

APITHERAPY NEW MEDICINES, SUPPLEMENTS, COSMETICS AND NEW TECHNOLOGIES

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HONEY - POWDER



► Dry or dehydrated honey.

- White, texture similar to corn flour.
- Sprayed dried into fine powder using **high heat**.
- Contains stabilizer that is made of wheat, starches or sugars such as maltodextrin and fructose.
- Commonly used as an ingredient in baking where the moisture content of recipes is limited. A 1:1 ratio is applied when replacing table sugar with the powder.
- Also popularly used as a sprinkle on cereal, puddings, biscuits, cakes, and breads.
- Has the benefit of non-stickiness, mess-free, no crystallization issues, and easy clean up.

Should we call it another form of honey when it is not made of 100% honey?



HONEY - MEDICINE

Medicinal honeys:

- excellent wound healing agent
- a good antibacterial

Defensin -1 - burns and skin infections (antibiotic resistant infections)



Activon® Manuka Honey Wound dressing selection guide

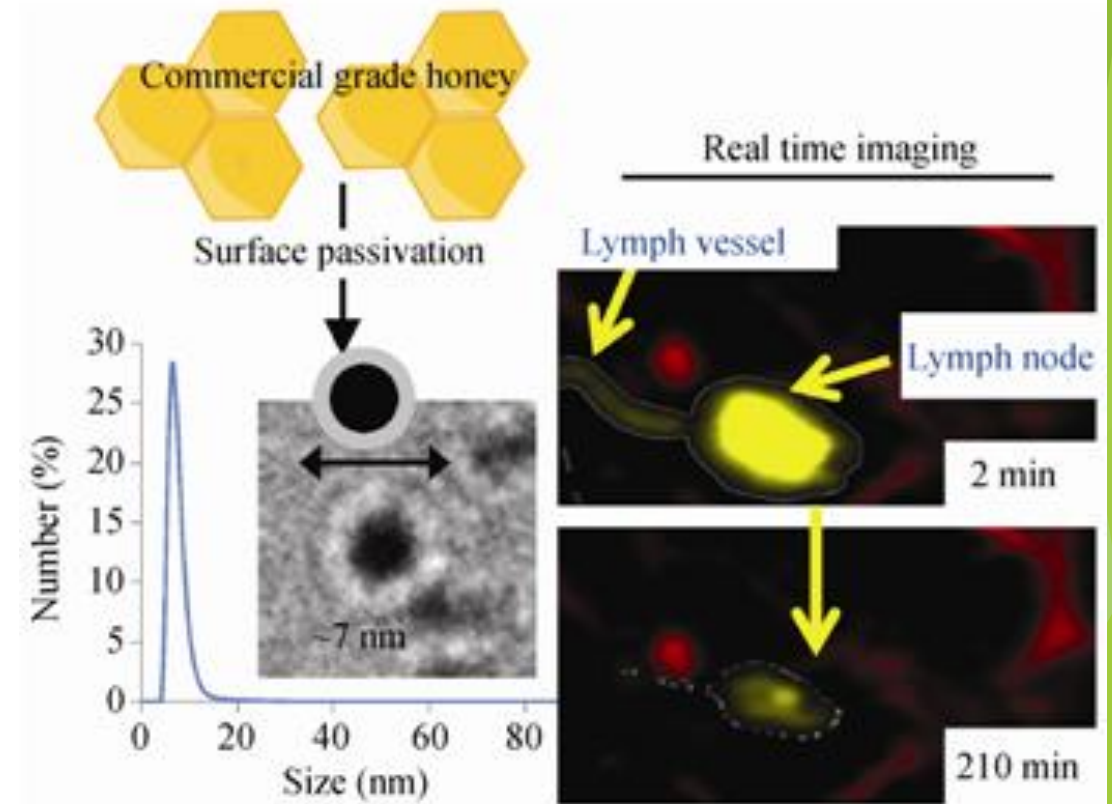
Type	Necrotic	Sloughy	Infected / Odorous	Granulating	Epithelialising
Aim	Debride <small>if needed (do not debride with active honey dressing)</small>	Remove slough	Reduce bacterial load / Eliminate odour	Promote granulation	Maintain moist environment
Product	Algivon® Algivon® Plus Algivon® Plus Ribbon Activon® Tube	Algivon® Plus Algivon® Plus Ribbon Activon® Tube	Algivon® Plus Algivon® Plus Ribbon Activon® Tube Actille® <small>in product</small>	Activon® Tube Actille®	Actille®

* because of the osmotic nature of honey, be aware that liquid can be drawn from the wound and this needs to be managed effectively with an appropriate secondary dressing, such as the Actiprep® range of super-absorbers
* pure manuka honey has no known bacterial resistance so therefore can be used to topically treat all infected wound types



HONEY USED IN NANOTECHNOLOGY

- ▶ Imaging sentinel lymph nodes (SLN) provide with critical information about the progression of a cancerous disease.
- ▶ A commercially amenable synthetic methodology for developing luminescent carbon nanoparticles from **food grade honey** with rapid clearance properties for real-time high-resolution photo-acoustic imaging.
- ▶ The naked carbon nanoparticles are derived for the first time, **from commercial food grade honey**.
- ▶ The results indicate an exceptionally rapid signal enhancement (~2 min) of the SLN.





HONEY IN COSMETICS

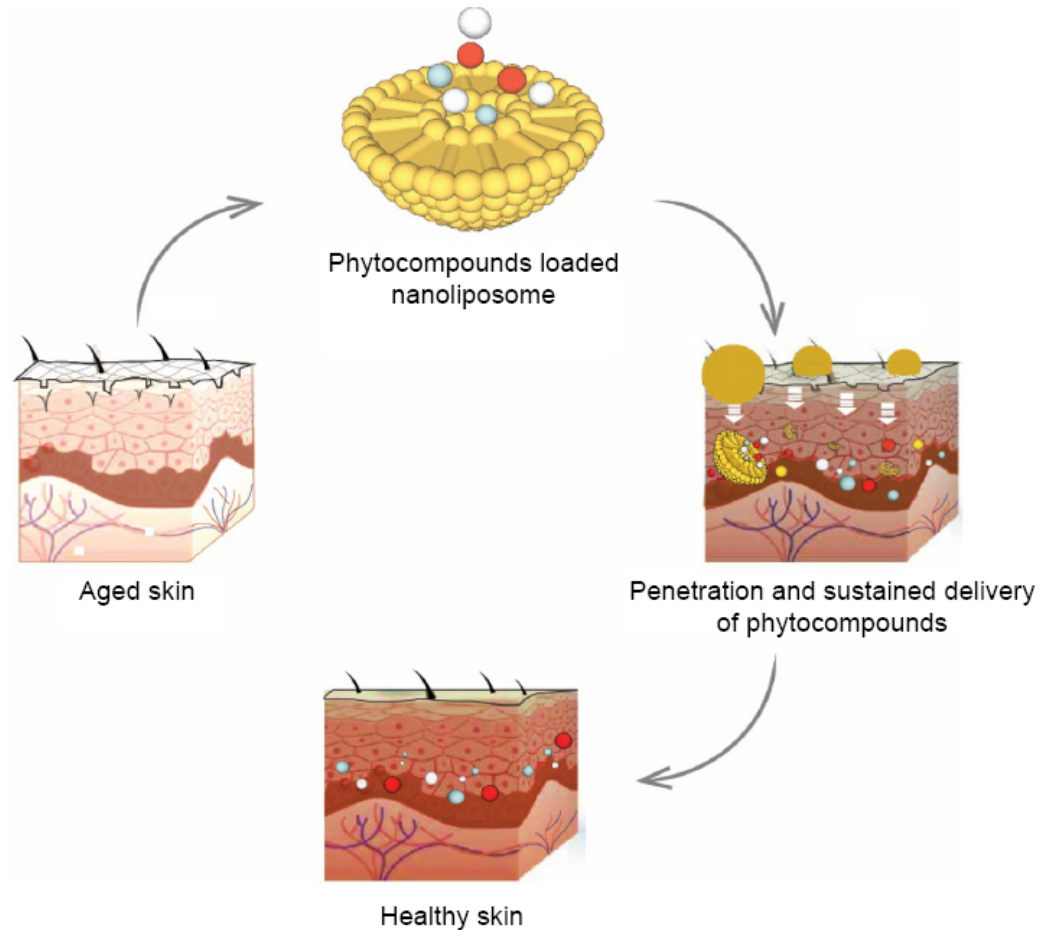


Figure 1 Nanoliposome-based delivery of antioxidants for skin wrinkles in antiaging treatment.



LAXATIV PRODUCT WITH HONEY FOR BABIES AND CHILDREN





BEE POLLEN





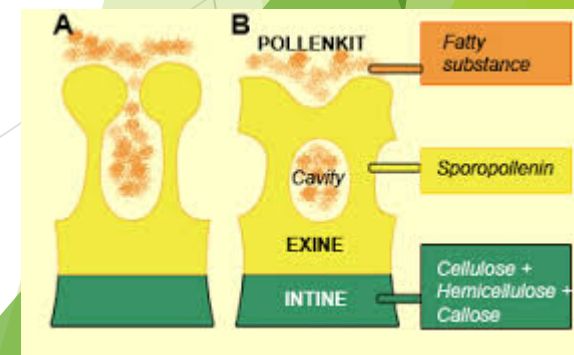
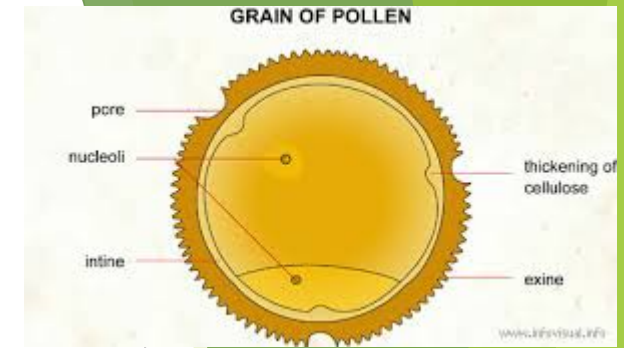
BEE POLLEN RESEARCH

Scientific research on bee pollen is directed towards:

- ✓ Development of the technology for bee pollen outer casings (exine) disruption and their removal
- ✓ Development of the technology for making rich bee pollen extract without bee pollen shells
- ✓ Study of biochemical parameters of bee pollen extract compared with raw bee pollen
- ✓ Development of the technology for oil extraction of bee pollen
- ✓ Development of the technology for waste less processing of bee pollen and development the whole range of new bee pollen health products.

Significant progress in the development of the technology for bee pollen outer casings disruption, and making active bee pollen extract.

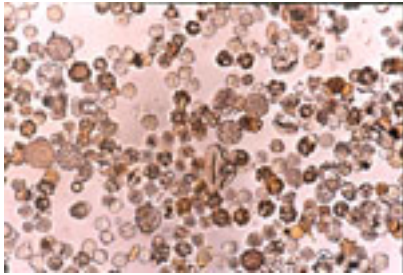
<http://www.apithealth.com/Apitherapy/Bee+Pollen+Extract.html>



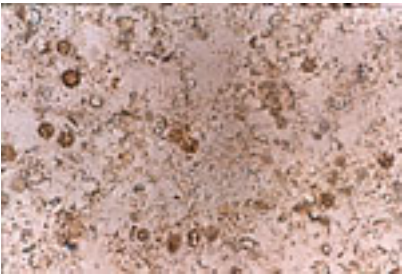


BEE POLLEN RESEARCH

Photomicrograph of pollen grains before disruption



Photomicrograph showing disrupted pollen



- ✓ High stability
- ✓ Preservation of all useful properties
- ✓ Low allergenic activity
- ✓ High concentration of the valuable nutrition components
- ✓ High digestibility
- ✓ High level of sterility

Hydroalcoholic extraction;

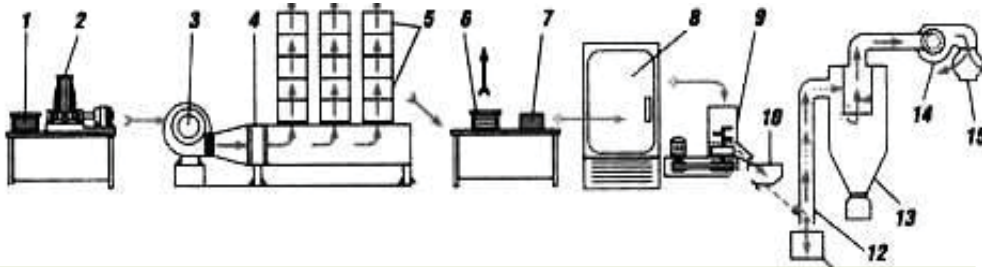
96% of the exine is disrupted

Allergic compounds at the level of the exine are removed

High degree of extraction of active bee pollen components.



BEE BREAD EXTRACTION TECHNOLOGY



Bee bread granules extraction: (1) outer layer of the bee bread granules, (2) scraping machine, (3) ventilator, (4) heater, (5) bee hives, (6) frames, (7) wax and bee bread, (8) freezer, (9) segmentation machine, (10) dosage machine, (11) container, (12) ventilation shaft, (13) cyclone, (14) ventilator, (15) dust container

- ▶ R. Akhmetova, J. Sibgatullin et al., *Procedia Engineering* 42 (2012) 1822 – 1825
- ▶ TECHNOLOGIES:
- ▶ soaking in water,
- ▶ manual extraction through vibration,
- ▶ drying;
- ▶ drying and separation of granules through vacuum
- ▶ drying; drying,
- ▶ freezing, segmentation and filtering of the wax particles.
- ▶ **ACOUSTIC DRYING**



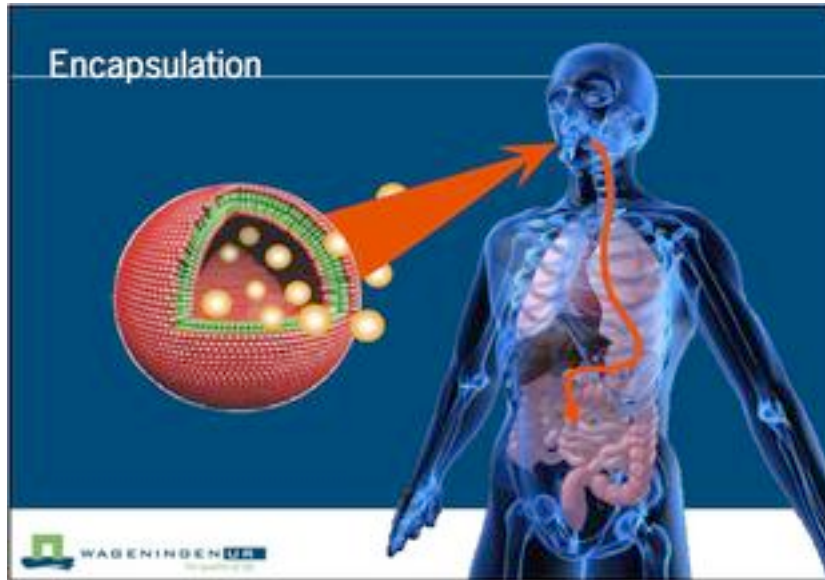
ACOUSTIC DRYING

- ▶ The equipment works the following way: Honeycombs are loaded into the dryer. Low frequency acoustic wave source is switched on. Equipment operates for several hours. Humid air is removed from the dryer.
- ▶ Frequency is held at 25 hertz. The infrasound spreads in the container with minor absorption. Harmonic waves of equal frequency and amplitude running towards each other from the source and reflected from the container walls form standing waves, which act in the process of drying more effectively. Almost 98% of bee bread is extracted, containing less than 5% of wax traces. Undamaged bee bread granules in the finished product compose 87% of total mass.
- ▶ The method for acoustic drying allows raising productivity and lowering the price of the drying equipment. Acoustic dryer includes drying container with soundproof walls, loading-unloading equipment, a source of acoustic waves, and hot air inflow equipment.

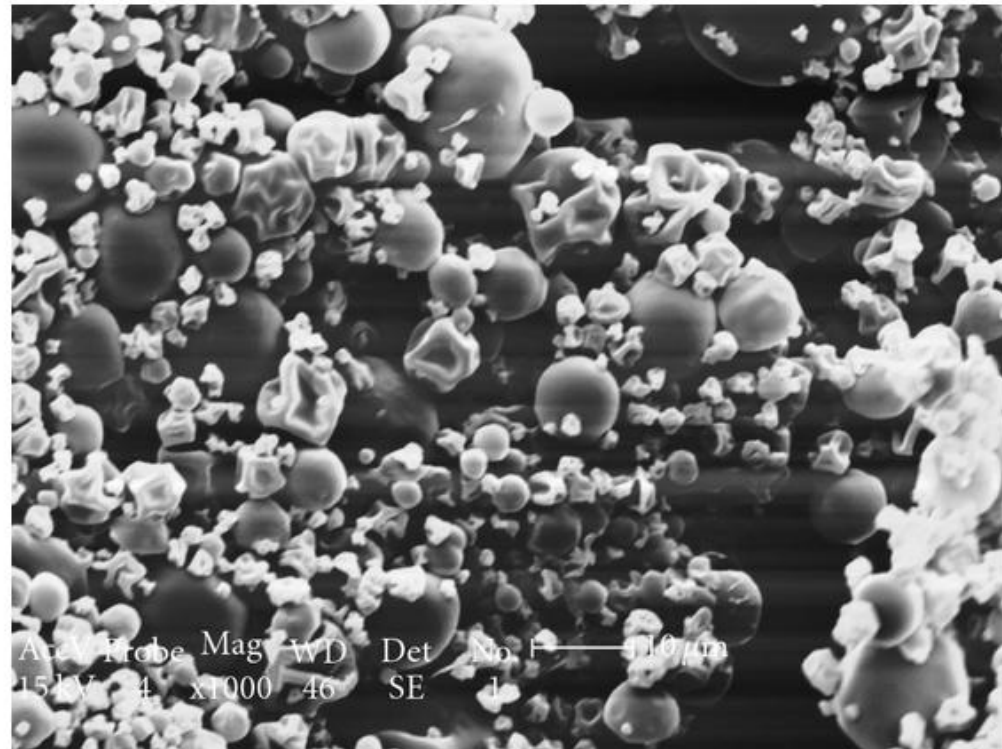




PROPOLIS



Nanoparticle6.wikispaces.com/2jet



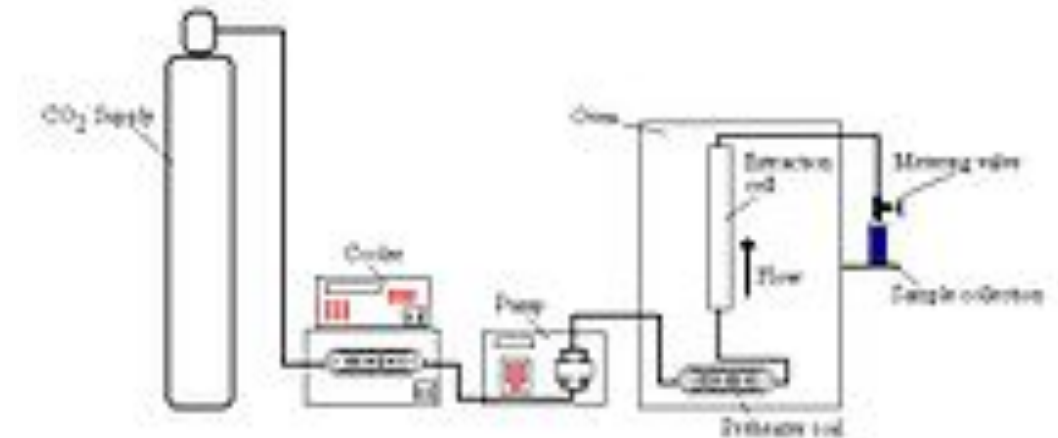


PROPOLIS EXTRACTION

Ultrasound Technology

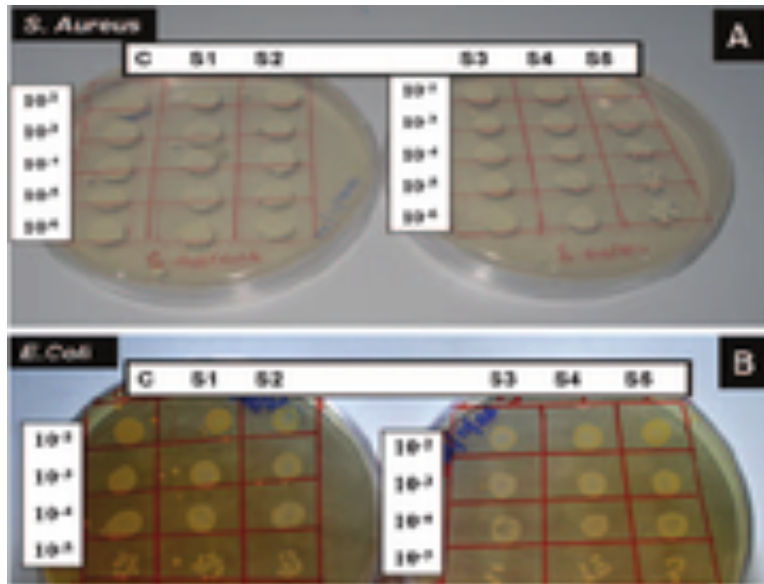
- ▶ Authors: [S. Sanpa](#), [Krit Sutjarittangtham](#), [T. Tunkasiri](#), [Sukum Eitssayeam](#), [P. Chantawannakul](#);
[Advanced Materials Research](#) (Volume 506)pp:371-374
- ▶ Method: ultrasound technology to reduce extraction time and increase extraction yields of propolis. ultrasound technology was applied for 15-60 minutes and the propolis extracts were examined to compare their biological activities.
- ▶ Result: The propolis extracted using ultrasound for 15 and 30 minutes showed inhibitory effects on tested fungi and bacteria as well as antioxidant activities.

Supercritical CO2 extraction technology





PROPOLIS TECHNOLOGY - NANOPARTICLES

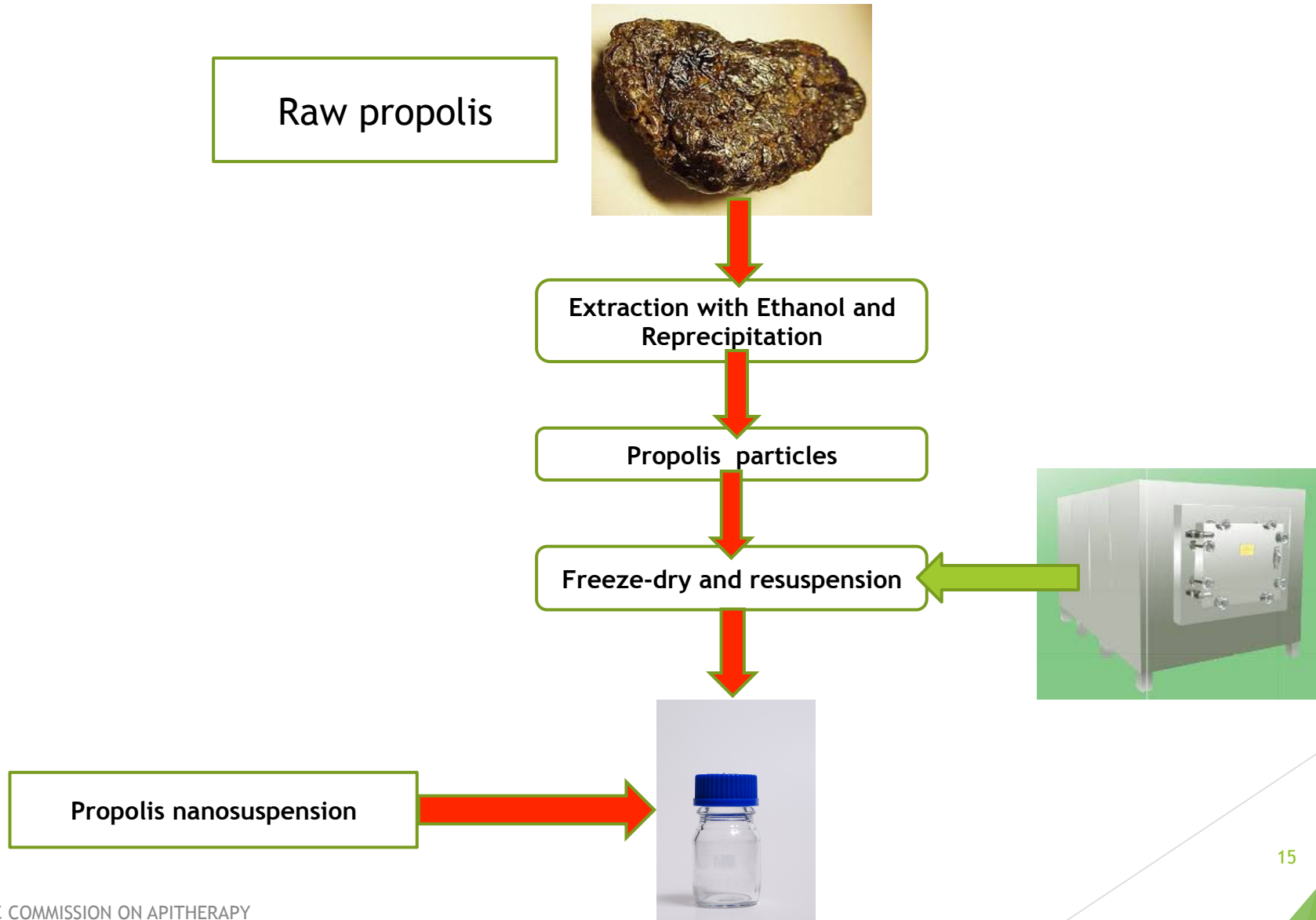


C-control
S1- 5 µg/mL of propolis nanoparticles
S2-10 µg/mL of propolis nanoparticles
S3-15 µg/mL of propolis nanoparticles
S4- 50 µg/mL of propolis nanoparticles
S5-100 µg/mL of propolis nanoparticles

- ▶ The **cytotoxicity** of propolis nanoparticles against MCF-7, A375, PC3 and PANC-1 cancer cell lines was tested using MTT assay and the minimal concentration toxic to the cancer cells were found
- ▶ The anti-microbial activity of the propolis nanoparticles was tested against Escherichia coli and Staphylococcus aureus and the minimum concentration of propolis nanoparticles that inhibit bacterial growth was found.
- ▶ The cell uptake studies of propolis nanoparticles on MCF-7 cells demonstrated internalization of the nanoparticles by the cancer cells. All these studies revealed that **propolis nanoparticles** could be a good substitute for the existing materials against cancer.



PROPOLIS NANOPARTICLES PREPARATION



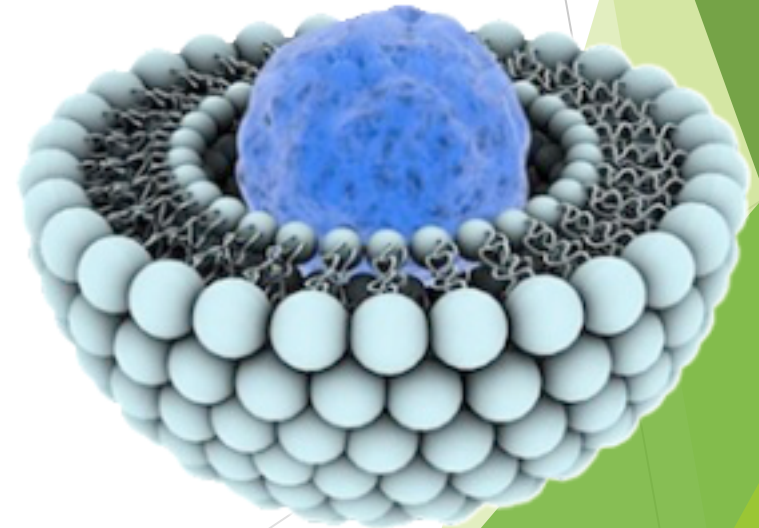


PROPOLIS LIPOSOMES

Optimization on Preparation Condition of Propolis Flavonoids Liposome by Response Surface Methodology and Research of Its Immunoenhancement Activity

- ▶ Propolis flavonoids (PF) liposome was prepared with ethanol injection method. Lecithin, cholesterol, and propolis flavonoids were dissolved in about 10mL of ethanol, and the ethanol was injected into the buffer (40°C, PBS) with a slow speed and continued to thermostatic mixing.
- ▶ Liposomes formed spontaneously after further evaporation of the residual ethanol.
- ▶ The resulting mixture is homogenized with ultrasonication for 30min to form the small single-chamber liposome (Ultrasonic Cleaner KQ5200B, Kunshan Sonicatic equipment Inc. China). Ultimately, the solution was filtered with 0.8 μm , 0.45 μm , and 0.22 μm millipore membrane successively
- ▶ Ju Yuan, Yu Lu, Saifuding Abula, et al., Evidence-Based Complementary and Alternative Medicine Volume 2013, Article ID 505703, 8 pages

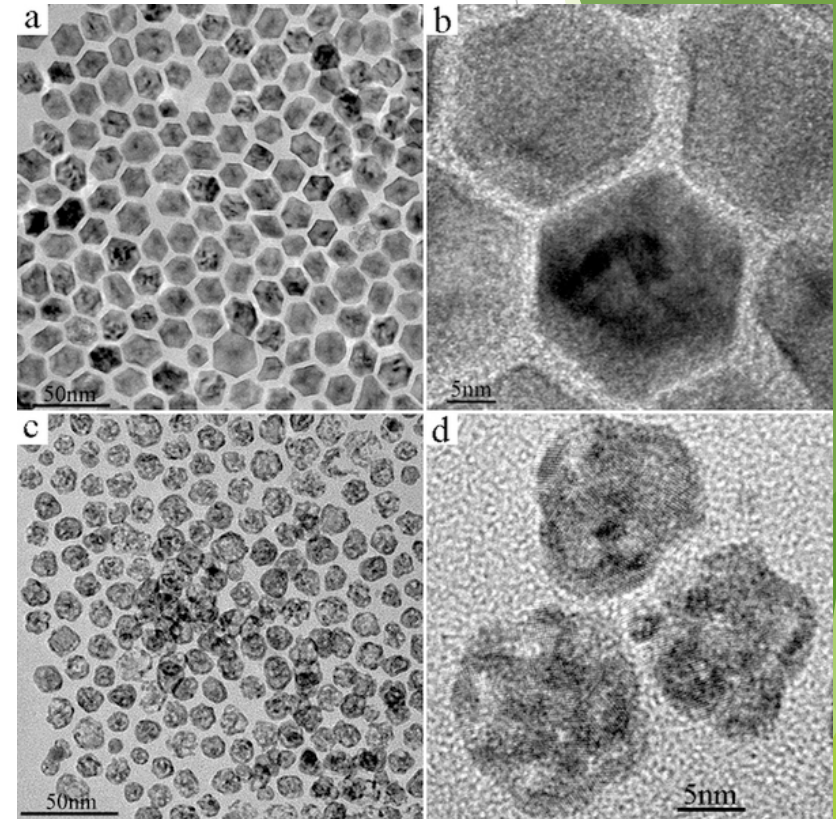
- ▶ Liposomes are microscopic spheres that have a natural affinity for living cells because their outer layers are composed of phospholipids that are virtually identical to the phospholipid composition of cell membranes





PROPOLIS LIPOSOME DRUGS

- ▶ Encapsulation efficiency is a critical factor to appraise the quantity of order to achieve high encapsulation efficiency of PFL, in the experiment the preparation conditions of PFL must be optimized.
- ▶ *In vitro*, PFL not only could significantly promote T lymphocytes proliferation singly or synergistically with PHA, but also could increase the expression levels of IL-2 and IFN- γ mRNA, demonstrated the stronger immunoenhancement activity, which provides the theoretical basis for the further experiment *in vivo*.
- ▶ PHA phytohemagglutinin





PROPOLIS SOLID LIPID NANOPARTICLES

- ▶ Propolis was used as a lipid material to prepare solid lipid nanoparticles (SLNs);
- ▶ SLNs are proposed bioactive medications for topical intranasal therapy.
- ▶ *In vitro* and *ex vivo* studies prove that drug and polyphenols do not cross the membranes; therefore, propolis-based SLNs could be used as delivery systems of diclofenac and flavonoids for the local treatment of nasal cavity diseases. Due to propolis composition, the proposed formulation could be used as a bioactive medication in which the carrier can exert a complementary effect with the loaded drug.
- ▶ Colloids Surf B Biointerfaces. 2015 Oct 31;136:908-917 Propolis as lipid bioactive nano-carrier for topical nasal drug delivery

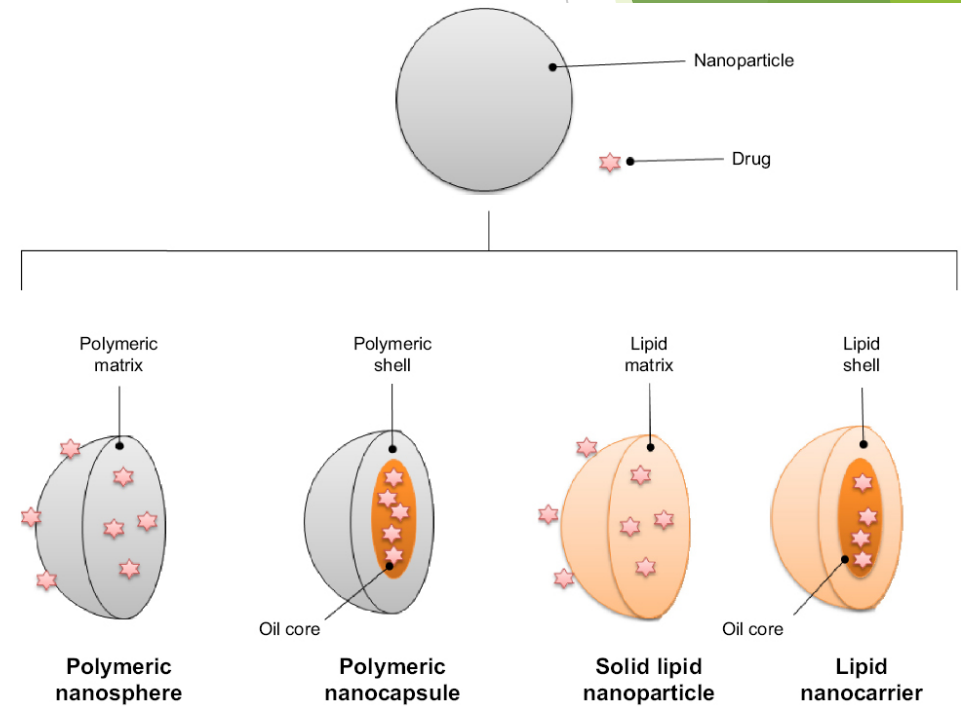


Figure 2 Schematic differences between nanocapsule, nanostructured lipid carrier, polymeric nanoparticle, and solid lipid nanoparticle drug delivery systems.



POLYMERIC NANOPARTICLES OF BRAZILIAN RED PROPOLIS EXTRACT

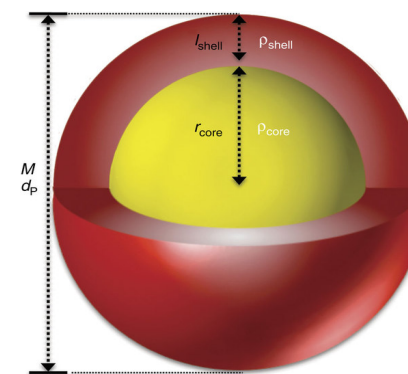
- ▶ polymeric nanoparticles loaded with red propolis extract were prepared with a combination of poly- ϵ -caprolactone and pluronic using nanoprecipitation method;
- ▶ encapsulation of the flavonoids from the red propolis extract into the polymeric matrix;
- ▶ (UPLC-DAD) identified the flavonoids liquiritigenin, pinobanksin, isoliquiritigenin, formononetin and biochanin A in ethanolic extract of propolis (EEP) and nanoparticles of red propolis extract (NRPE).



(a)



(b)





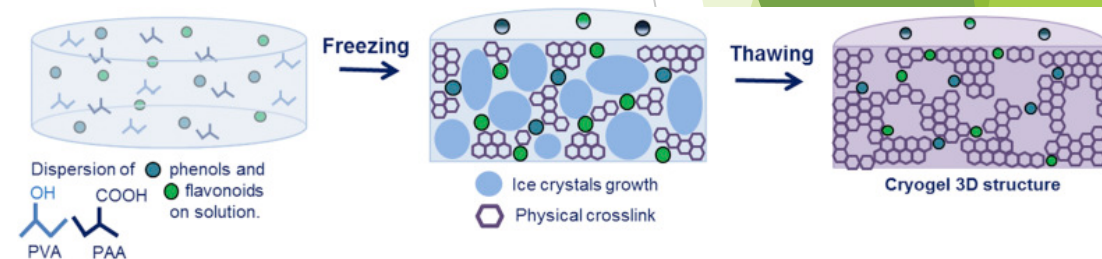
PROPOLIS HYDROGELS

► Properties of PVA Hydrogel Wound-Care Dressings Containing UK Propolis

Macromolecular Symposia Volume 368, Issue 1 October 2016
Pages 122-127 First published: 21 October 2016

Burns pose a potential threat to health, and often require dressings. PVA hydrogels present many characteristics of ideal dressings, but do not have any intrinsic antimicrobial properties. Propolis is a natural antimicrobial substance that can be incorporated in materials intended for wound-care. The goal of this work was to produce and characterize (in terms of swelling behaviour, microstructural and thermal analysis) PVA gels loaded with a UK propolis.

Propolis was loaded in the gels and it altered the crystallinity of the PVA gels. The thermal profile of the PVA-UK propolis gels was different from that of PVA gel alone. All gels presented at least ~200% of swelling degree. Weight loss as well as propolis release was high for samples with high amount of propolis.



Synthesis of propolis-loaded cryogels



PROPOLIS - GINGIVAL GEL

NANO-ANTIOXIDATIVE GEL



<http://nbfgingivalgel.ch/>

- ▶ **Nano-bio-fusion technology** (developed by NanoCureTech Institute (Institute for Nano-Bio Fusion Technology), which has formed in 2007.

it comes as a result of mixing two top technologies (on one side nano-technology, and on other Medical biotechnology)

A product that contains antioxidants in nanoemulsion state.

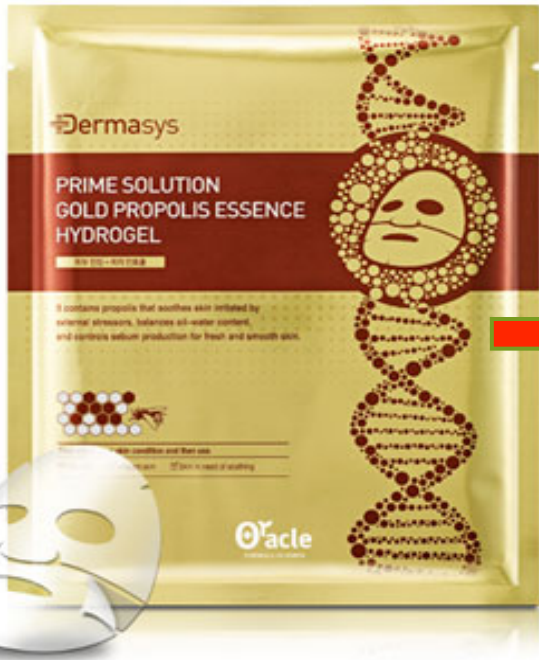
The use of topical antioxidants represents one of the main topics in medical science.

- ▶ AO may have beneficial effects on regulating fibroblast proliferation during gingival healing or periodontal repair

Propolis due to its adhesiveness and the nanoemulsion (lower surface potential) create a Nano-bioactive protective film.



GOLD PROPOLIS ESSENCE HYDROGEL IN COSMETICS



- ▶ Centella Asiatica, Hydrogel and high-concentration of **propolis**, it controls the excessive sebum while calming and soothing the skin .

www.youqueen.com



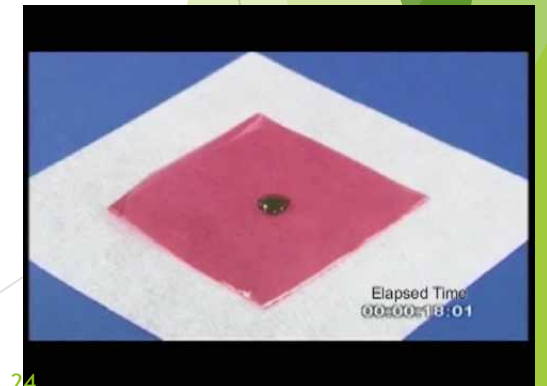
PROPOLIS DIETARY SUPPLEMENTS





ADHESIVE FILMS WITH ROYAL JELLY

- ▶ Oral mucosal adhesive films containing **royal jelly** accelerate recovery from 5-Fluorouracil induced oral mucositis. (Watanabe et al, 2013 - J.Pharmacol. Sci.,121(2), 110-8)





ROYAL JELLY

- ▶ A new technology of royal jelly harvesting and packing, which **excludes its contact with air oxygen.**
- ▶ The “wonders” of royal jelly are only possible if it is fresh - and has not lost its healing properties.
- ▶ Royal jelly harvested from royal jelly cups or, even worse, by vacuum suction from the queen bee’s cell, gets mixed with air. Air oxygen quickly, within two hours, oxidizes royal jelly.
- ▶ Only one Carl Jenter technology for royal jelly. The method includes the use of a **noble gas called argon** to isolate the product from air oxygen. This technology is rather labor-consuming, but it has shown that, royal jelly can be stored at the temperature of +5°C up to three (3) years without losing its properties or changing its composition.
- ▶ a new technology of native royal jelly harvesting and packing was developed, which **enables to exclude its contact with air oxygen.** The technology is less expensive than traditional approach, such as the noble gas method. For the first time it has become possible to supply customers with native royal jelly isolated from air oxygen and preserving all its properties. (LLC "Progalskiy,,)



ROYAL JELLY

- ▶ Comprehensive proteomic analysis reveals **novel proteins** and potential phospho/glycoproteins (Furusawa et al., 2008).
- ▶ Proteomic analysis of major RJ proteins changes under different storage conditions suggested that MRJP 5 protein is a reliable freshness marker and that the best way to maintain quality of royal jelly is under freezing conditions (Li et al., 2008)





AC Royal Jelly Extract - Cosmetic applications



- ▶ The nutrients in Royal Jelly have been shown to enhance cellular and tissue regeneration, thus providing healing properties.
- ▶ Royal jelly was also found to act as an antibiotic.
- ▶ When used on the skin Royal Jelly works to promote cell and tissue repair while simultaneously enhancing collagen production.
- ▶ The vitamins and minerals in royal jelly help to keep the skin hydrated and moisturized, an essential aspect of fighting wrinkles and aged, tired skin.

References

- ▶ 1) Koya-Miyata S, Okamoto I, Ushio S, Iwaki K, Ikeda M, Kurimoto M. Bioscience, Biotechnology, Biochemistry. 2004 Apr;68(4):767-73.
- ▶ 2) Park HM, Hwang E, Lee KG, Han SM, Cho Y, Kim SY. Journal of Medicinal Food. 2011 Sep;14(9):899-906.
- ▶ 3) Detienne et al. 2014. Experimental Gerontology. Royalactin extends lifespan of Caenorhabditis elegans through epidermal growth factor signaling. 60: 129-145
- ▶ 4) Yamaura et al, 2013. Pharmacognosy Magazine. Topical royal jelly alleviates symptoms of pruritus in a murine model of allergin contact dermatitis. 9(33): 9-13

TransEpidermal Water Loss

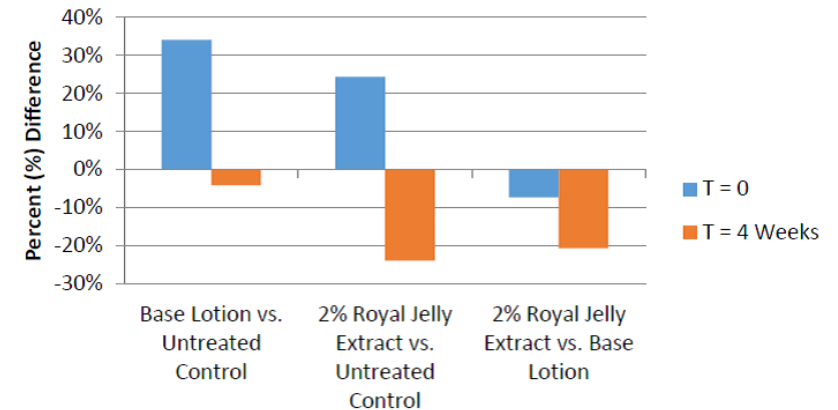


Figure 5. Percent change in TransEpidermal Water Loss

Collagen Ultrasound

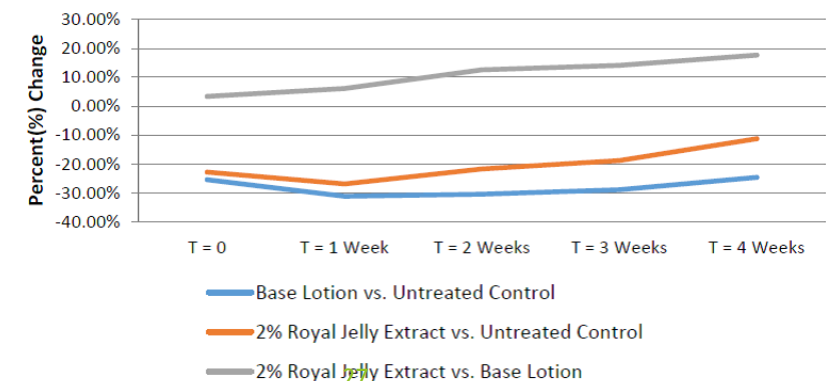


Figure 4. Comparative percent change in Collagen concentration vs. control and base



ROYAL JELLY - LIPOSOME TECHNOLOGY

This material is synthetic.

Composition:

- ▶ Butylene Glycol
- ▶ **10 -Hydroxydecanoic Acid**
- ▶ Sebacic Acid
- ▶ 1,10 -Decanediol

- ▶ 10-hydroxy-2-decenoic acid(10-HDA) is the special unsaturated fatty acid in royal jelly, which content is ruled in its quality. The lecithin as the main wall material, the 10-HDA **nanoliposome** was prepared by the ethanol injection-sonication method.
- ▶ Furthermore, five kinds of royal jelly product as the material, the content of 10-HDA was measured by HPLC, and then the 3 month-long stability experiment was carried out.
- ▶ Results showed that the envelope rate of 10-HDA may reach 90.3% using **nanocapsule technology** to prepare **10-HDA nanoliposome**; simultaneously its content stability could be improved. While the 10-HAD content of other four kind of royal jelly production was unstable, the content became lower along with the time.
- ▶ http://en.cnki.com.cn/Article_en/CJFDTOTAL-BGDH201116018.htm
- ▶ [major royal jelly proteins\(MRJPs\) pepsin and trypsin enzymatic hydrolysis technology ultrafiltration angiotensin I-converting enzyme inhibitory peptides](#)



ROYAL JELLY - LIPOSOME TECHNOLOGY

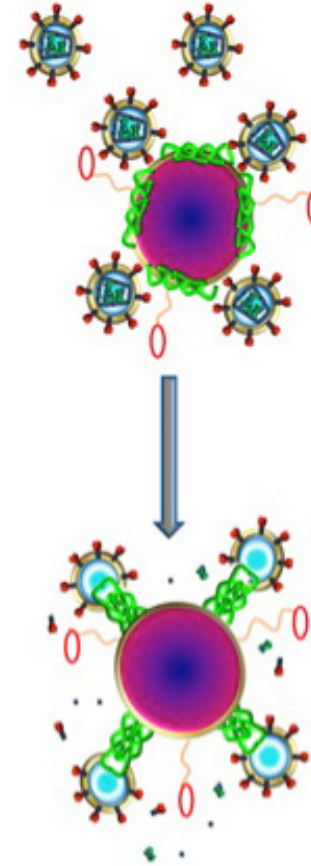


- ▶ **Royal Jelly Lift Concentrate**, the newest product in Jafra Cosmetics International's Signature Royal Jelly line, uses a combination of royal jelly, and *cutting edge technology* to stimulate cell renewal and help prevent the appearance of wrinkles.
- ▶ The product utilizes specially engineered liposomes, small mini-capsules that encapsulate active ingredients to deliver royal jelly to the skin more effectively. Because liposomes are similar in composition to the structure of skin cells, they absorb more easily, and are said to increase the Lift Concentrate's efficacy.
- ▶ www.jafra.com
- ▶ <http://cosmetics.specialchem.com/news/product-news/delivery-system-technology-in-a-new-lift-serum>



MELLITIN (BEE VENOM) NANOPARTICLES

- ▶ Nanoparticles loaded with bee venom kill HIV
- ▶ Nanoparticles carrying a toxin found in bee venom can destroy human immunodeficiency virus (HIV) while leaving surrounding cells unharmed, researchers at [Washington University School of Medicine](#) in St. Louis have shown. The finding is an important step toward developing a vaginal gel that may prevent the spread of HIV, the virus that causes AIDS.
- ▶ Melittin attacks double-layered membranes indiscriminately, this concept is not limited to HIV. Many viruses, including hepatitis B and C, rely on the same kind of protective envelope and would be vulnerable to melittin-loaded nanoparticles.
- ▶ Hood JL, Jallouck AP, Campbell N, Ratner L, Wickline SA. Cytolytic nanoparticles attenuate HIV-1 infectivity. *Antiviral Therapy*. Vol. 19: 95 - 103. 2013

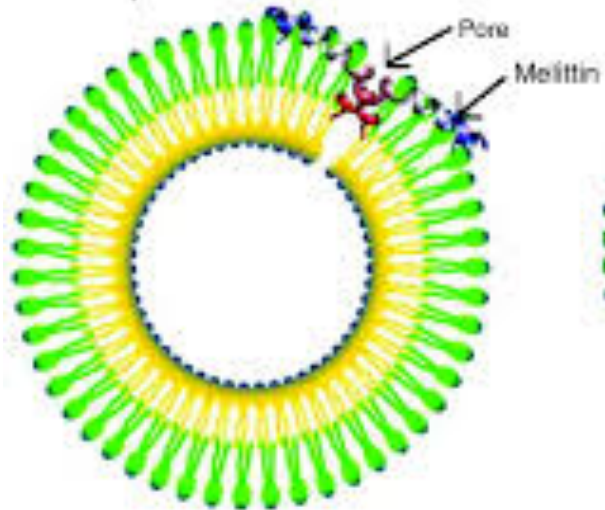


(Image: Joshua L. Hood, MD, PhD)

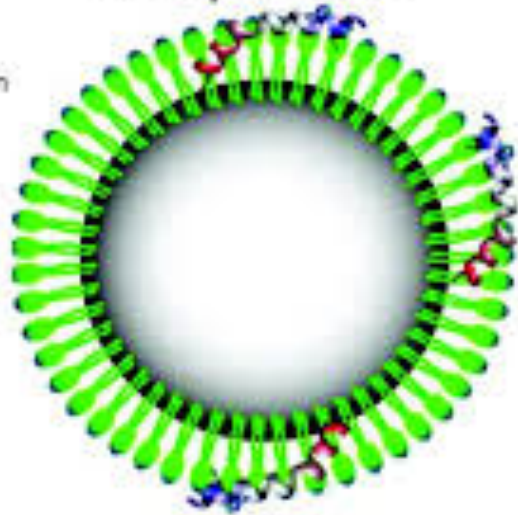


MELLITTIN IN LIPOSOMES AND NANOPARTICLES

Melittin in
Liposomes



Melittin in
Nanoparticles





CONCLUSIONS

- ▶ New pharmaceutical technologies
- ▶ New formulations
- ▶ Diversification



**THANK YOU FOR YOUR
ATTENTION!
GRAZIE !**

