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The Age of Biotransformation

Curcuminoids, the versatile pronutrient, is undoubtedly the most important and precious gifts to mankind from nature. However, the bioavailability of Curcumin had been an intriguing question to scientists all through the 1980s up until the year 2011. Experiments on the oral administration or intravenous injection of curcumin and its absence in the analysis of blood serum samples were research protocols that dominated publications until the concept of biotransformation of Curcumin was studied and understood.



Dr. Muhammed Majeed
Founder - Sabinsa Corporation

the metabolites and continued to bemoan the poor bioavailability of Curcumin. According to published PNAS report, Curcuminoids when ingested, immediately undergo biotransformation by the action of NADPH-dependent Curcumin/Dihydrocurcumin reductase (Cur A) to form Tetrahydrocurcumin, Tetrahydrodemethoxycurcumin and Tetrahydrobisdemethoxycurcumin¹; while through the action of other enzymes in the body, metabolites such as Hexahydrocurcumin, Octahydrocurcumin, Curcumin glucuronides, Curcumin sulphates and Ferulic acid are also formed.²⁻⁴

Curcumin is a versatile pronutrient that undergoes biotransformation in the biological system. A **pronutrient** is a nutritional supplement that is administered in an inactive or less than fully active form, and which is converted to its active form through microbial conversion and/or other active metabolic processes. It is a precursor chemical compound of a nutrient. Curcumin also undergoes microbial transformation in the gastrointestinal tract and forms various metabolites.



Reductive metabolites of Curcumin include Tetrahydrocurcumin, Hexahydrocurcumin and Octahydrocurcumin. Tetrahydrocurcumin has been evaluated the most and found to be highly bioactive.

Several studies report the various applications of Tetrahydrocurcumin such as antioxidant, anti-inflammatory, anti-glycation, cardioprotective, renal protection, hepatoprotective, anti-hyperlipidemic, cancer preventive, anti-diabetic, anti-alzheimer and anti-ageing.⁵

The biological role of hexahydrocurcumin has also been studied and found to be effective as an antioxidant, cancer preventive, for human platelet aggregation and as an antifungal agent.⁶⁻⁹

The metabolites - Curcumin glucuronides and sulphates - are inactive and do not contribute to any reported biological activities.¹⁰⁻¹² The antioxidant property is responsible for many of the pharmacological actions of curcuminoids.

The discovery that Curcumin undergoes microbial transformation in the gut as reported in a research paper in the prestigious Proceedings of the National Academy of Sciences (PNAS) of the USA in 2011, was the beginning of the answer to this intriguing question. It is not curcumin that one should look for, but the biotransformed products. However, everyone who looked into the bioavailability failed miserably to look for

But the Curcumin glucuronides are much poorer anti-oxidants compared to Curcuminoids.¹³

People thus looking for altered or modified forms of curcumin to address bioavailability claims, should be wary of the harmful effects such as cardiovascular outcomes, hemolysis and other ailments that are still unknown and are caused by the adjuvants used as bioenhancers. Bioavailability enhancers need to address core issues such as safety and therapeutically active quantities of Curcumin and its biotransformed metabolite Tetrahydrocurcumin to deliver one of the most powerful natural extracts of the century.

PEOPLE'S CORNER

Rick McNall

Sabinsa Corporation is pleased to announce that Rick McNall has joined the company as Regional Sales Manager. Rick comes to Sabinsa with extensive sales and marketing experience in the pharmaceutical and natural product industries. His career began with American Pharmaceutical Company where he assumed responsibility for expanding sales of the company's drug and nutritional supplement products in the retail drug channel, throughout the US and Puerto Rico. Recognizing tremendous growth in the natural products industry, Rick decided to join BioTherapies / Cartilage Technologies where he played a major role in developing and marketing the company's cutting edge nutraceuticals. Subsequent positions with Archon Vitamin Corporation, Tree of Life (Kehe) and Designs for Health enriched Rick's background with experience in nutritional supplement contract manufacturing, working with the nation's leading natural products distributor and gaining regional sales management experience in the "Professional" (health care practitioner) channel.

At Sabinsa, Rick will work closely with the management team to further the company's business development efforts and to support a high level of customer satisfaction. In the

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capacity of Regional Sales Manager, he will focus on building strong working relationships with existing accounts and will spend time developing new customers to expand the company's portfolio of brands in the Eastern region of the United States.

Jan A. Obirek

Jan has joined Sabinsa as a Regional Sales Manager for the State of California.



Jan is a top-producing business executive with 25+ years of success in sales management at the regional, national and international levels in the natural, mass & drug channels. He has broad consumer packaged goods and ingredient sales expertise with both branded and private label products. Jan has a proven ability to grow revenue, exceed sales and profit goals.

Jan has started his career with Giorgio Foods in Pennsylvania and has worked his way up the sales ladder and across the country with companies like Uncle Ben's, Corning and I.V.S., taking on increasing responsibilities and territories throughout the years. This experience proved valuable in his last assignment of helping build Tahiti Trader Company to a liquid dietary supplement category leader.

PRESS RELEASES

India's Former President Visits Sami Labs/Sabinsa. Dr. APJ Abdul Kalam Emphasizes Importance of Science

Sabinsa / Sami Labs Limited in Bangalore, India was honored by a visit from Dr. APJ Abdul Kalam, Former President of the Republic of India (2002–2007) on Sunday June 29, 2014. Dr. Kalam also participated in a discussion on the contribution and relevance of ancient Indian science to modern techniques. The other participants were Dr. Muhammed Majeed, Founder and Managing Director, SAMI/Sabinsa Group of Companies, Dr. S. Natarajan, Scientific Advisor, Sami Labs, Dr. Kalyanam, President, R&D, Sabinsa, and Dr. Sarang Bani, Head, Biological Research, Sami Labs.

Dr. Majeed welcomed Dr. Kalam, and conducted him on a tour of Sami Lab's Bangalore R&D facility, followed by discussions and a reception. More than 300 members of the Sami / Sabinsa staff were present, including 150 scientists involved in specialized work in the areas of phytochemistry, organic chemistry, bio chemistry and plant biotechnology for Sami / Sabinsa.

In his remarks, Dr. Kalam expressed his appreciation of the efforts of the young scientists in validating Ayurvedic knowledge with modern clinical documentation for health, personal care and cosmeceuticals benefits. "It is a great privilege to address the distinguished members of the Sami Group who've gathered here this morning," Dr. Kalam said. "One key aspect of science is to help people live a good life and not just be limited to inventions. While we have progressed on the lines of science and developed

products on every front, it is time now that we also realize the contribution of nature to these inventions and work in natural harmony."

Dr. Majeed said, "We are honored by Dr. Kalam's visit. He is a remarkable scientist and one of the top thought leaders of our time."



Dr. Kalam demonstrated his commitment to furthering India's scientific achievements as the Principal Scientific Advisor to the Government of India, a Cabinet Minister rank, from 1999 to 2001. He was the Chairman, Ex-officio, of the Scientific Advisory Committee to the Cabinet (SAC-C) and piloted India Millennium Mission 2020.

Sabinsa / Sami Labs Acquires Seventh Manufacturing Facility, Expands Biotech Foothold, Adds Natural Color To Product Line

Sabinsa's sister company and ingredient manufacturing arm Sami Labs Ltd., the Bangalore-based Indian multinational health science company which manufactures phytonutrients and standardized herbal extracts, specialty fine chemicals, and organic intermediates used in the nutritional, pharmaceutical and food industries, has acquired KCP Biotech, located in Hyderabad, India.

This acquisition will help Sami Labs gain another foothold in the growing biotech market and will aim to strengthen its product portfolio for world markets. The new facility, spread across 5 acres in Genome Valley with ultra-modern technology and world-class quality stringency, will be integrated with Sami's existing Hyderabad facility near by. This acquisition also adds three natural colors to the Sabinsa product line, red, yellow and orange made from paprika, turmeric and annatto, respectively.



"The additional biotech capabilities this acquisition brings will help us move more quickly bringing to market products and capabilities our dynamic R&D staff are constantly developing" said Founder and Managing Director Dr. Muhammed Majeed. "And adding natural colors to our product offerings complements our existing ingredient portfolio, which is having great success in the global supply chain."

Sabinsa's LactoSpore® Human Safety Study Cleared For Health Canada Access

Health Canada, the federal department that regulates the products that help the people of Canada maintain and improve their health, has reviewed and approved Sabinsa's shelf-stable probiotic LactoSpore® ingredient for sale in Canada. This pre-market safety approval is required prior to natural health products being offered for sale in Canada.

Sabinsa's LactoSpore® Masterfile has been substantiated with the required safety profile, paving the way for customers to request a Letter of Access from Sabinsa, with which the customer can apply for a Product License Application (PLA) with the Natural and Non-Prescription Health Products Directorate (NNHPD). Thereafter, manufacturers can obtain NPN number for their formulations containing LactoSpore® for purpose of sales in Canada as a Natural Health Product.

"Our investment in and commitment to LactoSpore® runs deep," said Shaheen Majeed, Sabinsa's Marketing Director. "Realizing in the late 1990's the potential of this ingredient, we invested in our own dedicated manufacturing facility to ensure ample and consistent supply of material meeting our quality standards. We made it a strong candidate for inclusion in functional foods by having it GRAS affirmed. We have now cleared the way for customers to sell products with our LactoSpore strain in Canada. These are exciting times for this brand and there's more to come this year."

A number of other Masterfiles on Sabinsa ingredients, such as BioPerine®, Curcumin C3 Complex®, Curcumin C3 Reduct® and ForsLean® are available for Letter of Access requests.

Sabinsa's LactoSpore® Enters Cosmeceutical Market

LactoSpore®, the proprietary *Bacillus coagulans* strain MTCC 5856 manufactured by Sabinsa Corporation for over 20 years, is for the first time included in cosmeceutical products with the launch of Massey Medicinals Candida Freedom® Soap and Candida Freedom® Bath Salts.

While use of probiotics orally for improving gut health and microflora is well known, the use of probiotics on skin is a relatively new area of interest.

Candida Freedom Soap is an all-natural handcrafted soap and provides *B. coagulans* topically for supporting healthy skin. This eco-friendly soap contains no synthetic fragrances, color or preservatives and is 100% biodegradable. LactoSpore® provides probiotic support to skin in addition to the oils of tea tree, lemon and lemongrass which additionally provide antifungal cleanser benefits. Candida Freedom Bath Salt formula is free of fragrances, dyes and essential oils for those with sensitive skin or low immunity.

Dr. Anurag Pande, Sabinsa's VP - Scientific Affairs says, "Microbes play an important role for our skin and such pathogenic bacteria in skin conditions such as Acne, atopic dermatitis, psoriasis, seborrheic dermatitis is well known. Hence, healthy microflora on skin can help create a good balance necessary for healthy skin."

"Candida Freedom Soap is a multifunctional probiotic soap which provides the benefits of lactic acid-producing bacteria *Bacillus coagulans* MTCC 5856 on skin," said Bryan Massey ND, founder of Massey Medicinals. "The skin is not only a barrier between the human body and environment but also contains an ecosystem on the surface of a wide variety of microbes that must be in balance. Candida Freedom Soap has skin-friendly pH, has a



soothing effect on skin and helps in tissue repair."

Sabinsa Launches New Cranberry Product LactoCran™ With Fruit D'Or Nutraceuticals

Sabinsa is pleased to announce an unique combination of its' shelf-stable LactoSpore® probiotic brand of Bacillus coagulans (MTCC 5856) combined with Cran Naturelle® cranberry seed powder from Fruit d'Or Nutraceuticals of Quebec, Canada. This patent pending combination is distinguished as a synbiotic blend, for use in foods, beverages and dietary supplements. It will be marketed and sold as LactoCran™ by Fruit d'Or.

Cranberry seed powder acts as a complete food source when combined with LactoSpore®, Sabinsa's room-temperature stable probiotic strain of bacillus coagulans, (MTCC 5856).

"Cranberry seed powder in this combination showed remarkable potential as a prebiotic food for growth of LactoSpore compared to commonly used prebiotics such as fructooligosaccharides (FOS)," said Dr. Anurag Pande, Sabinsa's VP - Scientific Affairs.

"We're excited to learn about this level of LactoSpore's growth activity using our cranberry seed powder," said Stephen Lukawski, Director of Business Development and Sales of Fruit d'Or. "We know that our cranberry seed powder contains over 50% fiber and as much as 25% natural protein, therefore this new combination could be the complete synbiotic solution for gut health and beyond."

"Sabinsa understands the importance of working directly with growers in order to source the highest quality ingredients for its customers, so we have that in common," Lukawski added. "Fruit d'Or is the only vertically integrated cranberry company in the Nutraceutical market, controlling quality from the planting of the seed to the retail shelf."

LactoCran™ provides support for healthy gut and digestive health while its prebiotic function also provides source of tocopherols and tocotrienols thus benefitting heart and circulatory health. LactoCran's non-lactose,

diary-free, non-GMO combination also works well in sports nutrition supplements as it contains a rich composition of 16 essential amino acids and 8 branch chain amino acids.

LactoCran™, blended in the United States, will be available worldwide beginning in early 2015.

Sabinsa Launches Animal Nutrition Division: Vetvitals®

Sabinsa Corporation today announced the formation of a new division focused on animal nutrition: VetVitals®. "Given the large percentage on nutritional ingredients that are used in the animal nutrition sector this is the next logical move for Sabinsa," said Shaheen Majeed, Sabinsa Marketing Director. "While Sabinsa has more than 100 ingredients for human nutrition, we have carefully selected about 20 ingredients that follow both AFFCO's guidelines and FDA CFR's for Animal Nutrition. This has allowed us to be extremely focused on bringing out precisely crafted nutrients, flavors, spices, seasonings, enzymes and probiotics to animals and pets, the world over. The proven safety and efficacy of our ingredients, position us to expand sales in this area rapidly."



One obvious offering Sabinsa will make available to the animal nutrition sector is curcumin. "Promoted as turmeric, as per AFFCO's definition, Sabinsa's C3 Complex and C3 Reduct can bring real innovation to both the animal feed and pet care marketplace," Majeed noted.

The array of offerings specific to the animal nutrition market were introduced at the Informa Events Petfood 2.0 show in Chicago September 23 and 24, 2014.

VetVitals® is being launched simultaneously worldwide, from all Sabinsa locations. In the US, the division is managed from the Utah office, and can be reached via pets@sabinsa.com

For more information: www.vetvitals.com

Sabinsa's Curcumin C³ Complex[®] and BioPerine[®] Combination Used In Published Study On Metabolic Syndrome

Another significant study on the combination of Curcumin C3 Complex[®] and BioPerine[®], Lipid-modifying effects of adjunctive therapy with curcuminoids–piperine combination in patients with metabolic syndrome: Results of a randomized controlled trial, by researchers at University of Medical Sciences, Mashhad, Iran, has been published in *Complementary Therapies in Medicine* 2014; 22(5): 851-857.

This study is the first trial investigating the efficacy and safety of adjunctive therapy with Curcuminoids-Piperine combination in patients with metabolic syndrome, receiving standard treatment. The results of the trial supported the effectiveness of the adjunctive therapy with significant decrease in serum concentration LDL-C, non-HDL-C, total cholesterol, triglyceride, Lp(a) and elevation in serum concentration of HDL-C in patients in comparison to the standard therapy alone. The present study also encouraged the efficacy of use of co-administering BioPerine[®] as a bioavailability enhancer.

"This research indicates additional benefits of Curcumin beyond inflammation, giving increased value to C3 Complex as the body of science grows" said Shaheen Majeed, Sabinsa Marketing Director. "And once again the C3 Complex and BioPerine combination has been shown to be a safe and effective supplement blend that can help keep people healthy."

Sabinsa's Curcumin C3 Complex[®] has been subject of over 72 research papers including 34 clinical studies published in peer reviewed journals. The combination of Curcumin C3 Complex[®] and BioPerine[®] has been studied in several independent clinical trials, including one published by Tufts University validating its safety and quality of ingredients and another on osteoarthritis from University of Medical Sciences, Mashhad, Iran.

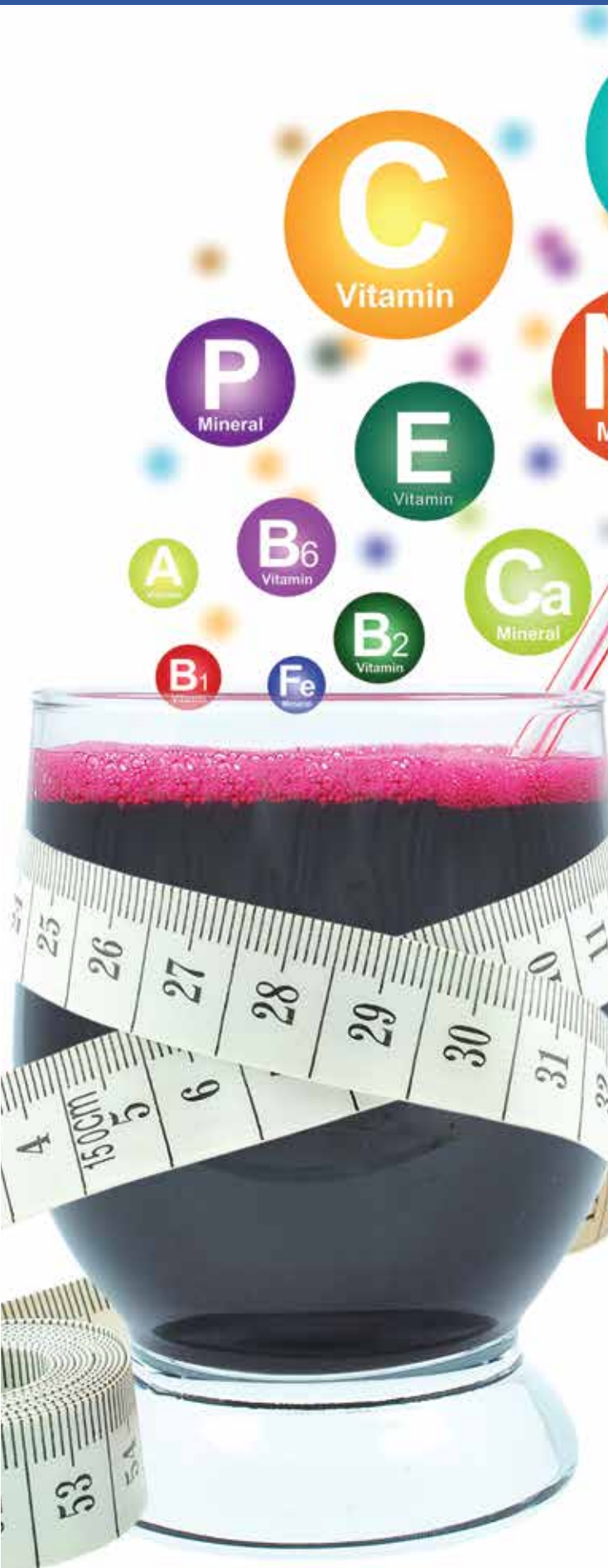


Sabinsa's Curcumin C³ Complex[®] and BioPerine[®] Combination Shows Significant Benefits In Osteoarthritis According To Study

In a significant study on the Curcumin C3 Complex[®] and BioPerine[®] combination, researchers at University of Medical Sciences, Mashhad, Iran observed considerable benefits of this combination in the management of knee osteoarthritis. The study was published in *Phytotherapy Research* and entitled *Curcuminoid Treatment for Knee Osteoarthritis: A Randomized Double-Blind Placebo-Controlled Trial*.

In this 8 week, 53 subjects, pilot randomized double blind placebo controlled parallel group study, patients suffering from mild to moderate knee osteoarthritis were administered Curcumin C3 Complex along with the natural bioavailability enhancer BioPerine (black pepper extract, piper nigrum) in three divided doses. BioPerine, trademarked and patented by Sabinsa, has been clinically studied for its safety and efficacy as a bioavailability enhancer for several dietary ingredients including Curcuminoids. The results show that the combination of Curcumin C3 Complex and BioPerine showed significant improvement in arthritic indices such as VAS (Visual Analogue Scale), WOMAC (Western Ontario and McMaster Universities Osteoarthritic Index) and LPFI (Lequesne's pain functional index) scores. Curcumin is a potent anti-inflammatory and scavenge free radicals, which cause oxidative stress thereby developing and progressing osteoarthritis. Study authors mention the combination of Curcumin with BioPerine as a novelty for this study, which improves the bioavailability by several mechanisms including the inhibition of curcuminoids glucuronidation in intestine and liver thus increasing the bioavailability of Curcuminoids.

"We're excited to see one of the many potentials of curcumin re-enforced, especially for consumers and marketing companies that use our patented Curcumin C3 Complex and BioPerine ingredients for this activity," said Shaheen Majeed, Sabinsa Marketing Director. "Rather than using altered, oil based or other modified forms of curcumins that are out there in the marketplace, this study gives compelling evidence to simply add BioPerine for enhancing the uptake of curcumin."



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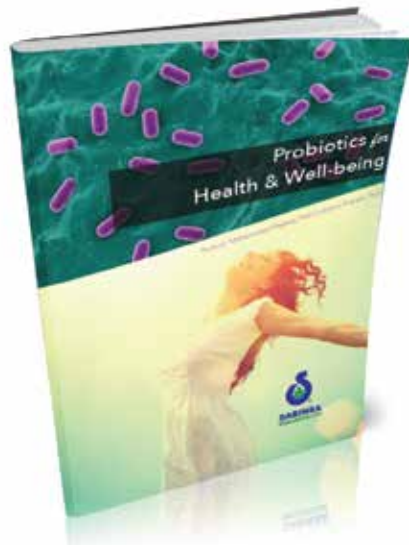
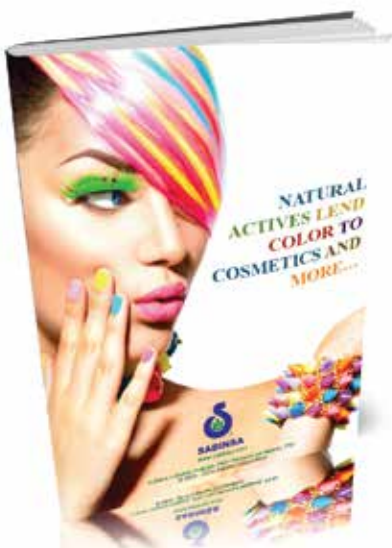
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