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Cosmeceutical benefits of stingless bee honey

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ABSTRACT

Introduction: There were about 500 stingless bee (SB) species that had been reported in Afrotropical, Indo-Australian and Neotropical provinces with the highest diversity species originating in the Neotropical. In Malaysia, there are more than 38 species and around 33 species were reported in Peninsular Malaysia. Due to its high nutritional and medicinal values, recently, stingless bee honey (SBH) has been highly demanded by the food, pharmaceutical and cosmetic industries. Thus, this paper will describe the cosmeceutical potential of SBH as an antiacne, skin moisturizing and anti-hypertrophic scar agent. SBH can treat acne by reducing inflammation and irritation during acne formation due to its high flavonoid and phenolic content. Besides, SBH also possesses antibacterial activity due to its acidity, osmolarity and hydrogen peroxide content which is unfavourable for *P.acne* growth. It functions as a natural humectant due to its ability to attract water from the dermis and deeper epidermis to the epidermis and its high water-binding capacity. SBH also can reduce scar formation by improving the wound healing process. This is due to the both pro-inflammatory and anti-inflammatory properties in which it triggers the production of the pro-inflammatory cytokines to initiate the inflammation and inhibit the production of the pro-inflammatory cytokines when inflammation is in progress to avoid prolonged inflammation. Furthermore, SBH can stimulate skin reepithelialization and wound contraction. These will reduce the damaged tissue that needs to be repaired and eventually minimise the scarring area. In cosmeceutical, further research regarding the effectiveness of honey/ SBH in various cosmetic formulations had been investigated and the formulations developed were proven to be effective in treating the acne, moisturising the skin and minimising the scar.

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Introduction

Stingless bee (SB) is normally found in tropical and sub-tropical areas (Fletcher et al., 2020; Rattanawannee & Duangphakdee, 2019). There were 500 SB species that had been reported in Afrotropical, Indo-Australian and Neotropical provinces (Fletcher et al., 2020) with the highest diversity species originating in the Neotropical. In Malaysia, there are more than 38 species (Mustafa, Yaacob, & Sulaiman, 2018) and around 33 species were reported in Peninsular Malaysia (Ghazi, Zulqurnain, & Azmi, 2018). However, only four species are commercially nurtured which are *Heterotrigona itama, Geniotrigona thoracica, Tetragonula leviceps* and *Lepidotrigona terminate* (Mustafa et al., 2018). There are two tribes of SB which are Meliponina and Trigonina (Jalil, Kasmuri, & Hadi, 2017; Zulkhairi Amin et al., 2018) Melipona tribe is bigger compared to the Trigona tribe (Figure 1) (Fletcher et al., 2020; Jalil et al., 2017). It is called a stingless bee due to its non-functional vestigial sting. Since SB do not have a sting, thus they protect their nests by biting or putting plant resin on the enemies' skin, entering body cavities or hiding in the hair (Barbiéri & Francoy, 2020).

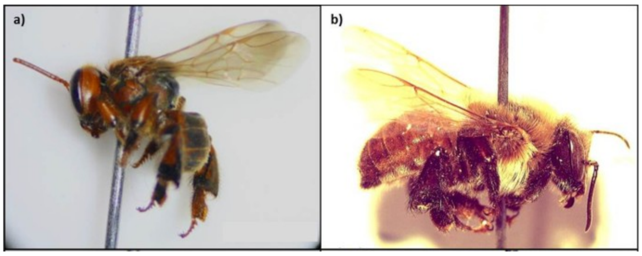

Figure 1 (a) Trigona genera (b) Melipona genera (Reyes-González, Camou-Guerrero, Reyes-Salas, Argueta, & Casas, 2014).

In Malaysia, the SB is known as *kelulut* (Mustafa et al., 2018). Nowadays, meliponiculture (stingless beekeeping) activities are very popular due to their easy management of the SB culture (Nordin, Sainik, Chowdhury, Saim, & Hj Idrus, 2018). As SB do not sting, therefore the extraction of honey, propolis and pollen are much easier compared to sting bee which needs proper safety equipment and training (Jalil et al., 2017; Nordin et al., 2018). Furthermore, the nesting behaviours of SB also make the meliponiculture activity easier since SB just construct their hive in the existing chamber or hollow area (Fletcher et al., 2020). Hence, the artificial hive can be used to control the colony and increase the honey production in meliponiculture activity (Jalil et al., 2017; Majid, Abu Bakar, Mian, Esa, & Kok Yeow, 2019; Nordin et al., 2018) Besides, the demand for stingless bee honey (SBH) has been increasing (Majid et al., 2019). This is because, over the last two decades, the food, pharmaceutical and cosmetic industries have become more interested in using SBH due to its highly nutritional and medicinal values (Ávila, Beux, Ribani, & Zambiazi, 2018).

SBH has been practised as a source in traditional treatment in many countries. The characteristics of SBH are amber-brown, sweet and sour taste, acidic and high moisture content (Rao, Krishnan, Salleh, & Gan, 2016; Zulkhairi Amin et al., 2018). It consists of carbohydrates, phenolic compounds, amino acids, organic acids, minerals, vitamins, enzymes and lipids (Fatima, Mohd Hilmi, Salwani, & Lavaniya, 2018). Its major constituent is fructose and glucose which are about 65% of sugars with a very minimal amount of hydroxymethylfurfural (Mustafa et al., 2018). However, the composition, bioactive compounds and physiochemical properties of the honey differ depending on the botanical source, geographical site, climatic condition, soil type, beekeepers' activities and storage treatments in commercial production (Mohammad, Mahmud-Ab-Rashid, & Zawawi, 2020). The amount of each constituent of SBH is listed in Table 1.

Table 1: The composition of SBH (Zulkhairi Amin et al., 2018).

Composition	Amount (%)
Total reducing sugars	54.90–87.00
Glucose	8.10–31.00
Fructose	31.11–40.20
Sucrose	0.31-1.26
Maltose	Not determined
Calcium	0.017
Potassium	0.07
Sodium	0.012
Magnesium	0.004
Ash	0.01–0.12

Minerals such as phosphorus, zinc, manganese, lead and iron are also found in the honey (Zulkhairi Amin et al., 2018). In *G. thoracica* and *H. itama* honey samples, there are four types of organic acids were indicated which are gluconic acid, lactic acid, acetic acid and citric acids (Shamsudin et al., 2019). The flavonoid and phenolic compounds of SBH are greater than in other honey types

(Mustafa et al., 2018) which makes it a potent antioxidant. As it has a high antioxidant capacity, thus SBH has the potential to treat numerous medical conditions such as cataracts and wounds. SBH also displays potential antimicrobial activity as a substitution treatment for inflammation and infection (Ávila et al., 2018).

STINGLESS BEE HONEY AS ANTI ACNE AGENT

Pathophysiology of Acne Vulgaris

One of the pathogenesis of acne vulgaris is increased sebum production. Sebum production is mediated by the androgen level in the pilosebaceous unit. The possible mechanism of high sebum production is either directly due to the high production of androgen hormones or the increased sensitivity of the sebaceous gland to normal androgen levels (Masterson, 2018). The level of androgen hormones including testosterone and 5α-dihydrotestosterone (DHT) will rise during puberty. This will lead to sebaceous gland hypertrophy, sebaceous lipogenesis and sebocyte differentiation. The sebocytes differentiation will possess abundant nuclear androgen receptors and peroxisome proliferator-activated receptors (PPARs) that make the sebaceous glands more hyperresponsive to androgens (Briganti, Flori, Mastrofrancesco, & Ottaviani, 2020). Besides, the high sebum in sebaceous follicles offers a nutrient source and anaerobic environment for *Propionibacterium acne* (Figure 2) to grow (Soleymani, Farzaei, Zargaran, Niknam, & Rahimi, 2020).

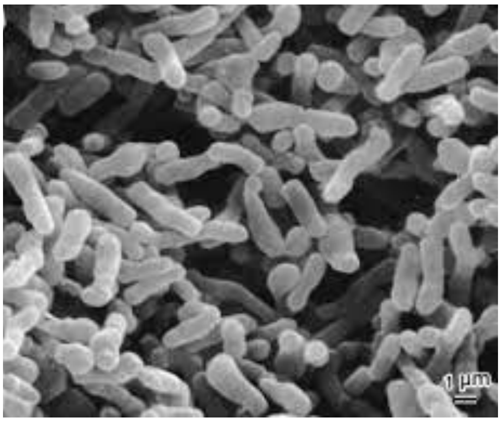

Figure 2: Scanning electron microscopic picture of P.acnes (Toyoda & Morohashi, 2001).

. The second pathophysiology of acne is the follicular hyperkeratinisation of the follicle. Many factors are believed to cause follicular hyperkeratinisation including reduced sebaceous linoleic acid concentration, increased androgen activity, inflammation and *P.acnes* biofilms. Reduced sebaceous linoleic acid concentration will enhance the cutaneous permeability to acne-causing inflammatory substances, thus disrupting the skin barrier function (da Cunha, Daza, Filho, da Veiga, & Fonseca, 2018). The proliferation and accumulation of keratinocyte cells at the follicle base will obstruct the pilosebaceous duct which leads to microcomedones formation. The microcomedone can be either a closed comedo (whitehead) in which the duct is almost entirely blocked or an opened comedo (blackhead) in which the duct is opened and exposed to the air (Figure 3). This opened comedo appears as a dark colour due to lipid and melanin oxidation (Brown, 2020).

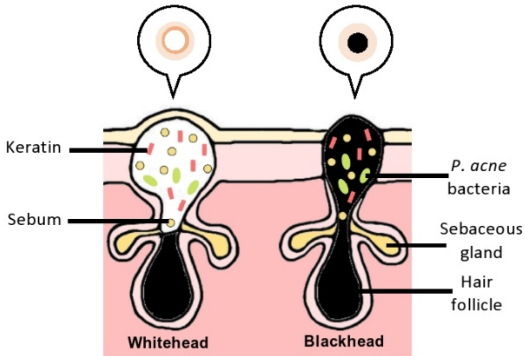

Figure 3: Illustration of whitehead and blackhead formation.

Furthermore, it is suggested that *Propionibacterium acne* does contribute to acne formation. Basically, *P.acnes* is one of the skin microbiota that acts as a first-line defence against external pathogens (Ramasamy, Barnard, Dawson, & Li, 2019). However, free fatty acids (FFA) produced by *P.acnes* triacylglycerol lipase activity are strong inducers for comedogenic, *P. acnes* biofilm formation and inflammation (Plewig, Melnik, & Chen, 2019). Lipase that is released by *P.acnes* will oxidise the squalene of the sebum and hydrolyse the triglycerides of the sebum into glycerol and FFA. Oxidised squalene can trigger the pro-inflammatory cytokines generation and PPARs activation. Meanwhile, glycerol can be the nutrient source for bacteria to grow and FFA promotes comedogenic, oxidative stress, inflammatory reaction and tissue destruction (da Cunha et al., 2018; Soleymani et al., 2020).

Lastly, inflammation is considered a significant element in acne pathogenesis. The expansion of microcomedone due to the buildup of keratin, sebum and bacteria will eventually cause the follicular wall to rupture and make the contents extrude into the dermis rather than above the skin surface. This will stimulate the inflammatory response and develop inflammatory acne lesions such as papules and pustules (Greydanus, Azmeh, Cabral, Dickson, & Patel, 2021). Inflammation is also mediated by the action of *P.acnes* through both innate and adaptive immune responses. *P.acnes* actuates the Toll-like receptor-(TLR)-2 on neutrophils and monocytes, then leads to the generation of proinflammatory cytokines such as tumour necrosis (TNF-α), IL-12 and IL-8 (Soleymani et al., 2020). The summary of the pathophysiology of acne vulgaris is illustrated in Figure 4.

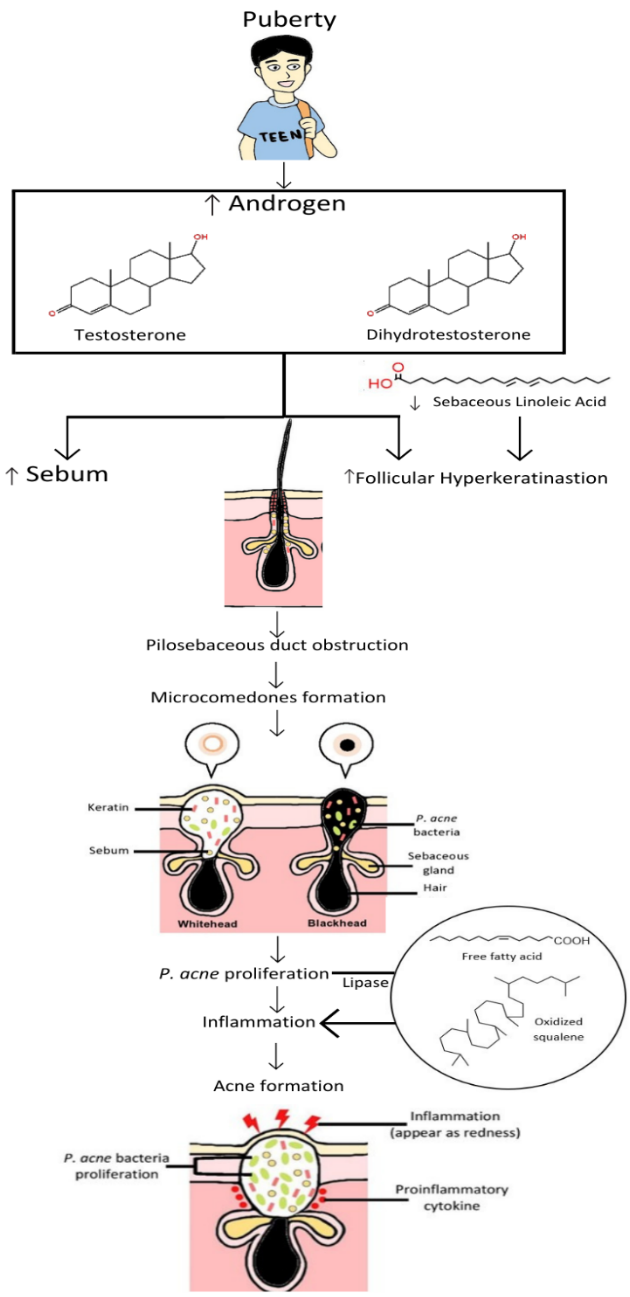

Figure 4: Summary of the pathophysiology of acne vulgaris.

Antioxidant and Anti-Inflammatory Activities of Stingless Bee Honey

As explained earlier, inflammation is one of the acne pathophysiologies. Oxidative stress that occurs due to ROS is known to cause many diseases either directly or indirectly. In acne, irritation during the infection is due to the free radicals formation specifically hydroxyl, superoxide and nitrous oxide. These free radicals are basically present in the sebum when the follicular walls of sebaceous glands become ruptured (Vora, Srivastava, & Modi, 2018). Antioxidative in honey produce anti-inflammatory properties which may decrease the inflammation during acne formation. Besides, studies show that the anti-inflammatory effects of honey can reduce the secretion of pro-inflammatory cytokines induced by *Propionibacterium acne* (Djakaria, Batubara, & Raffiudin, 2020). SBH possesses high antioxidative and anti-inflammatory properties since its polyphenolic compound is approximately ten times greater than other honey types (Mustafa et al., 2018). Research on the SB (*Trigona sp.*) in Malaysia indicated that the honey produced consists of a higher level of phenolic, flavonoids and total antioxidant activity compared with the honey produced by *Apis dorsata* (Ranneh et al., 2018).

Antimicrobial Activity of Stingless Bee Honey

The main mechanism of honey in treating acne is its antimicrobial property. Basically, the bacteria-killing effect of honey is attributed to its acidity, high osmolarity and hydrogen peroxide content (Albaridi, 2019). The acidic pH of honey will provide an unconducive environment for the bacteria, which in this case is *P.acnes* to grow as they favour neutral or slightly alkaline environments (pH 6.0 to 7.0) (Minden-Birkenmaier & Bowlin, 2018). Thus, the lower the pH, the higher ability of the honey to inhibit the growth of microorganisms (Fatima et al., 2018). SBH is considered the most acidic since it has the lowest value of pH (3.81 ± 0.02) when compared to *Tualang* honey (pH= 4.13 ± 0.02) and *Acacia* honey (pH= 4.20 ± 0.02) (Muhammad & Sarbon, 2021). Hence, this may deduce that SBH possesses potent antimicrobial activity since acidity contributes to its properties.

Moreover, it had been conjectured that reducing the water availability of the bacteria is a safe therapeutic approach for acne management (Eady, Layton, & Cove, 2013). Generally, honey is a supersaturated solution of sugar that has limited water content (Ab Hadi, Omar, & Awadh, 2016). Thus, this high sugar concentration of honey will induce a strong osmotic gradient on bacterial cells which makes the water from bacterial cells flow out through the osmosis process. This makes the bacterial cells dehydrated and unable to grow and proliferate in hypertonic sugar solution (Almasaudi, 2020). In addition, certain types of sugars have an effect on antimicrobial activity. For example, glucose and maltose are substrates for the growth of bacteria and fungi in small concentrations (Mizzi et al., 2020). Hence, it can be concluded that the individual sugars making up the honey play role in the bactericidal activity of the honey.

Another factor that contributes to the antibacterial property of honey is the presence of hydrogen peroxide (Jalil et al., 2017). The formation of hydrogen peroxide content in honey is catalysed by the glucose oxidase through the oxidation process of the glucose ($Glucose \xrightarrow[oxidase]{Glucose} Gluconic\ acid + Hydrogen\ peroxide$) (Febriyenti, Lucida, Almahdy, Alfikriyah, & Hanif, 2019). This hydrogen peroxide will increase the cytokine production for the inflammatory response to kill the bacteria (Jalil et al., 2017). Studies showed that just a low concentration of hydrogen peroxide can effectively inhibit many types of bacteria (Febriyenti et al., 2019) since hydrogen peroxide itself is one of the reactive oxygen species (ROS). Thus, it possesses antibacterial action by destroying the bacterial cell structure. This destructive action basically will depend on the concentration of hydrogen peroxide in the honey (Ab Hadi et al., 2016). The summary of SBH properties and their effects in treating acne is tabulated in Table 2.

Nowadays, many cosmetic formulations that included honey in combination with other natural ingredients were studied for acne treatment. A tamarind soap with honey was developed and assessed for its antibacterial effect against *Staphylococcus aureus*. The result showed it able to inhibit the bacteria, thus it can be considered to have potential antibacterial properties. This soap also was tested on acne patients and it was effective in reducing the amount and size of the acne and able lightening the acne scars' colour and skin colour (de Jesus et al., 2020). In another study, a moisturising cream that contains SBH and propolis was also developed by Regional Apiculture Center (RAC) and tested on 15 volunteers. The volunteers that used it for their acne claimed that the cream able to prevent further acne progression (Mostoles, Rosario, Pasiona, & Buenaagua, 2021). The effect of natural products consisting of two different concentration of honey (44% and 54%) were also evaluated in acne patients. The acne severity proved a significant improvement in post-treatment than in the pre-treatment state in both groups. However, in the post-treatment, more patients were transferred to a mild acne state in the group that received the 54% honey concentration compared to the 44% honey concentration group (Helal, Mohamed, Farag, & Abdel Rashed, 2017). Therefore, this reveals that inclusion of honey in cosmetic formulation able to treat acne and higher honey concentration will treat acne better.

MOISTURIZING EFFECT OF STINGLESS BEE HONEY

Pathophysiology of Dry Skin

Dry skin is characterised by focal or generalised dry, rough, flaky or scaly skin. It is commonly accompanied by loss of skin elasticity, fissure and pruritus (Henning et al., 2021; Proksch, Berardesca, Misery, Engblom, & Bouwstra, 2020). The skin may also feel tense, sore or burning. Besides, dry damaged skin can be the entry for skin infections. Dry skin can be a symptom of itself or a symptom of other skin conditions including atopic dermatitis, ichthyosis, irritant contact dermatitis, psoriasis or asteatotic eczema (Mekić et al., 2019; Proksch et al., 2020). Besides, certain chronic diseases such as diabetes, hypothyroidism, HIV and renal insufficiency and also the use of some drugs (diuretics, statins or chemotherapeutic agents) can be accompanied by dry skin (Mekić et al., 2019).

The overall prevalence of dry skin is about 29% to 85% worldwide and it is the most common skin condition in middle-aged and elderly populations. Thus, it can be considered as a part of physiologic skin ageing (Mekić et al., 2019). This is because the lipid and water content are reduced in ageing skin which eventually impairs epidermal barrier function. Impaired epidermal barrier function will result in water loss (Chang et al., 2018). The onset of dry skin is mediated by intrinsic and extrinsic factors that cause modifications in the stratum corneum (SC) such as defective keratinisation and lipid cement abnormalities (Henning et al., 2021). This lipid cement is mainly composed of ceramides (~50%) followed by cholesterol (25%) and fatty acids (10-20%) (Moore & Rawlings, 2017). The ceramide content has been observed to have a strong correlation with dry skin characteristics (Murphy et al., 2022). Many studies showed that ceramide content was reduced in dry skin

Table 2: Summary of SBH properties and their effects on treating acne.

Properties	Effective factors	Actions	References
Antioxidant and anti-inflammatory activities	Flavonoid and phenolic compounds	Reduce inflammation and irritation during acne formation	(Djakaria et al., 2020)
Antimicrobial activity	Acidity	Unconducive environment for bacteria growth	(Albaridi, 2019; Minden-Birkenmaier & Bowlin, 2018)
	Osmolarity	Dehydrate the bacterial cells	(Albaridi, 2019; Almasaudi, 2020)
	Hydrogen peroxide	Destruct the bacterial cells	(Albaridi, 2019; Jalil et al., 2017)

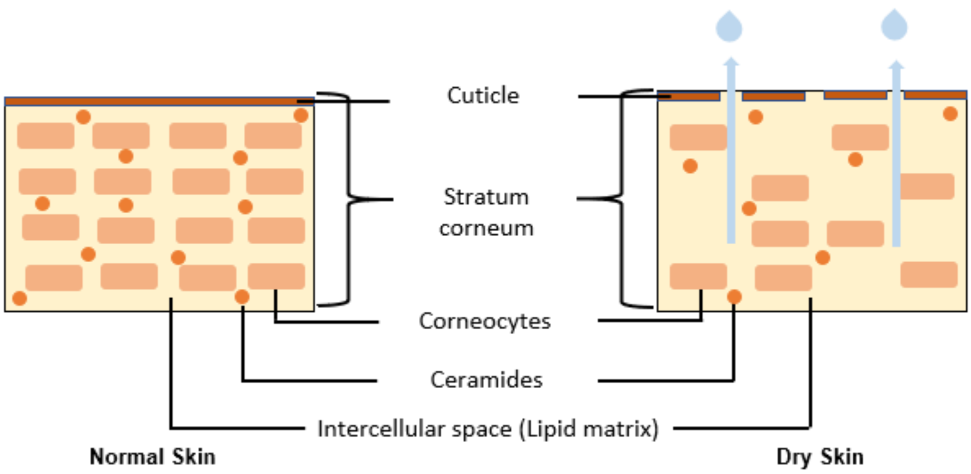

Figure 5: Illustration of the difference between normal and dry skins. The cuticle, corneocytes and ceramides number in the SC of dry skin are fragmented and depleted compared to normal skin. All these eventually lead to the loss of water.

(Moore & Rawlings, 2017). Some intrinsic factors are genetics, ageing and ethnicity meanwhile the extrinsic factors are sunlight exposure, low humidity, smoking, friction, bathing frequency and use of soaps (Henning et al., 2021; Proksch et al., 2020). A diagram illustrating the difference between normal and dry skin can be seen in Figure 5.

Role of Stingless Bee Honey as Humectant

Dry skin is normally been treated using humectants, occlusives or emollients to improve the SC's hydration and consequently repair the skin barrier (Murphy et al., 2022). Honey is a natural humectant due to its high moisture content (Ab Hadi et al., 2016; Eady et al., 2013). Humectants normally will possess emollient properties too (Purnamawati, Indrastuti, Danarti, & Saefudin, 2017). A humectant is basically a substance that acts like a sponge that draws water into the skin. It will attract water from the deeper epidermis and dermis and make the skin smoother by filling holes in the SC through swelling (Draelos, 2018). The presence of hydroxyl groups in honey

(Fletcher et al., 2020; Jalil et al., 2017) makes it has the water-binding ability and form hydrogen bonds with the water molecules. Hence, the hydrated skin condition can be preserved since the hydrogen bonds help to retain water in the SC by averting water loss through evaporation (Hadi, Razali, & Awadh, 2015).

Besides, the honey composition such as sugars, amino acids and lactic acid also exhibits a moisturizing effect (Fletcher et al., 2020; Jalil et al., 2017). SBH possesses high moisture content when compared to other types of honey. A study conducted in Malaysia showed that both SBH types (*Trigona thorasica* and *Trigona itama*) have high moisture content (28.3% to 33.7%) compared with the honey produced by *Apis dorsata* (24.8%) (Fatima et al., 2018). When compared to *Manuka* honey (*Apis mellifera*), the moisture content of SBH is also greater. The moisture content of honey by *Geneotrigona thorasica* and *Heterotrigona itama* range from 19.49% to 33.93% meanwhile *Apis mellifera* honey only consist of 14.74% water content (Shamsudin et al., 2019). Due to the great percentage of moisture content, thus SBH can be presumed to possess excellent moisturizing properties (Rao et al., 2016; Zulkhairi Amin et al., 2018). A diagram illustrating the mechanism of SBH preserves skin hydration can be seen in Figure 6.

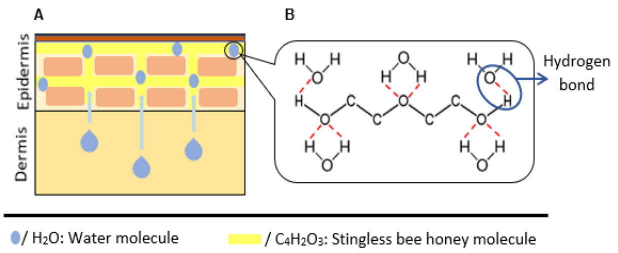

Figure 6: Illustration on how SBH preserves skin hydration by (A) attracting water from dermis to epidermis and (B) making a hydrogen bond with water molecules.

The effect on the skin of honey and bee products in cosmetic matrices had been studied. It showed that formulation consist of higher concentrations of honey hydrated the skin more effectively (Pavlačková, Egner, Slavík, Mokrejš, & Gál, 2020). More than 50% of volunteers rate the moisturizing effect of a bath soap consisting of SBH and propolis as acceptable (Mostoles et al., 2021). Furthermore, the moisture content of the lip balm formulation was enhanced with the presence of SBH. In this study, it shows that the higher the SBH concentration, the higher the moisture content of the lip balm. The lip moisture of all volunteers was also improved when applying the lip blam (Athirah, Yusof, Ajit, Sulaiman, & Naila, 2018). Hence, this indicates that the incorporation of SBH in cosmetic formulations enables to improve the skin hydration and also the moisture content of the formulation itself.

STINGLESS BEE HONEY REDUCES SCAR FORMATION

Formation of Scar

Scar formation is the result of the healing mechanism once the skin is injured. There are four corresponding stages in the wound healing process which are hemostasis, inflammation, proliferative and remodelling stages. Hemostasis and inflammation stages occur immediately after local aggression to restore the injury. Meanwhile, proliferative and remodelling stages involve the process of replacing the wound area with new skin. This new skin is formed by the deposition of collagen and the regeneration of new skin cells (Theoret, 2018). The summary of the wound healing process is illustrated in Figure 7.

Scar formation is a process that occurred in the remodelling phase. However, the extent of scarring will be depending on the severity of the trauma and the intensity of the inflammatory response. Although inflammation is one of the wound healing phases but once the inflammation fails to stop, the chronic inflammatory response will take over (Theoret, 2018). This will eventually impair the wound healing process and cause pathological scarring since permanent fibrotic scar tissue will accumulate at the site of injury. This fibrosis is characterised by the excessive accumulation of extracellular matrix (ECM) components including collagens, fibronectin and hyaluronic acid at the site of injury (Karppinen, Heljasvaara, Gullberg, Tasanen, & Pihlajaniemi, 2019; Theoret, 2018). This ECM will consequently form granulation tissue which is a secular connective tissue that contains macrophages, fibroblasts and capillaries (Karppinen et al., 2019).

Modulation of Pro-Inflammatory and Anti-Inflammatory Properties of Stingless Bee Honey

Honey possesses both pro-inflammatory and anti-inflammatory properties that may improve the wound healing process and eventually minimise scar formation. This is because honey will trigger the

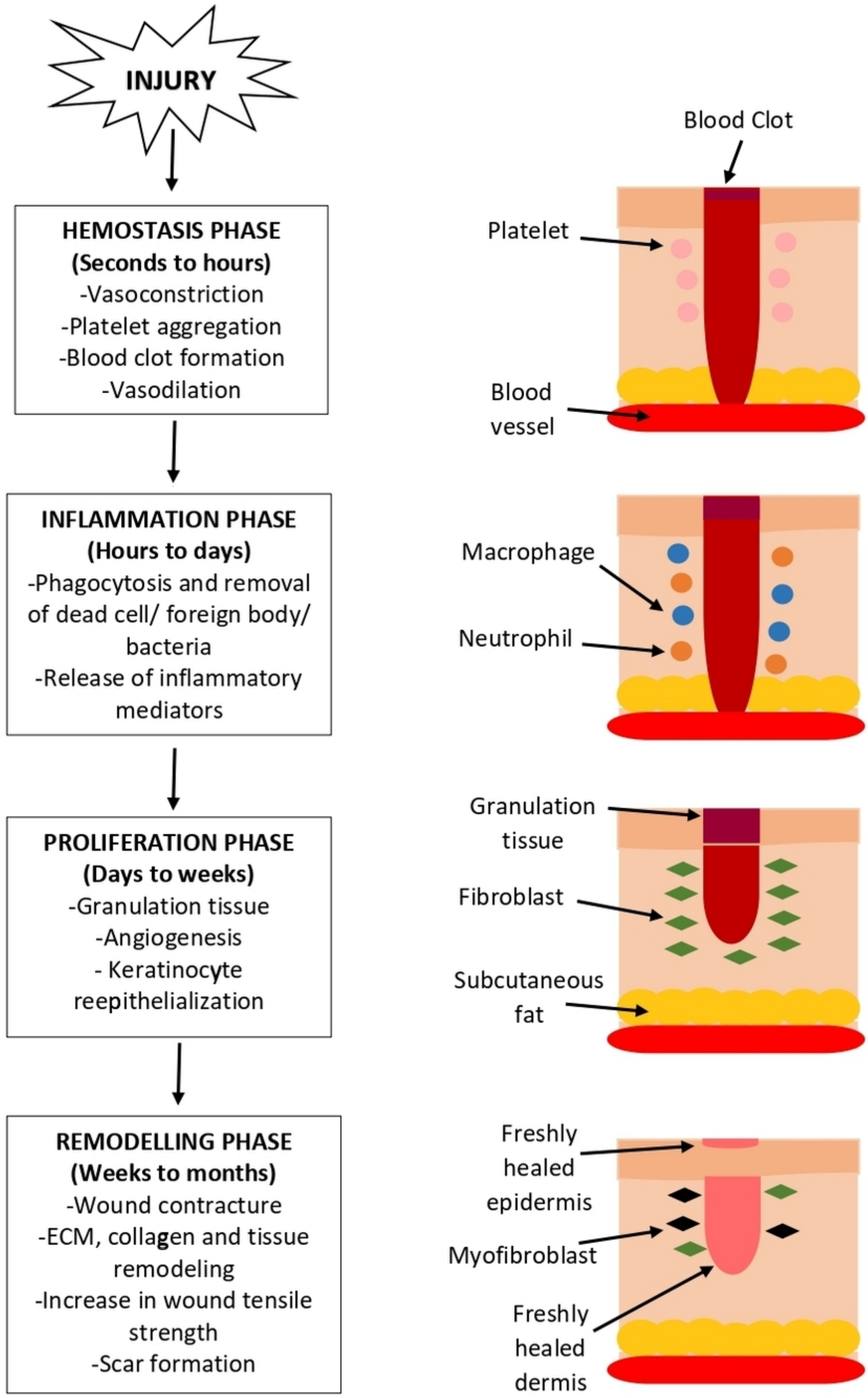

Figure 7: Illustration of the wound healing process.

release of inflammatory cytokines such as TNF-a IL-6, IL-1b, reactive oxygen species (ROS) and nitric oxide from the monocytes in the inflammatory phase. These cytokines play important roles in the initiation and magnification of inflammatory processes (Oryan & Alemzadeh, 2017; Oryan, Alemzadeh, & Moshiri, 2016). However, the prolonged inflammation phase can lead to tissue damage, impairs wound healing and eventually cause hypertrophic scarring due to hypergranulation and fibrosis. This is because the inflammatory mediators and cytokines are very cytotoxic and can destroy the essential components for the functional activities of all cells (Jalil et al., 2017). Hence, the use of honey can reduce tissue necrosis and hypertrophic scarring since honey possesses high anti-inflammatory properties.

The high anti-inflammatory properties of honey are attributed to the inhibition of leukocyte infiltration and reduction of matrix metalloproteinase-9 (MMP-9), cyclooxygenase-2 (COX-2), ROS and inducible nitric oxide synthase (iNOS) formation. This shows that honey can modulate both the pro-inflammatory and anti-inflammatory properties in which honey will trigger the production of the inflammatory cytokines when their concentrations are low. Meanwhile, the production of the inflammatory cytokines will be inhibited by the honey when inflammation is in progress (Oryan & Alemzadeh, 2017; Oryan et al., 2016) to avoid chronic wounds due to prolonged inflammation (Theoret, 2018). This anti-inflammatory property of SBH is contributed by the high flavonoid and phenolic compounds. Lastly, as mentioned before, SBH is a potent antioxidant. The antioxidant substances of SBH will remove and scavenge the ROS. It is important to prevent ROS formation as oxidative stress will increase tissue damage and prolong the wound repair process and form hypertrophic scar (Oryan et al., 2016).

Role of Stingless Bee Honey as Skin Reepithelialization and Wound Contraction Promoter

Honey which contains abundant sugars including SBH can stimulate skin reepithelialization by providing energy and a moist surrounding for the keratinocytes to migrate and proliferate to the wound surface in the proliferation phase (Oryan & Alemzadeh, 2017; Oryan et al., 2016). The high osmotic pressure of honey also facilitates skin reepithelialization acceleration by drawing out water from the tissue oedema and keeping the wound margin together. Besides, hydrogen peroxide content in honey also can promote epithelial cell growth (Nakajima et al., 2013). Wound contraction that occurred in the remodelling phase is basically a healing response that functions to decrease the damaged tissue size, so that lesser damaged tissue needs to be repaired and eventually minimise the scarring area. This response involves fibroblasts and myofibroblasts that are located adjacent to the wound (Lesperance, Francis, & Norton, 2006). As mentioned before, honey which is a source of energy promotes wound contraction by stimulating fibroblasts and myofibroblasts to deposit more collagen (Oryan & Alemzadeh, 2017; Oryan et al., 2016). The summary of the SBH effects on each wound healing phase in reducing scar formation is illustrated in Figure 8.

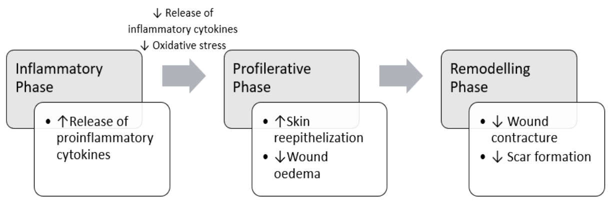

Figure 8: Summary of the SBH effects on each wound healing phase in reducing scar formation.

Recently, several formulations containing SBH had been developed and tested for wound healing. An *in vivo* healing efficacy test of PVA-natural biopolymer hydrogel incorporated with SBH on rabbit skin found that the SBH hydrogel exhibited an excellent wound healing property compared to no treatment and blank hydrogel. This is due to faster wound contraction and better wound closure was noticed in the SBH hydrogel groups (Abd Jalil, 2020). In another study, a nanofibrous composite membrane containing SBH and curcumin was developed for wound healing. The nanofibrous membrane-treated group showed a better healing rate (wound contraction and reduction) compared to the control group since significant collagen deposition and reepithelialization were observed (Samraj.S, Kirupha, Santhini, & Vadodaria, 2021). Besides, the volunteers of the RAC moisturising cream also mentioned that the skin irritations were easily reduced with little scar removal from the wounds (Mostoles et al., 2021). Hence, this shows that the addition of SBH in a formulation can promote wound healing and consequently reduce scar formation.

Conclusion

In conclusion, SBH may benefit the skin as it can treat acne, moisturise the skin and reduce the hypertrophic scar due to its constituents. SBH is a possible treatment for acne since it is highly antioxidant due to its high phenolic and flavonoid compounds. It also possesses anti-inflammatory properties that are contributed by the antioxidants which may decrease the inflammation during acne formation. Besides, the bacteria-killing effect of SBH is also attributed to its acidity, high osmolarity and hydrogen peroxide content. Moreover, honey's high moisture content is proven to give a hydrating effect on the skin due to the presence of hydrogen bonds in its chemical structure. This help to retain water in the SC of the skin by averting water loss through evaporation. Lastly, SBH honey can reduce hypertrophic scarring by modulation of both the pro-inflammatory and anti-inflammatory properties to avoid chronic wounds, stimulate skin reepithelialization and reduce wound contracture in the wound healing cascade. In cosmeceutical, further research regarding the effectiveness of honey/ SBH in various cosmetic formulations had been investigated and the formulations developed were proven to be effective in treating the acne, moisturising the skin and minimising the scar.

Conflict of Interest

None.

References

Ab Hadi, H., Omar, S. S. S., & Awadh, A. I. (2016). Honey, a Gift from Nature to Health and Beauty: A Review. *British Journal of Pharmacy*, *1*(1), 46–54. https://doi.org/10.5920/bjpharm.2016.05

Abd Jalil, M. A. (2020). Development of PVA-natural biopolymer hydrogel incorporated with stingless bee honey for wound healing (International Islamic University Malaysia). International Islamic University Malaysia. Retrieved from http://studentrepo.iium.edu.my/handle/123456789/10032

Albaridi, N. A. (2019). Antibacterial Potency of Honey. *International Journal of Microbiology*, 1–10. https://doi.org/https://doi.org/10.1155/2019/2464507

Almasaudi, S. (2020). The antibacterial activities of honey. *Saudi Journal of Biological Sciences*, *28*(4), 2188–2196. https://doi.org/10.1016/j.sjbs.2020.10.017

Athirah, A., Yusof, B., Ajit, A. B., Sulaiman, A. Z., & Naila, A. (2018). Production of Lip Balm From Stingless Bee Honey. *The Maldives National Journal of Research*, *1*(1), 57–72.

Ávila, S., Beux, M. R., Ribani, R. H., & Zambiazi, R. C. (2018). Stingless bee honey: Quality parameters, bioactive compounds, health-promotion properties and modification detection strategies. *Trends in Food Science and Technology*, *81*(September), 37–50. https://doi.org/10.1016/j.tifs.2018.09.002

Barbiéri, C., & Francoy, T. M. (2020). Theoretical model for interdisciplinary analysis of human activities: Meliponiculture as an activity that promotes sustainability. *Ambiente e Sociedade*, *23*. https://doi.org/10.1590/1809-4422ASOC20190020R2VU2020L4AO

Briganti, S., Flori, E., Mastrofrancesco, A., & Ottaviani, M. (2020). Acne as an altered dermato-endocrine response problem. *Experimental Dermatology*, *29*(9), 833–839. https://doi.org/10.1111/exd.14168

Brown, L. (2020). Acne and its management. *South African Pharmaceutical Journal Pharmaceutical Journal*, *87*(5), 37A-37H.

Chang, A. L. S., Chen, S. C., Osterberg, L., Brandt, S., von Grote, E. C., & Meckfessel, M. H. (2018). A daily skincare regimen with a unique ceramide and filaggrin formulation rapidly improves chronic xerosis, pruritus, and quality of life in older adults. *Geriatric Nursing*, *39*(1), 24–28. https://doi.org/10.1016/j.gerinurse.2017.05.002

da Cunha, M. G., Daza, F., Filho, C. D. A. M., da Veiga, G. L., & Fonseca, F. (2018). The relevance of sebum composition in the etiopathogeny of acne. *European Journal of Biological Research*, *8*(1), 21–25. https://doi.org/http://dx.doi.org/10.5281/zenodo.1184139

de Jesus, N., Zabala, E. C., Pineda, E. B., Loria, R. D., Pangilinan, E., & Soriano Jr, H. M. (2020). The Promotion of Beekeeping and Bee Product and By-Product Development at PSAU, Philippines. *AJARCDE | Asian Journal of Applied Research for Community Development and Empowerment*, *4*(1), 1–5. https://doi.org/10.29165/ajarcde.v4i1.29

Djakaria, S. A., Batubara, I., & Raffiudin, R. (2020). Antioxidant and Antibacterial Activity of Selected Indonesian Honey against Bacteria of Acne. *Jurnal*

Kimia Sains Dan Aplikasi, *23*(8), 267–275. https://doi.org/10.14710/jksa.23.8.267-275

Draelos, Z. D. (2018). The science behind skin care: Moisturizers. *Journal of Cosmetic Dermatology*, *17*(2), 138–144. https://doi.org/10.1111/jocd.12490

Eady, E. A., Layton, A. M., & Cove, J. H. (2013). A honey trap for the treatment of acne: Manipulating the follicular microenvironment to control propionibacterium acnes. *BioMed Research International*, *679680*, 1–8. https://doi.org/10.1155/2013/679680

Fatima, I. J., Mohd Hilmi, A. B., Salwani, I., & Lavaniya, M. (2018). Physicochemical characteristics of Malaysian stingless bee honey from Trigona species. *IIUM Medical Journal Malaysia*, *17*(1), 187–191. https://doi.org/https://doi.org/10.31436/imjm.v17i1.1030

Febriyenti, F., Lucida, H., Almahdy, A., Alfikriyah, I., & Hanif, M. (2019). Wound-Healing Effect of Honey Gel and Film. *Journal of Pharmacy & Bioallied Sciences*, *11*(2), 176–180. https://doi.org/https://dx.doi.org/10.4103%2Fjpbs.JPBS_184_18

Fletcher, M. T., Hungerford, N. L., Webber, D., Jesus, M. C. De, Zhang, J., Stone, I. S. J., … Zawawi, N. (2020). Stingless bee honey, a novel source of trehalulose : a biologically active disaccharide with health benefits. *Scientific Reports*, *10*(1), 1–8. https://doi.org/10.1038/s41598-020-68940-0

Ghazi, R., Zulqurnain, N. S., & Azmi, W. A. (2018). Melittopalynological Studies of Stingless Bees from the East Coast of Peninsular Malaysia. In *Pot-Pollen in Stingless Bee Melittology* (pp. 1–481). Springer, Cham. https://doi.org/10.1007/978-3-319-61839-5_6

Greydanus, D. E., Azmeh, R., Cabral, M. D., Dickson, C. A., & Patel, D. R. (2021). Acne in the first three decades of life: An update of a disorder with profound implications for all decades of life. *Disease-a-Month*, *67*(4), 101103. https://doi.org/10.1016/j.disamonth.2020.101103

Hadi, H., Razali, S. N. S., & Awadh, A. I. (2015). A comprehensive review of the cosmeceutical benefits of vanda species (orchidaceae). *Natural Product Communications*, *10Hadi*, *H.*(8), 1483–1488. https://doi.org/10.1177/1934578x1501000842

Helal, H. A., Mohamed, E. A. el Z., Farag, A. G. A., & Abdel Rashed, A. R. (2017). Study the Effect of Natural Products in Acne Patients. *Journal of Home Economics*, *27*(1), 101–110.

Henning, M. A. S., Ibler, K. S., Ullum, H., Erikstrup, C., Bruun, M. T., Burgdorf, K. S., … Jemec, G. B. (2021). The association between water hardness and xerosis-results from the danish blood donor study. *PLoS ONE*, *16*(6 June), 1–13. https://doi.org/10.1371/journal.pone.0252462

Jalil, M. A. A., Kasmuri, A. R., & Hadi, H. (2017). Stingless Bee Honey , the Natural Wound Healer : A Review. *Skin Pharmacology*, *30*, 66–75. https://doi.org/10.1159/000458416

Karppinen, S. M., Heljasvaara, R., Gullberg, D., Tasanen, K., & Pihlajaniemi, T. (2019). Toward understanding scarless skin wound healing and pathological scarring [version 1; peer review: 2 approved]. *F1000Research*, *8*(787), 1–11. https://doi.org/10.12688/F1000RESEARCH.18293.1

Lesperance, M. M., Francis, T. L., & Norton, B. (2006). Postsurgical Soft Tissue Healing. *Postsurgical Orthopedic Sports Rehabilitation*, 3–18. https://doi.org/10.1016/B978-032302702-1.50004-1

Majid, M., Abu Bakar, M. F., Mian, Z., Esa, F., & Kok Yeow, Y. (2019). Variations of physicochemical properties of stingless bee honey from different botanical origin in state of Johor, Malaysia. *IOP Conference Series: Earth and Environmental Science*, *269*(1). https://doi.org/10.1088/1755-1315/269/1/012028

Masterson, K. N. (2018). Acne Basics: Pathophysiology, Assessment, and Standard Treatment Options. *Journal of the Dermatology Nurses' Association*, *10*(1), S2–S10. https://doi.org/10.1097/JDN.0000000000000361

Mekić, S., Jacobs, L. C., Gunn, D. A., Mayes, A. E., Ikram, M. A., Pardo, L. M., & Nijsten, T. (2019). Prevalence and determinants for xerosis cutis in the middle-aged and elderly population: A cross-sectional study. *Journal of the American Academy of Dermatology*, *81*(4), 963-969.e2. https://doi.org/10.1016/j.jaad.2018.12.038

Minden-Birkenmaier, B. A., & Bowlin, G. L. (2018). Honey-based templates in wound healing and tissue engineering. *Bioengineering*, *5*(2), 1–27. https://doi.org/10.3390/bioengineering5020046

Mizzi, L., Maniscalco, D., Gaspari, S., Chatzitzika, C., Gatt, R., & Valdramidis, V. P. (2020). Assessing the individual microbial inhibitory capacity of different sugars against pathogens commonly found in food systems. *Letters in Applied Microbiology*, *71*(3), 251–258. https://doi.org/10.1111/lam.13306

Mohammad, S. M., Mahmud-Ab-Rashid, N. K., & Zawawi, N. (2020). Botanical Origin and Nutritional Values of Bee Bread of Stingless Bee (Heterotrigona itama) from Malaysia. *Journal of Food Quality*, *2020*, 15–17. https://doi.org/10.1155/2020/2845757

Moore, D. J., & Rawlings, A. V. (2017). The chemistry, function and (patho)physiology of stratum corneum barrier ceramides. *International Journal of Cosmetic Science*, *39*(4), 366–372. https://doi.org/10.1111/ICS.12399

Mostoles, M. D. J., Rosario, A. B. del, Pasiona, L. C., & Buenaagua, R. R. (2021). Utilization and Commercial Production of Stingless Bees and its Products in Bicol, Philippines. *AGRIKULTURA CRI Journal*, *1*(1).

Muhammad, N. I. I., & Sarbon, N. M. (2021). Physicochemical profile, antioxidant activity and mineral contents of honey from stingless bee and honey bee species. *Journal of Apicultural Research*, 1–8. https://doi.org/10.1080/00218839.2021.1896214

Murphy, B., Grimshaw, S., Hoptroff, M., Paterson, S., Arnold, D., Cawley, A., … Mayes, A. E. (2022). Alteration of barrier properties, stratum corneum ceramides and microbiome composition in response to lotion application on cosmetic dry skin. *Scientific Reports*, *12*(1), 1–11. https://doi.org/10.1038/s41598-022-09231-8

Mustafa, M. Z., Yaacob, N. S., & Sulaiman, S. A. (2018). Reinventing the honey industry: Opportunities of the stingless bee. *Malaysian Journal of Medical Sciences*, *25*(4), 1–5. https://doi.org/10.21315/mjms2018.25.4.1

Nakajima, Y., Nakano, Y., Fuwano, S., Hayashi, N., Hiratoko, Y., Kinoshita, A., … Wilkinson, J. M. (2013). Effects of Three Types of Japanese Honey on Full-Thickness Wound in Mice. *Evidence-Based Complementary and Alternative Medicine*, *2013*, 11. https://doi.org/10.1155/2013/504537

Nordin, A., Sainik, N. Q. A. V., Chowdhury, S. R., Saim, A., & Hj Idrus, R. (2018). Physicochemical properties of stingless bee honey from around the globe: A comprehensive review. *Journal of Food Composition and Analysis*, *73*, 91–102. https://doi.org/10.1016/j.jfca.2018.06.002

Oryan, A., & Alemzadeh, E. (2017). Potential Mechanisms and Application of Honeybee Products in Wound Management: Wound Healing by Apitherapy. *Recent Clinical Techniques, Results, and Research in Wounds*, 267–284. https://doi.org/10.1007/15695_2017_38

Oryan, A., Alemzadeh, E., & Moshiri, A. (2016). Biological properties and therapeutic activities of honey in wound healing: A narrative review and meta-analysis. *Journal of Tissue Viability*, *25*(2), 98–118. https://doi.org/10.1016/j.jtv.2015.12.002

Pavlačková, J., Egner, P., Slavík, R., Mokrejš, P., & Gál, R. (2020). Hydration and barrier potential of cosmetic matrices with bee products. *Molecules*, *25*(11), 1–13. https://doi.org/10.3390/molecules25112510

Plewig, G., Melnik, B., & Chen, W. (2019). Acne Pathogenesis. In G. Plewig, B. Melnik, & W. Chen (Eds.), *Plewig and Kligman´s Acne and Rosacea* (4th ed., pp. 45–61). Switzerland: Springer International Publishing. https://doi.org/10.1007/978-3-319-49274-2

Proksch, E., Berardesca, E., Misery, L., Engblom, J., & Bouwstra, J. (2020). Dry skin management: practical approach in light of latest research on skin structure and function. *Journal of Dermatological Treatment*, *31*(7), 716–722. https://doi.org/10.1080/09546634.2019.1607024

Purnamawati, S., Indrastuti, N., Danarti, R., & Saefudin, T. (2017). The role of moisturizers in addressing various kinds of dermatitis: A review. *Clinical Medicine and Research*, *15*(3–4), 75–87. https://doi.org/10.3121/cmr.2017.1363

Ramasamy, S., Barnard, E., Dawson, T. L., & Li, H. (2019). The role of the skin microbiota in acne pathophysiology. *British Journal of Dermatology*, *181*(4), 691–699. https://doi.org/10.1111/bjd.18230

Ranneh, Y., Ali, F., Zarei, M., Akim, A. M., Hamid, H. A., & Khazaai, H. (2018). Malaysian stingless bee and Tualang honeys: A comparative characterization of total antioxidant capacity and phenolic profile using liquid chromatography-mass spectrometry. *Lwt*, *89*, 1–9. https://doi.org/10.1016/j.lwt.2017.10.020

Rao, P. V., Krishnan, K. T., Salleh, N., & Gan, S. H. (2016). Biological and therapeutic effects of honey produced by honey bees and stingless bees: A comparative review. *Revista Brasileira de Farmacognosia*, *26*(5), 657–664. https://doi.org/10.1016/j.bjp.2016.01.012

Rattanawannee, A., & Duangphakdee, O. (2019). Southeast Asian Meliponiculture for Sustainable Livelihood. In R. E. R. Ranz (Ed.), *Modern Beekeeping - Bases for Sustainable Productio*. IntechOpen. https://doi.org/https://doi.org/10.5772/intechopen.90344

Reyes-González, A., Camou-Guerrero, A., Reyes-Salas, O., Argueta, A., & Casas, A. (2014). Diversity, local knowledge and use of stingless bees (Apidae: Meliponini) in the municipality of Nocupétaro, Michoacan, Mexico. *Journal of Ethnobiology and Ethnomedicine*, *10*(47). https://doi.org/10.1186/1746-4269-10-47

Samraj.S, M. D., Kirupha, S. D., Santhini, E., & Vadodaria, K. (2021). Fabrication of nanofibrous membrane using stingless bee honey and curcumin for wound healing applications. *Journal of Drug Delivery Science and Technology*, *63*, 102271. https://doi.org/10.1016/j.jddst.2020.102271

Shamsudin, S., Selamat, J., Sanny, M., Abd. Razak, S. B., Jambari, N. N., Mian, Z., & Khatib, A. (2019). Influence of origins and bee species on physicochemical, antioxidant properties and botanical discrimination of stingless bee honey. *International Journal of Food Properties*, *22*(1), 238–263. https://doi.org/10.1080/10942912.2019.1576730

Soleymani, S., Farzaei, M. H., Zargaran, A., Niknam, S., & Rahimi, R. (2020). Promising plant-derived secondary metabolites for treatment of acne vulgaris: a mechanistic review. *Archives of Dermatological Research*, *312*(1), 5–23. https://doi.org/10.1007/s00403-019-01968-z

Theoret, C. (2018). Physiology of Wound Healing. *Equine Wound Management*, *99*(8), 792–793. https://doi.org/https://doi.org/10.1002/9781118999219.ch1

Toyoda, M., & Morohashi, M. (2001). Pathogenesis of acne. *Medical Electron Microscopy*, *34*(1), 29–40. https://doi.org/10.1007/s007950100002

Vora, J., Srivastava, A., & Modi, H. (2018). Antibacterial and antioxidant strategies for acne treatment through plant extracts. *Informatics in Medicine Unlocked*, *13*, 128–132. https://doi.org/10.1016/j.imu.2017.10.005

Zulkhairi Amin, F. A., Sabri, S., Mohammad, S. M., Ismail, M., Chan, K. W., Ismail, N., … Zawawi, N. (2018). Therapeutic properties of stingless bee honey in comparison with european bee honey. *Advances in Pharmacological Sciences*, *2018*, 1–12. https://doi.org/10.1155/2018/6179596