Pharmacological effects of Royal Jelly on Human Skin

Oo, WM a,*

a Department of Biochemistry, University of Medicine-Magway, Magway, Myanmar.

*Corresponding Author
drwinminoo.ummg@gmail.com
(Oo, WM)
Tel.: +9595340338

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ABSTRACT: Honey is a medicinal agent that ancient medicine described as a common ingredient in different remedies for diseases long time ago. Recently, royal jelly, the essential nutrient for the development of the queen bee, becomes popular for dermatologic and cosmetic issues as studies have revealed in strong evidence regarding its benefits to the human skin. Current understanding of royal jelly affecting the skin supports not only aesthetic medicine but also clinical cases such as contact dermatitis. Therefore, a concise review on the benefits of royal jelly on the human skin becomes necessary. This review aims to evaluate current evidence of therapeutic and cosmetic values of royal jelly for dermatological purposes. The information provided in this review can be used to design and develop new pharmacological agents from royal jelly in cosmetic and clinical dermatology.

Keywords: Aesthetics, Honey, Pharmacological, Royal Jelly, Skin

1 Introduction

Royal jelly is produced from mandibular and hypopharyngeal glands of worker honeybees (Apis mellifera) and is necessary for the development of the queen honeybee [1]. Royal jelly is a yellow-white, acidic secretion, pungent in taste and odor [2]. Royal jelly is rich in nutrients such as proteins, lipids, amino acids, sugars and vitamins [3].

Ancient medicine mentioned honey to treat various diseases such as peptic ulcer, fatigue and wounds. Currently, research has focused on the effect of royal jelly on human skin and proved cosmetic benefits as well as clinical outcomes. Thus, an updated focused review becomes a need to evaluate the benefits of royal jelly to human skin.

Royal jelly becomes popular for its skin whitening and anti-aging effects in aesthetic medicine. Clinically, royal jelly carried advantages in treatment of wound healing and some inflammatory skin diseases such as atopic dermatitis. This paper aims to review the beneficial outcomes of royal jelly treatment on dermatological issues and underlying possible mechanisms.

2. Enhanced epidermal hydration

Dietary royal jelly improve epidermal hydration by modification of ceramide metabolism. In aged mice, supplementation with 1% royal jelly for 60 days increased the levels of epidermal hydration, individual ceramide, glycosylceramides, sphingomyelin, β-glucocerebrosidase and acidic sphingomyelinase. The mechanism is via enhancing ceramide metabolism not by gene expression control [4].

UV light can induce epidermal dehydration by reducing natural moisturizing factors (NMFs). Free amino acids are liberated when NMFs are degraded. Oral supplementation of royal jelly protects UV-induced epidermal dehydration by enhancing the expression of filaggrins and peptidylarginine deiminase-3 [5].

3. Skin whitening

Royal jelly whitens the skin by suppressing melanin synthesis. Melanin is synthesized by a pathway catalyzed by tyrosinase, tyrosinase related proteins (TRP)-1 and TRP-2 under the influence of melanocyte stimulating hormones (MSH) [6]. Water soluble royal jelly directly inhibits tyrosinase and downregulates tyrosinase activity. It also represses the mRNA and protein expressions of tyrosinase, TRP-1 and TRP-2. By these means, royal jelly
treatment significantly reduces melanogenesis even after the skin cells are stimulated with MSH [7, 8].

10-hydroxy-2-decenolic acid (10-HAD) extracted from royal jelly is responsible for anti-melanogenic effect. It inhibits tyrosinase activity and suppresses the expression of TRP-1, TRP-2, microphthalmia-associated transcription factor (MITF) in melanoma cells. In addition, topical application of 10-HAD improves the average skin whitening index [9]. This suggests 10-HAD from royal jelly might be used to treat excessive skin pigmentation.

4. Protection against photoaging

Skin aging composed of intrinsic aging occurring over time under the genetic influences and extrinsic aging contributed by certain environmental factors especially ultraviolet (UV) rays. Royal jelly particularly its major constituent, 10-HAD, prevents photoaging of the skin by boosting collagen production.

10-hydroxy-2-decenolic acid (10-HAD) was confirmed as honeybee royal jelly-derived collagen production -promoting factor after column chromatographic and molecular mass analysis. In fibroblast cell line, NHDF, 10-HAD promotes collagen formation by inducing TGF- β synthesis. The collagen-forming action of 10-HAD becomes blunted if neutralized by anti-TGF-β [10].

In the experiment using UVB-induced photoaging on human dermal fibroblast, treatment with royal jelly and 10-HAD significantly increased procollagen type I and transforming growth factor-β (TGF- β) [11]. In another study, royal jelly also enhanced collagen production in animal models with skin aging induced with estrogen deficiency. The procollagen type I concentration was increased in the ovariectomized animals fed with 1% royal jelly supplement [12].

10-HAD also protects ultraviolet A-induced damage in human dermal fibroblasts by promoting collagen synthesis, reducing reactive oxygen species and protecting against cellular senescence. 10-HAD represses UVA-induced expression of MMP-1 and MMP-3 and inhibits the signaling of the JNK and p38 MAPK in fibroblasts [13].

5. Wound healing

Ancient people used honey to heal wounds. According to scientific evidence, Major Royal Jelly Protein (MRJP)-1 induces mRNA expression of MMP-9, TGF- β, interleukin-1β and tumor necrotic factor-α in keratinocytes. MMP-9 can activate these cytokines from inactive forms and stimulate own secretion from keratinocytes. At the same time, MRJP-1 accelerates collagen type IV degradation via MMP-9 activation. In addition, it induces keratinocyte proliferation in human [14].

Royal jelly also affects fibroblast migration and modifies lipids in injured skin. Fibroblast migration is one of the essential steps in would healing and is accelerated significantly by royal jelly. Royal jelly also reduces cholesterol content and increases the levels of sphingosines, glycosylceramides and ceramides, which take part in wound healing [15].

In animal models, oral administration of royal jelly exhibited anti-inflammatory effect by promoting collagen synthesis and reducing exudation in granulation tissue formation. Royal jelly also shortened the period to heal desquamated skin damage [16]. Topical application of royal jelly significantly promoted wound healing of sterile incision in Balb/C mice and the effect was better than that of nitrofurazone [17].

5% royal jelly topical application is effective to treat diabetic foot ulcers and was first suggested to be a therapeutic potential in addition to standard treatments [18]. However, Siavash and colleagues found no significant superiority of application of 5% royal jelly over placebo in treating diabetic foot ulcers by conducting a double-blind placebo-controlled clinical trial [19]. Therefore, the effect of royal jelly on diabetic ulcers needs further investigations for confirmatory results.

6. Benefits in allergic dermatitis

Topical royal jelly ameliorates pruritus commonly encountered in chronic allergic dermatitis. In animal experiments, topical application of 0.1% and 1% royal jelly significantly reduced scratching and skin inflammation score in mice with chemically induced chronic contact dermatitis. The effect was comparable to that of betamethasone, but royal jelly does not induce nerve growth factor in the skin as seen in betamethasone treatment. This suggests royal jelly counteracts contact dermatitis by some different mechanisms [20].

Oral intake of royal jelly decreases serum immunoglobulin E level and inhibits histamine degradation from mast cells, suppressing the immediate hypersensitivity response. It raises interleukin (IL)-4 and reduced interferon (IFN)-γ, shifting Th2-dominant to Th1-
dominant type. At transcriptional level, royal jelly promotes IL-12 p40 and nitric oxide gene expressions while inhibiting prostaglandin E2 expression in macrophages [21]. Thus, royal jelly supplementation may be a potential for inflammatory skin disorders.

7. Benefits in atopic dermatitis-like skin lesions

Animal study showed royal jelly inhibited the development of atopic dermatitis-like skin disease induced by repeated application of picryl chloride. Royal jelly inhibited the infiltration of corium and epidermis by inflammatory cells, hyperkeratosis and hypertrophy in AD-like lesions. Royal jelly has a dual role at genetic level – suppressing the interferon (IFN)-γ expression and inducing nitric oxide synthase (iNOS) expression [22].

Macrophage requires IFN-γ activation to generate inflammation and royal jelly interfere this process. On another hand, by generating nitric oxide (NO) by iNOS, NO can scavenge superoxides that are harmful free radicals. As a result, royal jelly becomes an interest to treat atopic dermatitis.

8. Conclusion

Royal jelly has promising evidence of benefits in skin and related diseases. 10-HAD from royal jelly can be used cosmetic agent to whiten the skin and to protect against photo-aging. In clinical practice, royal jelly may be useful in wound management and inflammatory dermatitis.

References


**Competing Interests:**
The authors declare that they have no competing interests.

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