ETAS® Overview

Proprietary extract of *Asparagus officinalis*

ETAS® is a special enzyme-processed asparagus stem extract that has the ability to reduce stress and improve sleep. It works through an unusual pathway of triggering the release of the heat shock protein HSP70, which normally is produced by the body in response to the stress of exposure to excess heat. This effect is similar to the anti-aging and stress-relieving effects of hot springs. ETAS® has other benefits, including improving heart rate variability, enhancing cognitive performance, and reducing fatigue. ETAS® is rich in compounds known as hydroxymethylfurfural derivatives, which have been identified as novel compounds capable of inducing HSP70 expression (Ito, 2013). One of these compounds in ETAS® is a derivative known as asfural, from 5-hydroxymethyl-2-furfural (HMF-1). It has shown significant HSP70 mRNA expression-enhancing activity and has several biological activities, including antioxidant, antimyocardial ischemia, and effects for improving blood flow (Ito, 2013).

Derived from asparagus waste

The tender buds of asparagus stalks are a healthy, nourishing food often prepared and eaten in delicious, gourmet meals, though the tough stems are usually discarded and not thought to have any value. The waste part of the stalk has been found by researchers to have amazing wellness benefits after it is specially processed with enzymes and its elements have been extracted.

Heat shock protein background

Heat shock proteins (HSPs) are intracellular proteins induced by various stresses, principally from excess heat exposure. They help protect and repair the body's cellular proteins from heat damage that would otherwise deform and denature these proteins, rendering them nonfunctional. They are hypothesized to be the reason for the anti-stress and anti-aging effects of thermal and spa treatments. Heat shock proteins are also stimulated by exercise and calorie restriction, which are known to have life-extension effects in animal studies (Iguchi, 2012, Calderwood, 2009). Some HSPs (HSP70) directly protect cells against damage that would lead to earlier cell death known as apoptosis. However, the heat shock response declines in potency over one's lifetime, and a weakening of the response contributes to aging by allowing protein-aggregation diseases to develop. This in turn leads to reduction in cellular vigor and decreased longevity (Calderwood, 2009).

HSP70 (with a molecular weight of 70,000) has a number of beneficial physiological effects in the body, including reduced cell death, anti-inflammatory activity, and antioxidant activity. The protein is induced by several stresses such as heat, starvation, alcohol intake, and ultraviolet radiation (Doeppner, 2013; Matsuda, 2013; Agaki, 2013). It has been found that HSP70 also decreases with age and may be related to low-grade inflammation found in the aging process (Njemini, 2011).

Reduction in stress parameters

ETAS® markedly suppressed corticosterone, a stress hormone measured in sleep-deprived mice. Human studies have shown that ETAS® can reduce stress and improve sleep quality. In a study of 14 healthy volunteers divided into 2 groups, a placebo group and an ETAS® group (7 subjects in each group), it was found that the ETAS® group that ingested 300 mg of ETAS® daily for a week had 3 times the expression of HSP70 mRNA in white blood cells compared with before and after intake (Amino Up, sales bulletin, Hokkaido, Japan). Stress reduction was shown in a human clinical trial as HSP70 level in peripheral blood increased by the intake of ETAS® (Nishihira).

Another method of testing the stress-reducing effect of ETAS® was to observe its effect on the autonomic nervous system (ANS). This was done by analyzing heart rate variability (HRV) through measuring the pulse wave acceleration using the Pulse Analyzer Plus TAS9. In a human clinical study, 30 healthy volunteers were divided into 2 groups, placebo and ETAS®, with 15 subjects in each group. The group ingested 400 mg of either ETAS® or placebo daily for 4 weeks. The results of the study showed that ETAS® improved the stress response by improving the state of the ANS.

Sleep improvement

Sleep-related problems improved with ETAS® as demonstrated in a randomized, double-blind, placebo-controlled crossover clinical study at Hokkaido Information University. Sixteen healthy male volunteers with sleep-related problems were given 300 mg/day of ETAS®. Serum cortisol went up 45% in the placebo group, whereas in the ETAS® group the increase was only 10% (Amino Up, unpublished study). The ETAS® group suppressed the rise in blood-cortisol-caused stress by roughly 80%. Salivary cortisol increased by only 47% in the ETAS® group compared with 75% in the control group. A marker of psychological stress known as chromogranin A decreased 2.5 times more in the ETAS® group compared with the control group.

To find out what effect it has on sleep quality, an actigraphy analyzer was used in a human clinical trial to determine whether ETAS® would be effective for prevention of sleep disorders. An actigraphy instrument monitors rest and activity cycles during sleep with a sensor worn by a patient. The quality of sleep was significantly improved by ETAS® , which was safe and well-tolerated. The levels of serum cortisol, salivary cortisol, and chromogranin

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A all decreased, indicating an improvement in stress. ETAS® was effective for improving the quality of sleep and reduction of mental stress (Nishihira).

Another placebo-controlled study of ETAS® for sleep quality used the Athens Insomnia Scale, which examined sleep onset, night and early-morning waking, sleep time, sleep quality, frequency and duration of complaints, distress caused by the experience of insomnia, and interference with daily functioning. The ETAS® group was 0.40 points higher than the placebo group. Sleep quality and dreaming frequency decreased by almost 2 points in the placebo group, but in the ETAS® group it increased by 5.4 points. In the visual analogue scale of sleep quality-of-life measures, appetite was affected negatively by 6.1 points; however, in the ETAS® group it was improved by 9.1 points.

Improved mood and energy

ETAS® is effective in reducing fatigue and feelings of unhappiness (dysphoria) caused by stress at a dose of only 150 mg per day (Waki, 2013). In a randomized, double-blind, placebo-controlled crossover trial published in *Clinical Nutrition*, 25 healthy volunteers were given 150 mg/day of ETAS® or a placebo for 28 days with a 14-day washout period. The examination used a questionnaire survey of the subject's energy or fatigue condition in a sitting position and utilized mental arithmetic to cause psychological stress. The autonomic-nervous functions were measured by the heart rate variability analyses using an active orthostatic test. After the mental arithmetic test, different stress parameters were analyzed, including serum catecholamine hormones, sIgA (a salivary immune factor that is reduced from stress), and cortisol. The results of ETAS® intake for 28 days showed an increase in the levels of sIgA, reduced feelings of tiredness in daily living, and an improvement in the dysphoric condition.

Other beneficial effects on physiology

ETAS® has powerful beneficial effects on diverse areas of physiological functions. It has anti-inflammatory activity in liver cells through suppressing nitric oxide (Nishizawa, et al.). In intestinal epithelial cells, ETAS® reduces cell toxicity and excess cell proliferation under normal conditions and under oxidant stress. The addition of ETAS® to neuron cell cultures attenuates cellular stress through upregulation of HSP70 proteins. Pretreatment of ETAS® in PC12 nerve cells used in Alzheimer's disease research was able to prevent beta amyloid (βA)–induced cell death. ETAS® significantly attenuated βA-induced DNA damage as well as generation of reactive oxidized species. The results showed that ETAS® is especially capable of protecting brain cells from damage by enhancing cell viability in beta amyloid–treated (Ogasawara).

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