydration. *Dermatol Ther (Heidelb)*. 9:775–784.
18. Kresken J, Kindl U, Wigger-Alberti W, Clanner-Engelshofen BM, Reinholz M. (2018). Dermocosmetics for Use in Rosacea: Guideline of the Society for Dermopharmacy. *Skin Pharmacol Physiol*. 31(3):147-154.
19. Li G, Wang B, Zhao Z, Shi W, Jian D, et al. (2021). Excessive cleansing: an underestimating risk factor of rosacea in Chinese population. *Arch Dermatol Res*. 313(4):225-234.
20. Huang YX, Li J, Zhao ZX, Zheng BL, Deng YX, et al. (2020). Effects of skin care habits on the development of rosacea: a multi-center retrospective case-control survey in Chinese population. *PLoS One*. 15(4):e0231078.
21. Zuo Z, Wang B, Shen M, Xie H, Li J, Chen X, et al. (2020). Skincare habits and rosacea in 3,439 Chinese adolescents: a university-based cross-sectional study. *Acta Derm Venereol*. 100(6):adv00081.
22. Gonçalves MM, Pina ME. (2017). Dermocosmetic care for rosacea. *Braz J Pharm Sci*. 53(4):e00182.
23. Passeron T, Lim HW, Goh CL, Kang HY, Ly F, Morita A, et al. (2021). Photoprotection according to skin phototype and dermatoses: practical recommendations from an expert panel. *J Eur Acad Dermatol Venereol*. 35(7):1460-1469.
24. Baldwin H, Santoro F, Lachmann N, Teissedre S. (2019). A novel moisturizer with high sun protection factor improves cutaneous barrier function and the visible appearance of rosacea-prone skin. *J Cosmetic Dermatol*. 18(6):1686–1692.
25. Guerrero D. (2011). Dermocosmetic management of the red face and rosacea. *Ann Dermatol Venereol*. 138(3):S215-S218.
26. Emer J, Waldorf H, Berson D. (2011). Botanicals and anti-inflammatories: natural ingredients for rosacea. *Semin Cutan Med Surg*. 30(3):148-155.
27. Katiyar SK, Matsui MS, Elmets CA, Mukhtar H. (1999). Polyphenolic antioxidant (-)-epigallocatechin-3-gallate from green tea reduces UVB-induced inflammatory responses and infiltration of leukocytes in human skin. *Photochem Photobiol*. 69(2):148-153.
28. Hekmatpou D, Mehrabi F, Rahzani K, Aminiyan A. (2019). The Effect of Aloe Vera Clinical Trials on Prevention and Healing of Skin Wound: A Systematic Review. *Iran J Med Sci*. 44(1):1-9.