Chapter 5
Apitherapy – The Use of Honeybee Products

Theodore Cherbuliez

5.1 Introduction

In the bee world, the unit of life is the colony, not the bee. None of the three casts, i.e. queen, worker or drone, can survive alone nor reproduce itself. Swarming is a collective behavior by which the colony reproduces itself. For this purpose, the workers build special cells in which the queen deposits eggs. The hatching larvae are fed with a secretion of the worker bees, the royal jelly, which is necessary for the growth of the future queens. When laying eggs the queen is too heavy to fly; the bees then starve her to prepare her for swarming. When the queen cells are ready and the queen able to fly, about one-half of the bee population, together with the old queen, leaves the original nest to find another home.

By looking at the products of the hive one can see that here too, a product is not created by any single bee. In fact, honey, venom, pollen, propolis, royal jelly and wax each owe its existence to a succession of bee activities, each pooling their individual contribution to the "pot." Accordingly, for any use, only the amount contributed by many bees is large enough to be significant. An exception would be when the venom of a single bee is sufficient to achieve a desired result, e.g., applied on the big toe for gout would lead to a significant and prompt reduction in pain.

5.2 Apitherapy

The name Apitherapy comes from Latin "Apis", meaning bee, and Greek: θεραπεία, meaning serving and caring for. Interestingly, even the name Apitherapy is the result of a synergy.

T. Cherbuliez, M.D. (✉)
Consulting Medical Staff at Spring Harbor Hospital, Maine Medical Center,
13 Main Street, PO Box 155, South Freeport, ME 04078-0155, USA
e-mail: tcherbuliez@gmail.com

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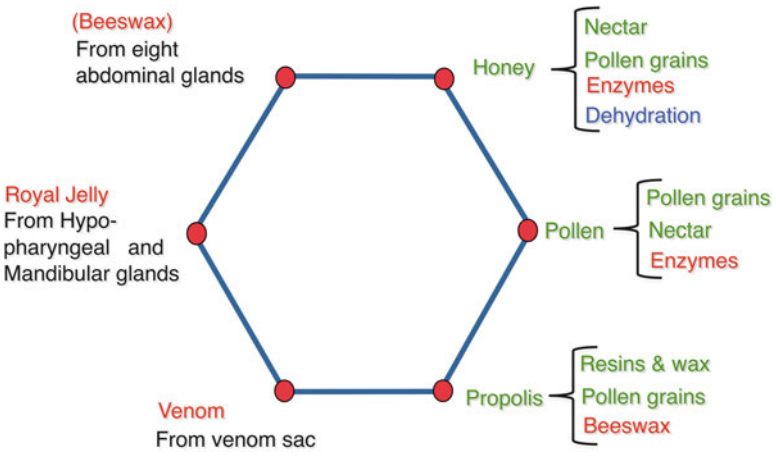

Fig. 5.1 Bee products: secretion (*red*), collection (*green*), modification (*blue*)

Apitherapy is the science (and art) of the use of honeybee products, to maintain health and assist the individual in regaining health when sickness or accident interferes.

In the past, the products of the hive, i.e. honey, pollen and propolis were frequently used as natural remedies for health maintenance and bee venom for treatment of ailments. More recently, the products of the hive have been incorporated into Western medical practice, where the focus of attention is mainly the illness and its prevention. This practice tends to use these products after they have undergone some processing, e.g. the irradiation of honey to insure sterility, or the use of bee venom extracts for ease of utilization. It is interesting to note that the concepts underlying the thinking in Apitherapy as a natural medicine differs from the corresponding ones used in Western medical culture. These concepts will be addressed below.

The main products of the hive used in Apitherapy and their origin are shown in Fig. 5.1.

5.2.1 Bee Products

Honey, pollen and propolis have in common that they begin as botanical material, respectively nectar, male gametes of flowers, and resins. These are collected by the bees who then add their secretions. The contribution of each bee is diverse, due to the variation of the botanical sources. The story of venom is different: its composition depends on the pollen the bee consumed and on the age of the bee as it matures with time. Royal jelly and wax are secretions of the bees, and they remain constant in their composition.

Table 5.1 Comparison of "Traditional" with "Western medicine" concepts

Traditional concepts	Western concepts
Uncertainty	Certainty
Variability	Constancy
Open system	Closed system
Synergy: multi-molecular systems	Specific molecule for identified action

5.3 Concepts of Apitherapy

As shown in Table 5.1, the concepts used in Apitherapy can be those of "Traditional Medicine" or those used in "Western Medicine."

I do not suggest that one set of concepts is superior to the other. Rather, that they are complementary and that Apitherapy can be viewed from either lens.

5.3.1 Uncertainty – Certainty

"Traditional concept" – **Uncertainty:** determining precisely the chemical composition of honey, pollen, propolis and venom is limited to establishing the formula of the sample tested, with the awareness that all other samples may be somewhat different. If we take the example of bee venom, we can see that if we take the venom of a given bee, we can either examine it to quantify its contents or effects, after which it is no longer available to use, or we can use it and we will not know exactly its composition.

"Western concept" – **Certainty.** The composition of a product can be reliably known and the product can be reproduced. One sample is identical to any other sample of the same product. It is then possible to know exactly the composition of a product one uses. It is also possible to create any amounts of the same product. When dealing with the products of the hive, working with one component, for instance melittin (out of the peptides of bee venom), respects the laws of certainty.

5.3.2 Variability – Constancy

"Traditional concept" – Products from the hive are **variable,** in function of both time and place, coming from many sources, such as pollen from different plants, and venom, which varies in its composition based on the age of the bee. Thus the products used in Apitherapy are never exactly the same, from one application to the next, and are not known nor are they reproducible or precisely measurable. The clinical consequences of this dimension are of great importance. A number of bee products have antibiotic properties. The products vary in their composition; these

variations cannot be predicted or known by germs. They, therefore, cannot get accustomed (become resistant) to a presence that varies constantly. Variability may have another value, that is the possibility, empirically often observed with natural products, that administration of several doses of a product showing small variations in their composition over time may be more effective than products that are rigorously homogeneous.

"Western concept" – A given product has the same known composition regardless of where and when it was made**. Constancy** in the composition of products allows the running of clinical protocols in very different circumstances, places, and times and pooling the results. Further consequence of this approach is the creation of multidrug resistant, MDR or "superbugs". This resistance turns hospitals into zones of risks, and communities into sources of epidemics of Methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin resistant enterococci (VRE). In the United States, the Center for Disease Control and Prevention (CDC) estimated (2006) that roughly two million hospital-associated infections, from all types of bacteria combined, cause or contribute to 99,000 deaths each year, more than doubling the mortality and morbidity risks of any admitted patient.

5.3.3 Open and Closed Systems

"Traditional concept": In an **open system** not all relevant variables are fully known, nor measureable nor controllable. (It is also the system in which life can be sustained). An Open system allows flexibility in the means used to achieve results. The participation and contribution of the individuals involved becomes one of the most important variables taken into account, a variable that increases in importance as the patient has more experience. In a therapeutic context, the lack of control over variables prevents proof of treatment effectiveness.

"Western concept": A **closed system** is necessary to reach a control, and a measure, of the relevant variables; those variables that cannot be controlled are to be discarded. The variables retained are described in detail, which allow proofs, valid within the limits of the observed situation. When the process observed takes place in people, the discipline leading to retain only controllable variables to define a process represents a "simplification" of the person(s) referred to. The progresses that such simplification of the person has allowed, in the development of medicine and of the knowledge of illnesses and their treatment, are immeasurable. The drawback of this simplification is the elimination of individual's humanity, initiative, adaptation, other than compliance with, and tolerance of, the instructions received. It should be emphasized that this only concerns the concepts of Western medicine and does not refer to the attitude of physicians treating patients. Western medicine, in its thinking, does not engage the individual to take responsibility nor does it acknowledge his power to do so.

5.3.4 Synergy

"Traditional concept" – An action is typically caused by a **synergy** of molecules, of components, or effects. The variations within time and space of many of these bee products, add to the fact that they are often used together.

"Western concept" – The emphasis is on reproducibility and precision. The goal is to find a **specific componen**t, for instance, a molecule, for each action of a product. Further, the search is for the reproducibility of such a component or molecule and for the predictability of its actions.

5.4 Bee Venom

The distinction between bee venom, defined by what a bee delivers when it stings, and Apitoxin, a patented name reserved to derivatives or extracts of bee venom, merits attention as there is major confusion in the literature regarding these two entities. The differences between bee venom and Apitoxin were evaluated by the Apitherapy Commission of Apimondia (Domerego 2012), which was carried out a study in the Chemistry Department of the Catholic University of Louvain in Brussels, Belgium. The study showed that fresh bee venom has about 3 % essential oils, from which 60 % are represented by esters. The latter are practically absent in Apitoxin and seem to be replaced mainly by acids and alcohols (Fig. 5.2). Observations further suggested that there are differences between the clinical effects of the two products, an issue deserving further research.

5.4.1 Treatment with Bee Venom

The treatment with natural remedies often includes the active participation of the patient and Apitherapy is particularly well suited to serve this way. Treatment for any condition can become an opportunity to involve patients intensely at each step, while their collaboration and decision making should utilized to the point that they should be able to continue their care on their own, assuming responsibility for their health.

A particularity of bee venom therapy (BVT) is that with each sting, there is an opportunity to observe several effects. A major part of the treatment is teaching patients to observe what is happening to their bodies with each sting, and progressively to determine themselves the indication to add another sting and if yes, where it should be applied. At first, before having any experience with this approach, people think mainly about the associated pain. As the treatment proceeds, they become more interested in the responses communicated by their body, such as differences in balance, a general feeling of relaxation and with some experience can even define when they have received an optimal amount of stings.

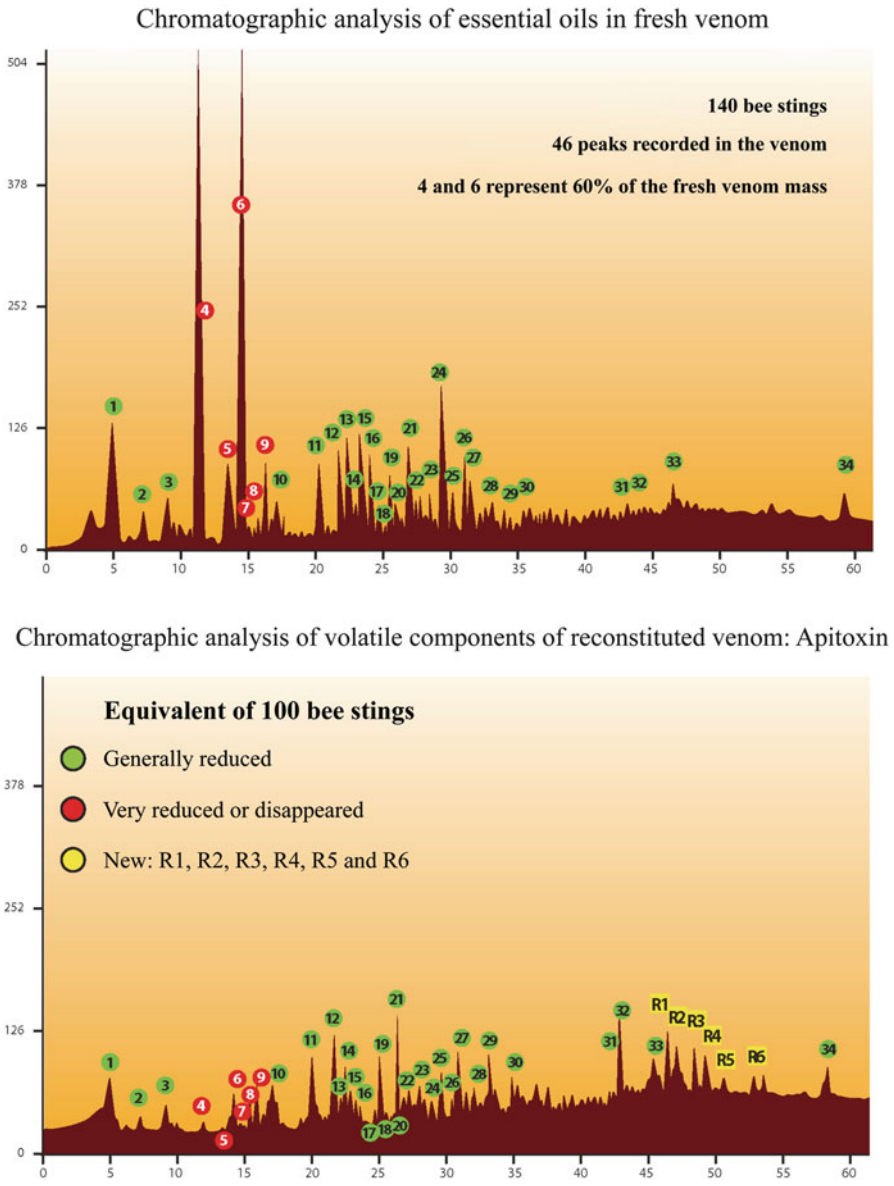

Fig. 5.2 Chromatographic analysis of essential oils in fresh honeybee venom (*above*) compared to the chromatographic analysis of Apitoxin (*below*)

Fig. 5.3 Separating the stinger from the bee

5.4.2 Practical Considerations When Administering BVT

In the practice, of BVT, because there is no possibility to combine venom with an anesthetic, as in the case with Apitoxin, one has to address the element of pain and apprehension from the very beginning. There are several techniques to decrease the effect of pain, one being the dosing of the venom determined by the type of sting.

There are three kinds of stings:

1. The regular or full sting, when the bee's stinger is kept in place for >5 min and the quantity of venom administered is approximately 150 μg.
2. The mini-sting, when the time before removing the stinger is shortened. In this case, the patient can also decide when to remove the stinger, which represents an important step in putting him in charge of his treatment. Here, the quantity varies usually from 20 to 30 μg to a full dose, depending on how long the stinger is left in place. Either the practitioner or the patient decides when to remove the stinger.
3. The micro-sting, when the therapist removes the stinger from the bee and applies it to the patient a number of times (Figs. 5.3 and 5.4). Experts in this technique can apply more than 100 micro-stings with one stinger. It is estimated that an averages of 1–2 μg venom is delivered with each sting. Another approach uses warm compresses just before application of the micro-stings. The patient feels only the light touch of the practitioner's fingers, not the stings themselves. This technique is totally painless and gives the clinician control over the stinging that even babies can be treated without discomfort.

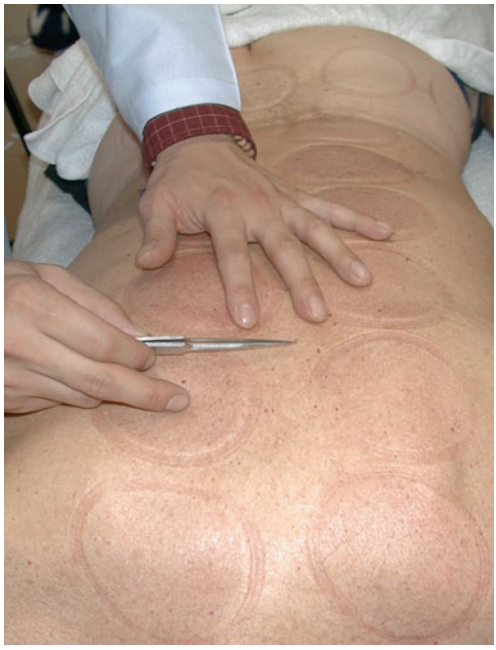

Fig. 5.4 The technique of micro-sting. It can be noted that on this case the skin had been prepared with cupping

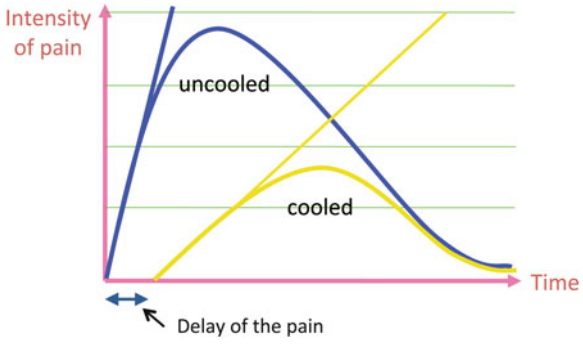

Fig. 5.5 Intensity of pain related to bee sting in *cooled* and *un-cooled* skin

Another way to decrease the pain experience is the cooling of the site before stinging, e.g. with a frozen object. The main effect of the cooling is the decrease of the gradient of pain (Fig. 5.5). For many people the pain of the bee sting has a marked component of fright due to the steepness of the gradient, which adds to the perceived pain. Cooling is contra-indicated while the stinger is on the skin, because this would stop the pumping action of the venom sack and impede the administration of the venom.

5.4.3 Protocol of Treatment

The treatment protocol of the present author includes having a trusting, personal relationship with the patient at the very beginning of the therapy. Both, the therapist and the patient, have to be clear about what is expected from the treatment, and, perhaps more important, how the therapy will engage the therapist and the patient. The patient is considered as the expert in his knowledge of himself, his abilities and goals. Accordingly, therapist and patient form a team and the team treats the patient. Anticipated reactions to venom are described in advance and the treatment is not initiated unless the potential reactions are acceptable to the patient. Discussing reactions and responding to patients concerns about reactions, minimizes fear, enhances trust and supports the relationship between the therapist and the patient.

In this context, one has to clarify the distinction between a tissue reaction to venom, which proceeds by extension from the site of the sting and is not, regardless of its dimension, an indication of allergy. An example is if a person is stung on the hand and has swelling from this area up to the elbow. As this swelling extends from the sting site, it is only an inflammation and not an allergic reaction. An allergic reaction is mediated systemically and accordingly its manifestations take place also on other sites of the body, e.g., if a person develops hives on the stomach after receiving a sting on the hand.

The American Apitherapy Society (AAS) has elaborated a desensitization program that proposes two starting points, which are shown in Table 5.2. The patient makes always the choice between these two.

The values presented in this table are presented as maxima; these numbers should be respected and only exceeded by very experienced practitioners who have achieved a trusting relationship with their patient. An important principle applicable to desensitization is the continuity of these administrations. Any interruption of the process exceeding a few days requires starting the process over from the beginning.

For this purpose, AAS gives yearly courses on BVT and on the testing for sensitivities. For example, AAS recommends that those practicing BVT have epinephrine available in case of an anaphylactic reaction. The use of anti-histamine tablets is also taught, with less emphasis on their use.

5.4.4 Side-Effects of BVT

Instances of allergy to venom are not rare; they practically never take place at the beginning of therapy and can be easily handled: the therapist faces the patient who lays down, relaxes and describes his experience in detail. The therapy is resumed as soon as the patient is ready, using small amounts of venom and increasing the quantity gradually. An injectable dose of epinephrine and anti-histamine tablets should always be available in the office of practitioner.

Table 5.2 Protocol for desensitization to bee venom with micro- and mini stings

	Starting with micro-stings		Starting with mini-stings
Time	Program 1	Time	Program 2
Day 1	5 tests with micro-stings		
Day 2	Day of rest		
Day 3	5 tests with micro-stings		
Day 4	Day of rest		
Day 5	5 tests with mini-stings	Day 1	5 tests with mini-stings
Day 6	Day of rest	Day 2	Day of rest
Day 7	5 tests with mini-stings	Day 3	5 tests with mini-stings
Day 8	Day of rest	Day 4	Day of rest
Session 5	1 test with a 30” mini	Session 3	1 test with a 30” mini
Session 6	1 test with a 60” mini	Session 4	1 test with a 60” mini
Session 7	1 test with a 90” mini	Session 5	1 test with a 90” mini
Session 8	1 test with a 2 min sting	Session 6	1 test with a 2 min sting
Session 9	1 test with a 5 min full sting	Session 7	1 test with a 5 min full sting
Session 10	2 tests with full stings	Session 8	2 tests with full stings
Session 11	1 more sting than the previous time	Session 9	1 more sting than the previous time

There are numerous observations suggesting that a trusting relationship between the two people involved in BVT, where the apprehension about venom has been reduced to a low, tolerable level, might lead to a decrease of the strength of allergic reaction. Some observations speak strongly in favor of the importance of the relationship in the protection against massive allergic reaction. In nearly 70 years of stinging experience, Charles Mraz, called the grandfather of BVT in the USA, never had to use epinephrine, the treatment of choice in bee venom related anaphylaxis. In 45 years of Apitherapy the present author observed only twice an anaphylactic reaction in a person stung. Both times were at congresses, where a speaker asked the audience for a volunteer for a demonstration of bee venom administration. In both instances a young man volunteered. The volunteer and the therapist did not know each other and they had no pre-established relation. The allergic reaction appeared very soon after the sting but was treated successfully thereafter.

5.5 Pollen

5.5.1 A Historical Note

Back as far back as 2735 B.C., Shen Nung, a Chinese emperor, had medical texts discussing the merits of pollen. There are also Egyptian papyri in which pollen is referred to as life-giving dust. In the 400s B.C., Hippocrates recommended pollen

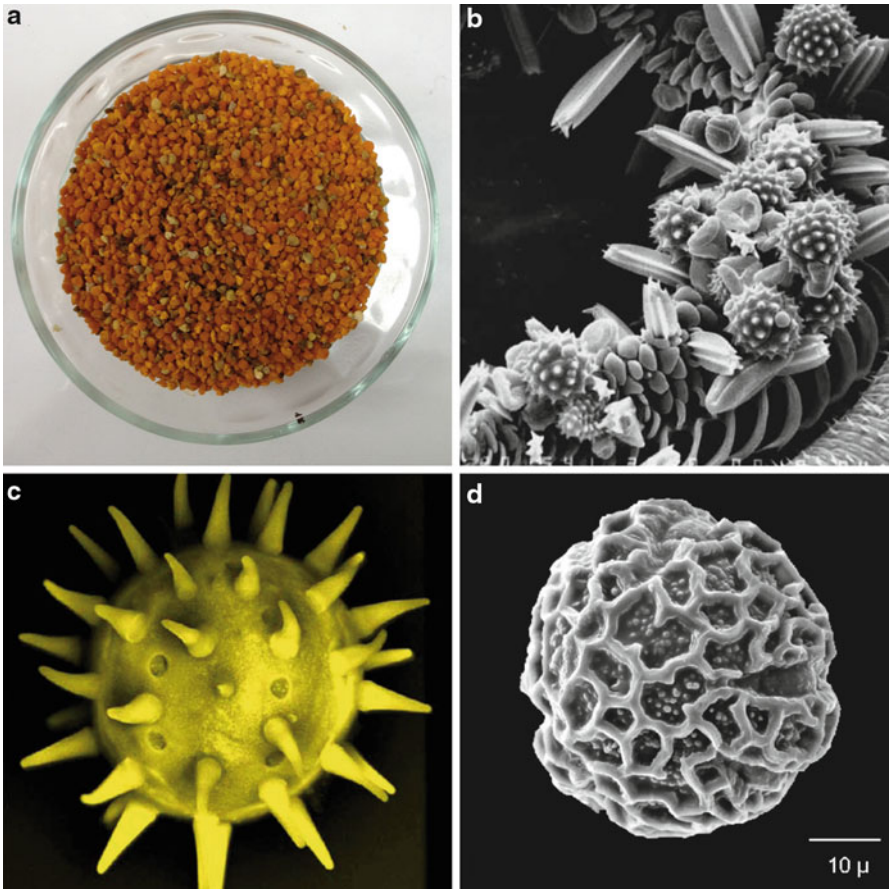

Fig. 5.6 Pollen grains collected by bees

as a remedy for multiple conditions and the Hindus taught that eating honey and pollen could produce health, vigor, happiness and wisdom.

5.5.2 What is Pollen?

Pollen grains are the male reproduction units (gametophytes) formed in the anthers of the higher flowering plants. The pollen is transferred onto the stigma of a flower (a process called pollination), by either wind, water or various animals (mostly insects), among which bees are the most important ones. Pollen from each species of flower is different and no one pollen type can contain all the characteristics ascribed to pollen in general (Fig. 5.6). The chemical composition of pollen is shown in Table 5.3.

Table 5.3 Chemical composition of pollen

Compound	Percentage and additional explanations
Water	5 % (dry) – 15 % (fresh)
Peptides	7.3–35 %
Sugars	15–55 %: Composed of fructose (60 %), glucose (40 %) and sucrose
Lipids	2–14 %: Primarily free unsaturated fatty acids, lecithin and phospholipids
Esters	Such as auxins, brassins, gibberellines and kinins
Carotenoids	Pro vitamin A
Antioxidants	Food with the highest value as measured by oxygen radical absorbance capacity test
Pigments	Yellow and orange
Gonadotropins	Increased levels of testosterone-like hormone
Estrogenic compounds	Antioxidant and chemo-protective activity
Minerals	>3 %: Bo, Ca, Cr, Cu, F, Fe, I, K, Mg, Mn, Mo, Na, Ni, P, S, Se, Si, Zn
Vitamins	A, B, C, D, E, K
Enzymes	>200
Hydroxycinnamic acid	Strong antioxidant activity (from a Brazilian pollen)
Undetermined	3 %

5.5.3 Foraging for Pollen

A foraging honeybee rarely collects both pollen and nectar from more than one species of flowers during one trip. Thus, the resulting pollen grains on her hind legs contain usually only one pollen species. The different colors are due to different flavonoids and carotenoids, which besides being anti-oxidants are also pigments.

During their collecting trips, bees add their saliva and nectar as they collect pollen. The collection process has two steps:

1. The bee, foraging for nectar, puts her head deep into the flower and accumulates pollen all over her body (Fig. 5.7a).
2. She then "cleans" herself by putting the pollen in the baskets of her third pair of legs, adding nectar and saliva to create a ball. The vibration of the bee's body during flight causes the pollen basket to become compact (Fig. 5.7b).

The nectar contains between five and eight strains of lactobacteria and three yeasts (Olofssos and Vásquez 2009). Honeybees therefore possess an abundant, diverse and ancient lactic acid bacteria microbiota in their honey crop with beneficial effects for bee health, defending them against microbial threats (Vásquez et al. 2012). They prevent the growth of other bacteria that may cause the pollen to spoil. This bacteriological "microflora" is perfectly preserved when the pollen is frozen, and varies in terms of quantities from between one and ten million bacteria per gram of pollen. However, when the pollen is dried, this microflora is destroyed. In itself, the pollen does not contain antibiotics; however, its microflora has a "barrier effect" that keeps the harmful bacteria such as *Proteus vulgaris* and *Proteus mirabilis* at bay (Percie du Sert 2006).

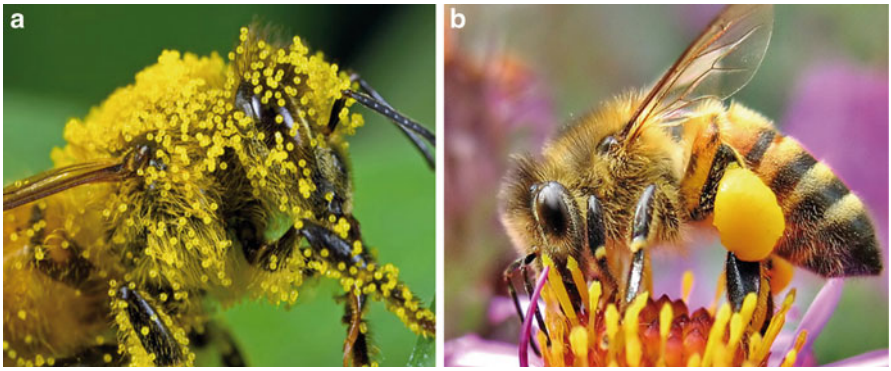

Fig. 5.7 Bees with pollen: (**a**) first step of collection; (**b**) pollen attached to the third leg of the bee

5.5.4 Bee Bread

Bees build three kinds of cells in the hive. By far the largest number of cells is for the workers, which are also the smallest. The cells destined for drones are larger in which bees can also store pollen. Both types are set horizontally. Cells that are built for queen larvae hang vertically. These queen cells are the only ones allowed to encroach into the space between combs and are never used to store pollen.

When a bee returns to the hive with a load of pollen grains, she transfers them to an other bee, who puts them in a cell and compresses each grain. When the cell is filled, they cover it with a thin layer of propolis; they have created bee bread (Fig. 5.8). Each cell contains the nutrition needed for one larva, in order to develop to an adult bee.

5.5.5 Trapping and Conservation

Pollen traps are devices that force bees to go through narrow holes as they enter the hive. The holes are calibrated so that the bees, passing through, drop approximately 70 % of their loads. These traps should be installed only on strong colonies, and for relatively short times (2–3 weeks), separated by similar intervals when bees may bypass them. Bees respond to pollen trapping by increasing their pollen trips. However, traps retaining more than 70 % of the load discourage bees from foraging further. A careful handling of traps allows for collecting about 6 kg of pollen a year from each hive, which is 10 % of the colony's production.

Several techniques are used to conserve the collected pollen, the easiest being the immediate freezing after removal from the hive. A good trap will yield pollen that is without debris, such as bee parts, and does not need to be cleaned. Special equipment is needed to freeze dry pollen. It can be dried in the dark at 30 °C for 20 h. Dried pollen kept at room temperature looses about 50 % of its antioxidant components, but none of its minerals, essential amino-acids or vitamins.

Fig. 5.8 Bee bread of *Apis mellifera*

5.5.6 Medicinal Properties of Pollen

Pollens from specific plants are known for their health effects, e.g. thyme: stimulating and antiseptic; sage: diuretic, regulates GI function, menstrual effects; sunflower: diuretic and laxative; canola: varicose veins; apple: myocardial effects; false acacia: sedative; chestnut tree: venous and arterial circulation, liver and prostate decongestant effects.

5.5.7 Commercial Preparations of Pollen

Pollen is sold as grains (fresh-frozen or dried), powder, tablets, capsules, coated pills, or as mixtures with honey or other foods. Formulations of pollen are prepared with water and alcoholic solutions in form of ointments, creams, lotions, capsules, suppositories, ovules often mixed with other bee products and/or essential oils.

5.5.8 Tolerance and Side-Effects

No contra-indications are known with the consumption of pollen, even in pregnancy. Allergy to pollen can be handled generally easily. (See below) There are no known incompatibilities with other therapeutics. Pollen is well tolerated even in long lasting administration and has no toxic effects even in high dosage. Recently, Hurren and Lewis (2010) reported a case, which suggests a probable drug interaction between bee pollen and warfarin.

The side-effects of pollen consumption or treatments with pollen formulations include unpleasant feeling of taste and flavor, when pollen becomes moldy, mild intestinal disorder such as diarrhea during the first days of use, gastric pain (when pellets are not well dissolved) and very rarely allergic reactions such as anaphylaxis.

5.5.9 Indications

5.5.9.1 Nutritional

Although pollen is a perfect food for the bee, this is not the case for humans as the nutrients are not always in the exact ratio needed for the human body. Particularly, pollen lacks the right amount of vitamin A, however it has a maximum percentage of essential amino-acids. Pollen is rich in proteins and 100 g of pollen can provide as much protein as seven eggs or 400 g of beef. Pollen contains all 22 essential amino-acids, as well as high amounts of proline and hydroxyproline, which serve as building blocks for collagen. Clinical tests have shown that orally ingested pollen is rapidly and easily absorbed, while most of its components pass directly from intestines into the blood stream. It should be also noted that pollens supply, in average, about 250 kcal per 100 g.

5.5.9.2 Treatment of Allergies to Pollen

The treatment of allergies should be started with one granule of pollen and the dose should be doubled each day as tolerated. Local unfiltered honey taken regularly over long periods can also keep the patient free of allergies. Whether taken directly or in honey, maintenance treatment, after cessation of symptoms, requires one dose of pollen monthly.

5.5.9.3 Asthma

In vivo activity assessment of a honey and pollen mixture formulation is claimed to be effective for the treatment of asthma, bronchitis, cancers, peptic ulcers, colitis, various types of infections including hepatitis B, and rheumatism by the herb dealers in northeast Turkey. Küpeli Akkol et al. (2010) concluded that their studies have clearly proved that mixing pure honey with bee pollen significantly increased the healing potential of honey and provided additional support for its traditional use.

5.5.9.4 Rheumatoid Arthritis and Digestive Track Disorders

The positive effect of flower pollen in patients with rheumatoid arthritis and concomitant disorders of the gastro-duodenal and hepatobiliary systems has been shown by clinical and biochemical, endoscopic and ultrasonic investigations (Voloshyn et al. 1998).

5.5.9.5 Ophthalmology

In Lithuania bee products such as honey, propolis, bee pollen and royal jelly are widely used in ophthalmology (Jankauskiene et al. 2006). The Mayas used to treat eye diseases with Melipona honey (Vit 2002).

5.5.9.6 Urinary Tract

In a double-blinded placebo controlled study on 60 men with benign prostate hypertrophy (BPH), pollen and placebo was administrated for a period of 6 months. At that time, 60 % of the treated and 30 % of the control men had improved or became symptom free (Buck et al. 1990). In another study with patients having BPH and prostatitis, alpha-blockers were recommended, but also included saw palmetto and bee pollen (Nickel 2006).

5.5.9.7 Metabolism

In 157 overweight and obese patients, who received honey and pollen, 18.3 % showed a decrease in the total cholesterol and 23.9 % in the LDL cholesterol levels. However, the improvement of blood lipid composition in those overweight (body mass index 25–30) and obese (BMI over 30) patients occurred only after loss in body mass (Kas'ianenko et al. 2011).

Chinese studies on humans and animals have demonstrated that consuming bee pollen for several days prior to moving to high altitude reduces the incidence of altitude sickness, and apparently improves the ability to adapt to lower levels of oxygen in the air (Peng 1990).

5.5.9.8 Radiation Protection

Mice bred to develop and die from tumors, were fed bee pollen at ratio of 1:10.000 in mice chow. In untreated mice, tumors developed in 100 % at an average of 31.3 weeks, while in pollen fed mice the average onset was at 41.1 weeks and some were still tumor free at about 60 weeks, when the test terminated (Robinson 1948).

5.5.9.9 Inhibition of Growth

A number of prostate inhibitory components were identified in pollen extract. A fraction designated as FV-7 maintained a strong time- and dose-dependent inhibitory effect on the growth of a prostate cancer cell line (Habib et al. 1995), while a sample of synthesized hydroxamic acid, structurally indistinguishable from FV-7, showed the same in vitro effects (Zhang et al. 1995).

It should be noted that there is a substantial number of warnings in publications, without confirming evidence, of the danger of bee pollen from anaphylactic reactions to a vast array of symptoms that cleared with the discontinuation of pollen.

5.6 Honey

It has been estimated, that bees must carry 120,000–150,000 loads of nectar and together have to fly about 50,000 km or 1.25 times around the equator to produce 1 kg of honey. They go through 120–150 regurgitation and swallowing cycles for each load. A strong bee colony is capable of producing up to 460 kg of honey per year.

5.6.1 Standards for Honey

The US Federal Drug Administration (FDA) does not have an official definition for honey. For internal operations, the Department of Agriculture established voluntary grade standards for comb honey in 1933 and for extracted honey in 1985. For exported honey, the standards included in The Codex Alimentarius Commission of the United Nation's Food and Agriculture Organization (FAO), are used. In the US, there are 48 floral varieties of honey, the essential oils of which, account, among other constituents, for its therapeutic properties.

5.6.2 Toxic Honeys

Some honeys can be toxic to humans, but are innocuous to bees and their larvae. An example is honey from *Rhododendron ponticum,* which contains alkaloids. The symptoms of honey intoxication vary from case to case and may include weakness, sweating, hypotension bradycardia, Wolff-Parkinson-White syndrome, gastritis, peptic ulcer, nausea, vomiting, faintness, leukocytosis, mild paralysis, dizziness, vertigo, blurred vision, convulsions and respiratory rate depression (Mayor 1995). Outside of Historical references, there are very few reports of accidental poisoning with honey, none fatal.

5.6.3 Composition of Honey

Carbohydrates comprise the major component of honey, which include monosaccharides, disaccharides and oligosaccharides. The monosaccharides in honey are fructose and glucose; the disaccharides include sucrose, maltose, isomaltose,

maltulose, turanose and kojibiose. The oligosaccharides present in honey, formed from incomplete breakdown of the higher saccharides present in nectar and honeydew, include erlose, theanderose and panose (Bogdanov et al. 2008; Erejuwa et al. 2012).

Various proteins and amino acids are also ingredients of honey. Enzymes include invertase, which converts sucrose to glucose and fructose; amylase, which breaks starch down into smaller units; glucose oxidase, which converts glucose to gluconolactone; which in turn yields gluconic acid and hydrogen peroxide; catalase which breaks down the peroxide formed by glucose oxidase to water and oxygen; and acid phosphorylase, which removes inorganic phosphate from organic phosphates. There are 18 free amino acids, the most abundant of which is proline.

Vitamins found in honey include trace amounts of the B vitamins riboflavin, niacin, folic acid, pantothenic acid and vitamin B6 and ascorbic acid (vitamin C) (Bogdanov et al. 2008). Additionally there are minerals, including calcium, iron, zinc, potassium, phosphorous, magnesium, selenium, chromium and manganese. Antioxidants include flavonoids, of which one, pinocembrin, is unique to honey and bee propolis. Ascorbic acid, catalase and selenium are other antioxidants in honey.

Organic acids such as acetic acid, butanoic acid, formic acid, citric acid, succinic acid, lactic acid, malic acid, pyroglutamic acid and gluconic acid, as well as a number of aromatic acids are found in honey. The main acid present is gluconic acid, formed in the breakdown of glucose by glucose oxidase (Bogdanov et al. 2008).

5.6.4 Indications for Honey

5.6.4.1 Health Maintenance

The earliest information on using honey in children's nutrition dates to about the ninth century BC. Ancient Germanic tribes and Greeks handled milk combined with honey and melted butter. In numerous historic texts, information about the therapeutic and prophylactic use of honey can be found. In Egypt, 3,500 years ago in the "Book of the Preparation of Medicines for all Parts of the (Human) Body", there are many recipes, which include honey. In an ancient Chinese script, honey was given this description: "*Honey heals internal organs, gives strength, reduces fever; long-term use increases its power, gives ease to the body, retains his youth, extending the years of life.*" The old Indian "book of life" says that extending human life can only be achieved with elixirs and diet, including honey and milk. In India, honey was used as an antidote to intoxication of any kind. The ancient philosophers and physicians of Rome and Greece including Pythagoras, Aristotle, Hippocrates, Dioscorides, Homer, and Galen wrote on the high healing properties of honey. The philosopher Democritus believed that honey had anti-aging properties. In the ancient script "The canon of the Avesta" from Iran, the use of honey and wax among other animal products are recommended. Avicenna, the tenth century Persian physician and philosopher, in his book "The Canon of Medicine" refers to dozens of recipes,

which included honey and wax as ingredients. For people older than 45 years, he recommended the systematic use of honey and walnuts. In the Middle Ages, honey was also widely used in medical therapy to treat wounds.

Honey as a healing product remained important in later centuries, and even in our days. It is widely used in folk medicine and is recognized as an official medicine throughout the world. Honey has earned fame as a universal energy product and for its remarkable pharmacological properties. It has tonic, antimicrobial, antitoxic, anti-inflammatory and sedative properties. Experience and tradition show that honey

- does not irritate the digestive system,
- does not need energy or enzymes to be digested,
- offers a fast availability of energy for mental and physical activity,
- does not generate byproducts to be metabolized by either kidney or liver,
- normalizes the intestinal microflora,
- shows a very light, natural, general soothing effect on the whole organism,
- has a very gentle diuretic effect,
- is safe to eat honey during pregnancy,
- calms the mood and is a most respected sleeping remedy and
- is a universal antitoxic remedy.

5.6.4.2 General Mechanisms for Wound Healing

Honey has many ways to assist in wound repair (Molan and Betts 2008). It is an effective thermal insulator and nurtures repair with a protective biofilm (Black and Costerton 2010). It reduces wound pain and thereby enhances patients' cooperation. The unlinked dehydrated gel of fructose and glucose in honey has twice the osmotic strength of an equivalent sucrose solution. Honey combats bacteria through osmotic pressure and draws fluid from wounds, decreasing tissue edema (Molan 2001). With its enzyme glucose oxidase, it reduces atmospheric oxygen to hydrogen peroxide (H_2O_2), which acts as a bactericide (Dustmann 1979). Hydrogen peroxide is toxic to bacteria but not to the fibroblasts and induces angiogenesis in the wound, particularly so in granulation tissue (Bang et al. 2003). The strength of this hydrogen peroxide is much lower than pharmacologic hydrogen peroxide, which is damaging to the healing environment of a wound. Few microbes grow in an acid milieu and chronic wounds have a high pH. Honey lowers the wound pH, and every 1 % reduction in pH is associated with a 1 % reduction in wound size (Gethin et al. 2008). Blaser et al. (2007) found a positive effect of medical honey on MRSA-colonized wounds and achieved healing where antiseptics and antibiotics had previously failed to eradicate the clinical signs of infection. Honey's glucose is a source of energy for cells involved in wound healing like fibroblasts, myofibroblasts and macrophages. Chronic wounds tend to dry, which promotes scab formation, associated with delay in wound closure. Honey inhibits drying and scab formation.

5.6.4.3 Infected Wounds

Between 1984 and 2009, at the Centre Hospitalier Universitaire de Limoges, France, 3,012 lesions, both infected and uninfected mainly on the abdominal wall were treated with honey (Descottes 2009). For 33 sacral cysts and 102 stoma closures, honey was systematically applied immediately after the end of the operation. Wound healing varied from 21 days for a lesion 10 cm squared, to 75 days for necrotizing abdominal wall lesions of over 30 cm squared. Wound healing was always aesthetically satisfactory except in cases where skin had been previously affected by radiotherapy.

A randomized controlled study of 108 patients with venous leg ulcers comparing Medihoney™ (standardized antibacterial *Leptospermum* [Manuka] honey from New Zealand) and hydrocolloid gel showed that honey eradicated MRSA (methicillin-resistant *Staphylococcus aureus*) in 70 % of patients, while hydrocolloid gel in 16 % only. For wounds contaminated by MRSA, honey supported better wound healing (Gethin and Cowman 2008).

As is often the case, Apitherapy takes more time than the standard medical approach, but also gets good results. Figure 5.9 illustrates the effects of treatment with honey of an infected wound caused by a fish bone puncture wound infected with *Staphylococcus aureus*. Healing was facilitated by 10 days of maggot therapy and 25 days of honey dressing (Dr. F. Feraboli 2006, personal communication).

5.6.4.4 Burns

Burn wounds are particularly at risk for infection and fluid losses of the patient if large areas are affected. Therefore, healing requires prevention or treatment of bacterial infections and prevention of excess fluid losses. There are several studies that present the effectiveness of honey in treating burn wounds (Molan 2001; Subrahmanyam 1991; Subrahmanyam et al. 2001).

Sukur et al. (2011) evaluated the effect of Tualang honey on wound healing in bacterial contaminated full-thickness burn wounds in rats. They found that topical application of honey on burn wounds contaminated with *Pseudomonas aeruginosa* and *Acinetobacter baumannii* gave the fastest rate of healing compared with other treatments.

The patient depicted in Fig. 5.10 was treated with local application of honey with added propolis extract for severe gasoline burns (Dr. A. Piñiero-Perez 2005, personal communication).

5.6.4.5 Prevention of Radiation Mucositis

In a recent meta-analysis Song et al. (2012) found promising results for the prevention of radiation induced mucositis with honey, but contended that further studies are needed to strengthen the current evidence prior to a firm clinical recommendation being given.

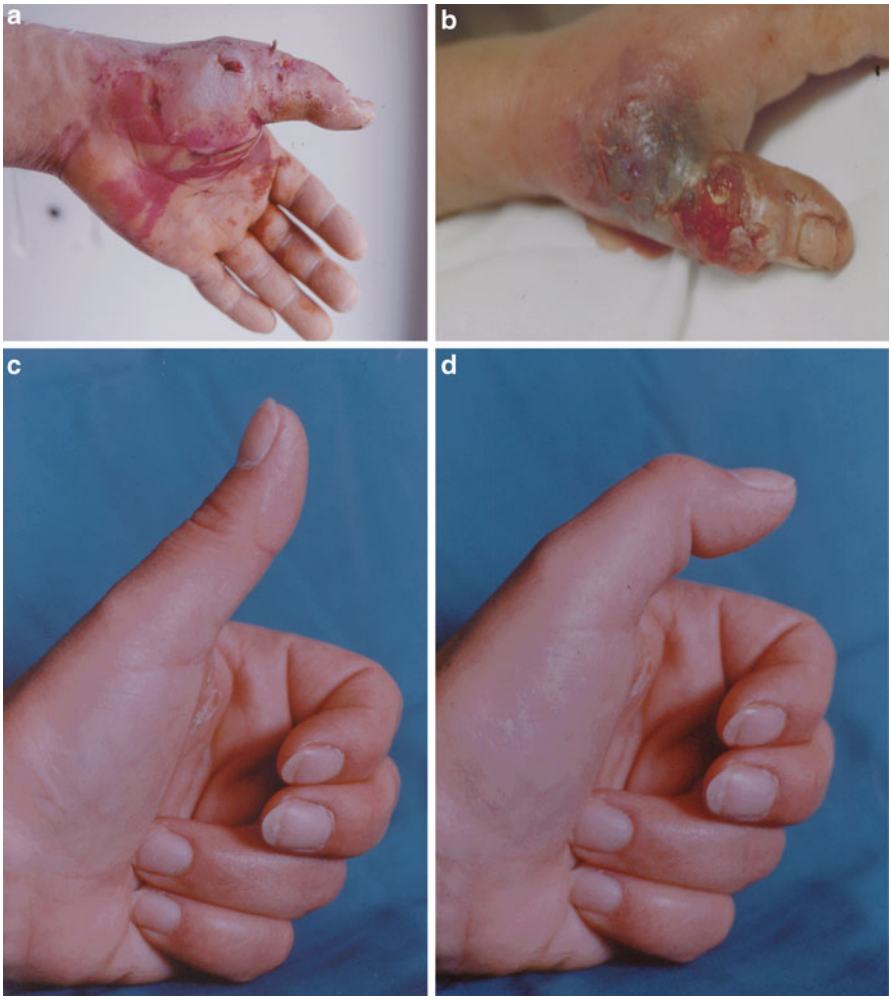

Fig. 5.9 (**a**) and (**b**) *Staphylococcus aureus* infected puncture wound after 7 days of unsuccessful antibiotic treatment; (**c**) and (**d**) The situation 1 year later after treatment with maggot therapy and honey (photo courtesy of Dr. F. Feraboli, Cremona, Italy)

5.6.4.6 Respiratory Tract

In a systematic review of honey for acute cough in children, Oduwole et al. (2012) found that honey is better than 'no treatment' and may be better than diphenhydramine (a first-generation antihistamine) in the symptomatic relief of cough.

Cohen et al. (2012) compared the effects of a single nocturnal dose of honey to placebo on nocturnal cough and difficulty sleeping associated with childhood upper respiratory tract infections (URI). Although there was a significant improvement in both

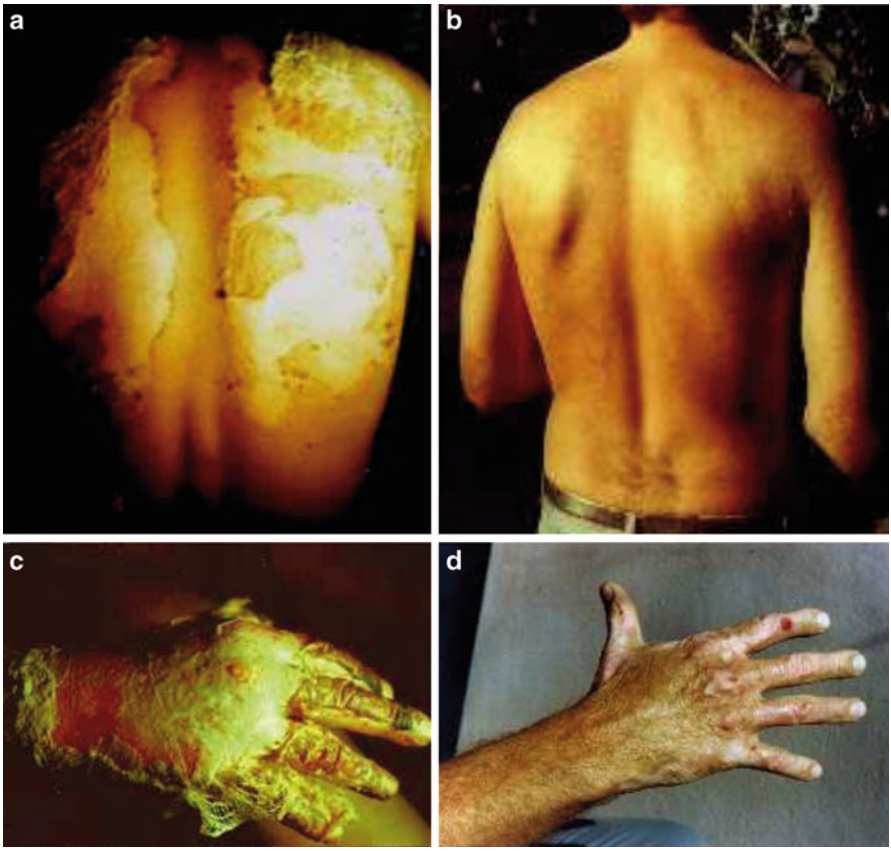

Fig. 5.10 A patient with gasoline burns soon after the accident (*panels* **a** and **b**) and healed 1 year later (*panels* **c** and **d**) (photo courtesy of Dr. J. Ramos, La Havana, Cuba)

groups, the improvement was greater in the honey group. They conclude that honey may be a preferable treatment for cough and sleep difficulty associated with childhood URI.

5.6.4.7 Gastro-Intestinal Tract

The finding that the bacterium, *Helicobacter pylori*, is a cause of stomach ulcers and the causative agent in many cases of dyspepsia has raised the possibility that the therapeutic action of honey for symptoms of dyspepsia may be due to manuka-honey's antibacterial properties. Somal et al. (1994) demonstrated that visible growth of *H. pylori* over the incubation period of 72 h was completely prevented by the presence of 5 % honey. A similar in-vitro antimicrobial effect of manuka-honey was reported against *Campylobacter spp.* (Lin et al. 2009).

5.6.5 Honey and Botulism

Honey sometimes contains dormant endospores of the bacterium *Clostridium botulinum*. Botulism causing bacteria thrive in areas with low acidity. In infants, the spores can survive and cause disease because the acidity of a baby's digestive tract is not strong enough to destroy the spores, leading to illness and even death. Therefore, the longstanding recommendation has existed to avoid giving honey to children under 1 year of age (Koepke et al. 2008). This position towards honey for the infant is not shared by all experts. The Apitherapy Commission of Apimondia is currently reviewing its scientific basis as well as its clinical history. However, there are no reports of botulism cases with honey applied on wounds.

5.7 Propolis

5.7.1 Description and Function in the Hive

Propolis is a complex compound of resins collected by bees on young buds, to which they add secreted enzymes and beeswax. The main function of propolis is to protect the colony, as it is used by bees as "architectural" and anti-infectious agent, which

- acts as space filler and "glue" to immobilize all structural elements,
- shapes and restricts entrances, making them easier to defend,
- excludes external moisture and light,
- smoothest the walls, therefore protecting the wings of the bees from fraying,
- inhibits fungal and bacterial growth in the hive and
- is used to mummify killed invading animals that are too heavy to be thrown out.

Basically, the warm (35 °C), humid (70–100 % humidity) and sweet (nectar and honey) hive is an ideal milieu for growth of germs, which the bees bring back from their trips. Bacterial overgrowth is inhibited by propolis. Additionally, propolis has been shown to have probiotic properties, supporting the presence of beneficial microorganisms in the bee. The best-known varieties are the red propolis from European poplar (*Populus spp.*) and the green propolis from *Baccharis dracunculifolia*, a medical plant from Brazil.

Although more than 300 constituents have been identified in propolis samples, biological activity is mainly due to few substances, such as flavonoids, terpenes, caffeic, ferulic and cumaric acids and esters. Propolis from different areas varies considerably in biochemistry. However, the medically active properties of propolis vary much less than its constituents. The principal composition of propolis is listed in Table 5.4.

Table 5.4 Composition of propolis

Component	Percentage
Resins/Balsams	45–55
Waxes and fatty acids	25–35
Essential oils	10
Pollen	5
Other organics & minerals	5

5.7.2 Major Properties of Propolis

5.7.2.1 Natural Antioxidants

Propolis is rich in phenolic compounds, which act as natural antioxidants, and are becoming increasingly popular because of their potential role in contributing to human health. These compounds can also be used as indicators in studies into the floral and geographical origin of the honey and propolis themselves (Russo et al. 2002).

5.7.2.2 Protection from Radiation

Propolis is effective in reducing and delaying radiation-induced mucositis in the animal model (Ghassemi et al. 2010). Free radical scavenging and antioxidant activities are probably the mechanisms that protect cells from ionizing radiation (Montoro et al. 2011).

5.7.2.3 Propolis and Cancer

In a recent in-vitro study, Kamiya et al. (2012) found that an ethanol extract of Brasilian red propolis induces apoptosis in human breast cancer cells. Búfalo et al. (2009), evaluating the effect of Brazilian green propolis on human laryngeal epidermoid carcinoma (HEp-2) cells demonstrated that propolis exhibited a cytotoxic effect in-vitro against HEp-2 cells, in a dose- and time-dependent way. Shimizu et al. (2005) investigated the effect of Artepillin C in Brazilian propolis on colon carcinogenesis and found that it dose-dependently inhibited cancer growth through the induction of a cell-cycle arrest. Additionally, inhibition of angiogenesis by propolis has been reported by several authors (Song et al. 2002; Dornelas et al. 2012; Kunimasa et al. 2011).

Abdulrahman et al. (2012) after a randomized controlled pilot study on honey and a mixture of honey, beeswax, and olive oil-propolis extract in treatment of chemotherapy-induced oral mucositis, recommend using honey and possibly other bee products and olive oil in future therapeutic trials targeting chemotherapy-induced mucositis. A detailed review on the anticancer activity of propolis can be found in Sawicka et al. (2012).

5.7.2.4 Tissue Regeneration and Wound Treatment

The effect of propolis on wound healing, especially chronically infected wounds has been studied extensively. Barroso et al. (2012) studying the effect of propolis on mast cells in wound healing, found that the anti-inflammatory action of propolis mediated by mast cells was more effective than dexamethasone in the inflammatory phase of healing. Additionally, propolis exhibited a significantly favorable effect on healing in experimental colon anastomosis in rats (Temiz et al. 2008).

Diabetic ulcers occur in 15 % of all patients with diabetes and precede 84 % of all lower leg amputations. Studying wound healing in a rodent model of experimental diabetes McLennan et al. (2008) found that propolis could possibly accelerate wound healing in diabetes. They conclude that their results and the established safety profile of propolis provide a rationale for studying topical application of this agent in a clinical setting.

One study has shown propolis to be effective in decreasing the number of recurrences and improve the quality of life in patients who suffer from recurrent aphthous stomatitis, a common, painful, and ulcerative disorder of the oral cavity of unknown etiology (Samet et al. 2007). Guney et al. (2011) found that propolis has some time-dependent beneficial effects on fracture healing.

5.7.2.5 Antibacterial Properties

Propolis was found to have antibacterial activity against a range of commonly encountered cocci and Gram-positive rods, including the human tubercle bacillus, but only limited activity against Gram-negative bacilli (Grange and Davey 1990).

Uzel et al. (2005) studied the antimicrobial activity of four different Anatolian propolis samples. Although propolis samples were collected from different regions of Anatolia, all showed significant antimicrobial activity against the Gram-positive bacteria and yeasts. They suggest that propolis can prevent dental caries and oral disease since it demonstrated significant antimicrobial activity against microorganisms such as *Streptococcus mutans*, *Streptococcus sobrinus* and *Candida albicans*.

5.7.2.6 Antiviral Properties

Schnitzler et al. (2010) analyzed the antiviral effect of propolis extracts and selected constituents (e.g. caffeic acid, p-coumaric acid, benzoic acid, galangin, pinocembrin and chrysin) against herpes simplex virus type 1 (HSV-1) in cell culture. Since propolis extracts exhibited high levels of antiviral activity against HSV-1 in viral suspension tests and plaque formation was significantly reduced by >98 %, propolis extracts might be suitable for topical application against herpes infection.

Sartori et al. (2011) investigated whether brown Brazilian hydroalcoholic propolis extract (HPE) protects against vaginal lesions caused by herpes simplex virus type 2 (HSV-2) in female mice. HPE promoted protective effect on HSV-2 infected

animals by acting on inflammatory and oxidative processes, probably due to its antioxidant and anti-inflammatory properties.

Studying the anti-HIV-1 activity of propolis in CD4+ lymphocyte and microglial cell cultures Gekker et al. (2005) showed that propolis inhibited viral expression in a concentration-dependent manner. Similar anti-HIV-1 activity was observed with propolis samples from several geographic regions.

Shimizu et al. (2008) reported an anti-influenza virus activity of Brazilian propolis along with a reduction of influenza symptoms in mice. The authors conclude that the Brazilian propolis studied may be a possible candidate for an anti-influenza dietary supplement for humans.

5.7.3 Clinical Effectiveness and Fields of Application

The Natural Medicines Comprehensive Database of the U.S. National Library of Medicine rates effectiveness based on scientific evidence and classified propolis as "possibly effective" for:

- Cold sores: Applying a specific 3 % propolis ointment might help improve healing time and reduce pain from cold sores;
- Genital herpes: Applying a 3 % propolis ointment might improve healing of recurrent genital lesions caused by herpes simplex virus type 2 (HSV-2). Some research suggests that it might heal lesions faster and more completely than the conventional treatment with 5 % acyclovir ointment;
- Improving healing and reducing pain and inflammation after mouth surgery.

According to the database more evidence is needed to rate propolis for indications like cancer sores, tuberculosis, infections, nose and throat cancer, improving immune response, ulcers, stomach and intestinal disorders, common cold, wounds, inflammation and minor burns. Therefore, additional clinical research is needed to gain more evidence of the effectiveness of propolis for these conditions.

5.7.4 Contraindications and Side Effects

Generally, propolis is well tolerated and exhibits a favorable safety profile. Not enough is known about its use during pregnancy and breast-feeding.

Propolis should be used with caution in individuals allergic to conifers, poplars, Peru balsam, and salicylates and it should be avoided in patients with asthma. Allergic reactions to propolis are generally limited to cutaneous manifestation. These usually resolve after discontinuation.

However, Li et al. (2005) report a patient with propolis-induced acute renal failure who required subsequent hemodialysis. The patient had cholangiocarcinoma and had ingested propolis for 2 weeks before presentation. Renal function improved

after propolis withdrawal, deteriorated again after re-exposure, and then returned to a normal level after the second propolis withdrawal.

5.8 Royal Jelly

5.8.1 Description and Function in the Hive

Royal Jelly (RJ) is a remarkable substance, both for its role within the colony but also for its composition and for the biological role it can play for our human cells.

It is secreted by the hypo-pharyngeal glands (clear fluid) and mandibular glands (white secretion) that are located in the front part of the head of the nurse bee, who is then 5–15 days old. Each egg laid in the hive is bathed during the first 3 days of its existence in Royal Jelly. Thanks to its presence, the egg's weight increases by 1,500 times in the first 6 days.

Different compositions of Royal Jelly are given to the bees in the hive:

- RJ given for 3 days to larvae of workers;
- RJ given for 3 days to larvae of drones;
- RJ given to the queen larva for the whole larval period;
- RJ given to queen during her lifetime as exclusive food.

Observing the life of the queen reveals Royal Jelly's full power. Every day of the summer the queen lays between 1,500 and 2,000 eggs per day, equaling almost her own weight.

Table 5.5 compares the queen with the worker bee demonstrating some of Royal Jelly's potential.

Kucharski et al. (2008) demonstrated that silencing the expression of DNA methyltransferase Dnmt3, allows for the development of queens with fully developed ovaries.

Royal Jelly has been known about for ages but has only been available in the last 50–60 years in quantities large enough for human consumption. China is acknowledged as the largest producer (over 2,000 tons yearly) and consumer (about 1,000 tons) of Royal Jelly. Table 5.6 lists the average composition of Royal Jelly. The pH of Royal Jelly is 3.6.

5.8.2 Pharmaceutical Preparations

Several pharmaceutical preparations of Royal Jelly are available: Fresh frozen, lyophilized (1 g fresh frozen RJ equals to 200–300 mg lyophilized RJ), tablets, granules, coated pills, lotions, creams, ointments, shampoos, emulsions, salves, suppositories and ovules.

Table 5.5 Parameters of queen bees compared to worker bees

	Queen bee	Worker bee
Food	Royal Jelly	Honey and pollen
Development	15.5 days	21 days
Size	17 mm	12 mm
Weight	200 mg	125 mg
Lifespan	3–5 years	4–6 weeks

Table 5.6 Average composition of Royal Jelly

Compound	Percentage and additional information
Water	67 %
Sugars	11 % (fructose 6 %, glucose 4 %, sucrose 1 %)
Proteins	13 % (fur)
Fat	5.6 %
Minerals	1 % (includes Ca, Cu, Fe, Mg, Mn, Na, K, Zn, Si)
Sterols	7–9 (sterols including sitosterol, cortisol, cholesterol)
Lipids	four phospholipids (from which cell walls are made); five glycolipids (which provide energy)
Vitamins	B1, B2, B3, B4, B6, B7, B9, B12 (Royal Jelly does not contain vitamins A, C; contains vitamin K in traces)
Gamma globulin	Mostly immunoglobulins which strengthen the immune system
10-Hydroxydecanoic acid	20–60 mcg/g; (its anti-bacterial and anti-fungal quality keeps Royal Jelly sterile)
Gelatin	Precursor of collagen for skin, tendon, ligaments
Acetylcholine	Up to 1 mg/g of Royal Jelly (important in nerve transmission and production and release of glandular secretions. Provokes adrenaline secretion)
Nucleic acids	DNA and RNA (the building blocks of genetic material)

Stocker et al. (2005) showed that in the RJ samples collected the concentrations of trace and mineral elements were highly constant, independently of the proportion present in the environment.

The best way to maintain the quality of RJ is by freezing it. Refrigerated and combined with honey it keeps for 3 weeks. However, lyophilized RJ will keep at room temperature indefinitely. Li et al. (2008) identified a protein (MRJP5) as a reliable freshness marker.

5.8.3 Mechanisms of Action and Possible Indications

5.8.3.1 Metabolic Activity

Narita et al. (2009) demonstrated on rats that ingested RJ tended to compensate for age-associated decline in pituitary functions. Inoue et al. (2003) showed on mice that RJ extended the life span by 25 %, possibly through the mechanism of reduced oxidative damage.

5.8.3.2 Hormonal Activity and Osteoporosis

Kafadar et al. (2012) investigated whether RJ and bee pollen reduce the bone loss due to osteoporosis in an oophorectomized rat model and found that bone tissue calcium and phosphate levels were higher in RJ and bee pollen groups compared to controls.

5.8.3.3 Wound Healing

Siavash et al. (2011) evaluated the efficacy of topical Royal Jelly on healing diabetic foot ulcers and concluded that Royal Jelly dressings may be an effective method for treating diabetic foot ulcers besides standard treatments. Koya-Miyata et al. (2004) showed that RJ promoted collagen production in skin fibroblasts by inducing TGF-beta 1 production. Park et al. (2012) studied RJ's protection against skin aging in rats with ovariectomy-induced estrogen deficiency and found that RJ may protect against skin aging by enhancing collagen production.

5.8.3.4 Irradiation Protection

Azab et al. (2011) investigated the possible protective effects of RJ against radiation induced oxidative stress, hematological, biochemical and histological alterations in male Wister albino rats. The authors suggested that the biochemical, hematological and histological amelioration observed in RJ treated irradiated rats might be due to the antioxidant capacity of RJ active constituents.

5.8.3.5 Anti-cancer Properties

Nakaya et al. (2007) investigated the effect of RJ on an environmental estrogen (Bisphenol A) that stimulates proliferation of human breast cancer cells. Royal jelly inhibited the growth-promoting effect of Bisphenol A (BPA) on human breast cancer MCF-7 cells, even though it did not affect the proliferation of cells in the absence of BPA. In addition, the observed inhibiting effect of RJ was heat-stable.

5.8.3.6 Anti-infectious Properties

Fujiwara et al. (1990) showed that Royalisin (a new potent antibacterial protein found in royal jelly of the honeybee with extensive sequence homology to two other insect derived antibacterial proteins) exhibited potent antibacterial activity at low concentrations against Gram-positive bacteria, but not against Gram-negative bacteria. They speculated that Royalisin may be involved in a defense system active against bacterial invasion of the honeybee.

5.8.3.7 Increase of Vigor and Physical Strength

Kamakura et al. (2001) investigated the antifatigue effect of RJ in mice in a swimming experiment. Their findings suggest that RJ can ameliorate physical fatigue after exercise, and that this effect seems to be associated with the freshness of RJ.

5.8.3.8 Biologic Activity

Nomura et al. (2007) investigated the effects of RJ on insulin resistance in Otsuka Long-Evans Tokushima Fatty (OLETF) rats, a type 2 diabetic model. RJ treatment tended to decrease systolic blood pressure and significantly decreased serum levels of insulin and the Homeostasis Model Assessment ratio, an index of insulin resistance. These results suggest that RJ could be an effective and functional food to prevent the development of insulin resistance.

Morita et al. (2012) conducted a randomized placebo-controlled, double-blind trial to investigate the effect of RJ in healthy volunteers. Six-month ingestion of RJ in humans improved erythropoiesis, glucose tolerance and mental health.

5.8.3.9 Immune Disorders

Sugiyama et al. (2012) reviewed the molecular mechanisms underpinning the biological activities of 10-Hydroxy-trans-2-decenoic acid or "royal jelly acid", which could lead to new therapeutic targets for the treatment of immune disorders.

5.8.3.10 Adverse Effects

Thien et al. (1996) observed symptoms of asthma and in some cases anaphylaxis following ingestion of RJ. These symptoms were true IgE-mediated hypersensitivity reactions. Katayama et al. (2008) reported the case of a Japanese woman who developed anaphylaxis after drinking a beverage of crude Royal Jelly including honey. They contended that Royal Jelly should be considered as a causative allergen in food-induced anaphylaxis.

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