Advitech SOLUTIONS

Taking it easy, naturally

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Stress affects your health

Did you know?

• Stress is directly linked to the six leading causes of death in the U.S.: heart disease, cancer, lung ailments, accidents, cirrhosis of the liver and suicide.

• The majority of back problems are related to stress.

• Nearly one in four full-time working mothers with children under 13 say they feel stressed almost every day.

Stress has become an important health concern in modern society. Stress is both additive and cumulative in its negative effects on individuals, organizations and societies. Stress is a worldwide phenomenon. when not translated in hours lost at work, are paid back in compromised health. Early signs of stress include headache, mood and sleep disturbances, difficulty concentrating, upset stomach, as well as deteriorating relationships with family and friends.

Stress is directly linked to the six leading causes of death in the U.S: heart disease, cancer, lung ailments, accidents, cirrhosis of the liver and suicide. Moreover many psychiatrists believe that the majority of back problems - one of the most common adult ailments in the United States - are related to stress. The Global Burden of Disease study, conducted by researchers at Harvard University, Cambridge, MA, found mental disorders, including suicide, ranked second only to cardiovascular conditions as social burdens for developed nations.

Is not surprising that people living in developed societies are searching for solutions to reduce the impact of stress in their lives, and the popularity of prescription drugs, even with the long list of their side effects, is increasing fast. But is there such a thing as a safe and effective natural option to stress relief? We believe so.

Coping with stress

Stress is an unavoidable part of life. It can result from many things, both physical and psychological. It can arise from a welcome event such as the birth of a child or a difficult situation such as divorce. Stress can be either chronic or acute and manifests itself in many different ways, depending on the individual.

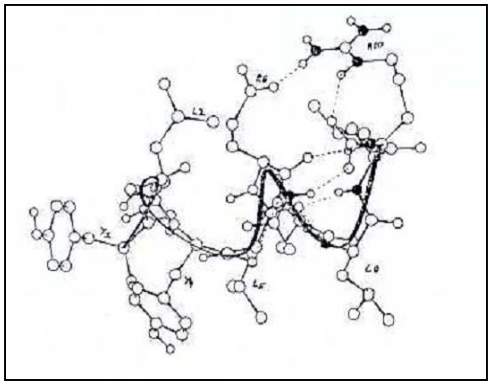
While stress is often viewed as a psychological problem, it has very real physical effects. The body responds to stress by triggering a chain reaction of physiological changes: increased secretion of adrenaline, elevation of blood pressure, acceleration of the heartbeat, greater tension in muscles, release of fats and sugars, rise in cholesterol levels as well as increased production of adrenocorticotropic hormone (ACTH) followed by the release of the hormones cortisone and cortisol. The increased production of adrenal hormones is responsible for a number of symptoms

associated with stress. The consequences of hormone imbalances can be exacerbated by hormone deficiencies. The result, especially with prolonged or recurrent stress, is that the body becomes deficient in many nutrients causing a number of stress related health disorders.

Proper nutrition and dietary supplements that include B-vitamins, minerals, essential fatty acids and amino acids combined with exercise, relaxation and the proper attitude are all part of a stress management program. Some supplements on the market offer promises of relaxation and well-being but it is not always clear how they work and how safe they are.

PNT 200®

PNT 200® contains a milk casein trypsic hydrolysate which has been tested for its anxiolytic effect. Using molecular separation technologies, a peptide having the specific anxiolytic-like activity was isolated from the hydrolysate. The bioactive compound called αs1-casein peptide binds to the benzodiazepine site of the $GABA_A$ receptors in vitro. These findings indicate that αs1-casein peptide carries the activity of the casein hydrolysate possibly by acting via the $GABA_A$ receptors(Miclo et al., 2001). Gamma-aminobutyric acid (GABA) is the predominant inhibitory neurotransmitter in the central nervous system (CNS).



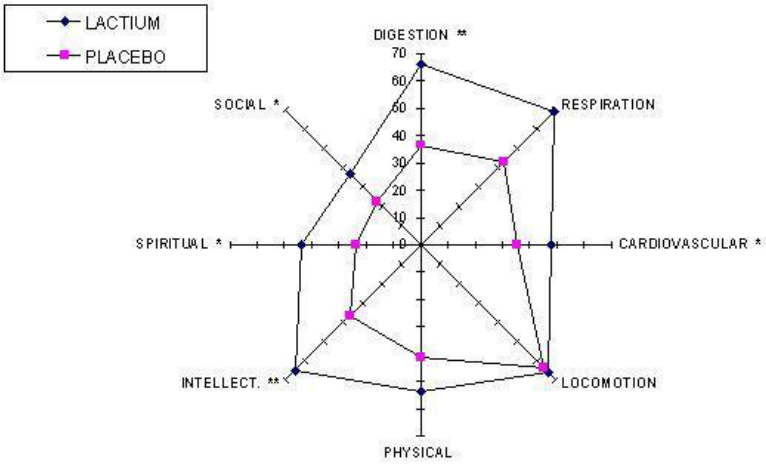
The anti-stress properties of PNT 200® were tested in pre-clinical studies on rats, as well as in clinical studies on humans (Lefranc, 2001). The potential anxiolytic activity of the casein hydrolysate was tested in rats using the conditioned defensive burying experiment (CDB), and its activity was compared to those of diazepam (chemical benzodiazepine compounds) and placebo. The anxiety global score was strongly reduced by an oral administration of PNT 200® compared to the placebo. The effect of the casein hydrolysate on anxiety was similar to the diazepam effect. Effects were observed 30 minutes after administration (Lefranc et al., 2001). Moreover, PNT 200® did not produce any subsequent behavioral, neurological or toxicolocigal effects nor did it cause dependency, amnesiac or tolerance effect.

Using the CDB test model, it was demonstrated that PNT 200® was more efficient in reducing stress responses than St. John's Wort or Kava Kava, whose effects were similar to the effect of placebo. Moreover, it was shown that PNT 200® was also more efficient than L-theanine at reducing stress. L-theanine, at 100 mg/kg, showed a similar response than PNT 200® at only 15 mg/kg.

Four clinical studies including more then 180 volunteers were also conducted. All studies were double-blind placebo controlled, one study followed also a cross-over design. The main results of the first 3 studies are summarized as follows:

Grenoble 24 healthy subjects	double-blind placebo controlled. Group 1, PNT 200® 2 x 150 mg; for 15 days Group 2, PNT 200® 2 x 75 mg; for 15 days Group 3, placebo; for 15 days Cattell and Spielberger stress scale. Stroop test at day 0 and day 15.	Volunteers with a high anxiety levels had a smaller increase in their global anxiety-state score in the PNT 200® group compared to the placebo group
NECKER HOSPITAL (Paris) 42 healthy volunteers	double-blind placebo controlled. 2 x 200 mg PNT 200 the day before test and 1 X 200 mg the day of the test mental stress test (Stroop test) and a physical stress test (Cold Pressor test)	- During the Stroop test, SBP and DBP had a significantly smaller increase in PNT 200® treated subjects than in control ones. - The plasmatic cortisol concentration of PNT 200-treated subjects significantly decreased while that of control ones remained stable.
CRSSA (La Tronche)52 healthy subjects	double-blind placebo controlled. 150 mg daily PNT 200® for 30 days Stroop test before the beginning of treatment at D0 (baseline); at D11 and at D 31 of treatment ; and at the end of a 12 day-period of washout (D43).	- The mean blood pressure (MBP) stress reactivity was lowered at D11 and D31 in subjects taking PNT 200® compared to subjects taking placebo. - The mean blood pressure reactivity was particularly significantly lowered in the PNT 200® group at D11 and D31 in high stress responder subjects. And this effect remained significant at D43 after the washout period.

A double-blind placebo controlled and cross-over designed study was carried on 63 female volunteers showing at least one symptom of stress. Subjects received 150 mg of the casein hydrolysate or a placebo for 30 days. A significantly greater positive evolution of stress symptoms was demonstrated in the PNT 200® group compared to the placebo group in 5 areas of health problems: digestive, cardiovascular, intellectual, emotional and social. PNT 200® had a greater effect on subjects having a high stress intensity score at the beginning of the study.



Improvement of the Major Stress Symptoms (%) at day 30 on the subjects with the highest initial Intensities (>4 at D0)

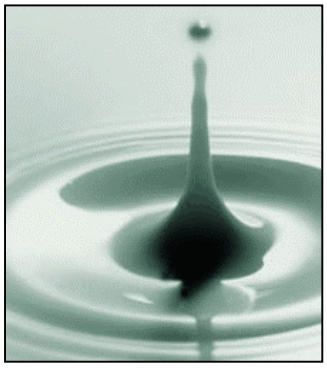
These previous studies strongly established the efficacy of PNT 200® compared to placebo in treating the effects of stress situations. PNT 200® produces a noticeable effect in as little as one hour and optimal results can be observed after 10 days of treatment. These results also suggest that PNT 200® reduces the intensity of the physiological reactions triggered by stress. In other words, it helps the body adjust better and become more equipped to deal with stressful situations.

Conclusion

Herbal compounds may present promising anti-stress and mood enhancing properties but generally, the lack of standardization and their adulteration makes difficult to ascertain a safe clinical use. Also, plant extracts are very rich in different bioactive compounds possessing a large spectrum of activities. For the majority of the plant extracts, the compound carrying the anxiolytic effect has not been well identified. Compared to herbal remedies, the PNT 200® bioactive compound and its activity are well characterized making possible a good standardization of the product. The natural peptide having the biological effect has been identified and characterized. Its spatial structure has also been modeled with NMR spectroscopy. The decapeptide binds to the $GABA_A$ receptors like benzodiazepines but does not induce side effects like dependence, tolerance, loss of memory and drowsiness (Lecouvey et al., 1997). Each capsule (200 mg) of PNT 200® contains 2.5 mg of the bioactive peptide.

Helps the body better adjust to stress:

- *Proven efficacy*
- *Controlled process*
- *No dependency*
- *No toxicity*
- *No memory loss*
- *No drowsiness*



Herbal remedies are considered to be safe. However, they may induce moderate side effects as photosentization, mild diarrhea and slight sedation, insomnia and irritability, as well as more severe side effects as mild nausea, heartburn, flatulence, feelings of fullness, and rumbling sensations. PNT 200® induces no side effects, which has been demonstrated in pre-clinical and clinical studies.

Clinical trials have a hard time demonstrating a true drug activity because of the high placebo response observed in the field of anxiety and depression disorders. In this respect, it is important that alternative therapies succeed to prove that they are more efficient compared to placebo in reducing stress or depression in well-controlled clinical trials. In general, herbal remedies need more quality clinical evidences to demonstrate their efficacy compared to placebo in reducing stress. PNT 200® has been shown to be very effective in reducing stress responses and stress symptoms compared to placebo in well controlled-clinical trials. Moreover, studies in rats using the CDB model have shown that PNT 200® is more efficient in reducing stress responses then St. John's Wort, Kava Kava and L-Theanine.

REFERENCES

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