Autoimmune Diseases: Investigation, Differentiation, And Treatment options

Autoimmune Diseases: Investigation, Differentiation, And Treatment options

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SYNOPSIS

INVESTIGATION

- Antibiotics vs. Antimicrobial Peptides
- Apitherapy
- Bee Venom Therapy
- Pharmacopuncture
- Apipuncture

DIFFERENTIATION

- Rheumatoid Arthritis
- Multiple Sclerosis
- Lupus

TREATMENT OPTIONS

- Therapy Strategies
- Point Logic

Antibiotics vs. Antimicrobial Peptides

- The rapid emergence of antibiotic resistant pathogens poses increasingly serious health concerns worldwide.
- Approximately 70% of bacteria that cause infections in hospitals are resistant to at least one of the antibiotics most commonly used to treat infections. [2]
- This antibiotic resistance is driving up health care costs by:
  - increasing the severity of disease
  - increasing the fatality of certain infections. [2]
- The annual cost of treating antibiotic-resistant infections in the US is estimated to be as high as $30 billion.[2]
- Sepsis is another serious medical condition resulting from severe inflammatory response to systemic bacterial infections.

Antibiotics vs. Antimicrobial Peptides

- Antimicrobial peptides (also known as natural antibiotics) comprise a large group of molecules that are capable of killing a broad spectrum of pathogens including:

  antibiotic-susceptible strains

  antibiotic-resistant bacterial strains[3]

- Antimicrobial peptides show extremely low risks of developing resistance.[3]
- Antimicrobial peptides have the capacity to bind bacterial endotoxins and neutralize bacterium-induced inflammatory response, thus treating sepsis.
- Because of the dual capability to kill bacteria and neutralize endotoxins, these antimicrobial peptides hold great promise as a new class of antimicrobial and anti-sepsis agents [4].
- Bee products, including honey, bee pollen, bee venom and propolis are antimicrobial peptides. [(1,2)]

Investigation
Apitherapy

- Overview
- Honey
- Aro-honeys
- Pollen
- Propolis
- Royal Jelly
- Bee Venom

APITHERAPY - Overview

- Emergence of antibiotic resistant strains of bacteria has confounded the current use of antibiotic therapy leading to the re-examination of honey and its by-products.
- Honey, propolis, royal jelly and bee venom have a strong antibacterial activity.
- Sensitivity of bacteria to bee products varies considerably within the product and the varieties of the same product. Botanical origin plays a major role in its antibacterial activity.
- Propolis has been found to have the strongest action against bacteria.
- Honey does not allow vegetative bacteria to survive. However, it does contain viable spores, including clostridia. Honey products should be filtered or otherwise checked for clostridia spores.

APITHERAPY

Honey

- Antiseptic/antibacterial properties
- Wound healing capacity
- Laxative
- Liver Protector

Aro-Honeys - Honey combined with aromatic essences or oils

- Honey helps in the assimilation of aromatic essences
- Honeys from specific geobotanical origins
  - Eucalyptus tree honey aids in in lungs/bronchial issues
  - Linden Honey for anxiety/sleeping difficulties

APITHERAPY

Pollen

- Pollen present in air can trigger allergies; taken by mouth can alleviate allergies
- Selenium content = detoxifying, antioxidant properties
- Anti-inflammatory effect

Propolis

- Antiviral action
- Antioxidant
- Rich in flavonoids
- Recent CRT showed Propolis extract addition to Mupirocin regimen was foiund to result in profound reduction in bacterial cell count and inflammatory response in the treatment of MRSA

APITHERAPY – Propolis

Propolis is used as by bees as a sort of mastic or bee glue not only as a building material but also to keep low concentration of bacteria and fungi in the hive .Thus, the action against microorganisms is an essential characteristic of propolis and why it is of interest to researchers. Bees collect resins from numerous different plant species; thus the chemical composition of propolis varies greatly and depends directly on the local flora and phenology of the host plants and indirectly on the locality and time of collection. It is believed that part of the substances collected undergoes chemical alteration by bee enzymes prior to incorporation in propolis, making propolis a substance considered to be of both plant and animal origin.

Honeybees frequently using propolis to reduce the size of the entrance to the hive in order to better defend it.

APITHERAPY

Royal Jelly

- Antibacterial
- Energetic
- Decreases perception of pain

Composition of Royal Jelly

Substance	Minimum	Maximum
Water	57%	70%
Proteins (N x 6.25)	17% of dry weight	45% of dry weight
Sugars	18% of dry weight	52% of dry weight
Lipids	3.5% of dry weight	19% of dry weight
Minerals	2% of dry weight	3% of dry weight

APITHERAPY- Royal Jelly

Royal Jelly is the foodstuff for queen bees that young worker bees have synthesized and manufactured within their bodies, using honey and flowerpollen as raw materials. More specifically, worker bees collect flower pollen, they knead this pollen together with honey from the flowers into a “dumpling” form that they carry back to the nest, these “dumplings” are fed to young bees for up to ten days after birth and to queen bees for life.

Queen Larva floating in Royal Jelly (FAO, 60).
Left: A 3-day old queen larva floating in royal jelly. The cell is almost ready for harvesting.
Right: A 5-day old queen larva in a newly sealed cell just before pupation; not much royal jelly is left.

APITHERAPY

Bee Venom

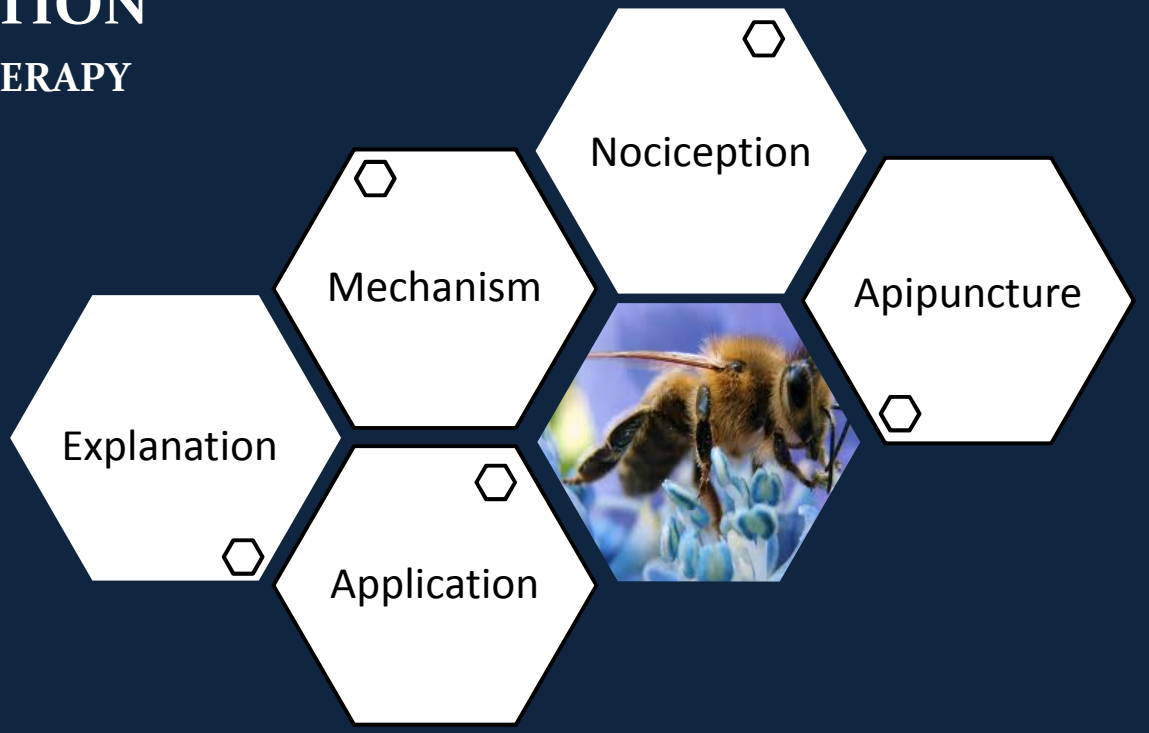
- Strong influence on nervous and circulatory systems
- Stimulates the immune system
- Anti-inflammatory properties

Class of Molecules	Component	% of Dry Venom
Enzymes	Phospholipase A2	10-12
	Hyaluronidase	1-3
	Acid phosphomonoesterase	
	Lysophospholipase	
	□-glucosidase	
Other proteins	**Melittin**	**50**
and peptides	Pamine	1-3
	Mast Cell Degranulating Peptide (MCD)	1-2
	Secapin	0.5-2.0
	Procamine	1-2
	Adolapin	
	Protease inhibitor	0.1
	Tertiapin	13-15
	Small peptides (w/less than 5 amino acids)	
Physiologically active	Histamin	0.5-2.0
amines	Dopamine	0.2-1.0
	Noradrenaline	0.1-0.5
Amino acids	t -Aminobutyric acid	0.5
	a-Amino acids	1
Sugars	Glucose & fructose	2
Phospholipids		5
Volatile compounds		

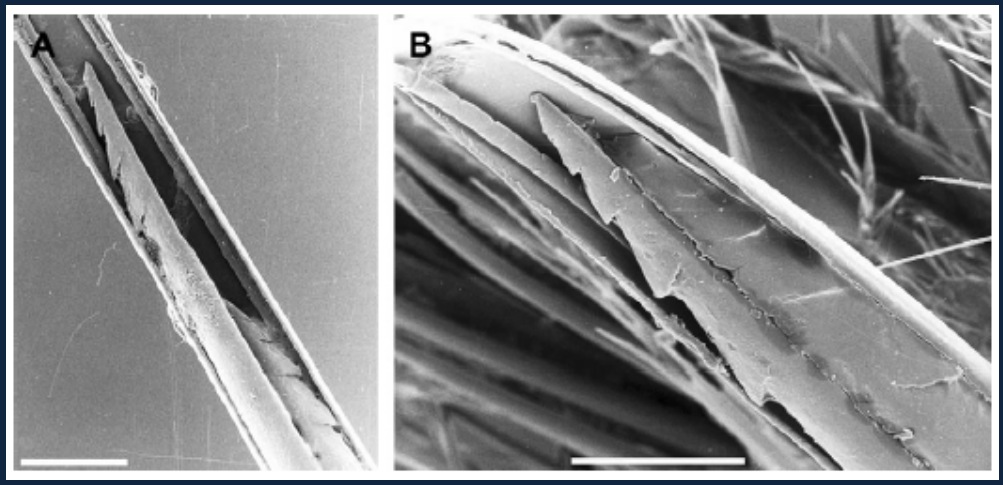
APITHERAPY – Bee Venom Therapy

Bee venom therapy (BVT) is the application of live honeybee stings to patients for therapeutic purposes. BVT is one of the most traditional complementary and alternative therapeutic methods that have long been believed to be effective in the treatment of many diseases, including rheumatic arthritis, bursitis, tendinitis, shingles (herpes zoster), multiple sclerosis, wounds, gout, burns and infections. The distinguishing feature for the application of this therapeutic approach to those disease sufferers is relief of pain and inflammation and restoration of normal body functions (Son et al., 2007). More recently, BVT is also being considered as a potential cancer treatment (Orsolic et al., 2003; Yin et al., 2005; Putz et al., 2006; Hu et al., 2006a,b,c; Liu et al., 2008b).

Investigation
Bee Venom Therapy



Investigation
Bee Venom Therapy



Venom apparatus of Osmia rufa. The two parallel lancets of the sting with backwards facing four barbs at the tip.
(Scanning Electron Microscopy-photo)

Bee Venom Therapy - Overview

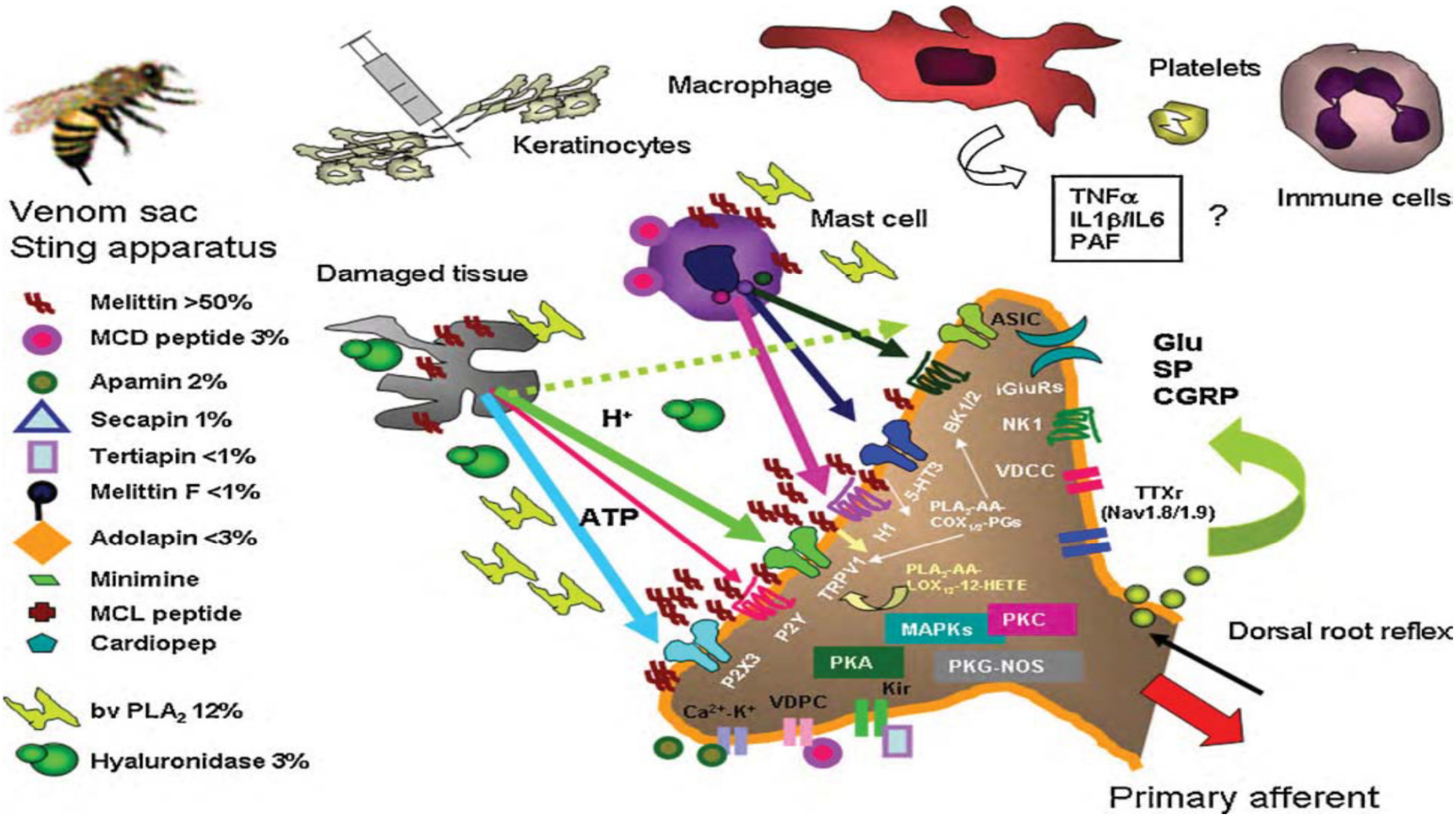
Bee venom (BV) contains a variety of peptides, including melittin, apamin, adolapin, the mast-cell-degranulating (MCD) peptide, enzymes (i.e., phospholipase [PL] A2), biologically active amines (i.e., histamine and epinephrine), and nonpeptide components which have a variety of pharmaceutical properties.

Melittin, a major peptide component of BV, has anti -inflammatory and anti-arthritis properties, and its inhibitory activity on nuclear factor kappaB (NF-κB) may be essential for the effects of Bee venom.

The anti -nociceptive effects of Bee venom have also been demonstrated in thermal, visceral, and inflammatory pain models. Acupoint stimulation (apipuncture) therapy into subcutaneous region may be important in the BV-induced anti –nociceptive effects. Multiple mechanisms, such as activation of the central and spinal opiod receptor, and α2-adrenergic activity, as well as activation of the descending serotonergic pathway have been suggested.

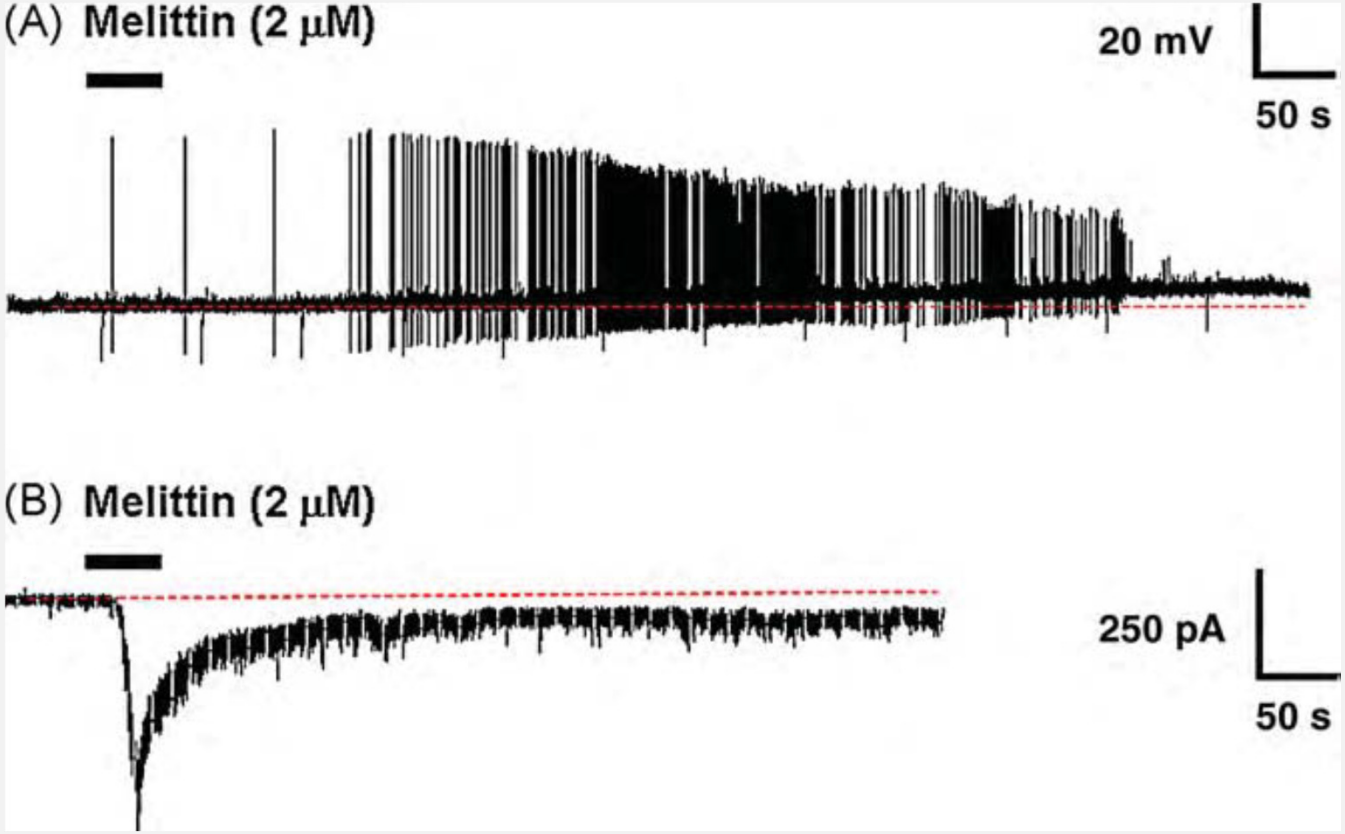
Bee Venom Therapy - Mechanism

Nociception is defined as "the neural processes of encoding and processing noxious stimuli.[1] t is the afferent activity produced in the peripheral and central nervous system by stimuli that have the potential to damage tissue.[2,3] This activity is initiated by nociceptors (also called pain receptors), that can detect mechanical, thermal or chemical changes above a set threshold. Once stimulated, a nociceptor transmits a signal along the spinal cord to the brain. Nociception triggers a variety of autonomic responses and may also result in the experience of pain in sentient beings.[3]

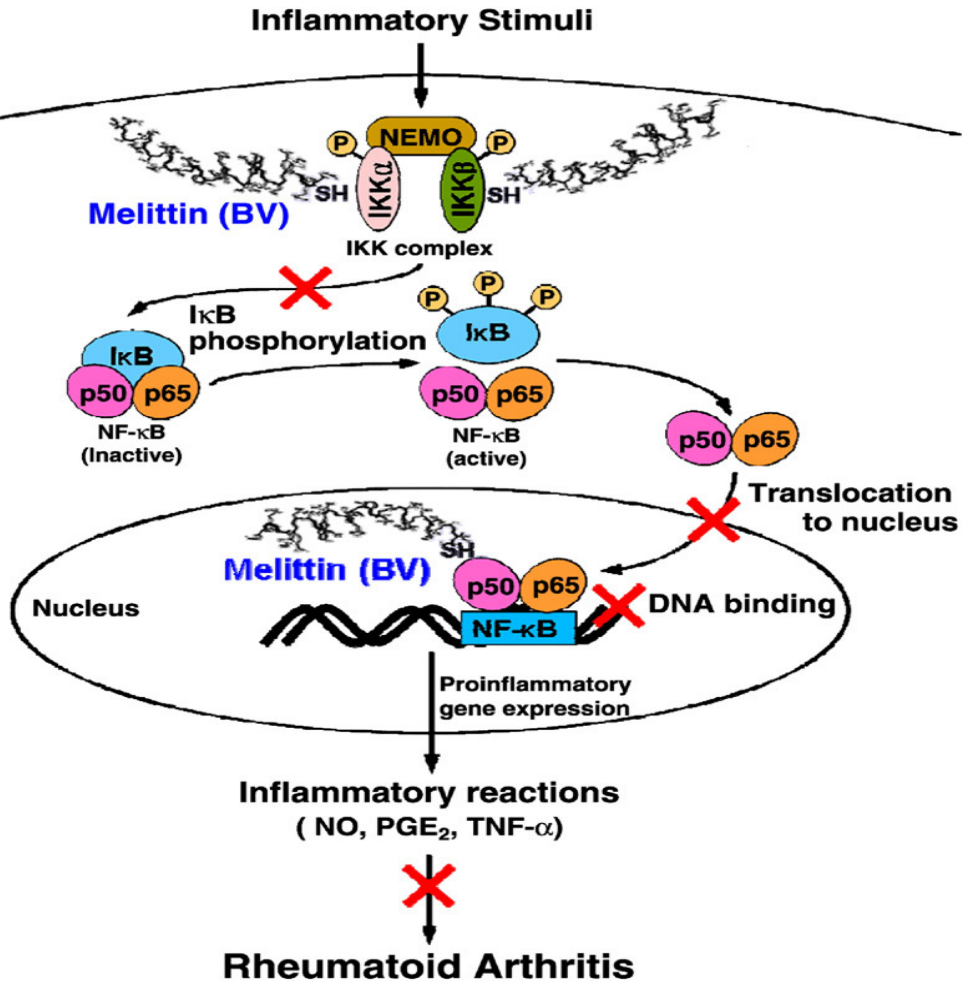

Venom sac
Sting apparatus
Melittin >50%
MCD peptide 3%
Apamin 2%
Secapin 1%
Tertiapin <1%
Melittin F <1%
Adolapin <3%
Minimine
MCL peptide
Cardiopep
bv PLA2 12%
Hyaluronidase 3%
Keratinocytes
Macrophage
Platelets
Immune cells
TNFα
IL1β/IL6
PAF
?
Mast cell
Damaged tissue
H+
ATP
ASIC
iGluRs
NK1
VDCC
TTXr
(Nav1.8/1.9)
Glu
SP
CGRP
BK-1/2
5-HT3
H1
TRPV1
P2Y
P2X3
PLA2-AA-COX1/2-PGs
PLA2-AA-LOX12-12-HETE
MAPKs
PKC
PKA
PKG-NOS
Kir
VDPC
Ca2+-K+
Dorsal root reflex
Primary afferent

Bee Venom Therapy - mechanism

Bee Venom Therapy - mechanism



Proposed anti-arthritic effect of BV (melittin). NF-κB activity is stimulated by many inflammatory stimuli. The IKK complex, which consists of the kinases IKKα and IKKβ and the regulatory subunit NEMO (also known as IKKγ), is a point of convergence for all 3 signaling pathways. The IKK complexes phosphorylate IκBα, which leads to its degradation and allows the NF-κB dimers to enter the nucleus, where they bind to the cognate DNA binding sites and activate the expression of the proinflammatory gene. Proposed anti-arthritic mechanism of BV (melittin) through its anti-inflammatory effects. BV (melittin) inhibits the release of IκB through the inhibition of IKKs. This inhibition might be due to an interaction between the sulfhydryl (SH) group of IKKα and IKKβ with BV (melittin) molecule, which results in NF-κB inactivation, and thus reduces the generation of inflammatory mediators. BV (melittin) may also interact directly with p50 of NF-κB and thereby inhibit the translocation of p50 into the nucleus. P, phosphorus; Ub, ubiquitin; NF-κB, nuclear factor-κB; IκB, inhibitor of NF-κB; IKK, IκB kinase; NEMO, NF-κB essential modulator.



Bee Venom Therapy - mechanism

Bee Venom Therapy

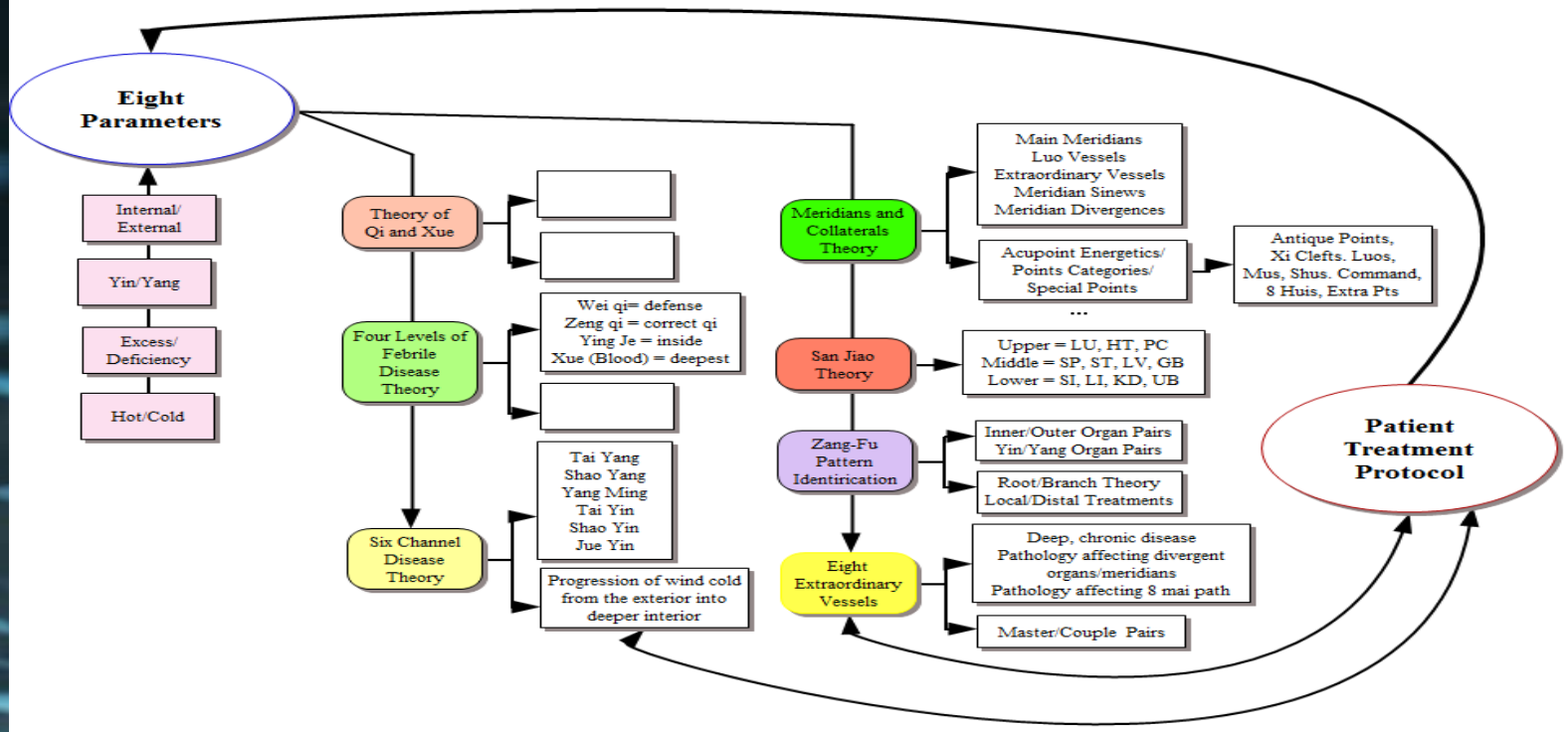
Future Considerations

Natural products may have a large variance in therapeutic components depending on their origin. Thus, the floral source of honey plays an important role on its biological properties. In consequence, it would not be surprising that the provenance of honey could determine its antibacterial properties. It is also possible that the mixing of bee products affect their antibacterial activity since those with lower antibacterial activities may mask the higher antibacterial activity of others. Bee products that are to be used for medicinal purposes have to meet certain criteria. As such, they have to be free of residual herbicides, pesticides, heavy metals, and radioactivity. They have also to be sterilized to prevent secondary infections. The problem of antibiotic residues should be highlighted. As long as beekeepers continue to use antibacterial drugs to control bee diseases, the risk of antibiotic residues in some bee products will remain. Even authorities have allowed a Maximum Residues Limit for each molecule. Consumers want honey free of residues because it is perceived as a pure, natural product. Only bee products warranted antibiotic residues free should be used for managing infections. Whichever bee product is used for medicinal purposes, consideration needs to be given to its quality. Further evidence and understanding of the antibacterial properties of hive products are needed to optimise their use in the clinical management of infections.

Differentiation

- Rheumatoid Arthritis
- Multiple Sclerosis
- Lupus

Treatment Options



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