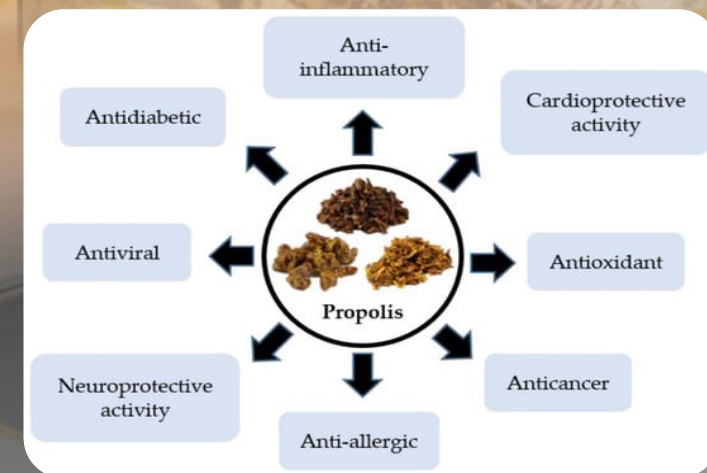


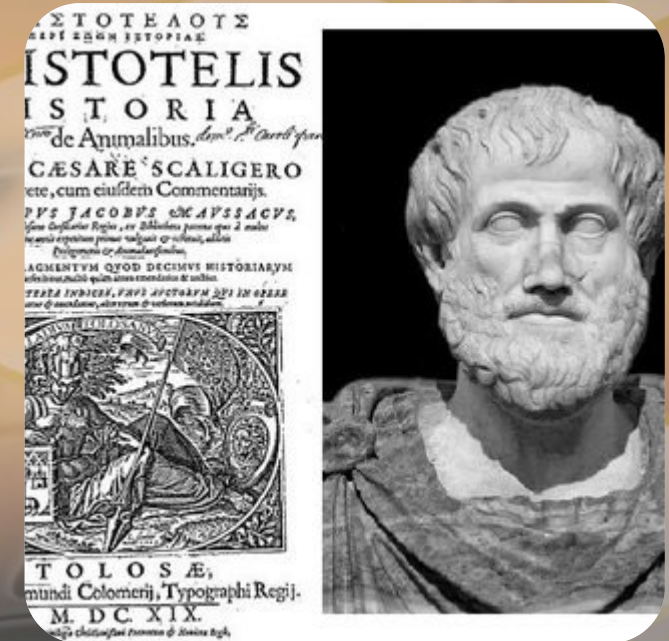
Introduction

- Nowadays, propolis is a natural remedy found in many health food stores in different forms for topical use. It is also used in cosmetics or as popular alternative medicine for self-treatment of various diseases. Current applications of propolis include formulations for cold syndrome (upper respiratory tract infections, common cold, and flu-like infections), as well as dermatological preparations useful in wound healing, treatment of burns, acne, herpes simplex and genitalis, and neurodermatitis. Propolis is also used in mouthwashes and toothpastes to prevent caries and to treat gingivitis and stomatitis. It is widely used in cosmetics and in health foods and beverages. It is commercially available in the form of capsules, mouthwash solutions, creams, throat lozenges, powder, and also in many purified products from which the wax was removed. Due to its antimicrobial, antiviral, and antioxidant properties, it is widely used in human and veterinary medicine, pharmacology, and cosmetics.
- Propolis is a lipophilic in nature, hard and brittle material and it becomes soft, pliable, gummy, and very sticky when heated [6]. It possesses a characteristic and pleasant aromatic smell and varies in color from yellow green to red and to dark brown depending on its source and age [2-7]. Depending on the origin of the resins, it also ranges from yellow to dark brown. But even transparent propolis has been reported.



History of Propolis

- The term propolis is derived from Greek and the pro means "defense" and the police means "city". From there, it was possible to reach a meaning such as the defense of the city or the hive. The discovery of propolis dates back to the years before Christ. The well-known Greek philosopher Aristotle wanted to study the bees' work by using a transparent hive, but the transparency of the hive was darkly covered with waxy substances. This dark colored substance is estimated to be propolis. The positive effects of propolis on human beings have been known since ancient times and their use among the people is based on ancient times. First BC. In 79-23 years, Pliny the Elder, a large school in Rome, described the pain-reducing, wound-healing activities of propolis.
- Propolis was also known by the Egyptians in ancient times and was used for the treatment of some diseases and for the embalming of the dead. The Greeks and Romans used propolis for centuries to treat skin abscesses. Hippocrates (460-377 BC) stated that propolis is used in the treatment of skin diseases, ulcers and digestive cystemia. In Africa, propolis has long been used as a medicine. Medical records of propolis used for oral, throat infections and dental health have been described in European records of the 12 th century. Another use of propolis based on ancient times is the use of varnish. In Italy, in the 17th year, Stradivari used propolis in the polishing of stringed instruments. The most important and well-known feature of propolis that has come from past times to the present is its effect against microorganisms. Propolis is used by people today because of its properties. In the century we live, this valuable bee product has numerous useful biological activities such as anti-inflammatory, anti-inflammatory, anti-ulcer, local anesthetic, antitumor, immunosuppressive as well as antibacterial, antifungal and antiviral properties; and its use in medicine, apitherapy, health food and biocosmetic fields. In recent years, propolis has gained importance as a health drink.



- It is also widely used in foods and it is thought that it improves human health and removes heart diseases. These properties of propolis have attracted the attention of scientists since the end of the 60s. Over the last 40 years, many studies have been published on biological use, pharmacological and therapeutic uses of chemical use. The first comprehensive research was published by Ghisalberti in 1978. Nowadays, much work has been done on the chemistry and biological activity of propolis. However, there are various difficulties associated with the administration of propolis.
- However, there are various difficulties associated with the administration of propolis. The main reason for this problem is that the chemical composition of propolis varies considerably depending on the vegetation and season of the region. Because different plants in different ecosystems and the secretions of these plants can be a source of propolis. For these reasons, the standardization of propolis has not yet been fully achieved.
- In today's world, the increasing number of events that threaten human health such as stress and environmental pollution have made the negative impact of environmental conditions more frequent. In spite of these negative effects of living conditions, propolis is being studied for various purposes in many countries due to its properties such as increasing body resistance, acting as an antibiotic and most importantly being a natural product. In many countries abroad, a variety of commercial products are produced using propolis. According to the literature, propolis was first used commercially in the 1950s. 1984 records of propolis; It includes the export of 55 tons of propolis from China, smaller quantities from Argentina, Canada, Chile and Uruguay, and at least 11 other countries with unknown quantities



- The effect of propolis against microorganisms, which is used as a natural antibiotic by discovering in ancient times, is the main character and has been used by people since ancient times due to its drug properties. The pharmacological properties of propolis have been described by the Greek and Roman physicists Aristotle, Dioscorides, Pliny and Galen. According to this definition, propolis can be used as an antiseptic in the treatment of wounds and oral infection. These properties of propolis were used in Europe and Arabia in the Middle Ages. Inca's used propolis as antipyretic. Propolis 17th century. In London, it is listed as the official drug and again in these years due to its antibacterial activity has gained importance in Europe. Propolis has gained importance with its excellent natural product characteristics which was discovered in the present century in order to contain 22 components that should be taken for human health. Propolis is a very interesting bee product for further research. In many countries, propolis contains some questions that have not yet been answered, although they are used against various medical problems.
- This limits the use of propolis in modern medicine. Propolis's different fields of use have attracted the attention of scientists and various researches have been started. Due to this interest, the commercial importance of propolis has also increased. Propolis is a natural product with great potential in veterinary and human health. On the other hand, unlike the products obtained from medicinal plants, their contents vary greatly. The chemical contents of the propolis samples collected in different countries vary widely. This diversity poses a serious problem for the medical use and quality control of propolis. The biggest problem faced is that the origin of propolis varies from region to region. The unknown origin of propolis causes serious problems in standardization. Today there are various uses of propolis, pure or aloe gel with pollen, as extract (hydroalcoholic or glycolic), as mouth spray (melissa, sage and / or mixed with rosemary), throat lozenges, creams and powdered, mouthwash is produced as and after the wax is removed. Despite the numerous effects of propolis, most of the reports are based on preliminary studies.
- The majority of studies are conducted in Eastern European countries. Applied studies and researches are mainly conducted in China. But the provision of information is difficult because of the language barrier. More detailed studies, especially intestines, skin and dental practices, will help to determine the possible benefits of propolis in medical use.

- Although there are no official official records of Propolis production, it is estimated that approximately 200 tons of propolis were sold in the world market in 1984. Among the countries producing the most propolis are China, Brazil, America, Australia and Uruguay (Figure 1). Japan is leading the processing and consumption of propolis. Lack of synthetic production of propolis, patent and standard problem, beekeeping of uneducated people; Honey, pollen and bee milk do not have a marketing network at the level and the source of income as a source of satisfaction of beekeepers and private firms to prevent the spread of propolis production is prevented. In Türkiye, propolis microscopic and chemical analyzes made by various researchers and Turkey of plant sources of propolis usually *Castanea sativa* and *Populus* spp. It has been reported to be. However, there are no detailed studies covering a region. Thus, Turkey has not established standards covering propolis. A study of the chemical composition of propolis Turkey Sorokin et al. (2001). In this study, from different regions of Türkiye (Bursa, Erzurum-Aşkale, Trabzon and Gumushane-Söğüttagil-Cascade) samples were collected and chemically analyzed by GC-MS was performed. According to the results of this study, similar chemical content was observed in propolis samples taken from Trabzon and Gümüşhane regions and Erzurum sample showed a different structure. In the samples collected from the Bursa region, flavonones, flavones and ketones were found to be quite rich. Eagle et al. (2002).



Propolis Characteristics - Physical Properties of Propolis

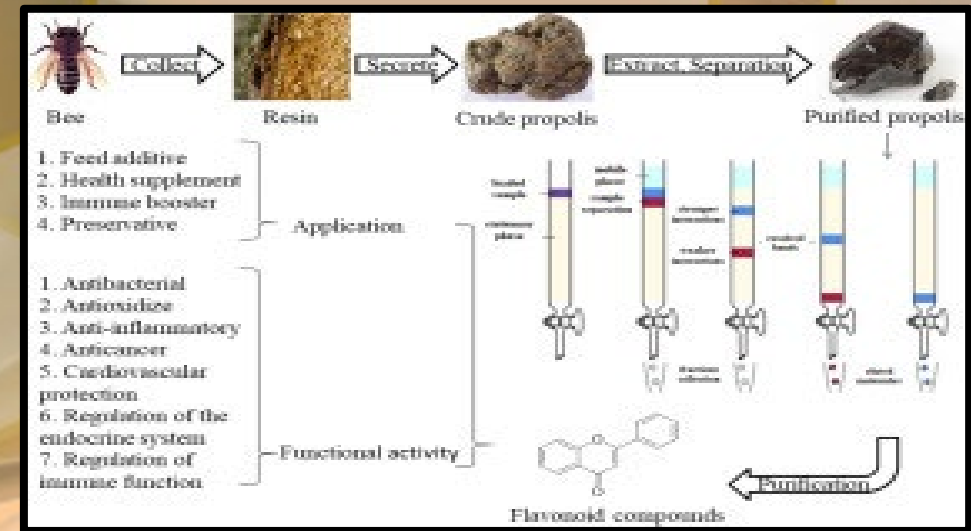
- Propolis, the color of yellow to dark brown, sometimes green. Figure shows the raw propolis in brown collected from the hive. Propolis color varies according to the region and season. For example, countries with temperate climates have more or less distinct brown, while in the tropical climate and in Australia, propolis is black.
- The Finland propolis is orange, and the Cuban propolis is dark violet. It is natural to observe differences in the color of the propolis due to changes in botanical origin.
- Propolis is a mixture of various amounts of beeswax and resins collected by the honeybee from plants, particularly from flowers and leaf buds. Since it is difficult to observe bees on their foraging trips the exact sources of the resins are usually not known. Bees have been observed scraping the protective resins of flower and leaf buds with their mandibles and then carrying them to the hive like pollen pellets on their hind legs. It can be assumed that in the process of collecting and modelling the resins, they are mixed with some saliva and other secretions of the bees as well as with wax.
- These resins are used by worker bees to line the inside of nest cavities and all brood combs, repair combs, seal small cracks in the hive, reduce the size of hive entrances seal off inside the hive any dead animals or insects which are too large to be carried out and perhaps most important of all, to mix small quantities of propolis with wax to seal brood cells.
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- The composition of propolis depends on the type of plants accessible to the bees. Until 2000, over 300 chemical components belonging to the flavonoids, terpenes, and phenolics have been identified in propolis. The characteristic constituents in temperate region propolis are flavonoids without B-ring substituents, such as chrysin, galangin, pinocembrin, pinobanksin. Caffeic acid phenethyl ester (CAPE) is a major constituent of temperate propolis with broad biological activities, including inhibition of nuclear factor κ -B; inhibition of cell proliferation; induction of cell cycle arrest and apoptosis. In tropical region propolis, especially Brazilian green propolis, the dominating chemical components are prenylated phenylpropanoids (e.g., artepillin C) and diterpenes. For propolis produced in the Pacific region, geranyl flavanones are the characteristic compounds which are also found in propolis from the African region [19]. The chemical composition of propolis is susceptible to the geographical location, botanical origin [20–23], and bee species [23]. In order to provide a theoretical basis for studying the chemical composition and pharmacological activity of propolis and plant sources, and controlling the quality, chemical components that were isolated for the first time from propolis between 2000 and 2012 were scouted and summarized from databases including BioMed Central, Biosis Citation Index, Medline, and PubMed. 2.
- Chemical Compounds in Propolis With the development of separation and purification techniques such as high performance liquid chromatography (HPLC), thin layer chromatography [24], gas chromatography (GC), as well as identification techniques, such as mass spectroscopy (MS) [25], nuclear magnetic resonance (NMR), gas chromatography and mass spectroscopy (GC-MS) [26], more compounds have been identified in propolis for the first time; including flavonoids, terpenes, phenolics and their esters, sugars, hydrocarbons and mineral elements. In contrast, relatively common phytochemicals such as alkaloids, and iridoids have not been reported. Two hundred and forty one (241) compounds have been reported for the first time from propolis between 2000 and 2012. Their chemical category, geographical locations, and possible plant source, are summarized below. 3. Flavonoids As the major constituents of propolis, flavonoids contribute greatly to the pharmacological activities of propolis. The quantity of flavonoids is used as a criterion to evaluate the quality of temperate propolis [27]. Flavonoids have a broad spectrum of biological properties, such as antibacterial, antiviral and anti-inflammatory effects. According to the chemical structure, flavonoids in propolis are classified into flavones, flavonols, flavanones, flavanonols, chalcones, dihydrochalcones, isoflavones, isodihydroflavones, flavans, isoflavans and neoflavonoids.

Collection, Processing and Storage of Propolis

- Contamination of propolis with wax, paint and other parts should be avoided. The cleanest collection method uses traps placed on top of the bucket. Traps are plates with small holes that are essentially similar to chambers or cracks in the sleeve wall. Bees try to close these holes to protect their hives from external factors and thus fill the trap with propolis. Thanks to the traps, the excess wax does not interfere with propolis and contamination does not occur during harvest.
- Trap harvesting is a faster and more productive method. In order to increase the production of propolis, traps are made of plastic, nylon or metal with openings of width (3 mm) that the bee cannot pass until the air cools down. The traps are mounted on the top of the hive. The openings on the traps are filled with propolis by bees working 12 to 21 days.



- Propolis is effective in the cleaning of the honeycomb eyes, the development of the eggs left by the queen in a sterile environment and the protection of the offspring. Propolis is also used by bees for shaping hive borders, hardening and repairing honeycomb edges, strengthening frame connections, fixing frames in hives, closing slits and cracks, and collecting for these purposes.
- The reason for the microorganism to be found in the hive is much less than the atmosphere is the presence of propolis in the hive. The inner walls of the hive are slippery when plastered with propolis and it is easier for bees to repel ants trying to enter the hive.
- Various insects that enter and die in the hive or other particles that cannot be removed from the hive are covered with propolis, thus preventing them from damaging the hive. It keeps the humidity in the hive to a certain level and protects the hive from the excessive moisture that will be seen after heavy rains. By preventing the development of various sports and the like, it ensures hygiene of the bucket.

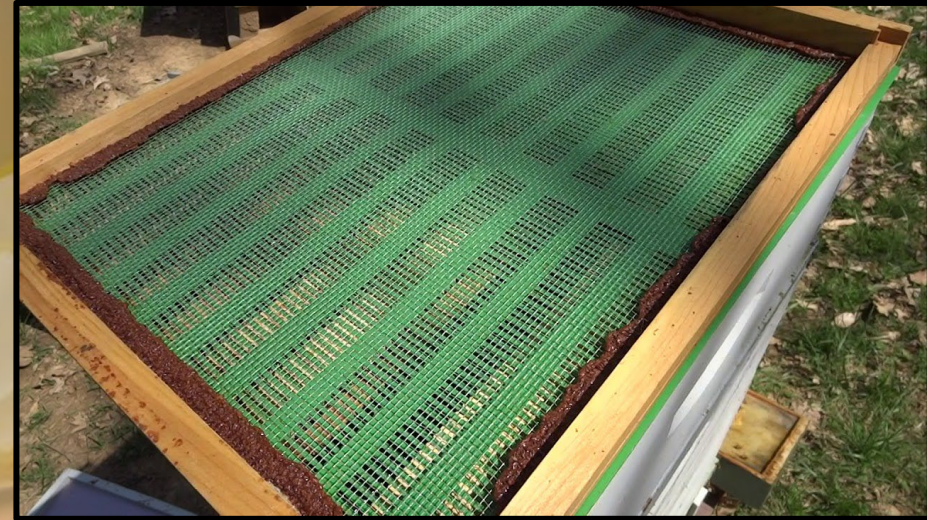
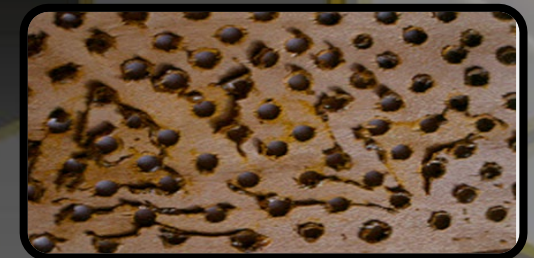
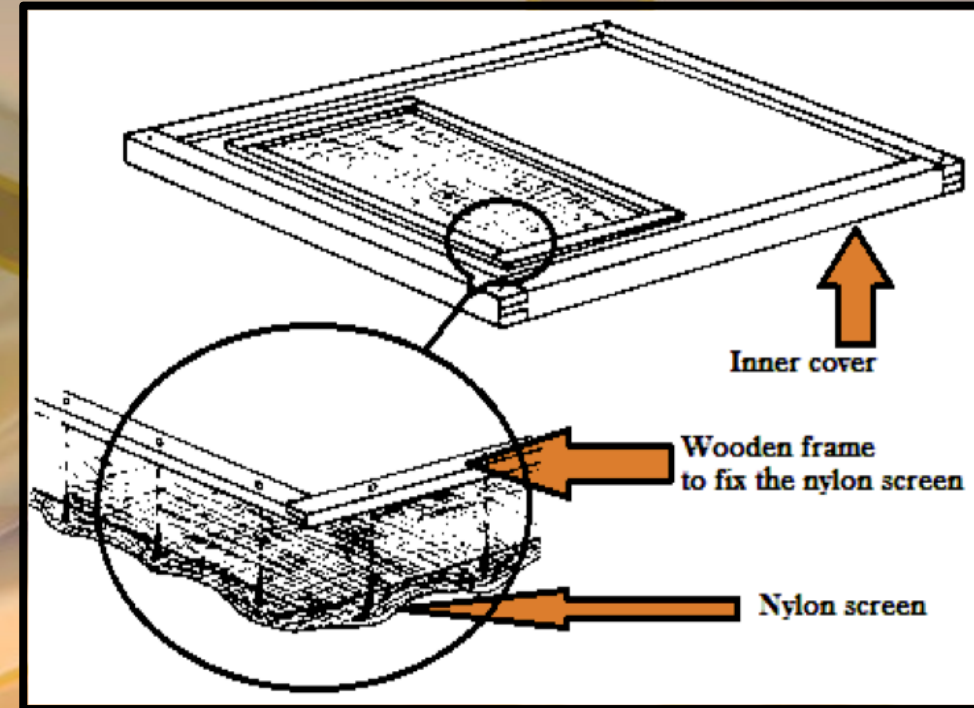


Figure 3. Traps filled with propolis by bees

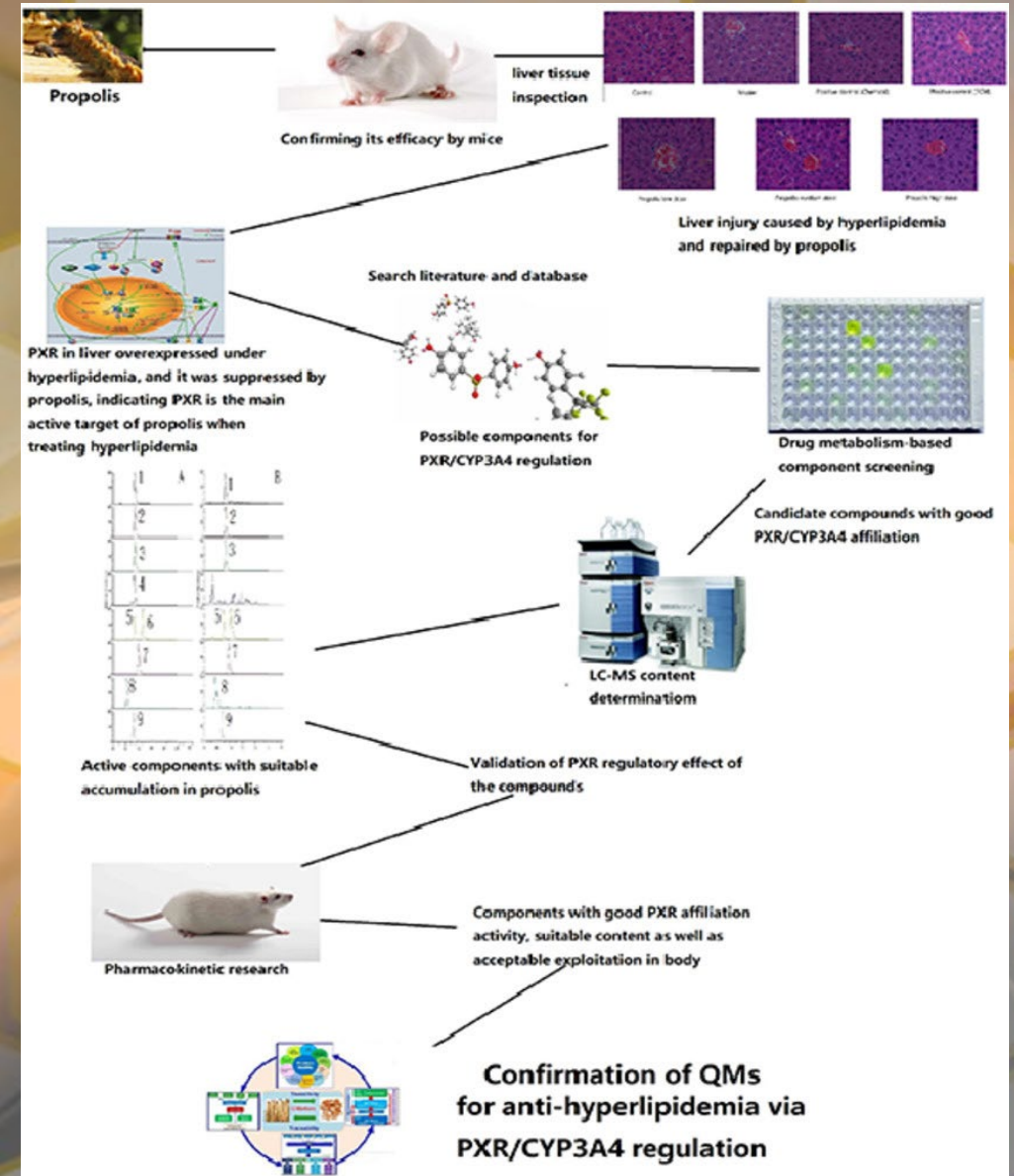


Quality Control in Propolis

- In the propolis, environmental pollutants, drugs and waxes can accumulate highly. Therefore, if propolis is to be collected for human use, it must be collected from hives not exposed to chemical treatment. A good propolis must first be free of all contaminants. Acaricides are used in many countries to control bee parasites and their residues can be found in propolis. Heavy metals can also accumulate in the propolis in dangerous amounts. Thus, the level of contamination of acaricides and heavy metals is an important parameter in the quality control of propolis. Propolis is not only free of toxins. The proportion of substances related to biological activity, insoluble parts, ash content should be recorded.



- If propolis is to be used for medical purposes, the concentration of substances with biological activity must be known. A good quality propolis should be free of toxic contaminants. The amount of wax, insoluble matter and ash should be low. The active components of the identified plant resource should be identified and the components with a high percentage identified. The most important of the studies related to propolis is the standardization of propolis. The wide variety of vPropolis from region to region makes it very difficult. However, the lack of standardization limits the use of propolis. Therefore, countries have started to establish their own standards



Processing of Propolis

- The crisp cool Autumn weather arrives at a time when the color of the leaves change, mice build nests in well-protected warm places, and bees finish plugging up the cracks in their hives with propolis in anticipation of Winter. The term propolis, (aka bee glue) originated with the Greeks who often observed a sticky resinous substance around the entrance to their hives. In Greek, “Pro” means coming before or in front of, and “Polis” is the Greek word for city or a body of citizens. Thus, propolis is what one could expect to find at the entrance to the city of the bees. Today beekeepers will often observe that the bees will use propolis to restrict or narrow the entrance to the hive to make it easier to defend. Honey bees use propolis as both a building material and as a way to sterilize and disinfect the cavity that contains the colony. This is because, as we will explore in this two part series, propolis is among the most powerful antimicrobial substances found in nature.
- Honey bees make propolis out of the resins they collect from deciduous trees such as cottonwood, birch, alder and poplar (aspen). As these trees bud, they exude these resins around the bud in order to protect is from fungi and other diseases. Foraging bees utilize their pollen baskets (corbicula) to carry globs of propolis resins back to the hive. Unlike with pollen however, foragers require the help of other bees within the colony to help them remove the sticky resins from their hind legs so it may be used by the colony.

Processing

While propolis can be found in many products from toothpaste and skin creams to healing salves, herbal tinctures, syrups and elixirs, propolis does not require any processing (other than cleaning) in order for it to be used. For gum, dental, or sore throat issues simply tuck a chunk of raw propolis between the gum and cheek and suck on it. This is the simplest way to use it, although its benefits may be limited and it may stick to your teeth if you are not careful. Here are some of the more usual commercially available forms that pure processed propolis can be found in.

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