MEDICAL IMPORTANCE OF BEE PRODUCTS

Ari Ürünlerinin Tibbi Önemi

(Genişletilmiş Türkçe Özet Makalenin Sonunda Verilmiştir)

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ABSTRACT

Apitherapy had been well documented in traditional medicine for treating systemic immune diseases, allergic diseases, viral diseases and organic-specific inflammatory diseases since more than one thousand years. Apitherapy or the medical uses of honeybee products are ranged from royal jelly to bee venom. It was used by the ancient Egyptians as a homeopathic remedy for arthritis. The history of apitherapy extends back to ancient Egypt, China and Greece. Apitherapy (the term comes from the Latin apis, which means "bee."), or bee therapy. Bee venom, bee pollen, raw honey, royal jelly, wax, propolis, and bee bread are products from bees that are generally considered to have medicinal effects. These products are effective against a wide range of ailments, from arthritis and chronic pain to multiple sclerosis and cancer, although few scientific studies have proved their benefits.

Key words: Bee venom, Bee pollen, Honey, Royal jelly, Wax, Propolis, Bee bread, Medical importance

INTRODUCTION:

Apitherapy (the term comes from the Latin apis, which means "bee."), or bee therapy, is the use of honeybee venom for therapeutic purposes. Bee venom, bee pollen, raw honey, royal jelly, wax, propolis, and bee bread are products from bees that are generally considered to have medicinal effects. Bee venom (BV) has been used traditionally for the control of pain and inflammation in various chronic inflammatory diseases, including rheumatoid arthritis (RA) in Oriental medicine. Today, medical importance of honeybee products has been taken the interest of medical and biologist scientists.

The medical importance of bee products was discussed here to prove this effectiveness of such products. Propolis, the resinous product collected by honey bees from plants, is used as folk medicine since ancient time.

Propolis

During the last ten years, immunoregulatory and anti-inflammatory properties of propolis have been published. The therapeutic characteristics of propolis have been well known for a very long time. It has been used in folk medicine for different nations as early in Egypt as 3000 BC (Hegazi, 1998). It has recently become a subject of increasing interest for chemists and biologists. It had various biological and therapeutic activities.

Propolis possesses variable biological activities: antiviral activity of Egyptian propolis was investigated by Hegazi, and Abd El Hady, (1993, 1995, 1997, 2001 2003 and 2004), antibacterial (Hegazi et al., 2000; Hegazi and Abd El Hady, 2002-b); fungicidal (Hegazi et al., 2000-b). The effectiveness of propolis against Salmonella spp. and Listeria spp (Gomes et al., 2011), *Enterococcus faecalis* (Kayaoglu et al., 2011), plaque and gingivitis (Pereira et al., 2011) and acute otitis media (Marchisio et al., 2010); antioxidant (Krol et al., 1996; Basnet et al., 1997, Hegazi and Abd El Hady, 2002- a), anti-inflammatory (Marcucci, 1995), antitumor activities (Matsuno, 1995 and Hegazi et al., 1998).

Oxidation of lipids is assumed to be implicated in the pathophysiology of atherosclerosis. It has been suggested that scavenging of lipid peroxyl radicals contributes to the ant atherosclerotic effects of naturally occurring compounds such as polyphenol compounds. These compounds are capable of inhibiting lipoprotein oxidation in vitro and suppressing formation of plasma lipid oxidation products in vivo (Stocker et al., 2004). Therefore, inhibition of LDL oxidation might be an important step in preventing atherosclerosis. Humans protect themselves from reactive oxygen species, in part, by absorbing dietary antioxidants (Kamiya et al., 2004). This group of polyphenolics includes flavonoids, phenolic acids and their esters and are present in relatively high concentrations in propolis

(Greenaway et al., 1990, Abd El-Hady and Hegazi, 2002-a; Hegazi and Abd El Hady (2008). Also propolis has activation of cytokines Hegazi (2009-b).

Caffeic acid phenethyl ester (CAPE) is an active component of honeybee propolis extracts. It has several positive effects, including anti-inflammatory, anti-oxidation, anti-cancer, anti-bacterial, anti-viral, anti-fungal, and immunomodulatory effects. In particular, the suppressive effect of NF-kappaB may disrupt a component of allergic induction (Jung et al., 2008).

The detailed mechanisms of actions of propolis and its components on immune cells, however, are still unknown. Inflammatory cytokines and oxidative stress have a central role in the pathogenesis of acute pancreatitis (Büyükberber et al., 2009). Propolis has anti-inflammatory and anti-oxidant effects.

Turkish propolis samples were evaluated the immunomodulatory effect (Büyükberber et al., 2009) by using the *in vitro* model of peripheral blood mononuclear cells, neopterin, tryptophan, kynurenine and pro-inflammatory cytokines, tumor necrosis factor-alpha and interferon-gamma (Girgin et al., 2009). Propolis has beneficial influences and could be able to antagonize aluminium chloride ($AlCl_3$) toxicity (Newairy et al., 2009; Türkez et al., 2010). The effectiveness of propolis in alleviating the toxicity of propetamphos on hematological and biochemical parameters in rats (Cetin et al., 2010).

The possible radioprotective effects of propolis constituents (caffeic acid, chrysin and naringin) on gamma-irradiated human white blood cells. The polyphenolic components of propolis were able to reduce the number of necrotic cells and diminishing the levels of primary and more complex cytogenetic DNA damage in white blood cells (Benkovic et al., 2009).

Bee Pollen

Bee Pollen is one of the richest and purest natural foods ever discovered, and the incredible nutritional and medicinal value of pollen has been known for centuries. The exact chemical composition of pollen gathered depends on which plants the worker bees are gathering the pollen from. Bee pollen rejuvenates our body, stimulates organs and glands, enhances vitality, and brings about a longer life span. It has been used to enhance energy, memory and performance, although there is no scientific evidence that it does. Bee pollen is also taken to prevent hay fever.

Researchers have demonstrated that there are several substances in bee pollen that inhibits the development of numerous harmful bacteria Basim et al., (2006), Özkalp and Özcan (2010), Abouda et al., 2011 and Graikou et al. (2011). Experiments have shown bee pollen contains an antibiotic factor effective against *Salmonella* and some strains of bacteria. On the clinical level, studies have shown that a regulatory effect on intestinal function can be attributed to bee pollen. The presences of a high proportion of cellulose and fiber in pollen, as well as the existence of antibiotic factors, all contribute to an explanation for this efficacious effect. It is reported that bee pollen in the diet acts to normalize cholesterol and triglyceride levels in the blood: a reduction of cholesterol and triglycerides was observed (Al-Shagrawi (1998). Selmanoğlu et al., (2009). High-density lipoproteins (HDL) increased, while low-density lipoproteins (LDL) decreased.

Bee pollen stimulates the metabolic processes leading weight-loss. It speeds caloric burn by lighting and stoking the metabolic fires (Cheng et al., 2009). Bee pollen is an excellent prophylaxis and therapeutic treatment against all the precocious symptoms of old age. It should be considered a universal geriatric treatment in the form of a natural remedy.

Bee pollen causes an increase in physical and mental abilities, especially of concentration and memory ability, activates sluggish metabolic functions, and strengthens the cardiovascular and respiratory systems. Matkovic et al., (2010) investigated the efficacy and safety of Astragalus membranaceus (AM) in the treatment of patients with seasonal allergic rhinitis (SAR). The study revealed a significant number of positive signals indicating the therapeutic effectiveness of the HMC in patients with SAR. Also pollen activates cytokines (Hegazi, 2010). A double-blind, placebo-controlled study was conducted by Kawase et al., (2009) to examine the effectiveness of *Lactobacillus* GG (LGG) and L. gasseri TMC0356 (TMC0356) in alleviating Japanese cedar pollinosis (JCP), a seasonal allergic rhinitis caused by Japanese cedar pollen.

Royall Jely

Royal jelly (RJ) is secreted from the salivary glands of worker bees, serves as food for all young larvae and as the only food for larvae that will develop into queen bees. It is taken extensively to promote en-

ergy and good health. Also it contains around 15% aspartic acid, which is important for tissue growth, muscle and cell regeneration.

It contains a mix of vitamins, minerals, proteins and fatty acids, along with acid glycosides and sterols. It contains approximately 12% protein with 5-6% lipids and 12-15% carbohydrates. Half of the dry weight of royal jelly is made of protein. It has 17 amino acids including all 8 essential amino acids. Its B vitamin content is high. 10-Hydroxy-2-decenoic acid (10HDA), a major fatty acid component of RJ (Kim and Lee, (2010); Ito et al., (2012), is known to have various pharmacological effects: vascular endothelial growth factor induced proliferation, migration and tube formation in human umbilical vein endothelial cells (Izuta et al., 2009), antimicrobial, antitumor, antihypertensive, and immunoregulatory activity. Additionally, effects on lipid profile, insulin-like action, and neurological and estrogenic effects have been demonstrated. However, clinical trials are lacking/royal jell activate cytokines (Hegazi, 2010), liver damage (Kanbur et al., 2009).

(RJ) has several physiological effects and is widely used in commercial medical products and health foods. RJ is known as a functional food containing many useful minerals. Nakaya et al., (2007) found an anti-environmental estrogen activity of RJ. Bisphenol a (BPA) is an environmental estrogen that stimulates proliferation of human breast cancer MCF-7 cells. RJ inhibited the growth-promoting effect of BPA on MCF-7 cells, even though it did not affect the proliferation of cells in the absence of BPA. In addition, this inhibiting effect of royal jelly was heat-stable.

Kamakura et al., (2001) found that royal jelly can ameliorate the physical fatigue after exercise, and this antifatigue effect of royal jelly in mice seems to be associated with the freshness of royal jelly, possibly with the content of 5 7-kDa protein. Also it used as dietary supplementation to decrease serum lipoprotein metabolism in humans (Guo et al., 2009). RJ was shown to exhibit immunomodulatory properties. Addition to IL-4, IL-5 and IL-10, antigen-specific interferon-gamma (IFN-gamma) production by spleen cells from ovalbumin (OVA)/Alum-immunized mice is inhibited by the administration of royal jelly (RJ). Since it has been shown that both Th1 and Th2 cytokines play pathogenic roles in the generation of atopic dermatitis (AD), Taniguchi et al., (2003) suggested that royal jelly suppresses the development of atopic dermatitis –like skin lesions in PiCl-treated NC/Nga mice, possibly by a combination of down-regulating TNP-specific IFN-gamma production and up-regulating iNOS expression.

Argentinean researchers Lamberti and Cornejo, (1975) discovered that royal jelly contains globulinic acid (gamma globulin), which works like an antibiotic, increasing resistance to bacteria and viruses. Also they documented that important element in royal jelly which slow down the aging process and which appear to lower blood and liver fats and cholesterol levels in animals and normalize LDL and HDL levels in humans.

RJ prevented the myelosupression induced by the temporal evolution of the tumor and abrogated the splenic haematopoiesis observed in EAT-bearing mice. The stimulating effect of RJ was also observed in vitro on the multipotent bone marrow stem cells (Bincoletto et al., 2005).

Blum et al., (1959) found that 10-Hydroxy-Delta (2)-decenoic acid, the major component of the lipid fraction of royal jelly, exhibits antibiotic activity against many bacteria and fungi. This fatty acid is less than one-fourth as active as penicillin against *Micrococcus pyogenes* and less than one-fifth as active as chlortetracycline against *Escherichia coli*. It also slows the growth rate of *Neurospora sitophila* and some unidentified molds. Boukraâ et al, (2009) concluded that the effectiveness of RJ against *Staphylococcus aureus* and *Escherichia coli*. Their findings suggest that combined mixture of RJ and starch could be used to treat infections that are resistant to conventional drugs, at a lower cost. RJ exhibited an antimicrobial action (Boukraa, 2008) against *Pseudomonas aeruginosa* (ATCC 27853) In C3H/HeJ mice that were fed a dietary supplement of RJ for 16 weeks, the levels of 8-hydroxy-2-deoxyguanosine (8-OHdG), a marker of oxidative stress, were significantly reduced in kidney DNA and serum.

These results indicated that dietary RJ increased the average life span of C3H/HeJ mice, possibly through the mechanism of reduced oxidative damage (Inoue et al., 2003). Nomura et al., (2007) found that RJ treatment resulted in significant reduction of the sympathetic nerve-mediated vasoconstrictor response to periarterial nerve stimulation (PNS) and potentiation of the calcitonin gene-related peptide (CGRP) nerve-mediated vasodilator response to PNS, compared with that in untreated OLETF rats.

Royal jelly promoted collagen production by skin fibroblasts in the presence of ascorbic acid-2-O-alpha-glucoside (AA-2G). Koya-Miyata et al., (2004) found that 10H2DA and 10-hydroxydecanoic acid increased the collagen production in a dose-dependent manner. Furthermore, 10H2DA induced the fibroblast cell line, NHDF, to produce transforming growth factor-beta 1 (TGF-beta 1) which is an important factor for collagen production. Hattori et al., (2007) stated that the royal jelly facilitates the differentiation of all types of brain cells (neurons, astrocytes, and oligodendrocytes). On the other hand, 10-hydroxy-trans-2-decenoic acid (HDEA), an unsaturated fatty acid characteristic of RJ, increased the generation of neurons and decreased that of astrocytes from NSCs.

Takaki-Doi (2009) found the long-lasting hypotensive effect of oral administration of royal jelly protein hydrolysate (RJPH) is dependent on the MWs of its ACE inhibitory peptides and the time required digesting them. Calli et al., (2008) suggested that royal jelly is effective in increasing healing of tympanic membrane perforations in guinea pigs. Abdelatif et al., (2008) study the effectiveness and safety of PedyPhar® Ointment (a new ointment prepared from natural royal jelly and panthenol in an ointment base) in the treatment of patients with limb-threatening diabetic foot infections.

Bee Venom

Apis mellifera L. bee venom is the most studied hymenoptera allergen. Allergologists seek evidence of the effectiveness of bee venom immunotherapy as this approach is the chosen treatment for systemic allergic reactions. The effectiveness of venom immunotherapy in bee venom (BV) allergy has been well established over the past 30 years. Goldberg and Confino-Cohen (2010) concluded that bee venom immunotherapy is effective in most patients immediately after the conventional maintenance dose has been reached. In the minority of patients who are not protected with this dose, an increased maintenance dose will provide appropriate protection immediately after it is achieved. Thus, the dosage of the maintenance dose seems to be the major factor affecting protection from re-stings rather than the accumulated venom dose or the duration on the maintenance dose. Venom immunotherapy high effectively may be responsible for local and systemic allergic reactions. There is a good theoretical basis for believing that purified aqueous and purified aluminium hydroxide adsorbed (so-called depot) extracts, commercially available in Europe, have the potential to reduce the incidence of venom immunotherapy side effects (Bilò et al., 2010).

Münstedt et al., (2010) collected data on the experience of beekeepers that underwent desensitization and continued beekeeping. They concluded that this study is the first to provide data on the experience of beekeepers who continue their activity after desensitization. Their results show that desensitization can result in a complete absence of symptoms after re-exposure to bee stings. The effect of bee venom on human basophils in vitro has not been studied in detail for many reasons, including the paucity of basophils in peripheral blood, inter-individual basophil response variability and the reliability and predictability of basophil activation tests. Chirumbolo et al., (2011) conducted a brief preliminary survey of the effect of *Apis* bee venom on healthy asymptomatic (non-allergic) subjects.

A dose of an aqueous commercial extract of *Apis* bee venom as high as 10 µg/mL activated resting basophils (CD63=+80–90%, CD203c=+30%), while it inhibited the expression of CD63 (-50%) following basophil stimulation by the soluble agonists formyl-Met-Leu-Phe or anti-IgE. The activation of resting basophils appeared to be dose-related. Only when basophils were activated with an IgE-mediated agonist, did bee venom extract exhibit a possible priming mechanism at the lowest doses used only via CD63, while it was ineffective via CD203c. Autocrine interleukin-3 may play a role in the observed biphasic behavior.

Bee venom (BV), well known as a traditional Oriental medicine, has been shown to exhibit anti-arthritic and anti-carcinogenic effects. However, the molecular mechanisms responsible for the anti-inflammatory activity of BV have not been elucidated in microglia. Moon et al., (2007) investigated the anti-inflammatory effect of BV and its major component, melittin (MEL), on lipopolysaccharide (LPS)-stimulated BV2 microglia. Their findings indicate that BV and MEL exert anti-inflammatory effects by suppressing the transcription of cyclooxygenase (COX)-2 genes and proinflammatory cytokines, such as interleukin (IL)-1beta, IL-6 and tumor necrosis factor (TNF)-alpha. These results demonstrate that BV and MEL possess a potent suppressive effect on proinflammatory responses of BV2 microglia and suggest that these compounds may offer substantial therapeutic potential for treatment of neurodegenerative diseases that are accompanied by microglial activation.

Yun and Sun, (2010) assessed the effectiveness of **apipuncture** treatment for central post-stroke pain for this study two female subjects with central post-stroke pain were treated with apipuncture. They found that both patients experienced a reduction in the intensity of pain after receiving apipuncture treatment without adverse effects. Bee venom (BV) acupuncture (BVA) involves injecting diluted BV into acupoints and is used for arthritis, pain, and rheumatoid diseases. Lee et al., (2012) evaluated the evidence for the effectiveness of BVA in the treatment of musculoskeletal pain.

Bee venom acupuncture involves injecting diluted BV into acupoints and is used for arthritis, pain, and rheumatoid diseases. A meta-analysis produced suggestive evidence for the effectiveness of BVA in musculoskeletal pain management. There is insufficient evidence to allow people with MS, clinicians or policy makers to make informed decisions on the appropriate use of the many treatments on offer. Only amantadine appears to have some proven ability to alleviate the fatigue in MS, though only a proportion of users will obtain benefit and then only some of these patients will benefit sufficiently to take the drug in the long term (Brañas et al., 2000).

Bee venom acupuncture (BVA) is growing in popularity, and is used primarily for pain relief in many kinds of diseases. Lee et al., (2005) evaluate the available evidence of BVA for rheumatoid arthritis and osteoarthritis. The anti-inflammation and analgesic actions of BVA were proved in various kinds of animal arthritic models. Two randomized controlled trials and three uncontrolled clinical trials showed that BVA was effective in the treatment of arthritis.

Bee venom (BV) has been used in patients with rheumatoid arthritis, a condition characterized by rheumatoid joint destruction mediated, in large part, by matrix metalloproteinases (MMPs). Nah et al., (2008) investigated the effects of melittin, a major component of bee venom, on the production of MMPs in human rheumatoid arthritic fibroblast-like synoviocytes (FLS). Mellitin had no effect on IL-1beta- or TNF-alpha-induced MMP1 or MMP3 production and did not decrease LPS-induced secretion of MMP1. Hadjipetrou-Kourounakis and Yiangou (1988) suggest that *in vivo* honey bee venom treatment affects the production of IL-1 by macrophages directly.

An anti-inflammatory effect of BV in osteoarthritis both in vivo and *in vitro* was demonstrated. Glutamate is the predominant excitatory neurotransmitter in the central nervous system (CNS). Changes in glutamate release and uptake due to alterations in the activity of glutamate transporters have been reported in many neurodegenerative diseases, including Parkinson's disease, Alzheimer's disease, and amyotrophic lateral sclerosis. Lee et al., (2012) assess if BV can prevent glutamate-mediated neurotoxicity, they examined cell viability and signal transduction in glutamate-treated neuronal and microglial cells in the presence and absence of BV. They induced glutamatergic toxicity in neuronal cells and microglial cells and found that BV protected against cell death. Furthermore, BV significantly inhibited the cellular toxicity of glutamate, and pretreatment with BV altered MAP kinase activation (e.g., JNK, ERK, and p38) following exposure to glutamate. These findings suggest that treatment with BV may be helpful in reducing glutamatergic cell toxicity in neurodegenerative diseases.

Data obtained by Moon et al., (2007) indicated that BV and MEL possess a potent suppressive effect on proinflammatory responses; they suggest that these compounds may offer substantial therapeutic potential for treatment of neurodegenerative diseases that are accompanied by microglial activation. Abd Raboo et al., (2008) found that bee venom is effective in treatment of psoriasis, with minimal tolerable side effects. Significant reduction in both PASI score and serum level of IL-1β was observed. Meiler et al., (2008) found after multiple bee stings, venom antigen-specific Th1 and Th2 cells show a switch toward interleukin (IL) 10-secreting type 1 T regulatory (Tr1) cells. Kim et al., (2008) found that bee venom. injected i.p at doses of more than 20 microl/100g mouse once a day for 14 days inhibited the ability of inguinal lymph node cells to produce T cell cytokines interleukin-1beta,-2,-6, tumor necrosis factor-alpha and interferon-gamma.

Extension of the intervals at which maintenance venom immunotherapy is administered has been attempted for many years. For that Goldberg and, Confino-Cohen (2007) examined whether the administration of a bee venom maintenance dose at 6-month intervals is safe and efficacious. They found the administration of maintenance venom immunotherapy at 6-month intervals does not provide suitable protection in BV-allergic patients, and they should continue maintenance venom immunotherapy at the accepted 1- to 3-month intervals. Hegazi (2009-a) reviewed the role of cytokines in bee venom therapy.

The general pharmacological effects of bee venom and venom extracts on a range of physiological parameters of the central nervous system, digestive, cardiovascular and respiratory systems in rodents were investigated. A single clinical dose of bee venom was taken as 5 µg/kg when administered by intradermal or subcutaneous route to human patients. Administered bee venom to mice, rats and rabbits in doses up to 200-fold was effective clinical dose (i.e. 1,000 µg/kg). Treatment with whole bee venom (at a dose 200 times the recommended clinical dose) did not produce any significant effect on the central nervous system (as determined by general behavior, sleep induction time and duration, spontaneous activity, motor function, body temperature, or drug-induced convulsions).

Bee venom was a potent antinociceptive agent without the side effects associated with many narcotic drugs. Bee venom treatment did not affect motor activity, intestinal peristaltic function or gastric function. Additionally, bee venom did not alter blood pressure and heart rate in rats nor respiratory rates in rabbits (Kim et al., 2004)

The molecular mechanisms of apoptosis induced by BV in human breast cancer MCF7 cells were investigated (Siu-Wan et. al., 2008). BV induced morphological changes and inhibited the proliferation of MCF7 cells; both effects occurred in a dose- and time-dependent manner. Flow cytometric analysis demonstrated that BV induced the production of reactive oxygen species (ROS) and dysfunction of the mitochondrial membrane potential (¢„m), and led to cytochrome c release, an increase in the levels of caspase-9 and Poly (ADP-ribose) polymerase (PARP) and then apoptosis. It also showed that BV induced S-phase arrest in MCF7 cells which may occur through the promotion of p53, p21, p27 and the exhibition of Cdk2.

Western blotting demonstrated that BV reduced Bcl-2 and increased Bax protein levels which may have caused the changes of ¢„m. BV treatment led to ROS production up to but after treatment led to a decrease in the levels of ROS, which may be associated with the observations of BV affecting glutathion S-transferase (GST), Zn-superoxide dismutase (Zn-v SOD), Cu/Zn-superoxide dismutase (Cu/Zn-SOD) and catalase. The Comet assay also showed that BV induced DNA damage while DAPI staining also confirmed that BV induced apoptosis in examined MCF7 cells. Our results also showed that BV increased the levels of AIF and EndoG in MCF7 cells. They concluded that the data demonstrated that BV induced apoptosis via a mitochondria-dependent pathway based on the changes of ¢„m, AIF and EndoG release in MCF7 cells. It has been previously reported that bee venom (BV) can induce apoptosis in many cancer cell lines, there is no information on the effect of BV on human cervical cancer cells and its molecular mechanisms of action are not fully elucidated.

Sw et al., (2008) found that bee venom induced morphological changes and decreased the percentage of viable Ca Ski cells in a dose- and time-dependent manner. They demonstrated that BV-induced apoptosis occurs via a Fas receptor pathway involving mitochondrial-dependent pathways and is closely related to the level of cytoplasmic Ca^{2+} in Ca Ski cells. Also Sw et al., (2011) found those Bee venom-induced cytotoxic effects, productions of reactive oxygen species and Ca^{2+} and the level of mitochondrial membrane potential (ΔΨm) which were analyzed by flow cytometry. Bee venom treatment induces both caspase-dependent and caspase-independent apoptotic death through intracellular Ca^{2+} -modulated intrinsic death pathway in human bladder cancer cells (TSGH-8301 cells). Bee venom-induced cell morphological changes and decreased cell viability through the induction of apoptosis in TSGH-8301 cell were found. Bee venom promoted the protein levels of Bax, caspase-9, caspase-3 and endonuclease G. The enhancements of endoplasmic reticulum stress-related protein levels were shown in bee venom-provoked apoptosis of TSGH-8301 cells. Bee venom promoted the activities of caspase-3, caspase-8, and caspase-9, increased Ca^{2+} release and decreased the level of ΔΨm. Co-localization of immunofluorescence analysis showed the releases of endonuclease G and apoptosis-inducing factor trafficking to nuclei for bee venom-mediated apoptosis.

The images revealed evidence of nuclear condensation and formation of apoptotic bodies by 4, 6-diamidino-2-phenylindole staining and DNA gel electrophoresis showed the DNA fragmentation in TSGH-8301 cells.

An anti-inflammatory effect of BV in osteoarthritis both in vivo and in vitro was demonstrated. Glutamate is the predominant excitatory neurotransmitter in the central nervous system (CNS). Changes in glutamate release and uptake due to alterations in the activity of glutamate transporters have been reported in many neurodegenerative diseases, including Parkinson's disease, Alzheimer's disease, and amyotrophic lateral sclerosis. Lee et al., (2012)

assess if BV can prevent glutamate-mediated neurotoxicity, they examined cell viability and signal transduction in glutamate-treated neuronal and microglial cells in the presence and absence of BV. They induced glutamatergic toxicity in neuronal cells and microglial cells and found that BV protected against cell death. Furthermore, BV significantly inhibited the cellular toxicity of glutamate, and pretreatment with BV altered MAP kinase activation (e.g., JNK, ERK, and p38) following exposure to glutamate. These findings suggest that treatment with BV may be helpful in reducing glutamatergic cell toxicity in neurodegenerative diseases.

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GENİŞLETİLMİŞ ÖZET

Apiterapi uzun zamandan beri geleneksel tıpta sistemik bağışıklık hastalıklarının, alerjik hastalıkların, viral hastalıkların ve ateşli hastalıkların tedavisinde 1000 yıldan fazladır kullanıldığı kaydedilmiştir. Apiterapi ya da arı sütünden arı zehrine kadar geniş yelpazedeki balarısı ürünleri tıbbi açıdan kullanılmaktadır. Eski Mısırlılar tarafından romatizmanın tedavisinde kullanmışlardır. Apiterapinin tarihçesi Mısırlılardan tutun Çin ve Yunanlılara kadar uzanmaktır. Apiterapi (Bu kelime Latince Apis: arı anlamına gelmektedir) ya da arı terapisi arıların ürettiği Arı zehri, arı poleni, bal, arı sütü, mum, propolis ve arı ekmeği arı ürünlerinin tıbbi etkisi olduğu düşünülmektedir. Bu ürünler çok az bilimsel çalışmanın etkilerini göstermesine rağmen romatizmadan tutun kronik ağrıya, multiple sklerosize ve kansere kadar geniş bir alanda etkili olduğu düşünülmektedir. Arı zehri geleneksel olarak ağrı ve değişik kronik ateşli hastalıkların (romatizmal hastalıklar, romatoid artritid, eklem iltihabı) kontrolünde kullanılmıştır, Günümüzde arı ürünleri biyologlar ve tıbbi bilim insanları tarafından dikkate alınmaktadır. Bu geniş derlemede arı ürünlerinin tıbbi önemi tek tek ele alınmış ve etkileri tartışılmıştır. Bunlardan birisi reçineli bir madde olan Propolis olup bitkilerden toplanmaktadır. Antibakteriyel ve antifungal özelliklere sahip olup antiseptik olarak kullanımı yaygındır. Bu madde çok eski yıllardan beri halk ilacı olarak kullanılmıştır. Diğer bir madde arı sütüdür. Son 10 yılda işçi arıların tükrük bezinden salgılanmakta ve genç larvaların yegane besinini oluşturmaktadır. Arı sütü enerji ve sağlık verir. Ayrıca %15 aspartik asit içerir ve bu madde doku büyümesi, kas ve hücre yenilenmesi için çok önemlidir. Aynı zamanda vitamin karışımı, mineral, protein ve yağ asitleri içerir, rakamsal olarak %12 protein, %5-6 yağ ve%12-15 karbonhidrat içermektedir. Arı sütünün kuru ağırlığının yarısı proteinden oluşur. 17 amino asit içerir ve bunlardan 8 tanesi esansiyel amino asittir. B vitamini miktarı çok fazladır. Arı sütündeki 10 hidroksi 2-dekanoik asit temel yağ asitini oluşturmakta ve farmakolojik etkileri bilinmektedir. Diğer bir arı ürünü arı polenidir ve keşfedilen en zengin ve en saf doğal besinlerden biridir ve yüzlerce yıldan beri tıbbi önemi bilinmektedir. Polen tam içeriği işçi arıların poleni topladıkları çiçeğe bağlıdır. Arı poleni vücudumuzu gençleştirir, organlarımızı ve bezlerimizi uyarır, canlılığı attırır, yaşam süresini uzatır. Herhangi bir bilimsel çalışma olmamasına rağmen, polenin enerji, hafıza ve performans artımında kullanılmaktadır, Ayrıca arı ürünlerinin etkilerini anlatmanın yanında bu ürünler ile ilgili yapılan bilimsel çalışmalara da geniş yer verilmiştir.