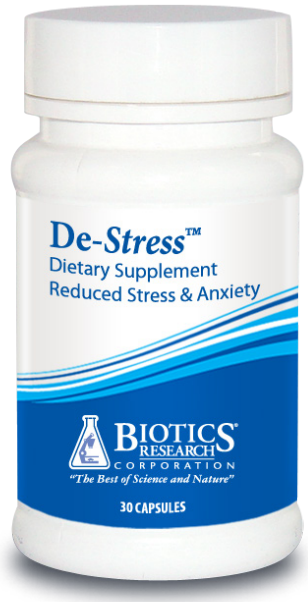
De-*Stress*™



For some mammalian species (including humans), the newborn is an external embryo. The milk they receive becomes the umbilical cord which links the newborn to the maternal organism (the mother). A baby's enzymatic system is different from that of the adult, especially concerning low pepsin levels, thereby displaying predominant trypsic activity.

Observing the baby's calm state after drinking warm milk, a research team from Nancy University observed the link between the trypsic activity in the milk and the calm state of the baby. This led to research on the milk casein hydrolysate fractions and peptides with anxiolytic activity.

De-*Stress*™, Defined

De-*Stress*™ is a patented, specially produced milk protein hydrolysate, which constitutes a specific peptide concentrate, having demonstrated anxiolytic activity. Anxiolytic activity refers to the action of medications prescribed for anxiety symptoms.

The Peptide

Identification of the peptide began with the laboratory production of an alpha-S1 casein trypsic hydrolysate (as1-casein), which demonstrated anxiolytic activity both *in vitro* (GABAA receptor-binding test and peripheral-type benzodiazepine binding assays) and *in vivo* (elevated plus maze test and conditioned defensive burying test, in rats).[1,2]

Amino acid sequencing identified the peptide as a "benzodiazepine–like decapeptide"[1] Utilizing molecular separation techniques, the peptide demonstrating specific anxiolytic activity, was isolated from the trypsic hydrolysate. The results of circular dichroism, two- dimensional NMR spectroscopy, and molecular modeling characterized the peptide as a 310 helix structure, initiated and terminated by an alpha-turn. In addition to the structural determination, it was observed that the decapeptide exhibited an amphiphilic characteristic, with the hydrophobic side chains located on one side of the molecule, and the hydrophilic side chains on the opposite side, thus indicating that it was "essentially flexible"[3]. Accordingly, the peptide was hypothesized to have the ability to cross both hydrophobic and hydrophilic membranes. Further classification of the peptide structure was confirmed by three-dimensional molecular modeling.[4]

Pre-Clinical Studies

The action of **De-*Stress*™** casein hydrolysate was demonstrated in randomized double blind studies, utilizing Wistar rats. The anxiolytic activity, reported as being similar to diazepam, was confirmed in these subjects. Results indicated that at a dosage of 3mg/kg, various activities demonstrated significance, including a decreased duration of probe burying ($P<0.005$), head stretches toward the probe ($P<0.01$), and the percent approaches towards the probe followed by retreats ($P<0.01$).[1] Additionally, rats given a 3mg/kg dose of the as1-casein tryptic hydrolysate (**De-*Stress*™**) were demonstrated to show a significant reduction in the action of pentylenetetrazole (PTZ) ($P<0.002$), which is similar to the action of diazepam (2mg/kg).[1]

The **De-*Stress*™** casein hydrolysate was also shown to have a "protective effect" on sleep, when subjects were exposed to chronic mild stress, observed as a maintenance of slow wave sleep duration," along with a minor increase in paradoxical sleep duration.[5]

Human Clinical Trials

In a double-blind, randomized, crossover, placebo controlled trial, sixty-three female volunteers were randomly assigned to receive either as1-casein (150mg/day) or placebo. Following a

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thirty-day treatment program, the as 1-casein hydrolysate group was observed to have reduced stress-related symptoms. The study correlated a reduction in stress related symptomatology to improvements in the following areas; digestion (P<0.05), cardiovascular (P<0.05), intellectual (P<0.05), emotional (P<0.05), and social (P<0.05) complications.[6]

In a subsequent study forty-two healthy male volunteers partook in a randomized, placebo controlled, double blind trial. The results indicated an "antistress activity in human subjects", as evidenced by a significant decrease in plasma cortisol in the as1-casein group (20.69%) (t=3.73; P=0.001), compared to placebo (3.39%) (t=1.05; P=0.30). Additionally, both the systolic and diastolic blood pressures were significantly higher in the control group as compared to the as1-casein group. A decrease in heart rate (P=0.05) was also noted in the as1-casein group, compared to placebo.

In another double-blind crossover study, sixty-three women volunteers, presenting with at least one symptom of stress, were randomized to either receive **De-*Stress*™** or placebo for thirty days. A 30d washout period was then performed, followed by a reversal in the treatment regiments. The subjects answered questionnaires on the 1st, 15th, and 30th day of each treatment period. The questionnaires covered three main areas and eight sub-areas potentially affected by stress. The results indicated a significant improvement on the digestive system (58% vs. 38.6% for placebo) and the cardiovascular system (53.4% vs. 21.8% for placebo) in those subjects initially demonstrating the highest intensities for their major symptoms. Additionally, a significant improvement in five areas was noted following the 30d treatment with **De-*Stress*™** in subjects initially demonstrating the highest intensities of symptoms (>4/day). The areas of improvement were noted in digestive function (66.1% vs. 36% for placebo), cardiovascular problems (48% vs. 35.5% for placebo), intellectual disorders (64.8 vs. 36.7% for placebo), emotional disorders (43.8% vs. 23.5% for placebo) and social problems (36.7% vs. 22.5% for placebo).[8]

Thus confirming evidence indicates that **De-*Stress*™** has anxiolytic activity. As such administration has shown beneficial results towards alleviating symptoms of stress, including digestive, cardiovascular and anxiety effects.

References

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De-*Stress*™ is available in 30-count bottles (#7707).

Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	% Daily Value
De-*Stress*™ hydrolysate † (as hydrolyzed casein concentrate)	150 mg	*

*** Daily Value not established**

Other ingredients: Capsule shell (gelatin and water).

Contains ingredients derived from milk.

† De-*Stress*™ supplies a decapeptide, as determined by its amino acid sequence, having anxiolytic activity. **‡ This statement has not been evaluated by the U.S. Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.**

Patent # 5,846,939

This product is gluten free.

RECOMMENDATION: One (1) capsule each day as a dietary supplement or as otherwise directed by a healthcare professional. **De-*Stress*™** can be taken during the day at time of intense stress or before bedtime.

KEEP OUT OF REACH OF CHILDREN
Store in a cool, dry area.
Sealed with an imprinted safety seal for your protection.

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