



# Therapeutic and Prophylactic Effects of Honey on Dermatitis and Related Disorders

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## Keywords

Honey · Dermatitis · Atopic Dermatitis · Eczema · Manuka Honey · Skin

## 11.1 Introduction

Honey is a stuff formed when honey bees collect nectar and sweet deposits from plants and further alter and store it in the honeycomb. It is an ideal mixture without allowing other substance (water and other sweeteners) to add on.

Nectar is a floral deposit and sweets are non-floral deposits from plants and upon mixing, modification and storage in the honeycombs by honeybees (*Apis* and *Meliponini*) form an unusual item of very beneficial value called honey (Namias 2003; Al-jabri 2005). Environmental and climatic settings along with botanical source of nectar play a vital part in defining the composition and quality of honey. Honey, based on its quality, can affect the health and nutritional status of people.

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Honey has, antioxidant, anti-inflammatory, and antimicrobial properties, hence beneficial actions have been attributed to it. Interestingly, honey is getting attention for being a complementary and/or an alternate basis of treatment in modern medicine. It has the potential not to select for further resistant strains and is effective against antibiotic-sensitive and antibiotic-resistant strains of microorganisms (White 1992).

## 11.2 Typical Composition

The composition of honey is highly inconsistent. Table 11.1 contains the various ingredients in natural honey.

## 11.3 Types of Honey

*Comb honey:* Honey existing in its unique comb.

*Extracted honey:* It is generally offered in numerous forms: (1) liquid (2) crystallized or preserved (3) partially crystallized; defined as per the *US Department of Agriculture Standards for Grades*. This is generally referred as “Honey.”

## 11.4 Sources of Honey

Source of honey defines its taste, fragrance, color, and ingredients, e.g.:

*Floral:* Specifies the nectar-producing flowers for the manufacture of honey.

*Non-floral:* Specifies extrafloral parts and honeydew (White 1992).

*Geographic origin:* Determines the area of manufacture and is in agreement with the *Code of Federal Regulations (CFR)*, mixtures containing honey of imported source must be labeled to specify their origin(s) (White 1992).

**Table 11.1** Ingredients of honey

Ingredients	Average $\pm$ SD	Range
Fructose/glucose ratio	1.23 $\pm$ 0.126	0.76–1.86
Fructose (%)	38.38 $\pm$ 1.77	30.91–44.26
Glucose (%)	30.31 $\pm$ 3.04	22.89–40.75
Minerals (Ash) (%)	0.169 $\pm$ 0.15	0.020–1.028
Moisture (%)	17.2 $\pm$ 1.46	13.4–22.9
Reducing sugars (%)	76.75 $\pm$ 2.76	61.39–83.72
Sucrose (%)	1.31 $\pm$ 0.87	0.25–7.57
pH	3.91 $\pm$ 0.2	3.42–6.10
Total acidity (meq/kg)	29.12 $\pm$ 10.33	8.68–59.49
True protein (mg/100 g)	168.6 $\pm$ 70.9	57.7–567

## 11.5 Forms of Honey

*Blended honey:* A regular combination of equal to or more than two honeys contradictory in flavor, plant source, geographic origin, shade, or thickness.

*Crystallized honey:* Also called granulated honey. Its glucose portion has naturally crystallized as monohydrate.

*Filtered honey:* formed when extraneous solids and pollen grains are filtered from honey.

*Organic honey:* Created, treated, and parceled in agreement with *State and Federal regulations on honey and organic products* and certified by a *State Department of Agriculture* or an *independent organic farming certification organization*.

*Raw honey:* As occurring in the hive or as we get without adding heat after mining.

*Commercially raw honey:* Acquired by least treatment.

*Strained honey:* Honey containing pollens but without particulate material (bits of wax, propolis, etc.).

*Whipped honey:* Honey produced by precise crystallization to a flat smooth texture. Also called churned honey, whipped honey, creamed honey, or candied honey (White 1992; Molan 1992).

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## 11.6 Honey Products

Although not meeting the compositional criteria for honey, these are the products containing entire or portion of honey;

*Artificial honey:* is a combination of dyed and flavored sweeteners to look like honey. This creation does not meet the criteria of honey or honey products.

*Deionized honey:* Formed on removal of selected ions by extra treatment.

*Deproteinized honey:* Formed on removal of protein by specific treatment.

*Dried honey:* On dehydration using drying aids and processing adjuncts, dried honey gets formed. It improves product stability.

*Honey extract:* It is formed by getting rid of particular constituents. The type of extract is defined by the nature of the constituent.

*Honey spread:* A diversity of eatable, very glutinous honey products. Spices, fruits, nuts, or aromas are sometimes blended with honey spread.

*Ultrafiltered sweetener:* When most proteins, enzymes, and polypeptides are removed from honey which do not pass through a submicron membrane give rise to ultrafiltered sweetener.

*Honey dew:* Secretions of insects who suck sap such as coccids or aphids and possibly secretions of fungi found on the faces of flora (White 1992; Molan 1992).

## 11.7 Therapeutic and Medicinal Properties of Honey

Natural therapeutic products are in use for times in the handling of numerous illnesses. Even though many have succeeded by orthodox pharmacological methods, presently there is renaissance in using honey and honey products by the common community. This unconventional division of medicine is named as *Apitherapy* (Ghosh and Playford 2003).

Honey has been treated as remedy by numerous humanities over extensive time. However, due to lack of technical report, it has inadequate use in medicine. Nowadays, honey is becoming standard as a trustworthy and operational healing agent. Its usefulness has been attributed to its antioxidant, anti-inflammatory, and antimicrobial properties as well as improving immunity (Krell 1996) (Table 11.2).

## 11.8 Skin Disorders

There are numerous skin disorders affecting *Homo sapiens*. The most usual disorders could have similar indications to some extent, thus it is imperative to know dissimilarities among them.

**Table 11.2** Therapeutic assets of honey and their valuable effects

Properties	Attributions	Activities	References
Antimicrobial (antibacterial, antiviral, antifungal, antiparasitic)	High acidity, osmolarity, hydrogen peroxide, and nonperoxide components	Inhibits or kills	Bansal et al. (2005) Fahey and Stephenson (2002) Irish et al. (2006) Manyi-Loh et al. (2010) Ndip et al. (2007)
Anti- inflammatory	Leucocytes	Reduces inflammation and minimize scarring of wounds	Dunford et al. (2000)
Antioxidant	Phenolic acids Flavonoids	Prevents free radical formation Hunt-free radicals	Gheldof et al. (2002) Baltrušaityt et al. (2007)
Immunological	Leucocytes macrophages	Cytokine formation Substrate for glycolysis	Tonks et al. (2007)

### 11.8.1 Permanent Conditions

They last for an extended time. Roughly may jump in early age and last till maturity. In some subjects, the ailment will not be existing all the time but will come up few times.

#### 1. Seborrheic dermatitis

Well-known as *cradle cap* in babies. Slimy and crusty skin patches get formed on the skin, maximally on the scalp. It diminishes on its own and is usually harmless.

In adults, it occurs at any place and is prone to appear and vanish for rest of lifetime. The exaggerated crust may be greasy, inflamed, and reddish. A yellow film may seem to be formed on surface of the skin as well. Relief from symptoms is brought by specific treatment (Fig. 11.1a) (Deleo 2004).

#### 2. Moles

Skin cells bunch up with surrounding tissue giving rise to common growths on the surface known as moles. Moles are often present and may develop over a period of time also. Moles are asymptomatic, but should be regularly checked for size, abnormality, and color change (Fig. 11.1b).

#### 3. Rosacea

It is generally linked with blush. Nevertheless, there are subcategories that give rise to other indications also:

- (a) *Erythematotelangiectatic rosacea* causes typical flushing and redness, prominence of blood vessels.
- (b) *Ocular rosacea* can lead to enflamed eyelids, irritated sore eyes, and indications similar to a style.
- (c) *Papulopustular rosacea* leads to swelling, inflammation, and breakouts looking like [acne](#).
- (d) *Phymatous rosacea* leads to thickening and bumpy texture of skin.

Rosacea has no treatment, but indications are to be treated to retain the disease (Fig. 11.1c) (Weiss et al. 2017).

#### 4. Lupus

[Lupus](#) is a complex sickness varying considerably. The illness affects the immune system, leading to pain and inflammation. Although it can upset any body part, signs on the skin comprise of sunburn-like rashes on the cheeks and nose, red spots on the surface, or rashes without itching or pain. Other symptoms include stiff or painful joints, [fatigue](#), [fever](#), and [headache](#). Treatment includes various drugs intended to help diminish the injury caused by lupus (Fig. 11.1d) (Khan and Ahmed 2016).

#### 5. Psoriasis

[It](#) is an autoimmune condition. Indications classically comprise blotches of unusual skin. Exaggerated area is usually scaly, sore, and itchy which differ in severity and size.

Mainly five forms exist:

- (a) *Plaque psoriasis* results in dense and inflamed patchy skin.
- (b) *Pustular psoriasis* gives rise to pustules enclosed by inflamed skin.



**Fig. 11.1** Permanent skin disorders. (a) Seborrheic dermatitis, (b) Moles, (c) Rosacea, (d) Lupus, (e) Psoriasis, (f) Eczema, (g) Vitiligo, (h) Actinic keratosis, (i) Melasma, (j) Melanoma, and (k) squamous cell carcinoma

- (c) *Erythrodermic psoriasis* gives rise to severe burn-like patches of skin covering bulky parts of body.
- (d) *Inverse psoriasis* gives rise to glossy inflamed rash in the skin folding.
- (e) *Guttate psoriasis* gives rise to tiny red plugs on the torso, face, limbs, and scalp (Fig. 11.1e) (Menter et al. 2019).

## 6. Eczema

It gives rise to rashes on wrists, ankles, legs, face, behind the elbows, neck, and on the scalp. The rashes may become thickened or bumpy and are very itchy. Generally, found in young age group. In adults, dry skin that is permanently itchy is formed which may cover the further area.

There are limited diverse forms, triggering their own signs. It either disappears of its own or treated with medicines and ointments. There is no known cure for eczema (Fig. 11.1f) (Oakley et al. 2016).

## 7. Vitiligo

Loss of skin color is referred as **Vitiligo**. Sunlight exposed parts of skin become patchy. People frequently lose their hair color early as well. Symptoms are restricted to one zone in some people while it spreads slowly to different parts in other individuals. Cure is not available. Although not right for everyone, there are rare surgical and medical cure possibilities (Fig. 11.1g) (Nguyen et al. 2016).

## 8. Actinic keratosis

Also well known as *Solar keratosis*. It is a coarse, crusty patch on skin developed due to sun exposure for years. Typically, it is less than 2 cm. Usually found on scalp, face, neck, hands, and arms. Typically pink in color but can have a gray, tan, or brown base (Fig. 11.1h) (Ratushny et al. 2012).

## 9. Melasma

It causes the appearance of dark patches, usually on the face. It is more frequent in people with darker complexion, pregnant women, and individuals having intense exposure to sunlight (chloasma). Staining of the skin is the only symptom. It may become permanent or go of its own within a year (Fig. 11.1i) (Rajaratnam et al. 2010).

## 10. Melanoma

Abnormal moles anywhere on the body that has multiple colors, asymmetrical shape, and irregularly shaped edges may lead to this grave and endangering **skin cancer**. It is more frequent in fair-skinned people (Fig. 11.1j) (Skin cancer 2019).

## 11. Squamous cell carcinoma

This cancer occurs in parts unprotected to UV radiation, as ears, face, and posterior of hands. There is a raised bump which progresses from scaly, reddish patch of skin, and continues to grow. There is a presence of bleeding growth which doesn't heal or heals and then reappears (Fig. 11.1k) (Muranushi et al. 2015).

### 11.8.2 Temporary Conditions

#### 1. Acne

It is an extensive short-term skin disorder that may be treated with medicine or ointments.

It has many forms:

- (a) Presence of **pimples** with **pus** at their apex known as *Pustules*.



- (b) Presence of raised red bumps called as *Papules* caused due to infection in hair follicles.
  - (c) Presence of painful *Nodules* lying beneath the skin.
  - (d) Presence of large painful *Cysts* which are pus-filled lying under the skin (Fitz-Gibbon et al. 2013).
2. Hives (Urticaria)
 

They are itchy bumps that are upraised from the skin. It is elicited due to illnesses, stress, or even tight clothes or allergic reaction in the body. Antihistamines and preventive practices are used to treat the condition (Yao et al. 2015).
  3. Warts
 

*Human papillomavirus (HPV)* is responsible for the cracks on the skin. Warts can appear on any part of the body and are contagious. Although they can appear anywhere but typically grow on the feet, hands, and joints. Usually perish on their own, but can be treated with medicated ointments or liquid nitrogen (King-Fan Loo and Yuk-Ming 2010).
  4. Fungal nail infection
 

An ailment in which fungus lives near, under, and around the nails, usually in the feet. The fungal buildup causes the nail's edges to dissolve away, creating white-yellowish scaling and flaking on the exterior of the nails. An antifungal cream or other fungal medicine is usually used for treatment.
  5. Cold sore
 

Typically found near the mouth. It is inflamed, fluid-filled sore. The blister is delicate or painful. Before the sore is visible there is itching or burning sensations on the site. They are produced by *herpes simplex virus*. The last until 2 weeks or may return. Cure comprises of medicines and creams (Usatine and Tinitigan 2010).
  6. Candidiasis
 

Caused by the overgrowth of *Candida albicans* fungus causing exasperated areas of skin. Typically present in the armpits, groin, knees, and under folds of skin. Could be prevented with proper hygiene, evading antibiotics overuse, and home remedies (Hu et al. 2013).
  7. Athlete's foot
 

A rash produced by a fungus that quickly grows in damp environments, such as athletic shoes. Indications comprise of inflamed, dry, and itchy skin. Presence of white, damp, and scaly skin between the toes or under the foot. Medicated ointments and good foot hygiene are the treatment options.

### 11.8.3 Internal Conditions

1. Carbuncle
 

When hair follicles get infected with *Staphylococcus aureus* bacteria, a sore, cross lump below the skin gets formed known as Carbuncle which quickly gets filled with pus and becomes puffy. Other indications include fever, itching, and





**Fig. 11.2** Skin disorders due to internal conditions. (a) Carbuncle and (b) Cellulitis

tiredness. Treatment options are antibiotics, drainage, and antibacterial washes to which they respond well (Dhar 2019).

## 2. Cellulitis

Infection in the inner coat of skin, bacterial in origin, which advances rapidly and could blowout speedily all over. Zone of skin may feel hot, painful, tender, become red, and swollen. It can occur all over the body but mostly in the legs. Mostly treated with antibiotics. This condition is considered as a medical emergency and severe infections may be life-threatening (Baiu and Melendez 2018) (Fig. 11.2).

## 11.8.4 Age-Related Conditions

### 11.8.4.1 In Children

#### 1. Hemangiomas

They are bulge out large growths initially arising from small red scratches or bumps. Mostly found on the head, neck, or face of infants. While hemangiomas are mostly found on the skin, they can also be found on various organs especially on the liver. Although some need elimination but usually they disappear by the age of 10.

#### 2. Measles

It is a viral disease, airborne, and highly infectious, with the indication of brown or red rash that spreads to other parts. It affects children and pregnant women. Other symptoms include small reddish spots inside the mouth, runny eyes and nose, fever, and cough. Measles disappears after 7–10 days, but indications should be treated (David et al. 2019).

#### 3. Impetigo

It is the most common and contagious skin infections in young children. It results in blisters and itchy sores around the face and mouth which later on erupts and leaving

a scab which desiccates leaving a mark. The entire development typically takes 3 weeks without action which can be reduced to 1 week with medicines.

#### **4. Dermatomyositis**

It is an uncommon inflammatory disease of skin. Children aged between 5 and 15 and adults of 40–60 years of age contract the disease. Typical signs comprise of a purple rash on the elbows, nails, chest, face as well as muscle weakness, and swelling. It can be managed with medicines with no cure available.

#### **11.8.4.2 In Adults**

##### **Shingles (Herpes Zoster)**

It is caused secondary to [chickenpox](#). It shocks with a pain, followed by a wide-spread pink, scorching rash within 2 days. Pain can be managed by antiviral treatment within the first 48 h. Vaccines are available against the disease (Ming-Chieh et al. [2017](#)).

##### **Seborrheic Keratoses**

Usually as people age, harmless bumps of skin appear with no medical significance. They are black or brown uneven blotches stuck to the skin.

##### **Age Spots**

Also called as liver spots. They are level skin spots with extra coloring than adjacent zone due to sun exposure for years. These spots are asymptomatic but disliked by many. Many surgical and medical treatment options are available.

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## **11.9 Benefits of Honey on Skin**

It is an unbelievable factor that does miracles for skin. This delicious golden liquid is nature's answer to skin complications. Using honey for skin is at all times a worthy idea. Regular application of honey on the skin results beyond fancy. It has the following benefits on skin.

### **1. Moisturizes and hydrates the skin**

It intensely moisturizes skin because of the presence of factors which assist its entry into the skin thereby preparing and relaxing it and that is the reason why it is a constituent for a wide variety of beauty artifacts. Honey keeps skin moisturized so is a "humectant."

### **2. Pore cleanser, anti-acne, and anti-pimples**

It has antibacterial, antiseptic, and antioxidant possessions, so it assists in removing blackheads by eliminating dust from apertures. It then tightens and hydrates skin apertures for unblemished complexion. It not only removes extra oil from the skin but also clears clogged pores, which will otherwise lead to acne and pimples.

### 3. **Gentle exfoliator**

Honey gently removes the dead skin cells and exfoliates skin which in turn creates a brighter complexion.

### 4. **Lightens scars**

It reduces swelling and aids in skin healing. Moreover, damaged skin is repaired by its antioxidant property.

### 5. **Beneficial in sunburn**

It recognized to be the top therapies for handling blisters and sunburns. It stimulates healing by lessening swelling and delivers nourishment to injured tissues.

### 6. **Antiaging property**

Antioxidants limit folds and fine lines present on the face. It increases the elasticity of skin making it look young and radiant (Molan 2001a, b).

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## 11.10 Honey: A Candid Antimicrobial or Microbicide for Skin Disorders

Honey has been documented for its skin-healing properties in old-style medicine. Persians recognized it to be operative in handling of inflammation, eczema, and wounds. The Greeks and Egyptians applied it topically to manage skin burns and wounds (Eteraf-Oskouei and Najafi 2013; Sepehr 2010). Microbes are linked with a series of dermatological ailments. *S. aureus*, *Pseudomonas aeruginosa* source infections in the wound. Presence of *Escherichia coli* and *S. aureus* is common in atopic dermatitis (Collier 2004; Ong 2014). Atopic dermatitis, psoriasis, Pityriasis versicolor, and Seborrheic dermatitis have the presence of *Malassezia yeasts* (Gaitanis et al. 2012). Conventional treatments like corticosteroids and UV radiation therapy cause skin thinning and skin cancer (Gasparro 2000).

In late 1800s, scientists stated antimicrobial properties of honey but with the advent of antibiotics in 1900s its role has faded away (Molan 2001a, b). Honey has again been researched again for medicinal use as the antibiotic-resistant microbial strains have emerged as a new global health concern (Molan 2001a, b; Fry and Barie 2011). In clinical setting, Manuka honey created by *Apis mellifera* in the form of impregnated dressings, ointments, and gamma-irradiated honey in gels is used topically for treatment of wound infections (Irish et al. 2011). In the Netherlands, wound care remedy is formed in form of Revamil honey and used in clinical practice (Kwakman et al. 2011). So it has a therapeutic potential of being used as antimicrobial agent for infective skin diseases.

A lot of in vitro research is going on antimicrobial action of honeys throughout the globe. A stingless bee, *Apis mellipodae*, in South Gondar, honey from Ethiopia is used in old-style medicine for the treatment of diseases along with skin disorders (Andualem 2013). Andualem et al. confirmed that *E. coli* and *S. aureus* were inhibited with minimal inhibitory concentration (MIC) of 12.5% and 6.25% honey individually by using agar well diffusion (Andualem 2013). In a study by Pimentel et al. using agar well diffusion assays, they showed that honey collected from

*Melipona compressipes manaosensis* during rains inhibited *E. coli* growth only in concentrated form, while honey collected during the dry season repressed the growth of *E. coli*, *S. aureus*, *Proteus vulgaris*, and *Klebsiella species* at diluted concentrations clearly indicating the effect of seasons on the antimicrobial action of honey. Seasons influence the health of the bee colonies hence affecting the antimicrobial action of product (Pimentel et al. 2013).

Scientists also compared *agar well diffusion* with *broth dilution assay* for accessing the antimicrobial properties of honey and concluded that the broth dilution assay gives better movement to antimicrobial factors in liquid broth compared to agar so a more sensitive method. By using HPLC, a flavonoid and antibacterial namely Rutin, was isolated from honey (Pimentel et al. 2013). Kuncic et al. found antibacterial action of Slovenian and pasture honeys obtained from Amazon, Brazil. They further reported the MIC of 2.5% against *S. aureus* and 50% against *Candida parapsilosis* and *Candida tropicalis*. *C. albicans* was not repressed Slovenian honeys (Kuncic et al. 2012). In other studies, growth of *C. albicans* was found to be inhibited by Jujube honey from Albaha, Saudi Arabia. Jujube honey is made by bees nourishing on *Ziziphus jujube* (Ansari et al. 2013; Al-Waili 2005a, b). These studies elucidate the prospectus of honey for treating *C. albicans* related skin disorders such as cutaneous candidiasis. The growth of methicillin-resistant *S. aureus* (MRSA), *S. aureus*, *Streptococcus pyogenes*, *P. aeruginosa*, and *E. coli* was found to be inhibited by Tualang honey, from *Apis dorsata*, Malaysia, in a broth dilution assay (Tan et al. 2009).

Scottish honey, called Portobello honey formed by honey bees in Portobello, Edinburgh, Scotland was tested for its antimicrobial action against *S. aureus*, *P. aeruginosa*, and *E. coli* using agar disc diffusion and a broth dilution assay in 2013. The results of agar method were inconclusive. The broth assay confirmed the activity of honey at MIC of 50% concluding that Portobello honey is a superior antimicrobial agent (Schneider et al. 2013a, b).

The antimicrobial activity of various honeys from different geographical locations was verified against MRSA, *S. aureus*, *E. coli*, *P. aeruginosa*, and *Acinetobacter baumannii* by Carnwath et al. using agar disc diffusion. All of them established antimicrobial activity, with Scottish heather honey being most effective, which suppressed growth of all microbes, with MICs going from <2% to 6% (Carnwath et al. 2014). Curiously, in vitro experiments establish that Scottish heather honey can backtrack antibiotic resistance, signifying that it might add to therapeutic effects when given in amalgamation with antibiotics (Jenkins and Cooper 2012). Honey might suppress *mecR1* gene product formation, a transducer in MRSA (Jenkins and Cooper 2012). Muller et al. stated that Manuka honey functioned along with rifampicin to inhibit the growth of MRSA and *S. aureus* growth (Muller et al. 2013). These experiments explain that honey has a capable antimicrobial action against skin pertinent microorganisms. Undeniably, there is comparable antimicrobial activity of sulfonamide family of antibiotics and honey from Iran (Tajik and Jalali 2009). The bacteria *S. aureus* is responsible for causing wound infections, furuncles, styes, and impetigo which is evidently repressed by honeys of different flower-patterned origins (Tajik and Jalali 2009). Honey may also be used in

the treatment of other skin disorders such as acne. Study of the antimicrobial activity of different types of honeys against other skin disease causing microorganisms ought to be stimulated.

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### 11.11 Honey: Effective Against Microbial Pathogenicity of Skin Relevant Microbes

The capability of pathogenic microorganisms to root illnesses is partially due to making of pathogenicity elements, for instance, *S. aureus* makes enterotoxins, epidermolytic toxins, catalase, and hemolysins (a, b, g, and d). Alphatoxin (a-hemolysin) injures tissue throughout wound infections by generating apertures in host cell crusts and by prompting production of cytokines followed by apoptosis. Amazingly, recent in vitro readings have revealed that honey might decrease bacterial pathogenicity more than being bactericidal. In MRSA, Jenkins et al. described that Manuka honey reduced the expression of a-toxin, genes related to cell division, virulence genes, and quorum sensing genes (Jenkins et al. 2014).

In vitro studies by Lee et al. stated that Korean acacia, Korean polyfloral, and American clover honeys considerably repressed *E. coli* O157: HA biofilm creation at a concentration of 0.5%. Moreover, Korean acacia honey condensed the curli genes (*csgBAC*), quorum sensing genes (AI-2 importer, indole biosynthesis), and virulence genes (*LEE genes*) expression in the microbial strain at low concentrations (Lee et al. 2011a, b). In *P. aeruginosa*, Manuka honey reduced siderophore formation (Krona et al. 2013). Studies showed cell shape alterations and cell lysis of *P. aeruginosa* following gestation with Manuka honey (Henriques et al. 2011). A honey flavonoid extract was found to disrupt integrity of membrane linked to virulence in *C. albicans* (Canonico et al. 2014). Manuka honey and Slovakian honeys significantly repressed *Proteus mirabilis* and *Enterobacter cloacae* biofilm formation (Majtan et al. 2014). These in vitro studies have made us understand the functions of honey to modify bacterial pathogenicity.

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### 11.12 Honey: A Medicine for Dermatitis

Honey is a nourishing substance that is conventionally known for its medicinal assets. For thousands of years, it has been used in this perspective in varied populations and is still extensively popular. Lately, in vivo and in vitro trials have documented its antimicrobial attributes (Kwakman et al. 2008; Maddocks et al. 2013; Carter et al. 2016) and have been an established wound healer (Lee et al. 2011a, b). In specific, Manuka honey that is chiefly derivative of *Leptospermum scoparium* was revealed to intercept cell partition of *S. aureus* (Jenkins et al. 2011). Additionally, it constrains leukocyte infiltration and cyclooxygenase 2 production apart from inducing nitric oxide synthase expression (Leong et al. 2012) as well as inflammation facilitated through (TLR)1/TLR2 pathway (Tomblin et al. 2014).

*Atopic dermatitis (AD)* also called as *Eczema*, is a popular continuing atopic inflammatory skin illness described by recurrent episodes of maculopapular rash and intense pruritus (Geha et al. 2011). It is a common long-lasting atopic swelling of outer layer of skin. Its prevalence in children and adults is 10–20% and 1–3%, respectively, and typically the first indicator of a series of allergic ailments as allergic rhinitis and asthma in a marvel known as “Atopic March” (Schneider et al. 2013a, b). Irritating skin, inflammation, blisters, redness, etc. are among the symptoms. Variants of dermatitis are diaper dermatitis, seborrheic dermatitis, etc. During pathogenic process, eosinophils, lymphocytes, mast cells, and macrophages crosstalk with keratinocytes as well as provocations from the external surroundings (Muñiz 2008; Mortz et al. 2015). In 70–90% of patients, skin gets colonized by *S. aureus* compared to only 5% of normal population resulting in secondary infections of dermatitis lesions (Thomsen 2014). Additionally, the making of extremely inflammatory elements such as exotoxins ( $\alpha$ ,  $\beta$ ,  $\gamma$ , and  $\delta$  cytolytins) and enterotoxins (SEA to SEE) worsen ongoing inflammation because they act as superantigens.

The administration of AD is perplexing in subjects where existing medications don't solve complications (Eichenfield et al. 2014). Some subjects prefer natural preparations and claim to improve when they used honey topically. Still, there is no strong signal in the literature to back these statements mechanistically or clinically. The topical use of honey displayed large progress in the management of disease (Burlando and Cornara 2013; Muñiz 2008). Manuka honey modulates the skin inflammation in AD due to its immunoregulatory and antistaphylococcal properties. As per the experiments by Alangari et al., Manuka honey is helpful in handling the diseases, predominantly, AD. They also detected that IL4-induced CCL26 was considerably decreased in a dose-dependent way by honey (Alangari et al. 2017). CCL26 is a main role player in the harshness of AD (Kagami et al. 2003; Owczarek et al. 2010) along with other illnesses where eosinophils are mainly responsible as eosinophilic esophagitis (Blanchard et al. 2006) and asthma (Larose et al. 2015). It is extra powerful than eotaxin1 (CCL11) and eotaxin2 (CCL24) in appealing eosinophils (Provost et al. 2013). Chemokine receptor (CCR)3 is a collective anti-ligand to all chemokines (Ponath et al. 1996), its manifestation is increased in AD abrasions (Yawalkar et al. 1999), and its obstruction by antibodies prevents enrollment of eosinophils (Shen et al. 2006). CCR3 is also present on basophils (Ugucioni et al. 1997), mast cells (Ochi et al. 1999), and activated Th2 cells (Sallusto et al. 1997). Hence, decrease in IL4-induced CCL26 release by keratinocytes by virtue of honey might clarify the phenomenon. Manuka honey may show its properties on CCL26 at protein levels and needs more learning. Manuka honey contains some flavonoids which are structurally similar to thiazolidinediones, which are PPAR $\gamma$  agonists and dose dependently reduce IL4-induced eotaxin release, nevertheless mechanism is unknown (Chan et al. 2013; Zhu et al. 2011). IL4 triggers IL8 release from epithelial cells (Strz et al. 1999; Mullings et al. 2001). This result is arbitrated through extracellular signal-regulated kinase (ERK) pathway, p38 mitogen-activated protein kinase (MAPK) (Ip et al. 2006). The large range of Manuka honey components seems to target

certain pathways, which are evident from the fact that honey did not control IL4-triggered IL8 release at mRNA or protein levels (Mullings et al. 2001).

Dermis and epidermis of AD patients contain an increased number of mast cells which in turn release histamine causing edema, local redness, and itching (Otsuka and Kabashima 2015; Simons and Simons 2011), disturbing skin barrier reliability (Wollenberg et al. 2014). The dose-dependent curb on histamine discharge by Manuka Honey may clarify its medical properties. Yet, its tool of action is controversial. Recently, in vitro experiments have shown that virulence genes in MRSA were repressed by Manuka honey, having extreme effect on *SEC3*, gene coding for Exocyst complex component 1 (Jenkins et al. 2014).

One more study has revealed the efficacy of olive oil, beeswax, and honey (in a ratio of 1:1:1 v/v), during the 7-day trial, for dermatitis, psoriasis, and skin fungal infections wherein they have observed that the mixture eradicated 50% of culture-positive patients infected with *C. albicans* probably owing to anti-inflammatory properties of the ingredients (Al-Waili 2003a, b, 2005a, b). As per another study, honey has bactericidal effect against *S. aureus* derived from canine dermatitis patients (Miorin et al. 2003). Natural raw honey is thought to quash the production and migration of inflammatory cells and in addition, it brings the enrichment in fibroblast/epithelial cell proliferation and production of pro-inflammatory cytokines thereby helping in the healing process through a twin influence on the inflammatory corridor (Mohammed et al. 2018). Honey from diverse floral varieties holds water content between 6 and 14% thus delivers the wanted moisture to the sore skin without producing maceration (Burlando and Cornara 2013; Mohammed et al. 2018).

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### 11.13 Honey, Olive Oil, and Beeswax: Its Topical Application in Diaper Dermatitis

In infants, diaper dermatitis is the most usual skin disease (Hurwitz 1981), present in 25–65% of children (Jodan et al. 1986), and is initiated by wearing a diaper, urine, and feces in a joint venture (Atherton 2001). There is presence of *Candida spp.* in diseased group when related to healthy controls; however, colonization by *S. aureus* does not diverge among the two groups (Ferrazzini et al. 2003). The safety of topical antifungal agents is not proven. So eosin, zinc paste, and corticosteroids are being used topically for the treatment (Hoppe 1997).

Olive oil, beeswax, and honey when applied topically affect formation of cytokines as they contain antioxidants, flavonoids, antibacterial/antifungal compounds (Tuck and Hayball 2002). Several studies have confirmed the effectiveness of this mixture for the treatment of psoriasis, dermatitis, and skin fungal infections (Al-Waili 2003a, b, 2004). In a study conducted by Al-Waili et al., the outcome of consuming this mix to treat the illness was explored. Fungal culture was done on glucose agar. The topical adjunct was made by scrupulously mingling natural honey, olive oil, and beeswax (1:1:1 v/v). In a 7-day trial, the management



was operative in treatment and removed *C. albicans* from 50% of culture-positive subjects (Al-Waili 2005a, b).

Anti-inflammatory properties may be responsible for the relief of symptoms. Osmolality, acidity, and hydrogen peroxide production could be the chief reasons for antimicrobial activity of honey (Molan 1999). Honey reduces prostaglandins and upsurges nitric oxide in biotic fluids as per previous studies (Al-Waili 2003a, b). Olive oil has been revealed to upsurge nitric oxide and lessen arachidonic acid by rat macrophages (Visioli et al. 1998). Nitric oxide released by sweat glands has antimicrobial action (Al-Waili 2003a, b, Akh and Zefirov 1999). Consequently, topical application could increase antioxidant and anti-inflammatory activity, decrease prostaglandin production, rise of nitric oxide levels, and inhibition of microbial sprout (Tuck and Hayball 2002; Noa and Mas 1998).

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### 11.14 Honey and Seborrheic Dermatitis

Honey has antibacterial, antifungal, and antioxidants actions and a high nutrient value. Seborrheic dermatitis is a long-lasting recurring inflammatory ailment resulting from metabolic changes in the cutaneous microflora including yeast, hyperactivity of sebaceous glands, and changed host immune task. In vitro studies have postulated that honey condensed the healing time via a twin influence on the inflammatory pathway. Firstly, honey defeats the manufacture and movement of inflammatory cells to place of damage; lastly, it increases propagation of fibroblasts and epithelial cells and making of proinflammatory cytokines (Tonks et al. 2001; Visavadia et al. 2008; Tomblin et al. 2014). In vitro studies revealed the effect of ingredients of honey on the making of inflammatory cytokines wherein they have established that Manuka honey improved manufacture of inflammatory cytokines, TNF- $\alpha$ , IL-1 $\beta$ /IL-6 via a TLR4-dependent mechanism (Riches 1996; Tonks et al. 2007).

Some other trials explored the possible usage of crude honey in the management of seborrheic dermatitis and dandruff when applied topically and concluded that crude honey could distinctly treat the disease and accompanying hair loss (Al-Waili 2001).

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### 11.15 Honey: A Wound Healer

Wound is an injury that characteristically includes cut or breach of a membrane-like skin. The underline tissue gets damaged causing obliteration of tissue, disturbance of blood vessels, and spillage of blood constituents and hypoxia (Porth 2006). It results in ache, uneasiness, and can lead to dangerous ailment or even death (Cooper et al. 2002). Wound healing is intercepted by endogenous and exogenous influences. Bacterial attack and development favor its infection (Porth 2006). Honey is one of unsurprising preparations useful in the management of wounds. It helps in the regeneration of tissue growth with little or no scars formation hence enhances

wound healing (Al-Waili et al. 2011; Bogdanov 2016; Lund-Nielsen et al. 2011; Misirlioglu et al. 2003). Honey is safe for external use in dressings, etc., with no allergic reactions with fast eradication of wound stink, decrease in quantity of exudates, and purification from microbes (Lund-Nielsen et al. 2011; Misirlioglu et al. 2003; Efem et al. 1992). As per Efem et al., unprocessed honey inhibited most of the fungi and bacteria except *P. aeruginosa* and *Clostridium oedematiens*. Skin defects are usually covered by split-thickness skin grafting which can lead to electrolyte imbalances, infection, delay in healing, and scar formation during the process of healing. The practice of using honey-infused gauzes is safe and effective leading to less pain and faster epithelization time due to conservation of moisture which is indispensable for timely healing (Misirlioglu et al. 2003; Efem et al. 1992). Therapeutic honey dressings have gained extensive recognition due to the influence of honey for curing different types of wounds. *Medihoney*<sup>®</sup> Dressing with 95% dynamic Manuka honey and 5% calcium alginate, manufactured by Derma Sciences received FDA approval for use in treating wounds like diabetic foot ulcers, venous or arterial leg ulcers, partial or full-thickness pressure ulcers/sores, first and second partial-thickness burns, and traumatic and surgical wounds (Group Health Cooperative 2010). A study by Subrahmanyam et al. showed that honey assists in healing of burns faster with less problems when equated to orthodox silver sulfadiazine gauze dressing (Subrahmanyam 1991). The accelerative influence of honey in ulcer, wound, and skin burn healing course is linked to its intricate chemical composition, hygroscopicity, hypertonicity, and lower pH. Ali-Wali et al. described the antimicrobial activity, nutritional trait, acidity, osmotic influence, antioxidant, and immune-modulating possession, when taken orally, as the chief causes for wound healing signifying that tissue growth factor may be implicated, rather than growth stimulus as a result of wound acidification or enhanced tissue nourishment (Al-Waili et al. 2011).

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### 11.16 Honey: Remedy in Skin Cancer

Management of malignant wounds due to various cancers is efficiently brought about by honey (Simon et al. 2006). Lund-Nielsen et al. proved that use of honey-coated bandages reduced wound size and enhanced wound hygiene in subjects with progressive malignant wounds (Lund-Nielsen et al. 2011).

Fernandez-Cabezudo et al. proved the antiproliferative and antiapoptotic activity of Manuka honey in three cell lines (Fernandez-Cabezudo et al. 2013). In addition, Pichichero et al. identified that acacia honey inducing cell cycle arrest in various cells (Pichichero et al. 2010). In vivo experiments in mice models have proved the tumor-constraining properties of intravenously administered Manuka honey apart from increasing overall animal survival and decreasing chemotherapy prompted toxicity with no changes in hematological and biochemical markers. In another study, UVB exposed keratinocytes treated with Tualang honey had decreased COX-2 and NF- $\kappa$ B activation and showed a drop in DNA damage. Hence, honey may protect the skin against the immunomodulatory and photo oncogenic effects of

sun exposure (Ahmad et al. 2012). Flavonoid and phenolic complexes in honey have been found to obstruct proliferation of melanoma cells through cell cycle seizure and apoptosis (Pichichero et al. 2010; Pichichero et al. 2011). Downregulation of tumor suppressor protein (p53) and antiapoptotic protein (Bcl-2) is brought about by honey in various neoplasms (Placzek et al. 2010).

Inflammation is a hallmark of cancer, so anti-inflammatory effects of honey define its anticarcinogenic activity (Jiang and Shapiro 2014). The anticarcinogenic traits of honey are encouraging but more investigation is essential for an elaborate understanding of the possible effectiveness of honey in the management or prevention of skin cancer.

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### 11.17 Honey: Be Aware of Risks

Top physicians of the world are of the opinion that there might be a possible allergic reaction to honey, predominantly if someone is already allergic to bees or pollen. There could be allergic reactions to proteins secreted by bees and from proteins derived from plant pollen (Simon et al. 2009). So it is imperative to do a patch test before using new skin-care products and look for any redness or allergic reaction in the area of application. Not all skin products contain Manuka honey. Original products are certified by *New Zealand's Unique Manuka Factor Honey Association* and have Manuka factor trademark.

It is worth to take into consideration that according to *The American Academy of Pediatrics* honey is not recommended for infants below 1 year of age. Fresh, unrefined honey increases the occurrence of botulism in infants where the honey is contaminated with spores of *Clostridium botulinum*. After consumption, *C. botulinum* dormant bacterium can sprout, develop, and yield toxin in lower bowel of infants less than 1 year, as the intestinal flora is not advanced (Brown 2000).

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### 11.18 Conclusion

Honey is a very intricate substance with possible therapeutic effect in dealing with various skin disorders. Upcoming explorations must intent to probe whether alike properties could be replicated with other types of honey. Manufacturing extra applied form of honey for topical skin use should accelerate scientific and medical inquiries. Additionally, these discoveries ought to built-up the gateway to the possible character of honey in the management of additional atopic disorders like allergic rhinitis or asthma. In this era of personalized medicine, it will not be wrong to say that honey doesn't do wonders on every individual. So people should not completely depend on honey for the treatment of skin disorders as there are allied allopathic ways to treat various disorders. Double-blinded randomized clinical trials are needed to find the most effective period, regularity, and kind of honey and more

severe technical experiments are needed to authorize its advantages a therapeutic invention of high value in dermatology.

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