



Garcinia double salts Patent concerns are unwarranted

Sabinsa Corporation pioneered market development efforts for *Garcinia cambogia* extract (trademarked Citrin®) in the early 1990's. Since then, *Garcinia* extract has gained recognition as an efficacious ingredient in weight management formulations. Several related research papers on hydroxycitric acid, the active principle in the extract, have been published globally in the last ten years.

The first product to be marketed was the calcium salt of hydroxycitric acid. Subsequently, end user needs prompted the development of water soluble salt forms.

In July 1998, Sabinsa Corporation was granted a patent for Citrin®K -"Potassium hydroxycitrate for the suppression of appetite and induction of weight loss" by the United States Patent and Trademark office. In light of this marketing history, it is surprising that Vittal Mallya Scientific Research Foundation (VMSRF), a research and development organization in Bangalore, India, recently filed a law suit against several companies, including Sami Labs Ltd., Bangalore, Sabinsa Corporation, USA, and other multinational companies.

The claim in the law suit was that the above companies infringed on their patented process for preparing *Garcinia* double salt. A postponement in legal proceedings effected by the Madras High Court has been annulled on application.

Sami Labs Ltd and Sabinsa Corporation maintain that we have our own patent for the manufacture of Mono Salts (Citrin®K) and that our process for manufacturing double salt is not covered by the recently issued VMSRF patent.

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New patent Applications

Four new patent applications were submitted to the United States patent and trademark office in January-February 2003:

1. Skin Care Compositions for Facilitating Depigmentation and Improvement in Skin Texture
Describes unique natural herbal extract compositions that effect skin smoothness, even out skin tone and reduce inflammation.
2. Analgesic, Anti-inflammatory and Anti-tumor Properties of Naturally Occurring Boswellic Acids and their Derivatives
D describes newly discovered additional beneficial effects of boswellic acids that have been long recognized for their anti-inflammatory effects, and outlines processes to prepare derivatives with enhanced biological activity.
3. Natural Ethyl p-methoxycinnamate: Method of Manufacture and its Use in Cosmetic Preparations
Describes processes to prepare natural from Zingiberaceae plants, such as Kaempferia galanga roots, and the novel use of this compound in anti-acne and other skin care preparations.
4. Process to improve the composition and accumulation of organic selenium compounds in *Allium sativum* Linn. (garlic) for nutritional supplementation
Describes a novel enrichment process to achieve an unique, bioavailable composition of natural organic selenium compounds in garlic bulbs.

Sabinsa successfully defends patent Infringement - lawsuit against QCI Nutrien

ForsLean®:

Sabinsa Corporation has once again successfully protected its intellectual property (IP). Mark C. Sysler, Sabinsa's Sr. EVP for Marketing and Sales today announced that the US District Court in New Jersey has entered a default judgment on behalf of Sabinsa against GCI Nutrients of Burlingame, CA.

Sabinsa filed suit against GCI in May of 2002 for infringement of its Forslean® Patent # 5,804,596 entitled "Method of Preparing a Forskohlin Composition from Forskohlin Extract and Use of Forskohlin for Promoting Lean Body Mass and Treating Mood Disorders".

The judgment stipulated that GCI had infringed Sabinsa's patent by importing, selling or offering for sale *coleus forskohlii* extract and that GCI was permanently enjoined from infringing or contributing to infringe or inducing the infringement of Sabinsa's Patent #5,804,596 for the remaining patent term. It further ordered that GCI pay Sabinsa's legal fees. Sysler commented that "this result was just and proper and should serve as a warning to anyone contemplating an encroachment upon Sabinsa's intellectual property rights. We are committed to our product development and new product research, and must enforce our IP rights in order to continue that commitment".

New clinical study on Forslean® in progress

Sami Labs, India, an associate group of Sabinsa Corporation, has completed the recruitment of volunteers for a 48 subject Clinical Study. The first round of volunteers have gone through Phase-I trials as well. ClinWorld Inc., subsidiary of the US based company, is organizing the study under ICH Guidelines. The final data will be available in the middle of summer 2003. Sami Labs is the producer of Coleus forskohlii extracts for Sabinsa Corporation.

REGULATORY DOSSIERS AVAILABLE

Sabinsa has Type II Drug Master File (DMF) available for the following products: Glucosamine sulfate potassium salt, Capsaicin USP and Gugulipid®. A facilities list file, type II for DigeZyme® is also available.

LOOK FOR US AT THE SCC SHOW

Sabinsa Corporation will participate in the Supplier's Day event on Tuesday, May 13 & Wednesday, May 14, 2003 (9:00 am to 4:00 pm) at the Meadowlands Convention Center, Secaucus, NJ. This annual event hosted by the New York Chapter of the Society of Cosmetic Chemists, is one of the largest shows of its kind anywhere in the world. Exhibits include a wide range of products and services related to the cosmetics industry, offering a comprehensive insight to professionals in the field.

Visit the Sabinsa booth to learn about our expanding range of natural extracts, fine chemicals and specialty chemicals and their versatile applications.

Shaheen Majeed (Executive Assistant to the CEO) and Kavita Subramanian (Manager, New Business Development) would be happy to share product information and application guidelines with you.

Clinical study validates efficacy of Nutritional bar

A snack bar formulation developed by Sabinsa Corporation was tested for clinical efficacy in supporting healthy blood sugar levels in sixteen type 2 diabetes patients (8 men and 8 women), 34 to 67 years of age.

The results of the open field, physician controlled study indicate that regular consumption of three bars per day for eight weeks, effects a gradual significant decline in blood fasting glucose levels and levels of glycosylated hemoglobin.

Cosmeceuticals: Versatile applications

Antioxidants:

Free radical chain reactions are implicated in most degenerative biological reactions. Free radicals on the surface of the skin therefore catalyze aging. Herbal extracts contain natural compounds that scavenge free radicals, or inhibit their propagation. These antioxidants are therefore useful in antiaging formulations and in formulations designed to maintain general skin health and integrity. Additionally, natural antioxidants also help to enhance the shelf life of fat-based topical formulations.

Skin rejuvenation:

Aging of the skin is a cumulative effect influenced by factors such as environmental pollution, chemicals, and atmospheric temperature fluctuations. The major contributor to skin damage is exposure to sunlight. Ultraviolet A and B radiation from sunlight penetrate the skin and accelerate damage due to free radicals. With prolonged exposure to sunlight, the collagen and elastin fibers which maintain the elasticity and integrity of the skin are broken down by the enzymes collagenase and elastase and the skin texture deteriorates. Herbal extracts and nutrients such as ursolic acid and rosemary extract which inhibit these enzymes and promote collagen and elastin synthesis therefore help to maintain the integrity of the skin. Such products are therefore useful in preventing wrinkling and aging and in improving the appearance of photoaged skin.

Other compounds that help in improving appearance and texture include alpha-hydroxy acids and aleuritic acid. These compounds accelerate exfoliation thereby helping to soften hardened skin areas.

Natural tyrosinase inhibitors

Darker skin tones, patches and blemishes result from increased formation of melanin and slow breakdown of preformed melanin on the surface of the skin. Hydroquinone products used historically for skin lightening are no longer acceptable on account of their toxicity. Agents that affect the melanin biosynthesis pathway are widely distributed in plant materials. These natural ingredients offer safer alternatives to hydroquinone for use in topical skin lightening compositions.

Some herbal extracts and phytonutrients regulate the overproduction of melanin through inhibition of the natural enzyme in the skin, tyrosinase, which is responsible for melanin production. Some

antioxidant compounds also help to break down preformed melanin. Typically compositions for skin lightening also include sunscreens, moisturizers and other functional ingredients that support skin health and appearance. Such compositions offer comprehensive protection to the skin and provide antiaging benefits as well.

Cosmeceuticals : Claims substantiation

Sami Labs Ltd., Sabinsa's associated group, has established a cosmeceuticals claims substantiation laboratory at its Bangalore research facility.

A summary of the current capabilities of the cell culture and biochemical validation laboratory is as follows:

Facilities available:

- Class 100 safety Hood (Class II level)
- Class 10,000 lab (sterile lab)
- Carbon-dioxide Incubator (thermo)
- Inverted microscope (Olympus) with CCTV and fluorescence attachment
- Microplate reader (BMG, Fluostar Optima) with Absorbance, Luminescence, Fluorescence detectors
- Temperature control Ultra centrifuge(20,000 rpm)
- Cryofreezer (-80oC)

Cell cultures Testing:

1. Toxicity evaluation

- Human fibroblast
- Mutagenicity against bacterial tester strain TA 102

2. Efficacy studies:

A. Melanogenesis promoters / inhibitors: Efficacy screening for skin pigmentation promotion or skin lightening, required in validating efficacious agents in vitiligo or skin fairness respectively.

- Melanocyte cell line (Melana A)
- Tyrosinase inhibition assay

B. Hyperproliferative studies / psoriasis evaluation

- SVK14 Keratinocytes proliferation, measurement of ATP/lactate dehydrogenase

C. Skin conditioning / anti-wrinkle properties

- Fibroblast proliferation and release of various enzymes and cytokines
- Anti-elastase activity
- Anti-collagenase activity
- Anti-hyaluronidase activity

D. Anti-inflammatory activity

- Evaluation of COX inhibition

E. Wound healing activity

- Proliferation of fibroblasts
- Proliferation of Keratinocytes

F. Antioxidant assay

- DPPH radical scavenging activity
- In vitro lipid peroxidation

G. Anti-acne/Anti-bacterial activities, Effectiveness against

- Propionibacterium acnes
- Staph. aureus
- Staph. epidermidis
- Strept. mutans
- E.coli
- Bacillus subtilis

H. Anti-dandruff activities

- Effectiveness against Pityrosporum ovale

One of the driving factors is the need for development of non-animal based efficacy studies. Alternative testing methods will be developed and validated at this laboratory

Garliselect® - Naturally enriched with Selenium

Dr. Muhammed Majeed, CEO of Sabinsa Corporation, announced the proposed introduction of Sabinsa's patent pending high selenium garlic product to the US and International markets. The product is expected to be launched in July 2003. Garlic bulbs are naturally enriched with an unique composition of organic selenium compounds, using a patent pending hydroponics technique developed at the tissue culture research facility at Sami Labs Ltd.

CO-MARKETING

New Concept in Nutraceutical Ingredient Marketing

Piscataway based Sabinsa Corporation and Sami USA have decided to co-market, Methyl Seleno Cysteine, an organic Selenium available in Garlic and found to be biologically more effective for certain cancers than regular L-Selenomethionine.

PEOPLE FOCUS:

Craig Nie



Craig Nie has been an integral part of Sabinsa's International Marketing group for over four years. Initially based at Sabinsa's New Jersey office, where he was International Marketing Analyst, Craig moved to Canada, from where he now coordinates Sabinsa's marketing efforts in the Canadian territory and in China.

S. Velmurugan



S. Velmurugan recently joined SabinsaNJ as Manager, Quality Control & Quality Assurance. He holds a Master's degree in Organic Chemistry from Annamalai University, India and brings with him over 8 years versatile experience in the analysis and quality assurance of herbal and synthetic products. Before joining Sabinsa, Velmurugan worked for two years at Sami Labs Ltd. Sabinsa's associate company in India, where he gained hands on experience in analytical method development and QA/QC issues related to the wide range of products on our list. Velmurugan's broad-based knowledge in these areas will be a valuable asset to customers looking for detailed technical information on products purchased.

Steven Figueroa



Steven Figueroa recently joined Sabinsa Corporation to help in the logistics of the day-to-day operations in the warehouse. With prior experience in tablet pressing and production of tablets, Steven has also trained under GMP practices and follows SOP's. We are pleased to welcome him on board with us.

SABINSA'S UPCOMING SHOWS

Suppliers Day SCC 2003 :
May 14-15
Secaucus, New Jersey,

Vita Foods 2003
May 13-15
Geneva, Switzerland

Product Focus

BioPerine® and Cosmoperine® enhance nutrient absorption

Do all nutritional supplements consumed, or all topically applied products provide optimal health benefits? A lot depends upon how well they are absorbed along their delivery route. Bioavailability encompasses availability, absorption, retention and utilization of nutrients. Absorption in the body is a key factor for the nutrient to be biologically effective.

BioPerine® is a standardized extract from the fruits of *Piper nigrum* L. (black pepper) or *Piper longum* L. (long pepper). It contains a minimum piperine content of 95% compared to the 3-9% and 3-5% found in raw forms of *Piper nigrum* and *Piper longum*, respectively. BioPerine® may be coadministered with various nutrients for both human and animal health.

When optimal oral delivery of nutrients is required, BioPerine® may be co-administered in low amounts (5 mg) with the nutrient's to increase absorption and bioavailability. The efficacy of BioPerine® in this regard is supported by clinical data as shown in Figures 1-4. BioPerine® has been termed a natural "Thermonutrient" and bioavailability enhancer .

Nutritional materials which may be co-administered with BioPerine®, include the following groups :

- Herbal extracts: (for example. Curcuminoids, Boswellia serrata extract, Ashwagandha, Ginkgo biloba extract, capsaicin, bioflavonoids and others)
- Water-soluble vitamins : (for example vitamin B1, vitamin B2, Niacinamide, vitamin B6, vitamin B12, Folic acid and Vitamin C)
- Fat-soluble vitamins : (for example. vitamin A, vitamin D, vitamin E, and vitamin K)
- Antioxidants : (for example. Vitamin A, Vitamin C, Vitamin E, alphacarotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein/zeaxanthin, pine bark bioflavonoids complex, germanium, selenium and zinc).
- Amino acids : (for example. lysine, isoleucine, leucine, threonine, valine, tryptophan, phenylalanine, and methionine)

- Minerals: (for example calcium, iron, zinc, vanadium, selenium, chromium, iodine, potassium, manganese, copper and magnesium).

BioPerine® enhances nutrient absorption by inducing thermogenesis, the production of heat energy associated with the digestion of food. This process, also called "food-induced thermogenesis", is attributed to the pungent principle piperine.

Sabinsa Corporation was granted four US patents and an International (European) patent on the use and manufacturing process for BioPerine® U.S. Patent #s. 6,054,585 (2000), 5,972,382 (1999), 5,744,161 (1998) and 5,536,506 (1996);

EP 0810868 (2001)-Sweden, Netherlands, Italy, United Kingdom, Ireland, Luxembourg, Monaco, Portugal, Spain, France, Denmark, Greece, Germany, Switzerland, Belgium, Austria Other International patents are pending.

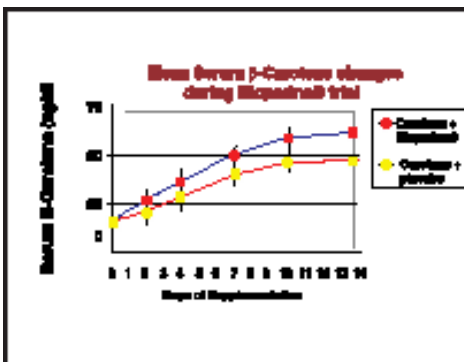


Figure 1. Effect of BioPerine® on the mean serum beta-carotene levels during a 14 day supplementation trial.

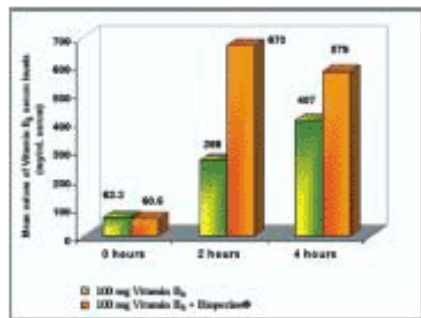


Figure 3. Efficacy of BioPerine® on the bioavailability of vitamin B6 absorption in human volunteers

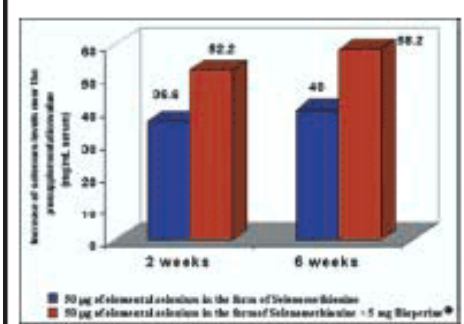


Figure 2. Effect of BioPerine® on serum selenium levels during a 6 week supplementation trial.

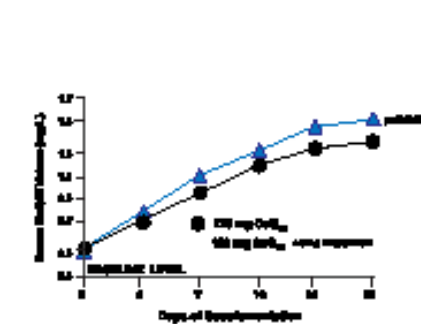


Figure 4. Effect of BioPerine® on serum CoQ10 levels during a 21 day supplementation trial.

Cosmoperine® is derived from black pepper or long pepper extract contains a minimum of 98% Tetrahydropiperine. When nutrients need to be delivered through the skin, Cosmoperine® added in low amounts (0.01-0.1%) to cosmetic formulations or topical delivery systems enhances the uptake and bioavailability of actives in the formulation.

Cosmoperine® is Tetrahydropiperine, prepared from black pepper or long pepper extract by a patent pending process. Its use in improving the skin penetration of active compounds is also covered by the pending patent.

Laboratory studies with betamethasone dipropionate (BMDP), a steroidal

antiinflammatory agent that is commonly used in topical anti-inflammatory formulations, revealed faster absorption of the drug when combined with Tetrahydropiperine.

Similar enhanced permeation was observed in studies with other active materials including Coleus forskohlii extract (forskolin). For example, the permeation of forskolin was enhanced when the concentration of Cosmoperine® was 5% of Forskolin concentration.

In view of these properties, Cosmoperine® is a potential transdermal "bioavailability" enhancer when co-administered topically with nutrients or other active compounds. Carotenoids, ascorbic acid, vitamin A, mineral nutrients, 7-keto DHEA, herbal extracts, amino acids and other topically beneficial nutraceuticals, may be better absorbed in the presence of Cosmoperine® in the formulation.

Cosmoperine® does not irritate the skin when used in cosmetic formulations, as revealed by an occlusive patch test performed on human volunteers.

References:

Badmaev, V. And Majeed, M. (2001 Jan/Feb) Skin as a delivery system for nutrients, nutraceuticals and drugs. THP a natural compound with the potential to enhance the bioavailability of nutrients and drugs through the skin. Agro-Industry Hi-Tech. 6-10.

Look for Sabinsa new product advertisements in the following trade publications this month:

- Chemical Market Reporter
- Cosmetics & Toiletries
- Soap, Perfumery & Cosmetics
- HAPPI
- Perfumery & Flavorist,
- Soap & Cosmetics

the ripple effect of research is clearly evident

BioPerine® works!

"Supplementation of 100 mg of Capsaicin Q10 with piperine (BioPerine®) produced an approximate 30% increase in bioavailability Q10 plus placebo." (J. Nutr. 136:1033-1038)

"...long-term nutrient supplementation may be an appropriate solution to nutritional deficiencies." (Nutr. 136:1033-1038)


"Even the window of opportunity for piperine-nutrient interaction has been closed, nutrient absorption is not enhanced." (Nutr. 136:1033-1038)

"Supplementation with beta-carotene plus piperine (BioPerine®) produced a 60% increase in serum beta-carotene." (Nutr. 136:1033-1038)

BIOPERINE®

BIOPERINE® was the first product ever developed specifically to increase the bioavailability of nutritional supplements. Seven years of use, millions of dosages consumed, four US patents, and a half dozen clinical studies later only serve to validate the safety and merit of this product.

If you haven't discovered the benefits of BioPerine yet, we invite you to do so now. Retailers, ask your manufacturers for it by name. Contact Sabinsa for a product information packet or visit www.bioperine.com.

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