Propolis: a valuable tool in dentistry

by Dr. Rafael Felitti

The study of propolis began in earnest in Europe in the 19th century, as a result of major advances in chemistry. Propolis researchers during that time included Vauquelin, Kostanecki, Emilewic, and Tambor, who were among the first to isolate and synthesize certain of its components.

Propolis contains more than 300 elements, including resins, wax, essential oils, pollen, and organic components: phenols, esters, flavonoids, and aromatic alcohols. Its major bioactive compound is caffeic acid phenethyl ester, or CAPE.

Flavonoids are the largest component of propolis. Several of these—notably chrysine, quercetin, and quercetin—are responsible for propolis’s antimicrobial, antiviral, antioxidant, anti-inflammatory, anti-tumor, and radio-protective actions.

The word “propolis” comes from the Greek word “promalasso,” meaning “before the city or suburb of the city.” It is well understood that bees produce propolis in order to help protect the hive. But propolis has another feature. In addition to sealing and repairing damage to the hive, propolis serves as a superb antiseptic, preventing infections in places where the larvae are reared or where the honey is stored.

Propolis’s many components have long made it a popular naturopathic agent, whether in ancient Greece (for healing ulcers, treating abscesses, healing phlegm, and soothing pain), ancient Egypt (for embalming cadavers), South America (for healing inflammation), or 19th-century battleground medicine (for treating wounds and treating infection; in Russia it was referred to as “Russian penicillin”).

In the 21st century, claims of the health benefits of propolis are wide-ranging. Among the disorders for which it is thought to be helpful are cancer, urinary infections, throat infections, gout, nasal congestion, influenza, bronchitis, gastritis, hearing problems, ulcers, and skin rashes.

Here we focus on propolis’s use in several areas of dentistry.

Preventing caries

The basic microorganism associated with the development of dental caries (cavities) is Streptococcus mutans, which can adhere to the teeth, produce acid, and resist a relatively low pH.

Propolis’s potential to prevent caries has been demonstrated in studies showing the reduction of incidence of caries and plaque accumulation in vitro and in vivo. Studies of rats also found this effect, through several mechanisms. And propolis-based solutions used as mouthwashes had less of an effect on gingival fibroblasts—which are responsible for the regeneration of gingival connective tissue—than did chlorhexidine-based mouthwashes. This property is directly related to the presence of flavonoids, phenols, and esters.

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From the Editor

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I n the most recent issue of this Journal, we promised to keep readers informed about research and other developments regarding the health of honeybees. With a wealth of news emerging this past spring, the promise was easy to keep.

That column in the Journal reported findings by scientists at the Harvard School of Public Health on the role of neonicotinoids—the increasingly popular and now most widely used class of synthetic pesticides—in contributing to colony collapse disorder. Their article, published in the May 9, 2014, issue of the Bulletin of Insectology, attempted to replicate colony collapse disorder in the field. The investigators monitored three groups of 18 colonies: one treated with tiny levels of imidacloprid (a popular seed coating for maize, sunflower, and canola), one with tiny levels of clothianidin (mainly used for seed coating of maize and canola), and a control group, which was not treated.

During the winter, the bees in six of the treated hives vanished, leaving behind empty colonies—the classic behavior of colony collapse disorder. Although research has suggested that bee die-offs may result from bees’ reduced resistance to mites or parasites as a result of exposure to pesticides, this study revealed that bees in the hives exhibiting CCD had almost identical levels of pathogen infestation as the control hives, most of which survived the winter. This finding suggests that the neonics are not only serving as a neurotoxin but also causing a biological mechanism in bees that in turns leads to CCD. In pointing out that honeybees normally don’t abandon their hives during the research, the authors suggest that neonics can impair memory, cognition, behavior, and other neurological functions.

Apparent confirmation of these results came in June. That month a task force of the International Union for the Conservation of Nature released the results of a four-year analysis finding what it terms “conclusive” evidence that neonics are “a key factor in the decline of bees.”

Predictably, three of the leading pesticide corporations—Syngenta, Bayer Crop Science, and Monsanto—have cast a veil of uncertainty over these findings. (This parallels the 1980s actions of Big Tobacco, a representative of which commented, “Doubt is our product.”) A major criticism is that the
study “overdosed” the bees. In response, the lead researcher notes that the dose used—0.74 micrograms per bee per day over 13 weeks—is small, and well below what scientists call the median lethal dose (the dose required to kill half the members of a tested population) for neonics. He also wonders what, according to Bayer, an “environmentally relevant” level of neonics might be. Further, he emphasizes that the treated bees showed no ill effects during the 13 weeks of the feeding. It was only well after exposure to the pesticides, during the winter, that they vanished.

On balance, while other scientists decline to consider the results to be a “smoking gun” of neonics’ complicity, they acknowledge that, with this study, evidence is mounting. As part of such a consensus, this past spring the U.S. Fish and Wildlife Service announced a gradual phasing out of neonicotinoids on National Wildlife Refuge Lands for the Pacific Region (Hawaii, Idaho, Oregon, and Washington), culminating in their elimination by the end of next year. The region comprises more than 8,700 acres of cropland; even though pesticides aren’t typically used in refuge management, it is likely that neonics enter the protected areas through the seeds of genetically modified organisms, or GMOs, which are engineered to be herbicide-resistant. The memo highlights neonics’ persistence in the environment and their tendency to drift to non-treated areas, as well as their potential for harming birds and small mammals. Although this column has argued in favor of the U.S. going further, i.e., banning neonics at least temporarily (as Europe as done), we agree that this is a significant step.

Also significant was President Obama’s signing, in June, of a memorandum spelling out new initiatives to promote the health of honeybees and other pollinators. In addition to calling for research into the causes of colony collapse disorder, the memo authorized the formation of a Pollinator Health Task Force of more than a dozen federal agencies, charged with creating a national strategy to protect pollinators. A June 30 lead editorial by the New York Times comments, “[The President’s] directive comes not a moment too soon.”

As other scientists argue for assessing the interplay of parasites, illness, food sources, and pesticides in bee health, biologist Mark Winston (in a July 14 essay, also in the New York Times) notes that the real issue in bee die-offs isn’t the number of problems or factors but rather the interactions among them: “the concept of synergy, where one plus one equals three, or four, or more.” A typical honeybee colony may contain residue from more than 100 pesticides. Each one itself represents a benign amount. “But together,” says Winston, “they form a toxic soup of chemicals” that can wreak havoc on bees immune systems, increasing their vulnerability to disease. A human equivalent is pharmaceutical interactions. Certain prescription drugs show harmful or fatal side effects when used together, particularly in people whose immune systems have been weakened by disease. This argues in favor of understanding pesticides’ synergistic impacts on our health and their interplay with human diseases.

Meanwhile, information on honeybee losses in the United States is unclear. In May a preliminary report by the U.S. Department of Agriculture and the Bee Informed Partnership found that during the most recent winter, just under 25% of hives collapsed. This was a decline from the year before and the smallest percentage since the onset of colony collapse disorder in 2005-06. (Losses peaked at 35% in 2007-08.) Notes entomologist Dennis vanEngelsdorp, a director of the partnership, “We’ve gone from horrible to bad.” While agrochemical industry representatives are encouraged by these figures, some scientists note that the numbers reflect nationwide averages and might mask significant regional losses. Ohio and Pennsylvania, for example, report 2013-14 losses exceeding 50%.

And now, another complication. Honeybee advocates, including this Journal, have long insisted that planting bee-friendly gardens can help hive insects survive. But as we learned to our dismay in June, the gardens we plant may actually be a source of harm to bees. That month a report by the Pesticide Research Institute and the environmental group Friends of the Earth was released. It found that more than 50% of the supposedly “bee-friendly” plants sold at major garden centers in the United States and Canada contain neonics. This means that gardens planted to save the bees—or even planted only in the belief that they aren’t contributing to CCD—may be doing the exact opposite.

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**RESEARCH ROUNDUP**

**PROPOLIS**

**Useful in sanitizing lettuce**

FRESH Vegetables, along with fruits, are a centerpiece of a wholesome diet. Eating fresh vegetables, though, poses a health risk if they are contaminated. Food-borne illnesses are a serious problem, particularly in people whose immune system has been compromised. Washing vegetables before eating them is therefore crucial.

The goal of their study was twofold. One aim was to determine the microbiological quality of commercially available ready-to-eat and fresh whole head lettuce. The other goal was to determine the efficacy of two washing solutions—sodium hypochlorite and propolis (tap water was a control)—on the microbial quality. Both treatments were effective in reducing the microbial load; propolis was slightly more effective.

In future work, the investigators will study the effectiveness of propolis in decontaminating other vegetables.


**Gel may help prevent radiation-induced oral mucositis**

For oral cancer patients at a late stage of the disease, surgery is not advised, and radiation treatment may therefore be the only option. However, approximately 80% of patients receiving radiation therapy for head and neck cancer develop mucositis, the painful inflammation of the mucous membranes lining the mouth.

In Brazil and elsewhere, propolis is popular treatment for diseases of the mouth. However, a lack of clinical studies of its efficacy means that dentists rarely prescribe its use. Now, in a phase II clinical study at the Irradiated Head and Neck Patient Clinic in Belo Horizonte, Brazil, investigators have verified the effectiveness of a Brazilian green propolis mucoadhesive gel in preventing oral mucositis in patients irradiated in the head and neck region.

A total of 24 patients—19 men and 5 women, ages 38 to 72—scheduled for radiation therapy for oral cancer were included in a phase II study of propolis. They were advised to apply 10 g of a mucoadhesive gel containing propolis 5% on the tongue and then spread it over the oral mucosa. The application was done three times a day, starting the day before radiation began and concluding two weeks after the completion of the seven-week therapy.

The investigators found that 20 patients did not develop mucositis, two patients developed grade 1 mucositis, and two patients developed grade 2 mucositis. None of the patients reported pain during use of the product, and no cases of candidosis were detected. In addition, none of the patients reported having a dry mouth. A possible explanation for this result is that propolis has an acidic content that can contribute to salivary flow.

While suggesting that mucoadhesive propolis gel might be considered a potential topical medication, the authors recommend a phase III study that would evaluate propolis in a larger number of patients and in comparison with other therapies.


**BEE VENOM**

**Benefits to patients with temporomandibular disorders**

Researchers in Poland have found that applying bee venom topically may help relieve pain in patients with temporomandibular joint dysfunction (TMJ), a painful disorder of the joint and muscles around the jaw.

In a randomized, double blind study conducted at the Medical University of Silesia in Katowice, the investigators studied 68 patients ages 22-34 with painful TMJ. Subjects in the experimental group were given 0.0005% bee venom ointment for topical skin application, while the placebo group subjects were given only Vaseline. Both groups applied the preparation three times a day for 14 days, locally over the masseter muscles (those used for chewing) on the left and right sides, during a three-minute massage. A reduction of muscle tension and pain was seen in both groups. However, in the bee venom group, the reduction was statistically relevant, whereas in the placebo group several measures of tension and pain were not statistically relevant.

The researchers conclude that while physical therapy alone is helpful in relieving muscle pain, the
effectiveness is greater when bee venom is used in the massage. In noting that muscle tension can be regulated by the bee venom protein melittin, they recommend further study to establish the optimal dose of bee venom, as well as the preferred frequency and duration of therapy.


HONEY

Effective in oral hygiene

Despite honey’s many benefits, some scientists suggest that it may be harmful to the teeth. One factor not considered in the debate, though, is the wide variation in antibacterial activities among various honeys. One honey with high levels of non-peroxide antibacterial activity is Manuka (Leptospermum scoparium), a function of a component known as Unique Manuka Factor (UMF). Now a team of researchers at a dental college in Kerala, India, have found Manuka honey to be effective in reducing salivary levels of Streptococci mutans in children.

For the study, children were divided into two groups, one using Manuka honey with regular tooth brushing, and the other continuing with regular brushing only. All the children brushed their teeth twice a day for 21 days, under professional supervision. Salivary samples were taken at the beginning of the study, at day 10, and at day 21. The children using Manuka honey showed statistically significant reduction in salivary S. mutans at both 10 and 21 days.


Improves quality of frozen sperm

Cryopreservation, a procedure that stabilizes cells at very low temperatures, can be used for human semen, typically when a man diagnosed with cancer faces the possibility that treatment will make him infertile. Cryoprotectants—low-molecular-weight, highly permeable chemicals—are often added to the sample to protect sperm from freeze damage. Among the substances used for this purpose are lipids, fatty acids, proteins, and now, according to researchers in Iraq, honey.

In their study, the investigators collected 30 semen samples from 30 infertile patients seen at a clinic at Al-Nahrain University. These were further divided into three samples: cryopreservation solution alone, cryopreservation solution enriched with 5% honey, or cryopreservation solution mixed with 10% honey. Sperm motility and activity were measured. Whereas the first two samples—cryopreservation solution alone and that supplemented with the lower concentration of honey (5%)—showed significantly decreased motility of the sperm after thawing, the sample supplemented with the higher concentration (10%) of honey showed a smaller decrease.


May help prevent dental problems

Young people often develop dental cavities and gingivitis after undergoing orthodontic treatment. Researchers in Saudi Arabia have now found that honey can reduce the occurrence of these conditions.

In their study, 20 female patients ages 12-18 were randomly assigned to one of three groups: those chewing honey, those given sucrose (a positive control), and those given sorbitol (a negative control). At 2, 5, 10, 20, and 30 minutes after the girls had chewed honey or rinsed with the control solution, the pH of their plaque was measured and the numbers of Streptococcus mutans, Lactobacilli, and Propionomas gingivalis in the plaque were determined.

Bacterial counts were significantly reduced in the honey group compared with the other treatment groups, and honey significantly inhibited the growth of all the strains compared to inhibition observed with antibiotics. Although both the honey and sucrose groups showed a maximum pH drop at five minutes, the pH in the honey group—in contrast to the sucrose group—did not drop below the critical decalcification pH of 5.5.

BEE VENOM

For osteoarthritis

A pimeds, a pharmaceutical company based in Seoul, South Korea, and headed by Christopher M.H. Kim, M.D., is sponsoring a year-long Phase I investigation to determine the efficacy of bee venom in treating osteoarthritis of the knee.

Investigators at Axis Clinical Trials in Los Angeles, California, are studying 330 patients ages 30-85 with diagnosed osteoarthritis of the knee. One group, randomly assigned, is receiving Apitox (purified honeybee toxin, lyophilized in saline), while a control group, also randomly assigned, is receiving a histamine injection. The subjects will be evaluated for relief of pain over a 12-week treatment period. Study results are expected at the end of 2014.

With acupuncture, for Parkinson’s

Parkinson’s disease symptoms typically develop when brain cells that make the chemical dopamine are destroyed. Acupuncture, which has long been used in Asia to relieve these symptoms, is thought to operate in several ways: by increasing dopamine levels, by protecting and easing inflammation in nerve cells, and by enhancing the effects and lessening the side effects of the drug L-dopa. Now the results of a small study in South Korea suggest that a combination of acupuncture and bee venom shows promise in treating Parkinson’s.

The research, presented at the 18th International Congress of Parkinson’s Disease and Movement Disorders in Stockholm, studied 35 Parkinson’s patients who had been on a stable dose of medication for at least a month. They were randomly assigned to three groups—one receiving acupuncture, the second receiving bee venom acupuncture (BVA), and the third receiving neither. The treatment was given twice a week for eight weeks. In the BVA treatment, bee venom was injected under the skin at an acupuncture point, with the goal of enhancing and prolonging the effects of stimulating acupuncture points.

Patients in the BVA group showed major improvement in Unified Parkinson’s Disease Rating Scale scores, the Berg Balance Scale, and the time taken to walk 30 meters. For acupuncture-only patients, the Unified Parkinson’s Disease Rating Scale and Beck Depression Inventory scores improved significantly. Patients in the control group experienced no change in their symptoms. A cautionary note: Some Parkinson’s symptoms include muscle spasms that can cause pain and difficulty moving. It is possible, therefore, that bee venom acts like botulinum toxin, causing a temporary paralysis or relaxation of these muscles.

Elizabeth Clausen, Acupuncture and bee venom acupuncture are beneficial alternative therapies for patients with Parkinson’s disease, news release, International Parkinson and Movement Disorder Society, Stockholm, Sweden, June 8, 2014.

For chronic neck pain

Chronic neck pain is a common condition most prevalent among middle-age people. As a mechanical pain without an accurately identifiable source, it may be related to neck pain, upper extremity pain, and headache. Although conventional and complementary alternative approaches are used widely to treat the disorder, their effectiveness has not been established by rigorous study.

In July 2013, researchers at the spine center at Kyung Hee University Hospital at Gangdong, South Korea, launched a pilot study to evaluate the feasibility of and refine the protocol for a full-scale randomized clinical trial of bee venom acupuncture (BVA) and non-steroidal anti-inflammatory drugs (NSAIDs) in patients with chronic neck pain.

For the study, 60 patients ages 18-65 with nonspecific, uncomplicated neck pain lasting at least three months will be recruited for random allocation into the BVA, NSAIDs, or combined treatment group. Patients from the BVA and combined treatment group will be treated with bee venom administered in predefined acupoints for six sessions over three weeks. Among the measures to be analyzed are pain intensity, neck disability index, quality of life, depression, and adverse experiences.

The study, which is registered with the U.S. National Institutes of Health Clinical Trials Registry (NCT01922466), will be completed by late 2014. The findings are expected to shed light on the cumulative effects of BVA repetition, the persistence of clinical impacts, synergistic advantages, and patient satisfaction.

Seo B-K et al, Bee venom acupuncture, NSAIDs or combined treatment for chronic neck pain: study protocol for a randomized, assessor-blind trial. Trials Volume 15, 2014.
For acne

The widespread use of antibiotics to treat acne has led to antibiotic resistance, prompting research to develop alternative therapeutic drugs. In one such effort, a double-blind study in South Korea, investigators randomly assigned cosmetics either with or without purified bee venom to 12 patients for two weeks. The patients’ lesion counts and skin microorganisms were subsequently evaluated.

Bee venom’s antimicrobial activity was directly correlated to its concentration. In a concentration of 0.5 micrograms (mcg), the colony-forming unit of P. acnes was reduced significantly. It declined even more in a concentration greater than 1.0 mcg. In the area of skin microorganisms, the subjects receiving cosmetics with bee venom showed a 50% decrease of adenosine triphosphate levels. In contrast, for those receiving cosmetics without bee venom, only a 5% decrease resulted.

In studies carried out at Venezuela’s Centro de Investigaciones Odontológicas de la Universidad de los Andes—Center for Odontological Research of the de los Andes University, it was observed that the growth of the S. mutans is inhibited in the presence of propolis.

**Periodontics**

Propolis has shown anti-inflammatory, antimicrobial, anesthetic, and wound-healing properties in cases of chronic gingivitis and recurring mouth ulcers. It also enhances periodontal treatment. Studies of propolis solutions have found that it acts at the level of plaque on the tooth surface above the gum line (in gram-positive bacteria), promoting the recovery of tissues and stimulating local immune response.

As an anti-inflammatory, propolis inhibits prostaglandin synthesis and helps the immune system by promoting phagocytosis (the process by which certain cells act to remove pathogens) and stimulating cellular immunity. Some researchers have created patches in the cheek to achieve the slow release of propolis, which has helped produce benefits. One study found that a mucoadhesive gel containing propolis applied to periodontal pockets could be used successfully in treating periodontal disease. Excellent results have also been achieved by use as an irrigant during periodontal treatment.

Propolis has been used in the treatment of herpes simplex virus. It has been determined that propolis solutions act by stopping the progression of changes in the skin during the first stages of the disease in addition to not causing cytotoxic effects.

**Operative dentistry**

Propolis has been used successfully to promote the regeneration of dental pulp in cases of accidental exposure, by direct application to the pulp covering. It is also used with great success in treating dental hypersensitivity. One group of researchers has proposed incorporating propolis extract in glass ionomer cements (dental restorative materials), following significant reductions in the amount of streptococci mutans on which propolis has been added. In one study, propolis was shown to be an effective agent in coating dental pulp, stimulating its formation comparing with traditionally used calcium hydroxide.

Propolis has advantages over calcium hydroxide. The hard tissue of the tooth (dentin) formed in contact with propolis showed improved quality; whereas dentin formed in contact with propolis was 100% tubular dentin, dentin in contact with calcium hydroxide was merely 14%. The high effectiveness of the direct coating of the pulp compared with that of calcium hydroxide is attributed to propolis’s ability not only to control inflammatory reaction but also to manage infection and induce high-quality dentin formation. One suggestion is that this results from the presence of flavonoids.

Propolis is also widely used in treating dental hypersensitivity. By using propolis gels (10% and 30%), researchers have been able to close up dentinal tubules. These are structures spanning the entire thickness of dentin. Flow of the fluid contained in these tubules can trigger a pain response.

**Endodontics**

Comparative studies of propolis as an intracanal medication were performed with calcium hydroxide, used to fill the root canal for the first stage of endodontic therapy. Propolis proved to be far superior. One study found that propolis is more effective than calcium hydroxide in reducing colonies of Enterococcus faecalis, a microorganism that is present in most endodontic failures. Propolis has also been compared favorably with sodium hypochlorite in its effectiveness as an irrigant. Its major advantage is the absence of inflammation of the tip of the root of the tooth and the protective effect on periodontal cells.

**Dental surgery**

Numerous studies have demonstrated that in preparing a lost tooth to be reimplanted, propolis is an excellent form of preservation for transport. One investigation found that it is superior to a milk or saline solution in achieving this result. Propolis has been used in post-extraction surgical wounds (hydroalcoholic solution 10%), as it promotes the production of new cells and the healing of wounds. It has also been used in cases of post-extraction complications such as inflammation. One study found that following surgery, propolis not only reduces inflammation but also has an analgesic effect.

**Prosthetics**

Dental stomatitis is frequent in patients using dentures. Candida albicans is associated with infection in cases of poor hygiene of the prosthesis and, as a result, the mucous membrane. Propolis-based products have strong antifungal properties, especially against Candida albicans, and may be used as mouthwashes or as a gel.
Conclusion

Propolis is a natural, safe product with great potential for use in dentistry. It has been studied by numerous investigators in treating pathologies in the mouth. To date no contraindications, allergic reactions, cases of toxicity, or overdoses have been reported.

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17. Kimberly Mariel, Huayhua Romani, Silvia Gisell, Nina Humire, “Accion antimicrobiana del propoleo de Apis mellifera et y de Solanum mammosum contra microorganismos de la cavidad oral (streptococcus mutans y streptococcus mitis).
In their investigation, the researchers purchased 71 “bee-friendly” plants at 18 Lowe’s, Walmart, and Home Depot outlets. For more than half of the plants, neonic residues in the flowers ranged from 2 to 748 parts per billion. (Toxicologists say that 192 parts per billion is enough to kill a honeybee; impaired bee navigation, memory, and foraging ability have been associated with levels below 30 billion.) We join the organization Friends of the Earth in calling on consumers to put pressure on retailers to remove neonic pesticides from their plants. And in order to ensure the safety of bees, we should buy organic plants.

If there are any silver linings to these developments, they may come in the form of greater understanding of honeybees and their health. Entomologists note that beekeepers are increasingly aware of the importance of maintaining their colonies properly. Eric Mussen of the University of California, Davis (quoted in the May 16, 2014, New York Times), notes, for example, “People are being forced now to look more carefully at their bees. If you don’t take care of them, you lose them.” And Mark Creighton, the official bee inspector of my home state of Connecticut, concludes that colony collapse disorder has increased the public’s awareness of the importance of pollinators—and has spawned demand for locally produced honey.

With my good wishes,

Patsy McCook
From the President

Once again the AAS is conducting an annual “Flower Power campaign,” in which we raise money through the sale of bulbs for planting in the fall—and blooming in the spring. Every purchase made on the site www.flowerpowerfundraising.com will return 50% to the AAS. The fundraiser concludes October 15.

Like any good not-for-profit group, we’re constantly contemplating additional ways to enlarge our coffers. Here are two recent ideas—which might be held as mini-events, in different regions of the United States:

A raffle. We could sell packs of tickets, and the winner would receive half the total amount. The other half would go to the AAS.

An apitherapy calendar. People could submit photos of honeybees and products of the hive. Votes would be cast, and each of the top 12 photos would be matched with a given month in the calendar.

Please send us your thoughts about these and other fundraising ideas. We welcome your creativity!

Frederique Keller, L.Ac.