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Suntheanine: A pure and safe L-theanine dietary supplement for relaxation and stress relief

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INTRODUCTION

Ever since the discovery of tea in China, it spread all over the world and has been consumed as a refreshing drink. At present, tea is consumed as green, oolong, and black tea, which are originated from the same plant *Camellia sinensis*. Green teas are subject to minimal oxidation, whereas Oolong and back teas are allowed to partially and extensively oxidize respectively. The taste of all types of teas can be attributed to the presence of many amino acids, in particular L-theanine (1) – an abundant free amino acid. Lately the refreshing or the relaxation property and many other neurological, physiological and some of the pharmacological functions of tea are attributed to the L-theanine (2).

L-theanine was first discovered in green tea leaves by Japanese scientists in 1949 (3) and later in other forms of tea (4,5). Its only other known natural occurrence is in the edible wild mushroom *Xerocomus badius* (6). The chemical nature was determined as L-glutamic acid- γ -ethylamide (Figure 1). In 1964, the Japanese Ministry of Health and Welfare approved L-theanine as a food additive in all foods except infant food (7,8). Since then, its popularity has spread from Japan to Europe, with more than 50 food products containing L-theanine available in those two places. In 2000, L-theanine was introduced as a dietary supplement in the United States (9).

Like most amino acids, theanine is also chiral and available in D- and L-enantiomers (10). The pharmacological effects of one enantiomer over another may vary significantly. L-theanine alone, the form in which it is found in tea, has been proved to have all the refreshing and beneficial functions. Suntheanine, a pure L-theanine enantiomer, the brand name of Taiyo

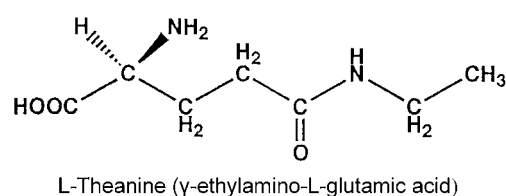


Figure 1 – Structure of L-theanine

Kagaku was produced by a patented L-isomer-specific enzymatic method (11) and proved to have all the benefits related to L-theanine.

Among various theanine products in the market, only Suntheanine meets all the safety standards and health claims set forth by the Dietary Supplement Health and Education Act of 1994 for use as dietary supplements. Taiyo has implemented strict quality control systems in the manufacturing of Suntheanine to ensure the GMP (good manufacturing practice) regulations of the US Food and Drug Administration. Above all, only Suntheanine was thoroughly studied for its purity and safety, and for its relaxation effects in several conditions of humans. Also, animal studies have confirmed several neurological, physiological and pharmacological functions of Suntheanine.

PURITY

Since the introduction of theanine as a dietary supplement, several commercial synthesized products are flooding into market. Theanine when extracted from tea leaves is predominantly in the L-form, as opposed to the enantiomeric racemic combination of L- and D-theanine found in many synthesized supplements labeled as L-theanine. Moreover, various research reports have assigned the refreshing neurological and physiological functions to L-theanine. While the functions of

ABSTRACT

In the competitive dietary supplement market for relaxation, many products are introduced labeled as L-theanine, but the purity and safety of these compounds are seldom checked. Suntheanine produced by a patented L-isomer enzymatic process is the only pure in its L-enantiomer composition. An API-MS analysis confirmed the isomeric composition of Suntheanine to be L-theanine (>99%). The safety of Suntheanine has been thoroughly examined following international protocols. Various human studies indicated that Suntheanine is effective in relieving the stress and inducing the sense of relaxation during anxiety, fatigue, physical stress, and PMS. Suntheanine is also effective promoting relaxed sleep and refreshed awakening in humans. Suntheanine is found effective in improving hypertension, learning performance, and concentration in animals. Immune enhancer and anti-obesity properties are also observed.

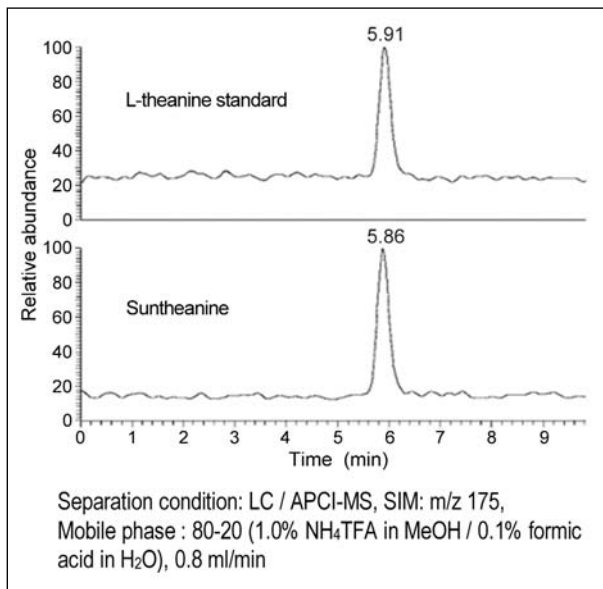


Figure 2 – Enantiomeric composition of Suntheanine

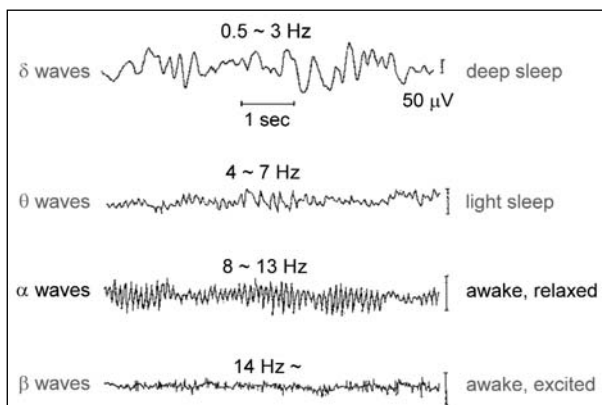


Figure 3 – Classification of brain waves

D-theanine are unknown, it warrants a caution to use such synthetic products. A product with predominant L-theanine is therefore necessary for the safety and for all the benefits of theanine.

Suntheanine is prepared by the way it is synthesized in the tea plant (12,13). Suntheanine is being produced using a soil-derived microorganism and the “starter” ingredients ethylamine and glutamic acid (two naturally occurring constituents of tea and the breakdown products of theanine). This method allowed standardized production of ultra-pure L-theanine in commercial scale. The enantiomeric purity of Suntheanine has been proven to be that of L-theanine.

Desai and Armstrong (14) established a method using the Chirobiotic T (teicoplanin) chiral stationary phase, native and derivatized theanine enantiomers were separated and detected via high-performance liquid chromatography (HPLC) coupled to atmospheric pressure ionization mass spectrometry (API-MS). They evaluated the enantiomeric composition of six commercially available L-theanine samples using the above method and confirmed with photodiode array detection. Among the six samples,

only Suntheanine has demonstrated >99% L-isomer purity (Figure 2). The other five samples tested contained a 50-50 (racemic) mix of D- and L-theanine.

SAFETY

Following the international protocols, the safety of Suntheanine has been evaluated in an acute toxicity study, a subacute toxicity study, a chronic toxicity/carcinogenicity study and a mutagenicity study.

28 Day Subacute Toxicity Study

Healthy male and female rats (five each) were administered daily with 2,000 mg of Suntheanine per kg of body weight for twenty eight days. The effects of ingesting Suntheanine were evaluated by urine analysis, hematology, ophthalmic testing, biochemical tests, a macro pathology study and examinations for clinical symptoms. There were no observed treatment related effects.

78 Week Evaluation of Toxicity and Carcinogenicity of Administration of L-theanine

Healthy male and female mice (150 each) were randomly divided, into three groups of 50 each. After keeping for 2 weeks on basal feed, they were allowed to consume freely 5.0%-Suntheanine test feed in first test group, 2.5%-Suntheanine test feed in the second test group, and to continue basal feed in the control group. Measurements of body weight and feed consumption volume were performed periodically on 4-week intervals. The administration period was set for 78 weeks. Thereafter the surviving rats were sacrificed and examined for carcinogenic and pathological indices in the internal organ and tissue. The results indicated that the long-term oral administration of Suntheanine did not cause any carcinogenesis or pathogenesis in any of the organs tested.

Acute Toxicity/LD-50 Determination

LD₅₀ value of Suntheanine was determined to be more than

5,000 mg/kg. No rat died consuming the above dose during a 7 day observation period.

Ames Salmonella/Microsome Plate Test for Mutagenicity

Suntheanine was found to be non-mutagenic in the Ames tests performed.

2 week Dietary Range Finding Toxicity Study in Rats

Suntheanine was well tolerated up to a dose of 6500 mg/kg/day in a two-week study. Assessment of toxicity was based on mortality, clinical observations, clinical pathology, organ weights and macroscopic observations. All animals survived and no remarkable clinical observations were observed.

RELAXATION EFFECTS IN HUMANS

Most people in modern times who live especially in urban areas are exposed too much to stress and mental pressures. Relaxation is the effective way to overcome these stress and mental pressures. Suntheanine is effective in stimulating the sense of relaxation and refreshness in various stress conditions of human.

Relaxation from Anxiety

Human brain-wave studies confirm L-theanine as Suntheanine produces a state of alert relaxation by generating the α -brain waves within 30 min from the administration (1). In one study (15), 50 female volunteers (18-22 years old) classified into five groups according to anxiety levels, were given Suntheanine solution (50-200 mg/100 ml) for 6 weeks and the brain waves were measured after intake. An electroencephalograph was used to record four sets of brain waves (Figure 3): alpha (awake and relaxed), beta (awake and excited), delta (deep sound sleep), and theta (drowsy, dozing, light sleep). The test results were compared with water placebo. Results

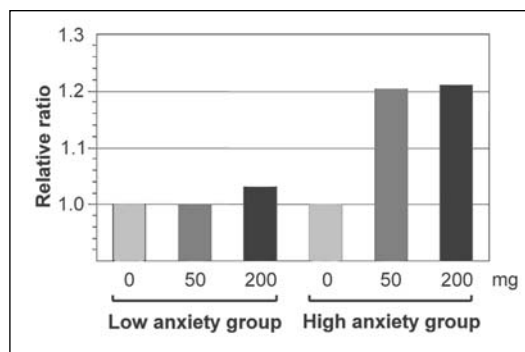


Figure 4 – Effect of Suntheanine® on emission of α -waves based on anxiety in women (2)

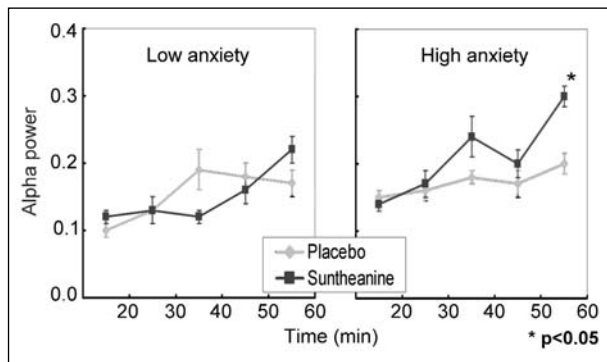


Figure 5 – Effect of Suntheanine® on α -power in the frontal channel of anxiety men

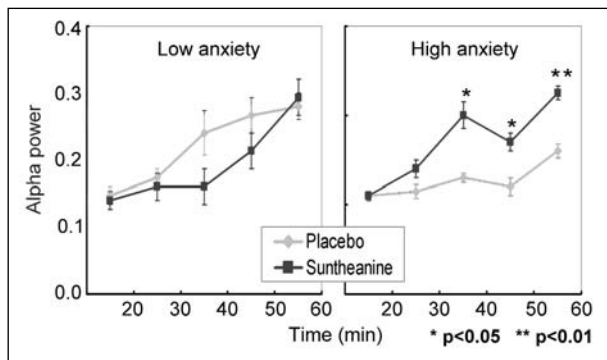


Figure 6 – Effect of Suntheanine® on α -power in the occipital channel of anxiety men

showed no alpha waves observed with the water solution. However, both groups experienced significant increases in their alpha waves 30 minutes after administration of both Suntheanine solutions, indicating they were in a relaxed state of mind. The intensity of the alpha brain wave emissions appeared to increase in a dose-dependent manner, in that the 200 mg L-theanine solution produced more alpha waves than the 50 mg solution, especially in the high-anxiety group (Figure 4). Moreover, the levels of theta waves in both groups remained unchanged during the observation period for all the test solutions, indicating that L-theanine did not induce drowsiness.

A similar brain-wave study (16)

examined the relaxation effects of Suntheanine using 15 healthy men (18 to 30 years old). In this study, the placebo and Suntheanine (200 mg) were in the form of tablets instead of oral solutions. Despite the different delivery form, the outcome confirmed the previous study's conclusion that L-theanine promoted the alpha power both in frontal (Figure 5) and occipital (Figure 6) regions, with the greatest impact on those with high anxiety.

and decrease in fatigue scores were observed after a week of taking the Suntheanine solution (Figure 7). This results proved the efficiency of Suntheanine in promoting mental relaxation and sense of refreshment in fatigue.

Relaxation from Physical Stress

Relaxation from physical stress with Suntheanine was examined with 14 non-smoking healthy male sport-students in a cross-over study (18). The down regulation after physical stress in the brain (measured by EEG-mapping) and in peripheral hormonal systems (plasma levels of catecholamines, cortisol, prolactin, serotonin, measured by HPLC) was examined. After exhaustive bicycle-

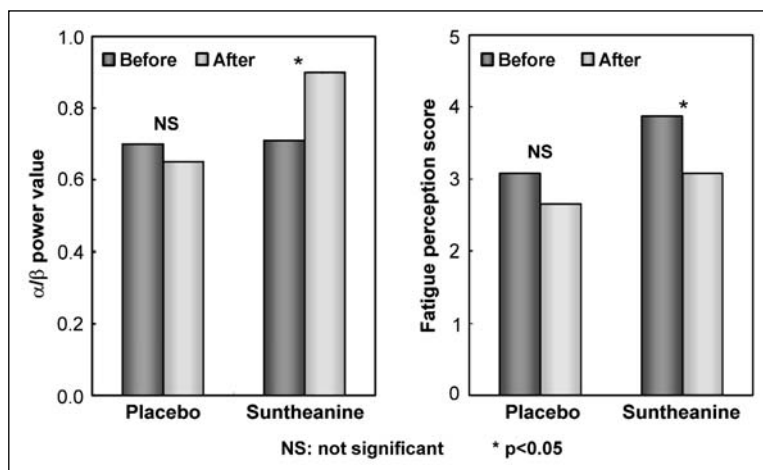


Figure 7 – Effect of Suntheanine® on α/β -power and fatigue in men

Relaxation from Fatigue

The relaxation and refreshing effects of Suntheanine were evaluated in another cross over study (17) with 20 healthy volunteers (30 to 55 years old), who experienced constant tiredness for more than one month without any known underlying disease as the cause. Subjects were given either a placebo or test solution containing 200 mg Suntheanine for seven consecutive days. They were then crossed over to the opposite treatment for another week. An EEG was used to measure brain waves for one hour after each administration, and a fatigue-sensitivity-scale questionnaire was given before and after each seven-day test period. A significant increase in alpha power

ergometer test the stress model subjects recovered by lying in a segregated shaded room. Three test drinks containing 0, 50 or 200 mg Suntheanine were given in a randomized, double-blind order. EEG-recordings (closed eyes) and peripheral hormonal analysis were carried out directly after exercise (M1) and 30 (M2), 45 (M3), 60 (M4), 120 (M5) min after the drink.

Suntheanine seemed to accelerate the normalization of EEG spectral power in high frequency waves. Qualitative different behavior trends were found in frontal-, central-, occipital-regions with increased alpha 1, theta (frontal) and decreasing beta relative-power earlier in recovery with the dose of 200 mg Suntheanine. These findings were related to relaxing effects. After ingestion of Suntheanine, alpha2-, beta1-power at occipital regions decreased faster (M2) to placebo recovery levels (M3/M4) (Figure 8). Also Suntheanine altered the correlations between EEG spectral power and some hormones (slow wave power/some catecholamines except norepinephrine/delta disappeared and new correlations with prolactin appeared). The results suggest that Suntheanine acts as the switch in the human brain for the peripheral stress regulation during the recovery after physical stress.

Relaxed Sleep and Refreshed Awakening

Sleep disorders generally associated with lack of good sleep and refreshed awakening. The effect of Suntheanine on sleep disorders was examined using standardized OSA sleep inventory questionnaire in 22 volunteers – 13 daytime workers of 25 to 36 years old and 11 students of 20 to 33 years old (19). Participants were free of significant psychopathology, medical disorders, and central nervous system active medications as determined by physical examination, medical history, and laboratory tests. The study was a

randomized, double-blind, placebo controlled, crossover study. Participants were given 200 mg L-theanine (four 50 mg Suntheanine tablets) or four placebo tablets one hour before bedtime. The study encompassed two six-night treatment periods, with an initial three-night adaptation period and a one-day washout between crossovers. The participants were asked to answer the

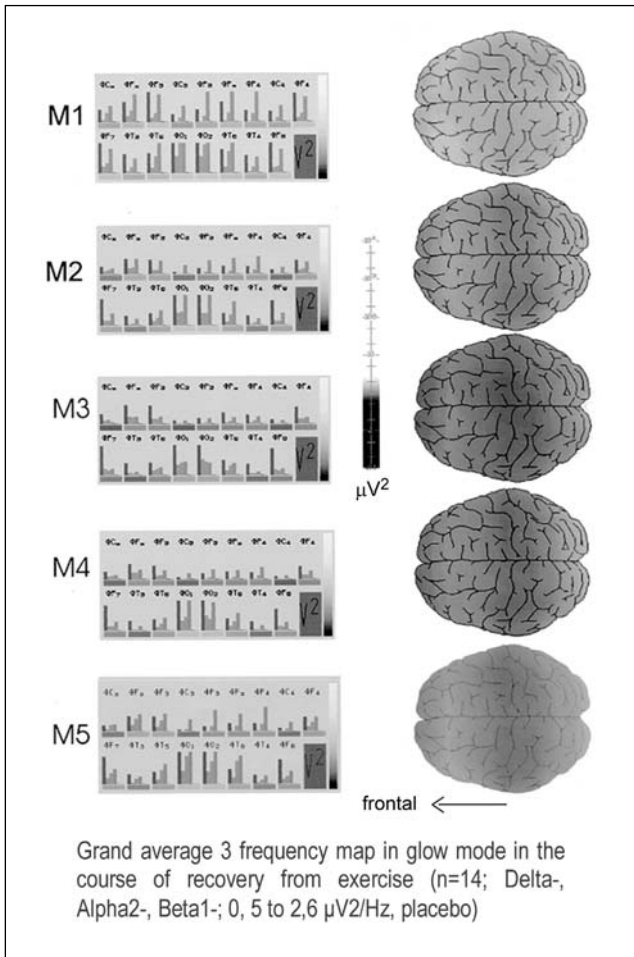


Figure 8 – Effect of Suntheanine® on physical stress

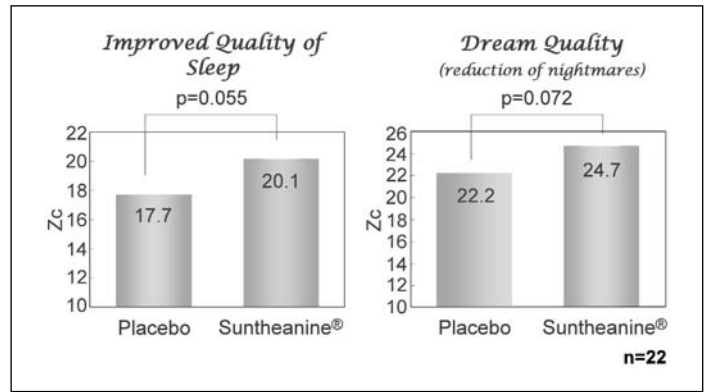


Figure 9 – Effect of Suntheanine® on sleep quality.
Quality of Sleep: Sleep latency, sleep induction and its maintain.
Dream: Reduction of nightmares and frequency of dreams.

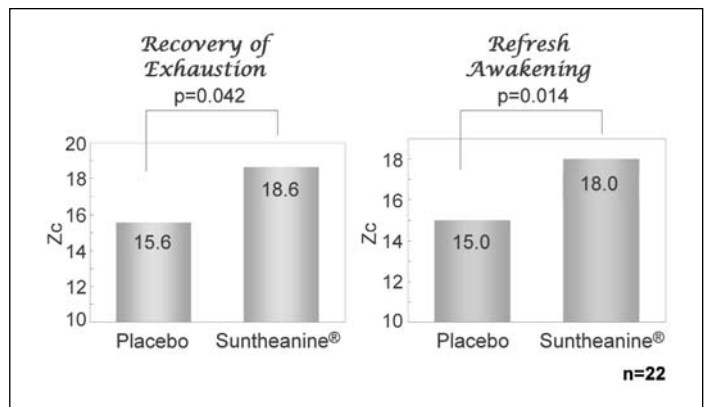


Figure 10 – Effect of Suntheanine® on mood at awakening

questionnaire about their state of sleep and mood upon waking on each day.

No significant difference in feelings of daytime sleepiness between the L-theanine and placebo treatments was observed, confirming that L-theanine does not cause drowsiness. However, compared with the placebo, the L-theanine treatment did improve sleep quality, dream quality and sleep onset, with a noticeable reduction in nighttime awakenings and nightmares (Figure 9). Even though sleep time was the same for both treatments, subjects taking L-theanine reported a feeling of prolonged sleep and a significant decrease in fatigue upon rising. They awoke feeling refreshed, good-spirited and more self-confident (Figure 10).

Relaxation from PMS

Premenstrual Syndrome (PMS) in women often reported to be high 1-2 days prior to menstruation. Typical symptoms of PMS are generally categorized as mental, physical and social symptoms. In a volunteer study (20), the effect of Suntheanine on PMS was examined in twenty subjects. The subjects were treated with tablets containing either Suntheanine or placebo. Subjects took two tablets twice a day equal to an amount of 200 mg Suntheanine per day

for two weeks before the beginning of their menstrual period. The test duration consisted of three menstruation cycles. The first cycle was regarded as the control, where subjects were randomly treated with Suntheanine or placebo. In the second cycle, the subjects were divided into either Suntheanine or placebo group and treated accordingly. In third cycle, the subjects in each group were treated crossover. Three days prior to the expected date of the beginning of

each menstruation cycle, the test subjects were asked to answer Moos's Menstrual Distress Questionnaire (MDQ) (21). The symptoms were ranked in 0 to 3 scales, where the high score represents severe symptoms. The survey results indicated that the subjects administered with Suntheanine scored low compared to placebo in both mental and physical symptoms (Figure 11). These results suggest that Suntheanine is very effective in relieving the symptoms of PMS.

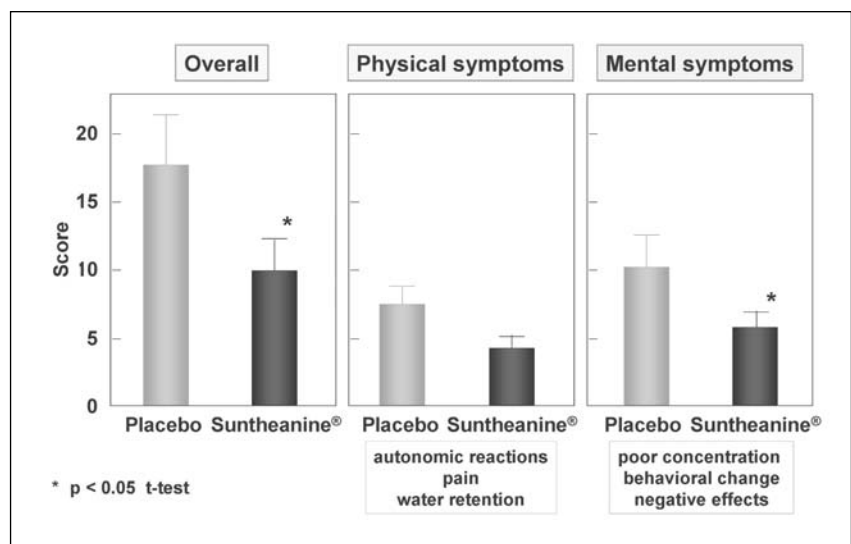


Figure 11 – Effect of Suntheanine® on PMS (MDQ scores)

CONCLUSION

Suntheanine, the brand name of Taiyo Kagaku Co. Ltd, Japan, is the pure and safe L-theanine enantiomer. Suntheanine has been studied for many years for its relaxation functions in various human stress conditions and proven to be effective in promoting the sense of relaxation during the anxiety, fatigue, physical stress, and PMS. It promotes relaxation without sedation to improve the quality of sleep and refreshed awakening.

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NutraCos news

TESTING THE EFFICACY OF BEAUTY PRODUCTS...

New literature is available from **Moritex** describing the latest version of its market-leading *Triplexense* skin counselling system.

The *Triplexense* is a hand-held, battery powered device equipped with three built-in CCD sensors that measure sebum (oiliness), moisture balance and skin elasticity. Operating *Triplexense* is as simple as one, two, three. Just enter the clients age, press the measure button and place the *Triplexense* on the area of a skin to be analysed. In 3 seconds the readings are complete.

WACKER RECEIVES EUROPEAN INNOVATION AWARD FOR COSMETICS AND CHEMICAL RAW MATERIALS

The Munich-based **Wacker Group** received a European Innovation Award for Cosmetics and Chemical Raw Materials on October 10 at the 53rd SEPAWA Conference in Würzburg, Germany. Developed for consumer products like skin-care articles, Wacker's novel linolenic acid / cyclodextrin complexes were awarded second prize in the "Most Innovative Natural Raw Material Concepts" category. In their fourth year, these Innovation Awards recognized outstanding achievements by the life-sciences industry in research, product development and training.

EHPM / ERNA RISK MANAGEMENT MODEL LEADS THE FIELD

As the EU debate on vitamins and minerals heats up, one risk management model has been hailed both useful and practical in determining safe maximum levels. The model, developed by the **European Responsible Nutrition Alliance (ERNA)** and the **European Federation of Associations of Health Product Manufacturers (EHPM)**, was deemed a useful tool in determining safe maximum levels for vitamins and minerals in food supplements across population groups, at a recent conference in Brussels. The vote of confidence came from a critical review conducted by research institute, **TNO Quality of Life**.

The model was praised for its practical approach to classifying all nutrients, providing a structured basis for risk management measures as opposed to a case-by-case approach.

SABINSA CORPORATION EXPANDS MANUFACTURING FACILITY IN UTAH

Sabinsa Corporation is completing the construction of a 17,000 square foot (ca. 1600 m²) expansion at its manufacturing and distribution facility in Payson, Utah, extending the company's current in-house manufacturing capabilities and capacity. This new facility includes cutting edge technology in design and function and will provide high volume capacity in fluid bed processing / granulation and high volume custom drum-to-hopper blends. Furthermore, analytical, microbiological and pilot laboratories are being constructed to assure product quality and consistency and

to facilitate product development and efficient batch scale-up. Discussions are presently being conducted to develop new business for this facility. Operations are scheduled to begin in March once all the installation qualifications and operational qualifications are completed.

NEW IMPROVED PEEL RIG FROM STABLE MICRO SYSTEMS

Stable Micro Systems has made significant improvements to its *Peel Rig*, which is used widely to evaluate the quality and strength of seals and adhesive bonds on pharmaceutical packaging. The new *Universal Peel Rig* incorporates a multi-position platform, allowing containers to be held flat or at 45° and 90° angles. As such, manufacturers can more precisely simulate the action of consumers, or handlers, to accurately assess both ease of use and stability of packaging seals.

CLA MAY SERVE CRITICAL ROLE IN PREVENTING WEIGHT AND FAT GAIN DURING YEAR-END HOLIDAYS

A study recently published online, in advance of publication in the prestigious *International Journal of Obesity*, suggest that **Tonalin® CLA** from **Cognis** could have long-term health benefits by preventing weight and fat gain commonly experienced by adults during the Christmas and New Year holiday season, and as part of the normal aging process. **Cognis Tonalin® CLA** (conjugated linolenic acid) is derived from natural safflower oil, is stimulant-free, and is the most clinically tested CLA on the market.