Honey in dermatology and skin care: a review

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Summary

Honey is a bee-derived, supersaturated solution composed mainly of fructose and glucose, and containing proteins and amino acids, vitamins, enzymes, minerals, and other minor components. Historical records of honey skin uses date back to the earliest civilizations, showing that honey has been frequently used as a binder or vehicle, but also for its therapeutic virtues. Antimicrobial properties are pivotal in dermatological applications, owing to enzymatic H₂O₂ release or the presence of active components, like methylglyoxal in manuka, while medical-grade honey is also available. Honey is particularly suitable as a dressing for wounds and burns and has also been included in treatments against pityriasis, tinea, seborrhea, dandruff, diaper dermatitis, psoriasis, hemorrhoids, and anal fissure. In cosmetic formulations, it exerts emollient, humectant, soothing, and hair conditioning effects, keeps the skin juvenile and retards wrinkle formation, regulates pH and prevents pathogen infections. Honey-based cosmetic products include lip ointments, cleansing milks, hydrating creams, after sun, tonic lotions, shampoos, and conditioners. The used amounts range between 1 and 10%, but concentrations up to 70% can be reached by mixing with oils, gel, and emulsifiers, or polymer entrapment. Intermediatemoisture, dried, and chemically modified honeys are also used. Mechanisms of action on skin cells are deeply conditioned by the botanical sources and include antioxidant activity, the induction of cytokines and matrix metalloproteinase expression, as well as epithelial-mesenchymal transition in wounded epidermis. Future achievements, throwing light on honey chemistry and pharmacological traits, will open the way to new therapeutic approaches and add considerable market value to the product.

Keywords: acacia honey, antimicrobial action, cosmetic and dermatological formulations, manuka honey, phytocompounds, skin cells, skin disease and aging, traditional medicine, wound healing

Ancient uses

Honey is one of the most used substances throughout human history, and its beneficial effects on the skin have an age-old repute. Starting from very old times,

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honey has been used extensively in toilet preparations or early skin remedies. Archaeological records from the predynastic age of upper Egypt have allowed to ascertain that nomadic tribes of the Tasian culture (around 4500 BC) mixed malachite, copper, spar, oil, fat, and honey for eye cosmetics. Ancient skin care uses of honey are also reported in a Sumerian tablet, dating back to about 3000 BC, and in the Egyptian Ebers Papyrus (around 1500 BC). It is also known that Egyptian women used honey together with sodium

bicarbonate for vaginal irrigations,³ probably due to its antibacterial properties. They also chewed scented pills made of honey and spices to sweeten their breath. Interestingly, a semisolid paste called "honey-mint" was used centuries later for a similar scope in ancient Rome. Other ancient reports about honey in cosmetics include writings from Aristotle, Dioscorides, and Pliny, as well as prophetic books of main cultural traditions, such as the Bible, Koran, Torah, and Talmud.⁴

In the antiquity, honey was frequently used as a binder, to hold other ingredients in a paste, or as a vehicle in creams and lotions. In his *Medicamina faciei feminae*, the Roman poet Ovid (43 BC- 17 or 18 AD) provided various recipes for face packs that contained honey and other herbal ingredients. A rare case of Medieval cosmetic treatise written by a woman, Trotula de Ruggiero, at the Schola Medica Salernitana (southern Italy), reports various uses of honey, such as skin moisturizer, hair dye, lip softener, and face mask. An anonymous Anglo-Norman treatise on body adornment, written in the XIII century, describes the use of honey mixed with parsley juice, pig blood, and white wine, for the preparation of a conditioner to make hair grow.

Historical reports from the Renaissance testify that the cosmetic use of honey was widespread at that age, with little change with respect to earlier periods. In Venice (Italy), women used to treat their hair with a lotion made of alum, sulfur, and honey, to obtain golden shades.8 Two manuscripts of the XVII century from the archives of Nantes (France) report various galenic forms containing honey and beeswax for external use in therapeutics and beauty care. 9 A review of herbal cosmetics in ancient India lists different formulae dating back to earlier than the XVIII century, including a face pack based on the lentil Masura (Lens culinaris Medik.) pounded with Madhu (honey). This source claims that such a paste, rubbed on the face for seven nights, confers it the shining of white lotus petals.¹⁰ In the Victorian age, makeup was considered improper for respectable women, but there was a restricted number of tolerated cosmetics, including face masks prepared with oatmeal, honey, and egg yolk.

Important ancient uses of honeybee products concern the preservation of corpses. Beeswax and honey were used in embalming techniques by Egyptians, while prominent historical figures are said to have been embalmed with honey. These include the King of ancient Sparta, Agesipolis I (reign 394–380 BC), Alexander the Great (356–323 BC), who was transported to his home country in a honey-filled coffin after his death in Babylon, King Herod the Great (73–4 BC), a

Roman-client ruler of Judaea, Nero's wife Poppaea (ca 30–65 AD), who was embalmed, in contrast to the Roman usage of burning dead people, and the later Roman emperor Theodosius I (347–395 AD).¹¹

Traditional uses

Honey is arguably the oldest skin care ingredient currently in use, as testified by many traditional uses in different countries. In East Asia, Japanese women are thought to maintain their hands devoid of wrinkles through a daily use of honey. Chinese women mix crushed seeds, particularly those of orange, to make a softening and cleaning cream for pimples and other unaesthetism. In Louisiana, Creole women rub their bodies with a lotion consisting of honey and water mixed with various herbal substances. Such a treatment is used as a cosmetic, as a remedy for skin ailments, and as a protective potion against evil ghosts. Women from the Arab Peninsula prepare antiage face masks consisting of honey mixed with egg yolk, avocado, lemon, and yogurt. 12

The medicinal use of honey for skin disease is cited in a number of ethnopharmacological and ethnomedical surveys. In these medicaments, honey is frequently used as a binder or vehicle for the external application of herbal extracts; however, specific therapeutic properties are also recognized. According to traditional Chinese medicine, honey prevents scars, removes discoloration and freckles, and improves the general appearance of skin. In Arab medicine, honey is used for fungal infections of the skin, 12 while in Burkina Faso, it is used as a skin cleansing agent by laborers. probably due to its bactericidal and sterilizing properties. 13 A review of remedies from the Eastern Mediterranean, based on animal products, reports uses of honey in skin diseases dating back since the Middle Age.14

An ethnobotanical study carried out in the state of Assam, India, has reported that honey is used for the topical application of disinfectant plants ground to powder or, alternatively, is mixed with rice flour and egg yolk to obtain a paste that is layered on the face for skin smoothing and spot removal. In Lithuania, honey is mixed with rye or wheat flour and applied as a poultice against furuncles and abscesses. Similarly, in women communities of Northern Pakistan, creamy honey is used as a base of herbal mixtures for skin smoothening, eyelid, and face protection, and the treatment for freckles and white spots.

In skin remedies of central Italy, honey enters in the preparation of toner and cleansing compresses, in a

formulation against furuncles, as a cream base for the application of silicon-rich horsetail (*Equisetum*) extracts to finger and toe nails, as a skin emollient with calcium bicarbonate, and as a soothening poultice for swelling. ¹⁸ In the Balkan region, special balms of Bosnia and Herzegovina known as "mehlems" are prepared by mixing fresh herbal parts with warmed conifer resins, lard, olive oil, and honey, and used as cosmetic or to cure skin and other external injuries or rheumatism. ¹⁹

Dermatological properties

Empirical evidence has established honey as a treatment for wounds and burns since ancient times. 14 The remarkable efficiency of these traditional uses has raised interest in modern clinical approaches to wound healing.²⁰ The physicochemical nature of honey makes it an ideal wound dressing, able to moisturize injured tissue, contrast microbial infections, sooth inflammation, and prevent gauze sticking to wounds.21 A good deal of literature about the wound healing properties of honey has been focused on antiseptic effects.²² However, emerging evidence argues for honey ability to interact with the complex cellular machinery carrying out tissue repair. Different studies have shown that honey is able to promote angiogenesis, granulation, and epithelialization,²³ stimulate lymphocytes and phagocytes, 24 induce the expression of tissue repair molecular markers, 25 and trigger epithelial-mesenchymal transition in keratinocytes.²⁶

Honey is included in the official pharmacopoeias of various countries, and γ-irradiated, medical-grade honey is available in the market. In the dermatological field, honey is principally exploited for its antimicrobial properties.²⁷ Antibiotic activities may vary among different honey types and are thought to depend in most cases on a combination of low water activity, low pH, and the release of hydrogen peroxide by the enzyme glucose oxidase. 4,28 In the treatment for vaginal candidosis, it has been shown that honey distillates are comparable to commercial antimycotic preparations.²⁹ In addition, superficial mycoses, such as ringworm and athlete's foot, have been successfully treated using honey types endowed with either hydrogen peroxide or nonperoxide antimicrobial activity.³⁰ Clinical trials have also been carried out about the use of honey for acne, herpes, skin rashes, and contact dermatitis.31

Floral sources can provide additional or exclusive antibacterial activities. Manuka honey is a widely known and marketed New Zealand unifloral honey derived from the Manuka tree *Leptospermum scoparium*

J.R. et G. Forst. This kind of honey has strong antibacterial activity and is even able to inhibit methicillin-resistant *Staphylococcus aureus* (MRSA) strains.³² These peculiar antibacterial properties seem not to depend on hydrogen peroxide, but rather on the presence of large amounts of the dicarbonyl compound methylglyoxal, a highly cytotoxic metabolite.³³ It has also been shown that Manuka honey produces positive effects against dental plaque, gingivitis, and dermatophytes that cause tineas.³⁴ Other honey types have shown antifungal effects against *Malassezia* yeasts, thus being profitable in the treatment for seborrheic dermatitis and dandruff.³⁵ Moreover, in a clinical study, honey has been successfully used to alleviate the symptoms of labial and genital herpes.³⁶

Even though double-blinded clinical tests are still lacking, a series of noncomparative or partially controlled, patient-blinded studies, have been carried out to test the potential curative properties of honey on various skin conditions. A mixture of honey, beeswax, and olive oil having antimicrobial properties³⁷ has been tested as an alternative topical treatment against pityriasis versicolor, tinea cruris, tinea corporis, and tinea faciei.³⁸ The same mixture has also been found effective in the management of diaper dermatitis, psoriasis, hemorrhoids, and anal fissure.³⁹ It has also been suggested that honey may ameliorate skin reactions induced by radio- or chemotherapies.⁴⁰

In vitro studies have brought evidence about the mechanisms of action of honey on skin cells. It has been assessed that the toxicity of honey on keratinocytes and fibroblasts is extremely low.26 In addition, a study on keratinocytes and excised skin fragments has shown that acacia honey induces the expression of cytokines (TNF- α , IL1- β , and TGF- β), and of matrix metalloproteinase 9 (MMP-9).⁴¹ This latter enzyme is able to degrade collagen IV and is involved in basal membrane disorganization during the re-epithelialization process of wound repair. Moreover, the release of cytokines (e.g., TNF-α) from monocytes seems involved in honey immunomodulatory effects. 42 It has also been suggested that the effect of cytokine release would be mediated by the 55-kDa glycoprotein apalbumin 1, or major royal jelly protein 1 (MRJP1), a main protein constituent of royal jelly and honey. 43

Cosmetic properties

Honey is included in the International Nomenclature of Cosmetic Ingredients (INCI) under the names of "Honey" or "Mel" (CAS no. 8028-66-8) and is classified as an emollient/humectant/moisturizing product.

INCI names for honey derivatives include "Mel Extract" (CAS no. 91052-92-5/8026-66-8, moisturizing), "Hydrogenated Honey" (humectant/skin conditioning), and "Hydroxypropyltrimonium Honey" (propanaminium, 2-hydroxy-N,N,N-trimethyl, 3-honey ethers, chlorides, CAS no. 223705-79-1, antistatic/hair conditioning). On regard of quality standards, the primary sugars of honey have been recognized as safe by the US Food and Drug Administration (FDA), while the safety of beeswax, which can also be present in various amounts, has been evaluated by an expert panel of the Cosmetic Ingredient Review (CIR). 45

Honey is considered particularly suitable for skin care, and its regular use is thought to keep the skin juvenile and retard wrinkle formation. A vast number of skin care formulas containing honey or other beekeeping products are available in the literature (see e.g., refs. 47,48). Honey is used in variable proportions depending on the kind of cosmetic. Generally, lower amounts are used in foaming products, creams, and emulsions (0.5–5%), while higher amounts are present in anhydrous ointments (10–15%).

Honey is hygroscopic, antibacterial, and fungicide, nurtures the skin, and contributes to regulate the mildly acid pH of the upper protective skin layer. Humectant properties make it suitable to be used as a natural component of a variety of moisturizing products, while its cleansing virtues can be exploited in skin soaps, bath and shower products, face creams and lotions. In addition, honey shows demulcent and anti-irritant properties that make it particularly fit for babies and other subjects with sensitive skins. Similarly, moisturizing and anti-irritant functions soothe the action of radiation-blocking agents in sun care and sun screen products. ⁴⁹

Honey derivatives are used in a growing number of products. Hydroxypropyltrimonium honey is considered a good conditioner for hair and scalp, 50 able to penetrate deeply into the hair shaft and restore hair elasticity and flexibility. Hydrogenated, intermediate-moisture, and dried honeys are also applied to the manufacture of cosmetics and soaps. 51 Besides the production of derivatives, honey refining techniques are also employed, such as membrane processing aimed at avoiding cloudiness or granulation, or at sterilizing and reducing viscosity. 52

The application to skin of honey alone, present in popular uses, is not generally utilized in the cosmetic industry, due to stickiness, thinning, and liquefaction. Honey is most often used in proportions ranging between 1 and 10%, in products like lip ointments, cleansing milks, hydrating creams, or gels, after sun,

tonic lotions, shampoos, and conditioners.⁴⁷ However, higher concentrations can be reached by mixing honey with oils, gelling agents, and emulsifiers, which can arrive to include as much as 70% honey, while maintaining a satisfactory performance for application.³¹ More in depth, technological solutions are also being pursued, like honey entrapment within polymeric gels consisting of acrylamide and glyceryl polymethacrylate, additioned with silicone fluids like cyclopentasiloxane.⁵³

Pharmacotechnical studies on honey-containing mixtures have also been carried out. An emulsion containing rosemary honey has shown a high degree of moisturizing/emollient power, thus rendering it a valuable eudermic treatment and an appropriate vehicle for dermatologically active principles. The mixture of antiseptic essential oils with honey has been proposed for cosmetic purposes, or as a medicinal formulation for the topical treatment of mycoses, acne, and other skin ailments. A patent claims that this kind of combination can be used in moisturizing, antiwrinkle, and slimming creams, soaps, hair, and mouth care products, as well as in hydrotherapy. 55

Technical progress in cosmetic industries concerns the use of honey as a moisturizing and emollient vehicle for the incorporation of herbal extracts, most frequently combined to botanical fats, in water-in-oil or oil-in-water emulsions (see e.g., refs. 56,57). Honey has been proposed as an alternative to emulsifiers in body-care preparation for bathing and shampooing, consisting of as high as 50% honey mixed to 50% surfactants.⁵⁸ The addition of 3–20% honey to a shampoo has been reported to confer abundance to hairs, maintain wave and lubricate, making it easier to comb.⁵⁹ Honey has also been claimed to possess keratolytic properties to be exploited in facial radiance-enhancing and antiwrinkle preparations. In this respect, association with α-hydroxy acids has been suggested, with the aim of improving performance while reducing irritation. 60 Another patented honey extract has been claimed to act as an optimal moisture regulator, improving turgor, elasticity, and the velvety smoothness of skin. 61 Depigmenting properties for skin and hair have also been reported.62

Active constituents

Honey active principles include as follows: sugars, mainly fructose and glucose; proteins and amino acids; vitamins, like ascorbic acid, biotin, nicotinic acid, pantothenic acid, pyridoxine, and thiamine; enzymes, such as diastase, invertase, glucose oxidase, and catalase; minerals, mostly potassium, magnesium, phosphorus,

calcium, iron, and copper; phytocompounds derived from botanical sources, and other minor components (Table 1). The mechanisms of action of these constituents on the skin tissue are largely unknown. The hydrating effect is mainly linked to the high content in fructose and glucose, forming hydrogen bridges with water and maintaining the moisture of the skin horny layer. ⁶³ Hydrating ability also derives from the presence of amino acids (mainly proline, but also arginine, alanine, glutamic acid, aspartic acid, lysine, glycine, and leucine), and of organic acids (mainly gluconic acid, but also in smaller quantities lactic, citric, succinic, formic, malic, acetic, maleic, and oxalic acids), which can supplement the natural moisturizing factors of the horny layer.

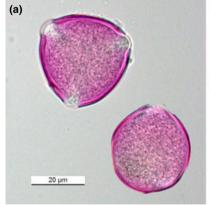
It is known that the biological properties of a specific honey type are conditioned by the flowers that provide

Table 1 Honey components with documented or presumed effects on skin

	Compounds	Properties
Sugars		Hydrating, ⁶³ antimicrobial
Amino acids		Humectant
Organic acids		Humectant
Vitamins		Nourishing, antioxidant
Minerals		Nourishing
Proteins	Glucose oxidase (H ₂ O ₂) Major royal jelly protein 1	Antimicrobial ^{4,28} Immunomodulatory ⁴³
Phytocompounds	Phenols Methylglyoxal (manuka)	Antioxidant ^{66–70} Antimicrobial ³³

the nectar, and thus, botanical sources are of great importance in the cosmetic field. Their determination is routinely achieved through pollen analysis. 64 but methods of chemical fingerprinting are becoming increasingly diffuse. 65 Two honey types that have attracted much attention are acacia and manuka honeys (Fig. 1). The honey produced from black locust (Robinia pseudoacacia L.), generally marketed as "acacia honey", is most common in cosmetics. This type of honey has a higher content of the more soluble fructose with respect to glucose, thus reducing the risk of crystal formation within the final cosmetic product. Manuka honey has been introduced into the world of cosmetics starting from its pronounced antibacterial and antifungal activities, which in the dermatological field can potentially find application in the treatment for acne and other infectious conditions. However, other skin care properties of this honey have been explored, including support to skin renewal processes and collagen strengthening.

Little is known about the role of phytocompounds in determining honey virtues. It is generally known that darker honeys, richer in phenolic compounds like flavonoids and tannins, possess the strongest antioxidant and radical scavenging activities. ⁶⁶ An analysis of the phenol content of multifloral, sunflower, almond, chestnut, and eucalyptus honeys found values from 194.9 to 1636.3 mg gallic acid equivalents (GAE)/kg, and total antiradical activities from 61 to 940 mg GAE/kg. ⁶⁷ In another study, multifloral honey exhibited flavonoid concentrations between 1.23 and 2.93 mg catechin equivalents (CE)/100 g. ⁶⁸ Sweet clover (*Melilotus officinalis* (L.) Pall.) honey was also found to possess



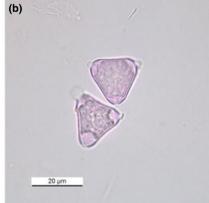


Figure 1 Micrographs of pollen grains from black locust *Robinia pseudoacacia* (a) and manuka *Leptospermum scoparium* (b), allowing the characterization of the respective monofloral honeys. Black locust pollen is isopolar, tectate, suboblate, tricolporate, subtriangular in polar view. Manuka pollen is oblate, syncolpate, and triangular in polar view, while the apertures are short furrows in a thickened portion of the wall.

high antioxidant activity, based on the reduction of polyphenol oxidase activity. ⁶⁹ Isolation of specific compounds in buckwheat honey showed a prevalence of gallic, p-coumaric, protocatechuic, caffeic, and ferulic acids. ⁷⁰

Allergies and noxious effects

Honey is known to occasionally produce systemic intoxications due to the presence of dormant endospores of *Clostridium botulinum*, ⁷¹ or to contamination by herbal drugs such as grayanotoxins from *Ericaceae* plants. ⁷² It has also been found that propolis and propolis-enriched honey can induce contact dermatitis, while urticaria from honey has been reported. ⁷³

Allergy to honey is uncommon,⁷⁴ but pollen and bee proteins in honey-based cosmetics can function as sensitizers,⁷⁵ causing problems to people with pollen allergies.⁷⁶ Royal jelly, widely used as a nutritional integrator, has sometimes been linked to dermatitis and other forms of acute sensitization. A proteomic study has identified major royal jelly protein 1 and 2 as main allergens.⁷⁷ In addition, the ingestion of royal jelly has been reported to induce sensitization to its topical application.⁷⁸

Concluding remarks

Honey is one of the oldest natural products used by humans, and yet, its biological properties and potential benefits to health are still far from being adequately assessed. Dermatological uses of honey are generally based on empirical knowledge, but nevertheless, there is a growing interest for scientific findings and applications. Due to large variations in the qualities of honeys from different natural environments, much interest is paid to the development of medical-grade honey, especially for the treatment for skin infections and wound healing. 27,79 The lack of knowledge about cellular and molecular mechanisms laying behind honey effects is a limit to the development of skin pharmaceuticals and cosmetics. However, the use of honey in the dermatological and cosmetic fields has undergone considerable expansion.

Future development in skin care applications of honey will benefit from studies carried out in various direction. First, ethnopharmaceutical surveys will possibly point out new relevant biological properties in the extraordinary variety of mono- and polyfloral honeys. Second, chemical and biological investigations will help to throw light on the chemistry of honey and its pharmacological traits, thus opening the way to new

therapeutic approaches to be validated in double-blind clinical trials. Third, the development of chemically modified forms of honey will provide formulators with new ingredients for the exploitation of honey virtues in a wider range of products. All these kinds of innovations will add market value to this extraordinary natural product, thus possibly also bringing support to the agricultural economies of developing and underdeveloped countries.

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