In the 1980s two pharmacologists, Dr. Jurgen von Bredow and Dr. James Vickwere, were assessing the physiological effects of certain drugs for arthritis. Intrigued by the numerous anecdotal reports of the benefits of bee stings, they began trials of bee venom on arthritic dogs. The dogs' improvement encouraged Drs. Von Bredow and Vick to collaborate with others to form the North American Apiotherapy Society (NAAS). The society’s annual symposia in the Washington, DC/Baltimore, MD area brought together researchers studying the health benefits of bee venom.

In the 1980s venom research declined as a topic of scientific study, and the NAAS ceased its operations, yet interest in bee venom and other products of the hive did not come to an end. The year 1989 marked the establishment of a nonprofit membership organization, the American Apitherapy Society, whose mission was to promote and teach the use of honeybee products to maintain and improve health, and to alleviate pain, suffering, and disability.

Like its predecessor, the AAS held scientific symposia, as well as workshops and annual meetings. One of the AAS’s founding members was Charles Mraz, a world-famous beekeeper and the pioneer of bee venom therapy in the United States. Charlie initiated clinical research with scientists at the Sloan-Kettering Institute and the Walter Reed Army Institute of Research. He also worked for the U.S. Food and Drug Administration to establish the standard for purity for dried whole venom, and he was the supplier of venom to pharmaceutical companies throughout the world.

In its early years the AAS began promoting not only bee venom therapy but also the use and study of other honeybee products. Noteworthy events of the 1990s included substantial publicity surrounding Charlie Mraz’s work; several AAS members’ trip to China to visit apitherapy clinics and meet with local practitioners; the launch of a website and a quarterly newsletter, Bee Well (successors were Bee Informed and the current Journal of the AAS); and the creation of an annual apitherapy training course (subsequently supplemented by a conference), the Charles Mraz Apitherapy Course and Conference, or CMACC, held in cities around the United States.

More recently the AAS has revised its website, integrating modern technology in the effort to educate about and promote apitherapy to the general public, to health care professionals and scientists, and to our members. CMACC is now a one -day basic apitherapy course, followed by a day and a half of a more advanced curriculum. The event is providing an increasingly thorough, scientific examination of apitherapy and coverage of new topics, including propolis and cancer, sports injuries, and veterinary apitherapy.

The American Apitherapy Society. Inc. (AAS) is a tax exempt, nonprofit membership corporation that educates the public and the health care community about the traditional and the scientifically valid uses of apitherapy for maintaining and enhancing well-being in illness and injury.

The American Apitherapy Society, Inc.
- Assembles information on apitherapy and collects data on the administration of and reactions to hive products.
- Advises the medical and scientific communities and the general public, both national and international, about apitherapy through this Journal; a website; and courses, conferences, and workshops.
- Maintains a network of people involved with apitherapy as apitherapists, beekeepers, and patients.
- Establishes guidelines for the professional conduct of apitherapists.
- Educates the public on the use of hive products to promote health.
- Statements made in this Journal have not been evaluated by the U.S. Food and Drug Administration and are not intended to diagnose, treat, cure, or prevent disease.
- These statements are provided as teaching for informational purposes only; they are not intended as a substitute for advice from a physician or other health care professional. Testimonials published here are based on individual experience and do not constitute a suggestion that another person will or can achieve the same results.
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EDITOR Deborah Klughers

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Happy 30th Anniversary to the American Apitherapy Society! To all of you who have been on this journey with AAS through the years, Thank You! And for all of our new members, Thank You too! Without our membership, we are but a few passionate apitherapists, busy beekeepers, and knowledgeable patients, buzzing along trying to introduce others to the healing power of the products of the hive; products that the honey bees so freely provide, even if it kills them!

And like the honey bees, we can’t do it alone. Each honey bee in a colony is comparable to a cell in a body. Although integral to the overall functioning, a single cell, or a lonely honey bee will die on its own. There is a critical number of honey bees that are necessary for colonies to not only survive, but to thrive. Once that threshold is met, many bees become available to forage outside the hive; to bring back sustenance to the workers within; to nourish the nurse bees, the comb builders, the queens attendants, and guards.

Those who leave the warm familiar confines of the hive, who step out of their comfort zone into mysterious and often dangerous places to ensure that future generations will be nourished and cared for, are the trailblazers, the leaders, the risk takers, and the ones who will ensure the survival of the colony and future generation as well. This is exactly what is happening at the AAS!

Please take a few moments to read our new AAS President’s letter, as well as his introduction that follows, and you will see that the direction the AAS is heading will require many workers bees to help us succeed. We plan to not just survive, with few venturing outside the hive to get what we can, but to thrive, and grow, and go places unfamiliar but necessary to ensure survival and sustainability.

We must take the leap, the chance, any chance we have to bring apitherapy to everyone. To do this we need you! We need your friends and your family. We need your coworkers and folks you don’t even know. I was in the airport on my way back from Apimondia a few weeks ago and saw a woman about my age struggling to walk with a few canes and too much luggage.

The next thing I knew, she was in a wheelchair behind me in the security line. I said hello, and asked if she had heard of apitherapy. She smiled and said she had not. I gave her my card and suggested she check out our website. I told her it might help her. She thanked me, sincerely, and that was that.

I hope she does look into apitherapy, because I do think it can help her. It wasn’t easy; I was a little nervous; I didn’t want to offend her; but I did want to give her information that she might be able to use someday. Maybe some day she can help us too! Ya never know unless you ask.

So, a simple interaction with a stranger in a foreign airport, will maybe, just maybe give us a new member of our hive. Our growing colony of eager workers can only help each other be the best we can be, if we offer this goodness to everyone. Please tell your friends and family about AAS and ask them to join. If you are a member, I know you are passionate about apitherapy, so go get others involved. There is nothing to loose and everything to gain! The more members we have the easier it will be to thrive. Just like in a colony of honey bees, there is power in numbers. There is also power in consistency. This consistency is what our new President discusses in his letter, and where the AAS is heading, as leaders in the apitherapy world.

Stepping onto a new path is difficult, but not more difficult than staying on an old one that does not nurture the whole. (M.Angelo)

My best to you and any bees you may keep.
Deborah Klughers
Hello Hive!!

Today is a big day for AAS, as it marks the publication of our 30th Anniversary issue of the Journal. As such, I would like to take this opportunity to introduce myself as the new AAS President. It is an honor, and a responsibility I take very seriously. For those of you who don’t know me personally, please allow me to share some of my background beyond my biography. Over the years I have worked to promote Apitherapy, and have served AAS with dedication, diligence, and benefit with multiple media events, a documentary, lectures, and a published article.

First and foremost, I am a practicing clinician with a focus on complex chronic conditions. Practicing an integrative approach, I utilize a variety of modalities to layer treatments-including Apipuncture. Secondly, I am also a patient, having utilized Bee Venom Therapy on myself for almost 20 years for chronic pain, resulting from my time in the service. Because of this, I have the unique perspective of my own personal experience, combined with the medical understanding of what venom and hive products can do. It has always been my goal to synthesize knowledge in order to legitimize what we have all already come to know, and believe my credentials are more than adequate to accomplish this goal.

For many organizations, including the AAS, moving forward has been a slow and difficult process as limitations such as time, money, and access to resources is scarce. My intention, albeit admittedly lofty, is to change that. So, I would like to share with you my vision for the AAS as we move into the future.

This is an exciting but also delicate time. As interest in natural therapies grows and we see increasing issues with things such as antibiotic resistance, microbiome alteration, failed surgeries and medication side effects, the medical community and more importantly patients are seeking answers.

Let me be frank however, I believe that without change, AAS, and in the broader scheme, natural medicine is doomed to fail. We have become marginalized for a variety of reasons, and that needs to change in order to ensure our success, both structurally as an organization, as well as philosophically in regard to the promotion of Apitherapy. To that end, myself, and our wonderful past President Frédérique Keller, along with the board have been working diligently to help guide AAS successfully into the future.

If you have not already seen it, we have redone and updated our website as a first step to spread our message. We are also trying to increase our social media presence, and attract a broader, more diverse group of followers.

Moving into to 2020 we have outlined what we believe to be a solid plan for expansion and increased legitimacy, not just for the organization, but for the “hive” to ensure we establish the AAS as the definitive organization for all things Apitherapy. Broad goals include a move towards unification and partnership with other organizations, as we believe that strength in numbers is of benefit to increase both our individual and collective missions within our community at large. To this end we have begun talks with the Biotherapeutics and Research Foundation and are establishing stronger relations with others.

We have identified lack of consistency in information and treatment methodologies from competing individuals and organizations who are promoting Apitherapy in non-scientific, poorly validated ways, but with significant followers and social media presence. To address this, we are also working on exciting changes to include more frequent regional events, and a formalized education program to ensure minimum competencies, and heightened professionalism.

At this time, it will likely include a two tiered program leading to either “Registered” status for non-medically licensed people and “Certification” for licensed medical providers. In this way we can formalize information, standards, and protocols leading to more recognized and consistent
information and data while increasing safety and In addition, we are hoping to expand the scope of the CMACC conference to become a true conference with updates and topic specific focus, as well as broadening the scope to be inclusive of health in the larger sense.

In order to accomplish all this we need your continued support. We believe these goals are attainable, and need the hive to work towards the greater good. We know you can because it has been you that has steadfastly pushed forward and it is you that we are working for.

Thank you all for allowing me the opportunity to serve as AAS President and it is my hope that I will both guide the AAS into the future and earn your respect along the way. Best regards to all.

In Health,
Dr. Chris Kleronomos, FNP; DAOM, MSc.

Currently Chris Kleronomos serves as the Comprehensive Pain Specialist for Vida Integrative Medicine. Formerly he was the Medical Director of the Fibromyalgia and Neuromuscular Pain Center, and served as Clinical Director of the Multi-Disciplinary Pain Rehabilitation Program, for Salem Hospital’s Comprehensive Pain Program

Practicing a comprehensive approach, he utilizes a variety of modalities to layer treatments incorporating the most current biomedical standards of care, with evidenced based Oriental and Natural Medicine through a Functional Medicine lens. He is board certified in Family Practice (AANP), and acupuncture (NNCAOM) and a board diplomate in Pain Management (AAPM), and Anti-Aging medicine (A4M), as well as a Professionally Registered Herbalist.

He is one of the leading experts on the application of Bee Venom Therapy and publishes and lectures on the subject around the country having served as the Vice president of the American Apitherapy Society for several years and currently is an active board member of the Biotherapeutics Research and Education Foundation.

He has been featured several times, on the television show “The Doctors”, and on “National Geographic Wild”. He has been published in the Pain Practitioner, Journal of the American Academy of Pain Management, and was a featured interview in Life Extension Magazine.

Chris Kleronomos became interested in medicine as a Corpsman in the U.S. Navy, where he served with the Marine Corps elite Special Operations Teams; Force Reconnaissance. Afterwards he studied for a master’s degree in Oriental Medicine, and completed a doctoral program focusing on oncology, chronic disease and pain management at Bastyr University. Due to his strong belief in Integrated Medicine, he continued his education to become an Advanced Practice Nurse Practitioner at Seattle University, as well as a Master of Science in Functional Medicine and Human Nutrition at the University of Western States.

Chris Kleronomos is married and has two adventurous boys following in his footsteps. His wife is a Health Psychologist specializing in cognitive behavioral training, and mind-body medicine. In his free time, he enjoys martial arts, traveling, hiking/camping, SCUBA and spending time with his family, and extended family including a giant St. Berdoodle named Buddha.
BEE VENOM: Overview of Main Compounds and Bioactivities for Therapeutic Interests

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Abstract

Apitherapy is an alternate therapy that relies on the usage of honeybee products, most importantly bee venom for the treatment of many human diseases. The venom can be introduced into the human body by manual injection or by direct bee stings. Bee venom contains several active molecules such as peptides and enzymes that have advantageous potential in treating inflammation and central nervous system diseases, such as Parkinson’s disease, Alzheimer’s disease, and amyotrophic lateral sclerosis. Moreover, bee venom has shown promising benefits against different types of cancer as well as anti-viral activity, even against the challenging human immunodeficiency virus (HIV). Many studies described biological activities of bee venom components and launched preclinical trials to improve the potential use of apitoxin and its constituents as the next generation of drugs. The aim of this review is to summarize the main compounds of bee venom, their primary biological properties, mechanisms of action, and their therapeutic values in alternative therapy strategies.

1. Generalities about Honeybees

Among honeybees, Apis mellifera (Figure 1.) is the main species used for crop pollination in the world [1]. The usage of all bee products, including bee venom and honey, dates back thousands of years as their medicinal properties were cited in religious books like the Bible and the Quran [2–4]. Apitherapy is a branch of alternative medicine that relies on the usage of honeybee products that consists of honey, pollen, propolis, royal jelly, and mainly bee venom (BV), which is also known as apitoxin [5,6].

Figure 1. Apis mellifera: Western honey bee or European honey bee. Queen honey bee (center) and worker bees.

Bee venom therapy (BVT) is the medicinal application of BV from honeybees into the human body for the treatment of some diseases, such as rheumatism arthritis [7]. This strategy has been used in alternative medicine for more than 5000 years. It consists of either indirect application, by extracting BV with an electric stimulus followed by its injection into the body or directly via bee stings [8]. (Figure 2.) The idea of using BV in the medicinal field was raised from the belief that beekeepers hardly suffer from rheumatism or joints problems.
BEE VENOM: Overview of Main Compounds and Bioactivities for Therapeutic Interests

Figure 2. Bee venom application via live honey bee. BV is produced by female worker bees and is known to contain many active components including: (i) peptides like melittin, apamin, mast cell degranulating (MCD) peptide, and adolapin, (ii) enzymes, such as phospholipase A2 (PLA2) and hyaluronidase, and (iii) amino acids and volatile compounds. Several studies assessed the therapeutic potential of these components in treating human inflammatory diseases as well as central nervous system diseases, such as Parkinson’s disease (PD), Alzheimer’s disease (AD), and amyotrophic lateral sclerosis (ALS), as well as many other conditions [9,10]. Interestingly, bee venom, in similarity to other animal venoms, has also shown beneficial anti-cancer and anti-viral potential against ovarian and prostate cancer, as well as HIV [11–14].

Bee venom is characterized by inducing allergic reactions following the sting. These reactions can take place in the skin, the respiratory track, the cardiovascular system, and the gastrointestinal system. Subsequently, severe anaphylactic shock could lead to cerebral or myocardial ischemia [15, 16]. These allergic responses are due to the presence, within the venom, of multiple protein allergens, most of which possess an enzymatic activity [9]. The major BV allergens and specific Immunoglobulin E (IgE) inducers are PLA2, melittin, and hyaluronidase. Apart from IgE-mediated mechanisms, studies suggest that allergens can also involve IgE-independent reactions, such as a bradykinin (BK) mediator, leading to various anaphylactic symptoms [17, 18]. The production of this non-immune mediator can be induced by melittin, known as a PLA2 activator that can mimic BK’s effects on tracheal tone [17, 19]. In addition, MCD-peptide or peptide 401 is able to induce an anaphylactoid reaction by degranulating mast cells [9, 20]. Beside molecular studies investigating the possible mechanisms behind inflammatory bee sting responses, many clinical studies are deeply looking into the potential use of BV for treating chronic diseases. Hence, the following parts of the review aim to highlight the primary biological properties of BV and its bioactive molecules that have potential in developing therapeutic strategies.

2. Main Compounds of Bee Venom

BV is an odorless and transparent liquid containing a hydrolytic mixture of proteins with acid pH (4.5 to 5.5) that bees often use as a defense tool against predators. One drop of BV consists of 88% of water and only 0.1 g of dry venom [10]. The latter is an extremely complex blend of peptides, including melittin, adolapin, apamin, and MCD-peptide. It also contains enzymes, most importantly PLA2, and compounds of low molecular weight like bioactive amines (e.g., histamine and epinephrine) and minerals [9].

2.1. Melittin

Melittin, a 26-residue peptide, is the main component of BV and accounts for 40–60% of its composition [21]. The carboxyl-terminal region of the peptide is hydrophilic and responsible for the lytic action, while the amino-terminal region of its sequence is predominantly hydrophobic with no lytic activity [22]. The amphipathic property of melittin makes it soluble in water in both its monomeric and tetrameric forms. It also allows melittin to be easily inserted into membranes by disrupting both natural and synthetic phospholipid bilayers. Previous studies have shown that the mechanism of action of melittin in disrupting membranes is mediated by pore formation lysing both prokaryotic and eukaryotic cells in a non-selective matter. In fact, melittin binds to membranes as monomers but acts on the membrane inclusively. Depending on its concentration, this biopeptide can induce either transient or stable pores [23]. When a transient pore is formed, only ions are able to diffuse through the membrane. However, in the case of stable pore formation, the membrane becomes permeable to relatively large molecules, such as glucose [24]. The pore formation induced by melittin is responsible of its hemolytic, anti-microbial, anti-fungal, and antitumor activities [12,25]. Lately, melittin has been shown to cause neural plastic changes along pain-signaling pathways by activation and sensitization of nociceptor cells. The mechanism involves the phosphorylation of mitogen-activated protein kinases (MAPK) as well as the activation of thermal nociceptive channels like TRPV1 (transient
receptor potential vanilloid receptor 1), ATP-gated P2X and P2Y purinergic receptors. Likewise, melittin can act as an activator of PLA2 [26]. It is also a major biologically active substance of BV that produces anti-nociceptive, anti-inflammatory, and anti-arthritic effects once administrated to the acupoint of the patient [27].

2.2. Apamin

Apamin is an 18-amino acid peptide containing two disulfide bridges. It is the smallest neurotoxin in BV [28]. This polypeptide is able to cross the blood-brain barrier and therefore it affects the central nervous system functioning via different modes of action. For example, it causes neurotoxic effects in the mammalian spinal cord, resulting in hyperactivity and seizures, as it has been shown in rats. By blocking calcium-activated K+ channels, apamin is also able to affect the permeability of cell membrane toward potassium ions (K+). In the vascular smooth muscle, the toxin is able to inhibit vascular smooth muscle cell proliferation and migration via the Akt and Erk signaling pathways [29]. This finding highlights the potential of apamin in atherosclerosis therapy strategies. Another study assessed the consequences of K+ channels sensitivity to apamin and showed that the neurotoxin can inhibit NO-induced relaxation of the spontaneous contractile activity of the myometrium in non-pregnant women [30].

2.3. Mast Cell Degranulating (MCD) Peptide

The MCD peptide, also known as peptide 401, is a BV polypeptide containing 22 amino acids with similar structure to apamin, as they both contain two disulfide bonds. It accounts for 2–3% of BV’s dry weight. The name MCD echoes the biological action in histamine release from mast cells. It is an epileptogenic neurotoxin, an important inhibitor of K+ channels, and can cause a significant reduction in the blood pressure of rats [31]. Some of MCD biological activities seem to have distinct mechanisms and may represent a good illustration of the structure function relationship. Studies describe MCD as a powerful anti-inflammatory agent and may serve as a potential candidate for the study of secretory mechanisms of inflammatory cells, such as mast cells, basophils, and leukocytes, leading to the design of compounds with therapeutic applications [32].

2.4. Adolapin

Adolapin is a basic polypeptide with 103 amino acids residues. It corresponds to 1% of the dry weight of BV. Researchers have shown that adolapin possesses anti-inflammatory, anti-nociceptive, and antipyretic effects by blocking prostaglandin synthesis and inhibiting cyclooxygenase activity [33]. The polypeptide can inhibit lipoxygenase from human platelets and may exert an analgesic effect according to Jung et al. [34].

2.5. Phospholipase A2

PLA2, the most lethal enzyme in BV, is a single polypeptide chain of 128 amino acids containing four disulfide bridges. Bee venom phospholipase A2 (bvPLA2) belongs to the group III sPLA2 enzymes and can act as a ligand for specific receptors. BvPLA2 represents 12–15% of BV’s dry weight and is extremely alkaline. BvPLA2 is a hydrolytic enzyme, able to specifically cleave the sn-2 acyl bond of phospholipids at the water/lipid interface [35]. Interestingly, its activity can be improved by melittin. This has been shown to occur during the process of erythrocyte lysis, proving the presence of synergistic action between both bvPLA2 and melittin [36,37]. In fact, it has been demonstrated that melittin helps in exposing membrane phospholipids to the catalytic site of enzymes via opening melittin-induced channels [38]. Additionally, new experimental data have demonstrated protective immune responses of bvPLA2 against a broad range of diseases, such as asthma, Alzheimer’s disease, and Parkinson’s disease [39–41]. BvPLA2 plays a neuroprotective role by inducing the microglial deactivation and reducing CD4+ T cell infiltration in the MPTP-induced mouse model of PD (MPTP: 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridin) [42].

2.6. Hyaluronidase

Hyaluronidase represents 1.5–2% of BV dry weight and is known to break down hyaluronic acid in tissues, such as in synovial bursa in rheumatoid arthritis. BV hyaluronidase allows the active components of BV to diffuse effectively into a victim’s tissue by affecting its structural integrity and increasing blood flow in the area. These two actions combine to intensify the wide spreading of the venom [43,44].

3. Bioactivities and Therapeutic Applications of Bee Venom and Its Major Compounds

3.1. Anti-Inflammatory Potential

Inflammation is a protective process for the body in response to harmful stimuli. Chronic inflammation can lead to the development of several diseases like rheumatoid arthritis (RA), diabetes, cardiovascular disease, obesity, asthma, skin diseases, and CNS-related diseases, such as PD, AD, and ALS [45].
Melittin, when administrated at high doses, causes local pain, itching, and inflammation. However, low doses of this BV compound can induce wide anti-inflammatory effects. Many reports investigated the anti-inflammatory mechanisms of melittin in different diseases such as RA and ALS [46,47]. In fact, it acts by inhibiting inflammatory cytokines like interleukin-6 (IL-6), IL-8, tumor necrosis factor-α (TNF-α), and interferon-γ (IFN-γ). Moreover, melittin decreases signaling pathways that activate inflammatory cytokines, including nuclear factor-kappa B (NF-κB), protein kinase Akt, and extracellular signal-regulated kinases (ERK1/2) in porphyromonas gingivalis lipopolysaccharide (PgLPS)-treated human keratinocytes. These findings indicate that, by blocking their primary signaling pathways, melittin inhibits inflammatory cytokines leading to a reduced inflammation in skin, skin, joint, and neuronal tissue [48].

Regarding skin diseases, a recent study by Kim et al. showed that BV reduces Atopic Dermatitis, the most common allergic chronic inflammatory skin disease [49]. In fact, the venom stimulates CD55 production by triggering ERK1/2 pathways, which leads to the alleviation of the disease’s symptoms [50]. Interestingly, a previous study by Shin et al. described the anti-inflammatory potential of bvPLA2 in skin diseases by showing that the enzyme attenuates Atopic skin inflammation through interaction with CD206 [51].

3.2. BV Application for the Treatment of Neurodegenerative Diseases

3.2.1. Parkinson’s Disease

PD is a degenerative movement disorder that leads to progressive disability in patients. The pathological hallmarks of the disease are the progressive loss of dopaminergic neurons in the substantia nigra (a basal ganglia structure found in the human brain), and the presence of Lewy bodies that contains aggregates of alpha-synuclein, a widely distributed protein in the brain [52,53]. Abnormal microglial activation is also a pathological sign in different neurodegenerative diseases, including PD [54]. Many preclinical trials investigated the effect of BV on the migration of leukocytes or microglial activation in animal and cellular models. Other tests evaluated the neuroprotective potential of BV acupuncture therapy (BVA) against rotenone-induced oxidative stress, neuroinflammation, and apoptosis in PD mice models [55]. Rotenone is a pesticide that may affect pathophysiological mechanisms that are implicated in PD [55]. Interestingly, BV proved its ability to prevent dopamine depletion after the administration of rotenone. In addition, the locomotor activity was re-established after treating PD mice models with BV. The treatment effectively repressed DNA damage and inhibited the expression of the apoptotic Bax, Bel-2, and caspase-3 genes in the brain of PD mice. These findings demonstrate that BV normalized all the apoptotic and neuroinflammatory markers and restored brain neurochemistry after rotenone injury [56]. It has also been shown that BV can protect dopaminergic neurons from degeneration in experimental PD models. Along with this finding, acupoint stimulation of lower hind limbs with BV was found to be protective in the MPTP (1-Methyl-4-Phenyl-1,2,3,6-TetrahydroPyridine) mouse model of PD [57].

3.2.2. Alzheimer’s Disease

AD is the most common neurodegenerative disease and many pathological processes are involved in its emergence [58]. However, the hypothesis of amyloid cascade and the toxicity of amyloid beta (Aβ) peptides have dominated research so far due to advanced studies showing that aggregates of this peptide are characteristic signs of the disease [59–61]. Although the etiology of AD remains unknown, the evidences suggest that inflammatory responses may play a crucial role in its pathogenesis [62,63]. The current treatments for cognitive loss related to AD rely on the usage of muscarinic or nicotinic receptor ligands and the acetylcholinesterase (AChE) inhibitor [64]. As an alternative strategy, Ye et al. showed that bvPLA2 can be used as a treatment to block the progression of AD in transgenic mice [40]. This is due to the ability of bvPLA2 to reduce the accumulation of Aβ and improve cognitive functioning in mice brains. The same study similarly shows that bvPLA2 can increase glucose brain metabolism and reduce neuroinflammatory responses in the hippocampus, which can limit AD pathogenesis [40]. A recent study also showed that regulatory T-cells populations could be modulated by bvPLA2 treatment in a 3xTg-AD mouse model. Therefore, authors suggested a new therapeutic approach to reduce the progression of AD by combining bvPLA2 treatment along with Aβ vaccination therapy to prevent its adverse inflammatory response [60].

3.2.3. Amyotrophic Lateral Sclerosis

ALS is a CNS disease that causes the death of motor neurons [65]. A significant trait of ALS is the abnormal accumulation of mutant SOD1 (mtSOD1)
protein aggregates [66]. A mice model of ALS carrying the mutated mtSOD1 gene with a Glycine to Alanine substitution (SOD1G93A) was characterized by Jaarsma et al., facilitating the understanding of ALS etiology [67]. Both in vitro and in vivo studies using the mutant SOD1 transgenic mice demonstrated various cellular pathogenic events in motor neurons like protein misfolding, dysfunction of mitochondria, and accumulation of neurofilament [67]. Interestingly, BV showed some potential for counteracting this disease. In fact, the administration of BV, at a precise and symptomatic stage of the progression of ALS, leads to an increase in motor activity in SOD1G93A mutant mice and a prolongation in life expectancy when compared with age-matched control mice. This could be caused by the blockage of activated microglia usually found in mice models of ALS [68]. Another study demonstrated that bee venom acupuncture (BVA) at ST36 inhibits neuroinflammation in the spinal cord of symptomatic ALS mice by significantly reducing the levels of inflammatory proteins like TLR4, CD14, and TNF-α [69].

3.3. BV and/or Melittin Applications in Cancer

The use of apitoxin, especially its main compound melittin, as a novel cancer-treatment strategy has gained wide importance recently [70,71]. In fact, melittin is known to be a nonspecific cytolytic peptide that can attack the lipid bilayer, thus leading to a significant toxicity when injected intravenously [72]. Nevertheless, many optimization approaches, including the use of nanoparticle-based delivery of melittin, have been exploited. Remarkably, the crude BV as well as melittin have shown antitumor activities against different cancer cell types including breast, liver, leukemia, lung, melanoma, and prostate cancer cells [70,72–75]. Wang et al. [76] investigated the mechanism behind melittin antitumor activity and showed that melittin can induce apoptosis of hepatocellular carcinoma cells (HCC) through the activation of the CAMKII-TAK1-JNK/p38 signaling pathway (CAMKII: Ca2+/calmodulin-dependent protein kinase; TAK1: Transforming growth factor-beta-activated kinase 1; JNK/p38: Mitogen-activated protein kinases). Moreover, melittin can sensitize TRAIL-resistant HCC cells (TRAIL: Tumor necrosis factor-related apoptosis-inducing ligand) to TRAIL-induced apoptosis, probably via activating the CAMKII-TAK1-JNK/p38 pathway and inhibiting the IKK-NF_B pathway (Figure 3). These findings are in agreement with the activation of calcium channels by melittin that leads to the increase of intracellular Ca2+ concentration and the activation of calcium sensitive CaMKII, as seen also in Figure 3 [76].

Park et al. [13] also reported that BV and its major component, melittin, induce an inhibition of cancer cells growth both in vitro and in vivo via the activation of caspases (3 and 9) pathways and the inhibition of NF-κB signaling and its downstream proliferative and anti-apoptotic gene products like Bcl-2, cIAP-2, iNOS, COX-2, and cPLA2 (Figure 3) [13]. Similarly, Zheng et al. [77] demonstrated that BV exerts an anti-proliferative effect and induces apoptosis via the activation of death receptors (DR4 and DR5). Another interesting finding emerged about melittin by highlighting its anti-metastatic and antigrowth properties [73]. In cancer, metastasis and the invasion of malignant cells are the main reasons behind the progression of the disease. Therefore, researchers in the cancer field focus on understanding the molecular mechanisms that regulate malignant cell migration and the possible way to prevent it, as a crucial step in their fight against cancer [78,79]. In this context, it has been found that melittin inhibits in vitro and in vivo HCC cells motility by suppressing Rac1-dependent pathways [73]. On the other hand, a recent study proved that the combination of melittin with a chemotherapeutic agent like temozolomide remarkably decreases growth along with the invasion of melanoma cells, compared to conditions where TMZ or melittin were used alone [71].

These findings show the great potential of melittin in cancer treatment by acting on different key points and be further dissected. Despite the convincing data regarding specifically melittin, against a variety of cancer types, its applicability to humans remains very challenging because of its nonspecific cytotoxicity.
Current optimization methods are focusing on nanoparticle-based delivery of melittin in order to avoid such problems. Due to nanotechnology, it has been possible to develop and effectively test conjugates of melittin against a broad range of human cancer types in preclinical models [81]. Cheng et al. aimed to develop an efficient yet safe delivery system for melittin, which can reduce its hemolytic activity while conserving its cytotoxic advantages. Therefore, a dual secured nano-sting (DSNS) was designed via the combination of a zwitterionic glycol chitosan and disulfide bonds. Melittin loaded DSNS showed almost complete cytotoxic effect on many cancer cells types at very low concentrations while leaving red blood cells unharmed [82]. Furthermore, it has been shown that intravenous administration of melittin prodrug-loaded nanoparticles, using per fluorocarbon nanoparticles, in a melanoma mouse model efficiently reduced the tumor growth rate compared to saline and blank nanoparticle treatment [83].

3.4. Antiviral and Antibacterial Properties

It is well known that BV and its two major components (melittin and PLA2) present antimicrobial activities and thus can be used as complementary anti-bacterial agents [84–87]. These compounds exert their effects against bacteria by inducing pores through their membranes leading to their cleavage and then lysis [36]. Nevertheless, the antiviral effect of BV has not been mentioned much in literature. A recent study investigated BV antiviral potential and came out with interesting findings both in vivo and invitro. This study showed that BV and melittin have significant antiviral effects against numerous enveloped viruses (vesicular stomatitis virus, influenza A virus, herpes simplex virus, etc.) and nonenveloped viruses (enterovirus-71 and coxsackie virus) in vitro [88]. The study also showed that melittin protected mice that were exposed to lethal doses of influenza A H1N1 virus. Although the precise mechanism of action by which BV and melittin act as antiviral agents remains unclear, it has been confirmed that BV interacts directly with the viral surface. Moreover, BV and its componants can stimulate type I interferon (IFN), and therefore suppress viral replication in the host cell [89].

Additionally, researchers at Washington University School of Medicine in St. Louis have reported the possible application of nanoparticles loaded with melittin in destroying the human immunodeficiency virus while leaving non-infected cells unharmed. In this approach, the authors suggest a preventive strategy in which these nanoparticles are used in developing a vaginal gel that inhibits the spread of HIV. Its theoretical principle is as follows: Melittin molecules present on nanoparticles fuse with the viral envelope forming pore-like attack complexes, thus breaking the viral envelope [14]. Another study showed that bvPLA2 can also block the replication of the virus. The same team further identified the peptide sequence of bvPLA2 responsible of the inhibition of HIV replication [89–92].

4. Conclusions

The use of BV for medical applications can be traced back thousands of years. Here, the therapeutic interests of crude bee venom and/or its main compounds, particularly melittin, are discussed. The latter grants broad anti-inflammatory properties by affecting primary inflammation signaling pathways and inducing the inhibition of pro-inflammatory genes expression. BV also possesses a neuroprotective potential in neurodegenerative diseases such as PD, AD, and ALS by significantly blocking their progression and improving cognitive functioning in mice models. In terms of antitumor activity, both melittin and BV have a cytotoxic effect on cancer cells and a significant anti-metastatic activity.

Optimization approaches are currently focusing on the possible use of nanoparticle-based delivery of melittin, or even BV, in order to avoid their nonspecific cytotoxic effect. The antiviral activity of BV is also promising since BV and melittin have notable toxic effects against a broad spectrum of enveloped viruses, including the challenging HIV, and few non-enveloped viruses. Finally, the clinical application of BV therapy is still a long way ahead, but researchers believe that the ongoing work on this topic will eventually allow BV and its compounds to be considered as definitive candidates in various therapies in upcoming years.

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CHEMICAL COMPONENTS OF INSECT VENOMS

Insect venoms can vary significantly in their composition. They commonly contain a complex mix of proteins, peptides, and enzymes, as well as smaller molecular weight components. This graphic aims to give a broad overview of some of these components.

The circle surrounding each component is color-coded to indicate whether it is present in bee, wasp, hornet, or ant venom. Note that this represents a general overview, and venoms will vary from species to species.

- **Bee Venom**
- **Wasp Venom**
- **Hornet Venom**
- **Ant Venom**

**Melittin**: A peptide, and a major basic component of bee venom. Can bind to & disrupt cell membranes.

**APamin**: Can pass through the blood-brain barrier & affect the central nervous system, and block or alter neuronal activity.

**Cytokinins**: Cytokinins are plant hormones that promote cell division and growth.

**Histamine**: Causes smooth muscle contraction and dilatation of blood vessels, and increased blood flow.

**Formic Acid**: A major component of ant and bee venoms, particularly those that sting their victims rather than chew.

**Piperine Alkaloids**: Class of compounds found in bee and ant venom, and large contributors to the pain of stings.

**Lethal Doses of Venom**:
- Honey Bee: 2.8 mg/kg
- Yellowjacket: 3.3 mg/kg
- Giant Hornet: 4.6 mg/kg
- Harvester Ant: 0.12 mg/kg

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Bee Pollen for Better Sleep
by Michael Szakacs – Boynton Beach, Florida

Sleep provides an opportunity for the body to repair and rejuvenate itself. Sleep also helps us consolidate and understand the information we’ve been collecting all day long. We know that sleep is good for memory, mood regulation and growth hormone production. Growth hormone is a complex protein produced by the pituitary gland in the brain and is essential for cell regeneration and tissue repair. In order for these nightly repairs to happen we must fuel our bodies properly.

There are four stages of sleep: Light Sleep (N1); Light Sleep (N2); Deep Sleep; and Dream (or REM) Sleep. In stage 1 we experience a light transitional sleep. This is where drowsiness and sleep begin. In stage 2 chemicals produced in the brain block the senses making it difficult to be woken. Stage 3 is deep sleep where fatty acids and amino acids are needed for growth hormone production, restorative sleep, cell regeneration and digestion. Dream sleep revitalizes the memory. In this stage brain activity is very high and intense dreaming is likely to occur. Bee pollen is high in protein and is considered a “complete protein” because it contains all the amino acids needed to break down proteins. Additionally, bee pollen is known to improve mood and vitality, decrease inflammation in the body, lower stress levels, boost levels of vitamins A, C, D, and E, and provide fatty acids, amino acids and nutrients.

<table>
<thead>
<tr>
<th>VITAMIN</th>
<th>SLEEP STAGE</th>
<th>DESCRIPTION (BENEFITS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Deep</td>
<td>Growth and development, vision, maintenance of the immune system.</td>
</tr>
<tr>
<td>C</td>
<td>Dream</td>
<td>Biosynthesis of certain neurotransmitters, metabolism of protein.</td>
</tr>
<tr>
<td>D</td>
<td>Deep</td>
<td>Maintaining strong bones, needed by muscles, nerves, and the immune system.</td>
</tr>
<tr>
<td>E</td>
<td>Deep</td>
<td>An antioxidant that boosts the immune system.</td>
</tr>
</tbody>
</table>

A 53-year-old male was suffering from poor-quality sleep. He frequently woke up at 3 am to urinate; had difficulty waking up in the morning to go to work and was not able to remember his dreams. He started taking bee pollen and gradually worked up to three heaping teaspoons twice a day (approximately 40g per day). After about three weeks the results were conclusive. He was able to sleep through the night. He started waking up, fully refreshed, about 5 minutes before his alarm clock went off, as if his body was anticipating the alarm. Lastly, he was able to remember the details of his dreams. Pollen was the appropriate fuel his body and brain needed to be able to complete all the nightly tasks for both deep sleep and dream sleep.

Chemotherapy Induced Peripheral Neuropathy
Improved with Propolis
By Tina McDonald – Tiverton, Rhode Island

My Mom, Gail Aubin-Fischer, became sick in 2017, and when the diagnosis finally materialized it was devastating: stage 4 metastatic gastric/stomach cancer. Gail was managed in a palliative approach with chemotherapy and traditional Western treatment under excellent medical care at Women & Infants Hospital in Providence, RI. It was clear that it was not a curable situation from the start, but rather being managed to slow the progress of her aggressive cancer. Unfortunately Mom was unable to eat, and because of the extent of her stomach cancer, she required a nasogastric tube (NGT), placed through her nose to her stomach in order to empty her stomach contents regularly throughout the day to prevent vomiting and discomfort. She was able to sip liquids occasionally, but often...
had to be placed on mechanical suction through the tube as fluids were unable to pass through her intestines.

I had attended my first Charles Mraz Apitherapy Course and Conference (CMACC) in Redondo Beach 2016, and remembered Glenn Perry presenting on the benefits of propolis. He was a passionate speaker, and I took a good amount of notes on his lectures. I looked back, and as I had recalled, propolis was effective to shrink cancer, and specifically gastric and stomach cancers! I was excited to make this discovery, and it was easy to convince Mom to give propolis a try. As the mother of a beekeeper, she was always supportive of the bee medicine, but also she didn’t have to taste it, as it was administered directly through her NGT. She was proud to include propolis on her list of medications, and would happily explain to her medical team what propolis was. I did not have hopes that it would cure her cancer, although I was hopeful that it would shrink the tumors, or possibly even prevent them from growing or progressing further. Propolis gave us hope.

The beauty of propolis, is that it is not an “alternative” therapy, where you have to choose either chemo/Western medicine or the alternative treatment. Propolis is considered an “adjunct” therapy, supporting the body during cancer treatment and does not interfere with the treatment when given together. Many natural treatments are alternative, and not recommended with chemo or radiation. When faced with the decision it can be difficult to choose one or the other, and for my Mom it was powerful to be able to decide to add propolis to her grueling chemo regimen- to be able to say, “Hey! I want this, too!” I started researching anticancer properties of propolis and found many journals covering this subject including The Journal of Functional Foods and Clinical Reviews in Allergy & Immunology. I felt confident that administering propolis to my Mom was a beneficial thing to do.

I used water soluble Brazilian green propolis (BGP) in Mom’s treatment. BGP is the most studied propolis in scientific research, and I felt the most reliable. I was concerned about resin building up in the NGT and compromising patency of the tube. The water soluble property of this propolis was perfect for preventing complications with the tube. If Mom’s tube became blocked, it meant she needed to go to the hospital to have it replaced, which was an extremely uncomfortable experience and one that we avoided at all costs.

Mom’s propolis treatment started in March 2018, and we kept records of her other medications, responses and comments to each administration of propolis. Mom cheerfully called herself a “beesperiment” as I recorded all her reactions to the treatment. She often had stomach upset, as was common while anything was in her stomach, and sometimes had to have suction applied to the NGT to avoid vomiting. This made it difficult to determine how much propolis was being absorbed into her body, as it most likely did not move far into her intestines. Although I started with a ¼ teaspoon BGP daily dissolved in about 45cc water, I had to decrease to 1/8 teaspoon fairly quickly due to gastric upset. Within 3 days Gail noticed improved neuropathy in her feet, but we did not attribute it to propolis initially.

Gail was treated with 5FU and Paclitaxal chemotherapy drugs over her course of treatment, which caused the side effect of severe neuropathy up to her thighs.

Peripheral neuropathy symptoms include numbness, paresthesias and burning pain in all extremities, although most commonly in the feet and legs. Patients commonly report the symptoms in toes and fingers, which Mom experienced as well. I documented Mom’s comments and responses to treatment, and although she stated an improvement in her neuropathy after 3 days of treatment with propolis, it wasn’t until a month after that I started relating it to her propolis treatments. “What am I taking that is helping my neuropathy?”

In my defense, she was receiving several different medications, and improved neuropathy wasn’t the response that I had expected. Once I started putting 2+2 together, I started researching the literature. Unbeknownst to me this is a studied benefit of propolis! I found recent research from Tanta University in Egypt, and it became clear once I
made the correlation that her improved neuropathy occurred when she was able to tolerate the propolis. Mom had several falls, but benefited from improved mobility at times when she was able to tolerate the propolis treatments.

My Mom lived for 1 year after diagnosis of stage 4 stomach cancer- which was the higher end of her prognosis. It was our intention to write this testimonial together, and I am honored to share her thoughts and feelings as I recall them from our time together. Do I think propolis contributed to the longevity of her life? I can’t say that. It was my original intention, for sure. But I definitely without a doubt believe it improved her chemo induced peripheral neuropathy, improving her safety and quality of life. I am most grateful to the medicine of the honey bees.

Today is My 6-month Bee-versary!
By Lauren Rothman– Brooklyn, New York

I thought I'd give an update on how I'm doing. I responded to BVT for Lyme disease from the very first week or so, but my progress has been slow and incremental, not fast or dramatic. BVT has also been the roller coaster everyone says it is, with ups followed by downs, rinse and repeat. However, my ups are higher than they were before BVT and my lows are also higher.

I am currently only at 9 stings, which is outside of the "official" protocol, but my body has told me to go slower with the ramping so that's what I've done. I hope to get to 10 stings within the next two months or so. I detox diligently with an at-home sauna, coffee enemas, and charcoal. My diet is more or less normal and very varied, but I eat all organic and grass fed/free-range and I don't eat processed sugar or gluten.

Symptoms that are gone:
- Brain fog, inability to read or follow the plot of a TV show or movie.
- Depersonalization, derealization, and the extreme fear and anxiety they caused.
- Chronic fatigue syndrome, being bedridden and housebound.
- Irregular/missing period. (I now have a 28-day cycle.)
- Stabbing foot pain. ( Likely from Bartonella,)
- Internal vibrations, like a cell phone was going off inside my body.
- Waking up seeing stars and light shows in my eyes/brain.

Symptoms that are better but not gone:
- Fatigue and tiredness. I'm now able to walk more, ride my bike short distances and occasionally (1-2x/week) I take a yoga class.
- Fear/anxiety/panic.
- Bone and body pain.
- Muscle tightness.
- Hair loss/hair not growing.
- Itchiness all over body, internal itchiness. (Almost gone, but not totally.)

I strongly believe in BVT as my best option for making a full recovery and am committed to stinging for the full 3 years if necessary. I also have grown very fond of the bees and read about bees and beekeeping daily. I hope to have my own hive someday when I am well.
The Bees Allow Me to Manage an Injury in a Medication Free Way
By Carolyn Essaunce – Langley, British Columbia

Five years ago I was on a multi-day hike on my way down a slippery wet mountain in the Kootenay region of British Columbia, Canada, and I slipped on a boulder and shattered my left wrist. Surgery and a long recovery followed. After a year or two the strength and flexibility had finally returned. A few years later, one winter after a particularly intense season as a commercial beekeeper, I felt pain in that same wrist. I massaged it and stretched it, making it much worse!

Within a few days the pain and swelling was so bad I thought I was going to need a second surgery. I couldn’t even use it to turn the steering wheel on my truck. Remembering my apitherapy course from the Commercial Beekeeping Program I had taken at Kwantlen Polytechnic University, along with my easy access to honeybees, I decided to try BVT.

I took an older, (unlucky) bee from the inner cover of a nearby colony on a cold winter day, waited for her to bend her abdomen just right, and gently pressed her stinger against the bulge on my wrist caused by the swelling. The pain from the sting lasted about 30 seconds, but I left it in there for a full 5 minutes until the muscle attached to the venom sac stopped pulsing. The relief was instant. By nightfall, there was a bit of swelling which restricted full movement of my wrist; this lasted a day or so.

By the third day, I was driving to work and easily made the left turn I used to switch hands for in order to avoid the pain in my wrist. Mid-turn I realized I didn’t have to put my coffee down. My wrist was completely pain free, like it never happened! The swelling was gone and my wrist was completely pain free.

About twice a year the sharp pain comes back, and 1 or 2 unsuspecting bees makes the sacrifice. These girls (the bees) allow me to manage an injury that I will live with forever in a non-invasive, medication free way. I am forever grateful.
Bee Propolis for Energy and Good Health
By Cora Kuiper – Grand Rapids, Michigan
and Kristine Jacobson

I asked for a testimonial from Cora because she had been using propolis capsules since January 2019. She is in the midst of her second bout of breast cancer treatments, after a period of remission. I suggested she include the propolis capsules in order to help reduce side effects of treatment, to support and enhance her immune system, and to assist with more energy during her healing process. She has been maintaining a dose of 16 grams per day. (Kristine Jacobson)

EVENTS

October
The Romanian Apitherapy Congress, Expo, and Workshops will be held in Bucharest, Romania from October 11-14, 2019. For more details, visit apiterapie.ro/en/ or contact Dr. Stefan Stangaciu at drstangaciu@gmail.com.

November
The National University of Natural Medicine is partnering with the BioTherapeutics, Education, and Research Foundation and The American Apitherapy Society, Inc. to host a Biotherapy Conference on November 9 and 10, 2019. Learn about biotherapy treatments such as maggot debridement, leech therapy, phage therapy, service animals, and last but not least, bee venom therapy. An overview of these therapies, their clinical applications, specific evidence, and rationale for treatment will be presented through hands-on demonstrations, informative lectures, panel discussions and more. Continuing education credits are available for attending this conference! AAS's Frederique Keller and Dr. Chris Kleronomos will present on apitherapy, Dr. Patrick Fratellone will participate in a panel discussion, and Amelia Moody will be leading a practical demo.
For more details and registration information please visit career-alumni.nunm.edu .

December
The International Symposium on Apitherapy will be held from December 3-5, 2019 in Cairo, Egypt. This years theme, "Latest Innovations in Apitherapy" allows a unique platform for global experts to explore scientific collaborations and networking, with the AAS President, Chris Kleronomos as an invited guest speaker.
Contact Chris at aasoffice@apitherapy.org for more information.

January
The American Beekeeping Federation will hold its annual Conference & Tradeshow from January 8-11, 2020 in Schaumburg, Illinois. Partnering with industry experts, researchers, exhibitors, and beekeepers, ABFs annual conference offers the latest knowledge in best practices and bee health. During the Saturday workshop sessions, there are six apitherapy related offerings, with the AAS Editor Deborah Klughers presenting "Value Added Products from the Hive for Health and Wealth."
For more information visit abfconference.com .
**Frederique’s Amazing Propolis Salve/Lip Balm/Suppository Formula**

You will need a glass measuring cup, double boiler, hand blender, measuring spoons, and a mixing tool.

**Ingredients**
- 16 oz. extra virgin olive oil (other base oils can be used)
- 6 ounces pure beeswax
- 1 tablespoon propolis powder or non-alcohol extract
- 1 tablespoon raw honey
- 1/2 teaspoon rosemary extract
- 1/2 teaspoon lavender essential oil
- 1/2 teaspoon tea tree essential oil

Essential oils may be varied according to desired properties and flavor. **Do not use fragrance!**
Use less beeswax for a softer consistency.

**Directions**
Melt beeswax in olive oil in a double boiler.
Set up all the lip balm trays or pots.
To prevent scalding, let mixture cool down, then add all remaining ingredients, with essential oils last.
Use stick blender to evenly distribute.
Pour quickly and carefully into tubes or pots.
Let cool completely before capping.
Store at room temperature. In very hot weather you can store in refrigerator to prevent melting. (Bring to room temperature before use.)

Makes 25 ounces, enough for 100 lip balms or 25 one ounce pots.

---

**Soothing Facial Scrub**

**Ingredients**
- 1/4 cup oatmeal
- 1/2 cup raw honey
- 2 tablespoons olive, coconut, or sunflower oil
- 1 drop essential oil or 1/4 tsp extract*

*(Oil or extract is your choice or optional. Be sure to test a small area for sensitivity prior to first use.)*

**Directions**
Chop oatmeal into small pieces with knife or grind in a food processor.
Combine oatmeal with honey and olive, coconut, or sunflower oil.
Add essential oil or extract and mix well.
Apply to face with a circular motion. Relax.
Leave on face for 5-10 minutes then rinse with warm water.

---

**Exfoliating Face and Body Scrub**

**Ingredients**
- 1 tablespoon sea salt
- 1 tablespoon brown, white, or raw sugar
- 1/4 cup oatmeal
- 2 tablespoons olive, coconut, or sunflower oil
- 1/2 cup raw honey

**Directions**
Combine sea salt, sugar and oatmeal. Add oil and honey and mix well.
Apply to skin and gently scrub with circular motion.
Leave on skin for 10 minutes and then rinse well.
Store unused scrub(s) in an airtight container.
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BEE VENOM: Overview of Main Compounds and Bioactivities for Therapeutic Interests

BEE VENOM: Overview of Main Compounds and Bioactivities for Therapeutic Interests
