

Life Extension Magazine April 2011

COVER STORY

Widely Used in Europe... Natural Sedative Restores Youthful Sleep

If you find yourself routinely struggling to fall asleep—or to stay asleep—you're not alone. A staggering **30%** of Americans suffer from **chronic insomnia**,¹ while approximately **60** million experience problems falling asleep in a given year.²

In addition to its adverse impact on mood and quality of life, chronic insomnia can increase one's risk for most degenerative diseases.³⁻¹⁰



In the search for natural ways to combat this health threat, researchers have isolated a set of nutritional compounds called **bioactive milk peptides** that promote sustained and restful sleep patterns while inducing a state of relaxation.

Bioactive Milk Peptides: A Natural Sedative?

For generations, mothers have given their children a warm glass of milk before bed as a way to help them fall asleep. As far back as **1934**, this home remedy gained scientific validation when it was observed that people who ate milk and cornflakes were more likely to enjoy a full night of uninterrupted sleep.¹¹

In **1997**, pediatric researchers added to the evidence by demonstrating that newborns given an infant formula containing milk fell asleep not solely due to nursing and being held, but owing specifically to something in milk itself.¹²

In **2000**,¹³ researchers identified what that “something” was. It turns out that nutrients found in cow's milk called **bioactive peptides** (chains of amino acids) exert a *sedative* effect on the brain and induce sustained sleep patterns.

These **bioactive milk peptides** have since been shown to act on the brain's **GABA-A** receptors,¹⁴ the same mechanism of action that makes the class of sedatives known as *benzodiazepines* so effective.¹⁵ The advantage of milk peptides, of course, is that they induce relaxation and sleep without the side effects associated with long-term benzodiazepine use.

In pre-clinical models, milk peptides^{15,16} markedly reduce anxiety and improve sleep in animals subjected to chronic stress.¹⁷

In *human* studies, a proprietary **bioactive milk peptide** compound used widely in **Europe** has been shown to effectively induce relaxation, leading not only to deeper, more restorative sleep, but also to substantial improvements across a wide range of **stress markers**.

Bioactive Milk Peptides: Reducing Stress, Restoring Sleep

When given this proprietary **bioactive milk peptide** compound, aging individuals suffering from stress-related symptoms and chronic insomnia consistently exhibit substantial reductions in biomarkers associated with the stress response. These stress response biomarkers include elevated **cortisol**, **heart rate**, and **blood pressure**, along with physical and **psychological symptoms**.



In a number of especially noteworthy published studies, the improvements in **stress-related markers** proved to be both significant and system-wide.

For example, a group of over 60 women suffering from a constellation of stress-related problems was given **150 mg per day** of this **bioactive milk peptide** compound.¹⁸ Before treatment, they suffered from a broad range of symptoms, including digestive, cardiovascular, pulmonary, emotional, cognitive, and social disorders.

Compared to controls, after just 30 days, significant improvements were observed for the **milk peptide** group in symptoms related to digestion (**65.6%** improvement—21% greater improvement than the placebo group), cognitive function (**62.5%** improvement—16.3% over placebo), cardiovascular function (**48.9%**—9.9% over placebo) and social difficulty (**40.2%**—9.7% greater than placebo).¹⁸

Interestingly, for those women exhibiting symptoms of the highest intensity at the outset of the study, the 30-day improvements were dramatic:¹⁸

As evidenced in the table below, compared to the placebo group, these women saw their stress-related conditions slashed across the board, with improvement almost **30% higher** in some symptom categories.¹⁸ Similarly compelling results have been observed in men.

PERCENTAGE IMPROVEMENTS IN STRESS-RELATED CONDITIONS*			
Symptom	Placebo Group	Milk Peptide Group	% Difference
Digestive	36.6	66.1	29.5
Cardiovascular	35.5	48.0	12.5
Pulmonary	43.1	68.9	25.8
Cognitive	36.7	64.8	28.1
Emotional	23.5	43.8	20.3
Social	22.5	36.7	14.2

* Recorded in women with the highest intensities of symptom manifestation.

Cortisol Levels Slashed in Human Study

In a double-blind study involving over 40 healthy male subjects,¹⁹ two groups were subjected to psychological and physical stress tests, with cortisol concentrations, heart rate, and blood pressure levels measured at specific intervals.

Each of these three stress response markers were substantially lowered in the group taking the proprietary **bioactive milk peptide** compared to controls.¹⁹

Cortisol levels in the **placebo** group—measured before and after administration of stress testing—saw a net change of only **-3.39%**. This means that the harmful spike in cortisol typically caused by stressful situations was almost entirely unaffected in the group that did not receive treatment. By comparison, the **milk peptide** group experienced a net reduction in **cortisol** of **-20.69%**. In other words, the release of cortisol was kept under control by the **milk peptides**, limiting its detrimental effects.¹⁹

WHAT YOU NEED TO KNOW: NATURAL SEDATIVE RESTORES YOUTHFUL SLEEP

- Over 30% of Americans suffer from chronic insomnia, while approximately 60 million experience problems falling asleep in a given year.
- The dire health consequences of sleep debt range from chronically elevated levels of cortisol (the stress hormone), insulin resistance, and increased fat storage to greater risk of mortality from all causes, including cancer and cardiovascular disease.
- A proprietary set of bioactive milk-derived peptides used widely in Europe has been identified that operate along the same neurological pathways as anti-anxiety drugs—without side effects.
- Published studies show they effectively combat the stress response, blunt elevations of cortisol, and relieve anxiety.
- Milk peptides decrease the amount of time it takes to fall asleep, improve sleep efficiency, and increase daytime wakefulness.
- By improving several aspects of healthy sleep, milk peptides may offer protection against the many health disorders associated with sleep deprivation.



Cardiovascular Benefits

The **milk peptide** group also experienced an almost **50% lower** increase in heart rate when placed under stress than those in the placebo group.¹⁹

The same beneficial effects were observed in **blood pressure** readings in the milk peptide group after placement under experimental stress. Following the mental stress test, for example, systolic blood pressure increased **21.25%** in the control group, but only **14.65%** in the milk peptide group. Similarly, diastolic blood pressure readings increased **21.24%**, compared to **15.26%** in the peptide group.¹⁹

The proprietary milk peptide yielded positive outcomes in nearly all indicators measured, for both men and women.

Human Studies Verify Sleep Efficacy

Recent studies validate milk peptides' capacity to *restore* more restful sleep patterns while enhancing daytime performance and cognition.

In a placebo-controlled study of 165 healthy adults with a history of **insomnia**, participants were given **150 mg** of milk peptides or placebo each day for one month.

Changes in their ability to relax and fall asleep were evaluated using established diagnostic tools that measure **27 individual indicators** of sleep disorders and insomnia-related problems (including daytime cognition and overall function).²⁰

THE KEY TO FALLING ASLEEP: COMBATING CORTISOL AND THE STRESS RESPONSE

At the core of this proprietary milk peptide compound's sedative effect is a demonstrated power to effectively blunt the **stress response**, a primary causative factor in chronic insomnia.

Stress, anxiety, and sleep deprivation share one crucial feature in common:²² each prompts your adrenal glands to secrete **cortisol**,^{23,24} the stress hormone. Since most people now encounter significant stress in their daily lives, chronic cortisol overexposure probably accounts to a great extent for the extraordinary prevalence of insomnia today.



As an evolutionary adaptation to temporary external dangers, cortisol enhances alertness, raises your heart rate, and increases blood pressure. It mobilizes energy *toward* handling a challenging situation and away from a relaxed, inattentive state. This may enable you to manage a sudden crisis effectively, but it also makes it difficult, if not impossible, **to fall asleep**. In this sense, cortisol release evolved as a temporary, stopgap measure, but our physiology is not structured to withstand sustained cortisol exposure.

Cortisol also boosts **insulin levels**.²² This in turn creates a metabolic environment that predisposes aging individuals to fat storage. Sleep deprivation also causes us to consume an average of **221 more calories** the next day than we normally would.²⁵

Interestingly, researchers have discovered that the adverse metabolic impact of even short-term cortisol elevations (increased blood sugar and higher insulin levels) is **more pronounced in the evening than in the morning**.²⁶

Together with other similarly harmful effects, chronically elevated cortisol levels can set in motion a cascade of pathologic physiological processes that hastens the onset of virtually all degenerative diseases. This is no longer a matter of scientific conjecture: over the past two decades, insufficient or poor-quality sleep has been definitively linked to **increased mortality from all causes**.²⁷⁻³⁰

The proprietary milk peptide yielded positive outcomes in **nearly all indicators measured**, for both men and women.²⁰ Sleep quality, sleep efficiency, sleep disturbances, and daytime dysfunction were all improved, especially in individuals who suffered from moderate symptoms of anxiety or depression.

These results were confirmed by yet another clinical analysis of bioactive milk peptides in adults suffering from **pronounced sleep disturbances**.

Thirty-two healthy men and women suffering from insomnia during the preceding six months took a **150 mg capsule** of patented milk bioactive peptide one hour before bedtime—or placebo—for a month.²¹

After two weeks, the bioactive milk peptide group experienced a **50%** improvement in *sleep quality*. At four weeks, they needed **30%** less time to fall asleep and experienced improvements in daytime alertness and function.²¹



Summary

The dire health consequences of sleep deprivation range from elevated levels of cortisol (the stress hormone), insulin resistance, and increased fat storage to greater risk of mortality from all causes, including cancer and cardiovascular disease. In both animal and human studies, a proprietary set of **bioactive milk-derived peptides** used widely in **Europe** has been shown to effectively combat the stress response, blunt elevations of cortisol, and substantially eliminate stress-related symptoms across multiple systems of the body. The result is improved ability to relax and fall asleep. Using established diagnostic tools that measure sleep disorders and insomnia-related problems, this proprietary **milk peptide** yielded positive outcomes in **nearly all indicators measured**, for both men and women.

If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-864-3027.

THE DEADLY EFFECTS OF CHRONIC INSOMNIA: AN UNFOLDING PANDEMIC



When your body is chronically deprived of sleep, levels of the stress hormone **cortisol** tend to rise, especially at the end of the day.³¹ This, in turn, raises insulin levels. Insulin promotes a metabolic environment that encourages the storage of fat. Stress, anxiety, and mild depression are the most common causes of chronic insomnia.³²⁻³⁷ Together, these unwanted phenomena negatively affect circadian rhythms and modify both sleep duration and sleep quality.³⁸

The range of data published during the last decade reveal a horrific, ever-growing epidemic of stress-related insomnia in the US.

According to a published 2001 scientific poll, **38%** of American adults reported obtaining **8** hours of sleep; by 2009, that number had decreased to only **28%**.³⁹

People suffering from chronic sleep debt can expect to experience adverse physiological changes in blood pressure, endocrine function, glucose and lipid metabolism, and sympathetic and parasympathetic nervous system balance. In contrast, studies show that sleeping 7 to 8 hours each night *reduces mortality from all causes*,⁴⁰ including automobile accidents due to drowsiness (drowsy driving causes more than 100,000 crashes a year, resulting in 40,000 injuries and 1,550 deaths).⁴¹

In addition to dermatological disorders, sleep studies have linked chronic insomnia to the following conditions:

- Anxiety and depression^{32,33,35}
- Cancer^{3,42,43}
- Impaired cognitive function (concentration and memory loss)^{4,44-46}
- Metabolic syndrome^{5,47}
- Cardiovascular disease⁴⁸⁻⁵¹
- Diabetes^{6,7,52}
- Impaired insulin action^{53,54}
- Impaired glucose control^{55,56}
- Increased body mass index (BMI)^{8,57}
- Elevated C-reactive protein levels^{9,58}
- Elevated evening cortisol levels^{6,59}
- Hypertension^{10,60}

References

1. Roth T. Insomnia: definition, prevalence, etiology, and consequences. J Clin Sleep Med. 2007 Aug 15;3(5 Suppl):S7-10.
2. Available at: <http://www.npr.org/templates/story/story.php?storyId=90638364>. Accessed January 14, 2011.
3. Arendt J. Shift work: coping with the biological clock. Occup Med (Lond). 2010 Jan;60(1):10-20.
4. Thase ME. Correlates and consequences of chronic insomnia. Gen Hosp Psychiatry. 2005 Mar-Apr;27(2):100-12.

5. Violanti JM, Burchfiel CM, Hartley TA, et al. Atypical work hours and metabolic syndrome among police officers. *Arch Environ Occup Health*. 2009 Fall;64(3):194-201.
6. Gangwisch JE. Epidemiological evidence for the links between sleep, circadian rhythms and metabolism. *Obes Rev*. 2009 Nov;10 Suppl 2:37-45.
7. Hayashino Y, Fukuhara S, Suzukamo Y, et al. Relation between sleep quality and quantity, quality of life, and risk of developing diabetes in healthy workers in Japan: the High-risk and Population Strategy for Occupational Health Promotion (HIPOP-OHP) Study. *BMC Public Health*. 2007 Jun 28;7:129.
8. Buscemi D, Kumar A, Nugent R, Nugent K. Short sleep times predict obesity in internal medicine clinic patients. *J Clin Sleep Med*. 2007 Dec 15;3(7):681-8.
9. Meier-Ewert HK, Ridker PM, Rifai N, et al. Effect of sleep loss on C-reactive protein, an inflammatory marker of cardiovascular risk. *J Am Coll Cardiol*. 2004 Feb 18;43(4):678-83.
10. Kim J, Jo I. Age-dependent association between sleep duration and hypertension in the adult Korean population. *Am J Hypertens*. 2010 Dec;23(12):1286-91.
11. Laird DA, Drexel H. Experimenting with food and sleep. I. Effects of varying types of foods in offsetting sleep disturbances caused by hunger pangs and gastric distress-children and adults. *J Am Diet Assoc*. 1934;10:89-94.
12. Blass EM. Infant formula quiets crying human newborns. *J Dev Behav Pediatr*. 1997 Jun;18(3):162-5.
13. Clare DA, Swaisgood HE. Bioactive milk peptides: a prospectus. *J Dairy Sci*. 2000 Jun;83(6):1187-95.
14. Delini-Stula A, Holsboer-Trachsler E. Treatment strategies in anxiety disorders--an update. *Ther Umsch*. 2009 Jun;66(6):425-31.
15. Miclo L, Perrin E, Driou A, et al. Characterization of alpha-casozepine, a tryptic peptide from bovine alpha(s1)-casein with benzodiazepine-like activity. *FASEB J*. 2001 Aug 15;15(10):1780-82.
16. Violle N, Messaoudi M, Lefranc-Millot C, et al. Ethological comparison of the effects of a bovine alpha s1-casein tryptic hydrolysate and diazepam on the behaviour of rats in two models of anxiety. *Pharmacol Biochem Behav*. 2006 Jul;84(3):517-23.
17. Guesdon B, Messaoudi M, Lefranc-Millot C, Fromentin G, Tome D, Even PC. A tryptic hydrolysate from bovine milk alpha(S1)-casein improves sleep in rats subjected to chronic mild stress. *Peptides*. 2006 Jun; 27(6):1476-82.
18. Kim JH, Desor D, Kim YT, et al. Efficacy of alphas1-casein hydrolysate on stress-related symptoms in women. *Eur J Clin Nutr*. 2007 Apr;61(4):536-41.
19. Messaoudi M, Lefranc-Millot C, Desor D, Demagny B, Bourdon L. Effects of a tryptic hydrolysate from bovine milk alphaS1-casein on hemodynamic responses in healthy human volunteers facing successive mental and physical stress situations. *Eur J Nutr*. 2005 Mar;44(2):128-32.
20. So Ken Study: Effect of Lactium® on sleep disorders. October, 2006.

21. de Saint-Hilaire Z, Messaoudi M, Desor D, Kobayashi T. Effects of a bovine alpha S1-casein tryptic hydrosylate (CTH) on sleep disorder in Japanese general population. *The Open Sleep Journal*. 2009;2:26-32.
22. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. *Lancet*. 1999 Oct 23;354(9188):1435-9.
23. Weissman MM, Greenwald S, Niño-Murcia G, Dement WC. The morbidity of insomnia uncomplicated by psychiatric disorders. *Gen Hosp Psychiatry*. 1997 Jul;19(4):245-50.
24. Leproult R, Copinschi G, Buxton O, Van Cauter E. Sleep loss results in an elevation of cortisol levels the next evening. *Sleep*. 1997 Oct;20(10):865-70.
25. Nedeltcheva AV, Kilkus JM, Imperial J, Kasza K, Schoeller DA, Penev PD. Sleep curtailment is accompanied by increased intake of calories from snacks. *Am J Clin Nutr*. 2009 Jan;89(1):126-33.
26. Plat L, Leproult R, L'Hermite-Baleriaux M, et al. Metabolic effects of short-term elevations of plasma cortisol are more pronounced in the evening than in the morning. *J Clin Endocrinol Metab*. 1999 Sep;84(9):3082-92.
27. Grandner MA, Hale L, Moore M, Patel NP. Mortality associated with short sleep duration: The evidence, the possible mechanisms, and the future. *Sleep Med Rev*. 2010 Jun;14(3):191-203.
28. Wingard DL, Berkman LF. Mortality risk associated with sleeping patterns among adults. *Sleep*. 1983;6(2):102-7.
29. Lavie P, Herer P, Peled R, et al. Mortality in sleep apnea patients: a multivariate analysis of risk factors. *Sleep*. 1995 Apr;18(3):149-57.
30. Punjabi NM, Caffo BS, Goodwin JL, et al. Sleep-disordered breathing and mortality: a prospective cohort study. *PLoS Med*. 2009 Aug;6(8):e1000132.
31. Leproult R, Copinschi G, Buxton O, Van Cauter E. Sleep loss results in an elevation of cortisol levels the next evening. *Sleep*. 1997 Oct;20(10):865-70.
32. Perlis ML, Giles DE, Mendelson WB, Bootzin RR, Wyatt JK. Psychophysiological insomnia: the behavioural model and a neurocognitive perspective. *J Sleep Res*. 1997 Sep;6(3):179-88.
33. Sukegawa T, Itoga M, Seno H, et al. Sleep disturbances and depression in the elderly in Japan. *Psychiatry Clin Neurosci*. 2003 Jun;57(3):265-70.
34. Hall M, Buysse DJ, Nowell PD, et al. Symptoms of stress and depression as correlates of sleep in primary insomnia. *Psychosom Med*. 2000 Mar-Apr;62(2):227-30.
35. Benca RM. Mood disorders. In: Kryger MH, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine*. 3rd ed. Philadelphia, PA: WB Saunders; 2000:1140-57.
36. de Saint Hilaire Z, Straub J, Pelissolo A. Temperament and character in primary insomnia. *Eur Psychiatry*. 2005 Mar;20(2):188-92.
37. Vollrath M, Wicki W, Angst J. The Zurich study. VIII. Insomnia: association with depression, anxiety, somatic syndromes, and course of insomnia. *Eur Arch Psychiatry Neurol Sci*. 1989;239(2):113-24.

38. Bonnet MH, Arand DL. Hyperarousal and insomnia. *Sleep Med Rev.* 1997 Dec;1(2):97-108.
39. National Sleep Foundation. 2009 Sleep in America Poll™. Washington, D.C.
40. Cappuccio FP, D'Elia L, Strazzullo P, Miller MA. Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. *Sleep.* 2010 May 1;33(5):585-92.
41. Available at: www.nhtsa.gov/Driving+Safety/Distracted+Driving/Research+on+Drowsy+Driving. Accessed January 2, 2011.
42. Rosa Neto JC, Lira FS, Venancio DP, et al. Sleep deprivation affects inflammatory marker expression in adipose tissue. *Lipids Health Dis.* 2010 Oct 30;9:125.
43. Kloog I, Portnov BA, Rennert HS, Haim A. Does the modern urbanized sleeping habitat pose a breast cancer risk? *Chronobiol Int.* 2011 Feb;28(1):76-80.
44. Roth T, Ancoli-Israel S. Daytime consequences and correlates of insomnia in the United States: results of the 1991 National Sleep Foundation Survey. II. *Sleep.* 1999 May 1;22(Suppl 2):S354-S8.
45. Verstraeten E. Neurocognitive effects of obstructive sleep apnea syndrome. *Curr Neurol Neurosci Rep.* 2007 Mar;7(2):161-6.
46. Ferrara M, De Gennaro L, Casagrande M, Bertini M. Selective slow-wave sleep deprivation and time-of-night effects on cognitive performance upon awakening. *Psychophysiology.* 2000 Jul;37(4):440-6.
47. Hall MH, Muldoon MF, Jennings JR, Buysse DJ, Flory JD, Manuck SB. Self-reported sleep duration is associated with the metabolic syndrome in midlife adults. *Sleep.* 2008 May 1;31(5):635-43.
48. Mullington JM, Haack M, Toth M, Serrador JM, Meier-Ewert HK. Cardiovascular, inflammatory, and metabolic consequences of sleep deprivation. *Prog Cardiovasc Dis.* 2009 Jan-Feb;51(4):294-302.
49. Alvarez GG, Ayas NT. The impact of daily sleep duration on health: a review of the literature. *Prog Cardiovasc Nurs.* 2004 Spring;19(2):56-9.
50. Sabanayagam C, Shankar A. Sleep duration and cardiovascular disease: results from the National Health Interview Survey. *Sleep.* 2010 Aug 1;33(8):1037-42.
51. Ikehara S, Iso H, Date C, et al. Association of sleep duration with mortality from cardiovascular disease and other causes for Japanese men and women: the JACC study. *Sleep.* 2009 Mar 1;32(3):295-301.
52. Bass J, Takahashi JS. Circadian integration of metabolism and energetics. *Science.* 2010 Dec 3;330(6009):1349-54.
53. González-Ortiz M, Martínez-Abundis E, Balcázar-Muñoz BR, Pascoe-González S. Effect of sleep deprivation on insulin sensitivity and cortisol concentration in healthy subjects. *Diabetes Nutr Metab.* 2000 Apr;13(2):80-3.
54. Buxton OM, Pavlova M, Reid EW, Wang W, Simonson DC, Adler GK. Sleep restriction for 1 week reduces insulin sensitivity in healthy men. *Diabetes.* 2010 Sep;59(9):2126-33.
55. Chaput JP, Tremblay A. The glucostatic theory of appetite control and the risk of obesity and diabetes. *Int J Obes (Lond).* 2009 Jan;33(1):46-53.

56. Scheen AJ, Byrne MM, Plat L, Leproult R, Van Cauter E. Relationships between sleep quality and glucose regulation in normal humans. *Am J Physiol.* 1996 Aug;271(2 Pt 1):E261-70.
57. Park SE, Kim HM, Kim DH, Kim J, Cha BS, Kim DJ. The association between sleep duration and general and abdominal obesity in Koreans: data from the Korean National Health and Nutrition Examination Survey, 2001 and 2005. *Obesity (Silver Spring).* 2009 Apr;17(4):767-71.
58. Patel SR, Zhu X, Storfer-Isser A, et al. Sleep duration and biomarkers of inflammation. *Sleep.* 2009;32(2):200-4.
59. Scheen AJ. Clinical study of the month. Does chronic sleep deprivation predispose to metabolic syndrome? *Rev Med Liege.* 1999 Nov;54(11):898-900.
60. Röst M, Nilsson P. Sleep disorders--a public health problem. Potential risk factor in the development of type 2 diabetes, hypertension, dyslipidemia and premature aging. *Lakartidningen.* 2002 Jan 17;99(3):154-7.

**These statements have not been evaluated by the Food and Drug Administration.
These products are not intended to diagnose, treat, cure, or prevent any disease.**

Life Extension does not provide medical advice, diagnosis or treatment. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.

All Contents Copyright ©2019 Life Extension® All rights reserved

LifeExtension