

**Zen Plus** is a food supplement consisting of **9 plant extracts**, L-theanine, D-Ribose and **complete B complex**, bringing balance and keeping the **nervous system** healthy. The **25 ingredient** formula contains, per capsule, 335 mg of plant extracts, 118 mg of B group vitamins and 100 mg of theanine making it a highly concentrated and complete formula.

**HEALTH CLAIMS (Regulation EU N° 432/2012):** Vitamins B1, B2, B3, B6 and B12 contribute to keeping the nervous system healthy and B1, B3, folates and B12 help maintain a normal psychology. Vitamin B5 contributes to a normal intellectual performance. Ashwaganda supports the body's resistance to stress and helps maintain mental balance. Passionflower helps to induce calm, rest and sleep. Astragalus supports physical and mental well-being.



**FORMAT:** 30 and 60 vegetable capsules

## FORMULA

**Ingredients:** L-Theanine, ashwagandha root extract (*Withania somnifera*), holy basil leaf extract (*Ocimum tenuiflorum*), passionflower extract (*Passiflora incarnata*), rhodiola extract (*Rhodiola rosea*), **oat** extract (*Avena sativa*), choline bitartrate, D-pantothenate calcium (vit. B5), inositol, para-aminobenzoic acid (PABA), thiamin hydrochloride (vit. B1), riboflavin (vit. B2), pyridoxine hydrochloride (vit. B6), D-ribose, astragalus root extract (*Astragalus membranaceus*), inositol hexanicotinate (vit. B3), phellodendron bark extract (*Phellodendron amurense*), red jujube fruit (*Ziziphus jujuba*), nicotinamide (vit. B3), magnolia bark extract (*Magnolia officinalis*), anticaking agents: magnesium salts of fatty acids and silicon dioxide, calcium-L-methylfolate, D-biotin, riboflavin-5'-phosphate sodium (vit. B2), pyridoxal-5'-phosphate (vit. B6), methylcobalamin (vit. B12), vegetable capsule (glazing agent: hydroxypropylmethylcellulose; purified water).

<b>Nutritional information:</b>	<b>1 capsule</b>	<b>NVR*</b>
L-Theanine	100 mg	
Ashwagandha ( <i>Withania somnifera</i> ) (2,5% withanolides)	75 mg	
Holy basil ( <i>Ocimum tenuiflorum</i> ) (10% ursolic acids)	50 mg	
<b>Oat</b> extract ( <i>Avena sativa</i> ) (10:1)	50 mg	
Passionflower ( <i>Passiflora incarnata</i> ) (4% flavonoids)	50 mg	
Rhodiola ( <i>Rhodiola rosea</i> ) (5% rosavins)	50 mg	
Astragalus ( <i>Astragalus membranaceus</i> ) (3% astragalosides)	25 mg	
Phellodendron ( <i>Phellodendron amurense</i> ) (0,1% berberine)	15 mg	
Red jujube ( <i>Ziziphus jujuba</i> )	12,5 mg	
Magnolia ( <i>Magnolia officinalis</i> ) (50:1, 80% magnolol+honokiol)	7,5 mg	
D-Ribose	25 mg	
Thiamin (vit. B1) (from 25 mg thiamin hcl)	22,3 mg	2.027%
Riboflavin (vit. B2) (from 25 mg riboflavin + 2,5 mg riboflavin-5'-phosphate sodium)	26,9 mg	1.921%
Niacin (vit. B3) (from 7,5 mg nicotinamide + 17,5 mg inositol hexanicotinate)	23,4 mg NE	146%
D-Pantothenic acid (vit. B5) (from 25 mg D-pantothenate calcium)	22,9 mg	382%
Vitamin B6 (from 10,5 mg pyridoxine hcl + 5 mg pyridoxal-5'-phosphate)	12 mg	857%
Folate (calcium-L-methylfolate)	500 µg	250%
Vitamin B12 (methylcobalamin)	75 µg	3.000%
Biotin	37,5 µg	75%
Choline (bitartrate)	25 mg	
Inositol	25 mg	
PABA ( <i>para</i> -Aminobenzoic acid)	25 mg	

\* NRV Nutrient Reference Value in %

## Cautions:

Do not use if you are pregnant or breast-feeding, if you have bipolar disorder or if you are taking cyclosporine or sedatives. Consumption with alcohol is not recommended.

**ZEN-PLUS** should not be administered while taking tricyclic antidepressants (like Melitracene). A minimum of 14 days should pass, or as indicated by your doctor, before starting treatment with ZENPLUS after the administration of this type of medication.

---

## Recommended daily dose:

1-2 capsules daily with food. Do not exceed the stated recommended daily dose.

---

## Indications and uses:

Different studies have shown that the ingredients in ZEN-PLUS can be of help for:  
People in situations of physical or mental stress, those who need to reinforce physical and/or intellectual performance, stress-related anxiety disorders, nervousness, irritability, feeling run-down and mental fatigue.

---

## DETAILS:

ZEN-PLUS is a formula elaborated with ingredients which are attributed adaptogenic properties, increasing the body's resistance to multiple forms of stress. It regulates the main mediators involved in stress response and contributes to better physical resistance and cognitive performance, strengthening concentration and critical ability. ZENPLUS reduces nervous irritability and anxiety while favouring emotional and mental well-being.

---

## INGREDIENTS:

**L-THEANINE:** This amino acid is present almost exclusively in the green tea plant, synthesized in the root and concentrated in the leaves. L-theanine has been widely studied for its health benefits. It has a relaxing effect in situations of stress because it increases the activity of alpha brain waves, a sign of induced relaxation. In the brain, L-theanine increases GABA, a neurotransmitter that participates in the regulation of the excitability balance, as well as increasing dopamine and serotonin levels which elevate mood. A study carried out in Japan suggests that oral ingestion of L-theanine could have anti-stress effects by inhibiting cortical excitement neurons <sup>(1,2)</sup>.

**ASHWAGANDHA:** The root of *Withania somnifera* has been traditionally used for treating states of anxiety and nervous hyperexcitability, among other applications. It is made up of abundant withanolides and to a lesser extent, alkaloids and saponins<sup>(3)</sup>. In the monograph of the WHO, its anti-stress activity is explained in detail, it improves reaction time, has antioxidant power, is immune-stimulating and has a neuroprotective capacity. In ayurvedic medicine it has been used because of its adaptogenic ability to improve physical and mental health, increase resistance to disease and external pollutants, and increase longevity <sup>(4-6)</sup>.

**HOLY BASIL:** This aromatic plant has a long trajectory in traditional ayurvedic medicine and is considered an adaptogen that balances different bodily processes and helps it adapt to stress. In India it is considered a holy plant. Also known as Tulsi, there is ample scientific evidence describing its therapeutic potential. Recent research has shown that eugenol, an active component of *Ocimum tenuiflorum*, is the active principle responsible for its activity. In a recent study, the anxiolytic activity of *Ocimum tenuiflorum* on patients with generalized anxiety disorder was revealed <sup>(7,8)</sup>.

**OAT:** The EMEA approves the traditional use of the uppermost parts of the plant to relieve mild symptoms of stress and to help induce sleep. In fact, it is attributed a mild sedative action because of the presence of an indole alkaloid similar to the alkaloid contained in passionflower, so they surely act in synergy. The E Commission describes the use of oat for treating acute and chronic anxiety, as well as for stressful situations, states of excitement and neurasthenic syndrome <sup>(9,10)</sup>.

**PASSIONFLOWER:** The active part of this plant is the outermost stamen. Flavonoids are abundant in its chemical composition as well as other phytochemical compounds that act synergically and justify its therapeutic use. Its monograph can be found in prestigious publications such as those by the ESCOP, WHO or EMEA, indicating that in addition to treating insomnia, it is useful for anxiety, nervousness, irritability and palpitations, among others. It is frequently combined with other plants to strengthen its effect or to treat different types of insomnia <sup>(11-13)</sup>.

**RHODIOLA:** this plant with a neuroendocrine tropism contains numerous active ingredients, in particular various phenols including flavonoids (including proanthocyanidins) but also and above all phenylpropanoids (rosavin, rosin, salidroside, etc.). An adaptogen par excellence, Rhodiola supports the body's ability to adapt and resist the many forms of stress that affect it. Its beneficial effects on stress are linked to: regulation of the hypothalamic-pituitary-adrenal axis; modulation of the main mediators in the stress response (Hsp70, DAT-16, cortisol, NO, etc.); and its influence on the activity of neurotransmitters such as monoamines and opioid peptides. <sup>(14-18)</sup>.

Numerous studies have shown its anti-stress effect and its ability to improve cognitive performance (memory, mental calculation, concentration) especially under stressful conditions. One study showed that patients under certain stressful conditions significantly improved cognitive and perceptual brain function after taking 170 mg of Rhodiola extract for 15 days. Rhodiola helps increase physical and mental endurance by increasing resistance to exertion and decreasing recovery time after exertion, and some studies suggest it is useful in athletes and in patients with impaired immune systems. <sup>(14-21)</sup>.

**ASTRAGALUS:** The part of this plant used for therapeutic purposes is the root. The main active components are triterpenoid saponins and polysaccharides. Numerous studies have confirmed the immune-stimulating effect of the root, which can exert a beneficial effect in situations in which the immune system is compromised, such as stress. The immune-stimulating activity seems to be associated with its polysaccharide fraction. In a recent study, the anti-stress effect of astragalus was assessed in a model of induced stress. The results were very conclusive, observing that the administration of astragalus readjusted the levels of certain neurochemical transmitters during stress. A significant reduction of tyrosine hydroxylase was detected in the neurons of the locus coeruleus, as well as an increase in cholinergic activity in the hypothalamus, improving spatial learning and memory, and reducing stress <sup>(22,23)</sup>.

**PHELLODENDRON:** The part of this plant used for therapeutic purposes is the bark, whose main component is berberine. This compound has shown its anxiolytic activity in different experimental models. This activity has also been proven in a study carried out on stress-associated overweight women, in which a combination of phellodendron and magnolia reduced cortisol levels as well as perceived stress, helping them maintain their weight <sup>(24-26)</sup>.

**RED JUJUBE:** In traditional Chinese medicine, the fruit of this plant has been used for insomnia, fatigue, poor appetite and anxiety. Its main components are triterpenes and triterpenic saponins. There is scientific evidence of a hypnotic effect in jujubosides, influencing circadian rhythm and the serotonergic system. In the WHO monographs, its benefits are described for treating insomnia-associated irritability <sup>(27)</sup>.

**MAGNOLIA:** The bark of this plant contains magnolol and honokiol as its main components, and these are attributed anxiolytic and anti-depressive action since both compounds have a certain selectivity for determined sub-types of the GABA-A receptor. In a study performed in 2008, the synergic effect of magnolia and phellodendron was shown, both of which help maintain cortisol and DHEA levels, which are hormones related with the symptoms of stress, providing relief for premenopausal women suffering from transitory anxiety <sup>(28-31)</sup>.

**D-RIBOSE:** It's a simple carbohydrate molecule found in all cells of the human body. Physical stress can increase the loss of nucleotides (such as ATP, ADP and AMP) in the heart and skeletal muscles. D-ribose is fundamental for the continuous production of ATP, the molecule which gives the heart and muscles the energy they need to function. Ribose helps with energy production at the cellular level and improves muscle recovery time and resistance <sup>(32-34)</sup>.

**VITAMIN B COMPLEX:** This consists of a set of vitamins that work together for good health. They generally maintain good nervous system conditions, care for mental health and strengthen the immune system, among other functions <sup>(35,36)</sup>.

**Vitamin B1 (Thiamine HCl):** This is needed to transform food into energy so the brain can absorb the glucose it needs in order to function properly. When there is a deficiency of this vitamin, problems of depression, fatigue, disinterest, poor memory or low mental agility appear. It is necessary for adequate nourishment of the nervous system. Supplementation of this vitamin helps to reduce the negative symptoms of depression upon stabilizing thiamine levels. It is useful in cases of dementia and for overcoming stress <sup>(37)</sup>.

**Vitamin B2 (Riboflavin):** Vitamin B<sub>2</sub> is necessary for proper nerve cell function. It positively influences determined nervous disorders such as stress, insomnia and anxiety <sup>(38)</sup>.

**Vitamin B3 (Inositol-hexanicotinate/niacinamide):** A slight deficiency in this vitamin can cause alterations to the nervous system like nervousness, irritability, insomnia and depression. We've incorporated vitamin B<sub>3</sub> in the form of inositol-hexanicotinate and niacinamide (non-reddening) <sup>(39,40)</sup>.

**Vitamin B5 (calcium D pantothenate):** This vitamin intervenes in adrenal gland function, which is responsible for releasing cortisol, a hormone related with vital tone and the state of alertness <sup>(41)</sup>.

**Vitamin B6 (Pyridoxine):** Necessary for haemoglobin production in the blood, along with the rest of the B vitamins it participates in the maintenance of the nervous and immune systems. It favours improvement in depression since supplementation elevates serotonin levels and favours memory maintenance in the elderly <sup>(42,43)</sup>.

**Vitamin B9 (folate):** Some of the symptoms related to a folic acid deficiency are weakness, depression, poor memory and bad mood, among others <sup>(44)</sup>.

**Vitamin B12 (Methylcobalamin):** Vitamin B<sub>12</sub> is involved in the activity of numerous organic enzymes and collaborates in maintaining a healthy nervous system <sup>(45)</sup>.

**Vitamin B7 (Biotin):** This vitamin helps the body use pantothenic acid and folic acid. It participates in the metabolism of fat, protein and carbohydrates, and a deficiency of biotin can manifest in the form of nervous alterations <sup>(46)</sup>.

**CHOLINE BITARTRATE:** This is necessary for the formation of acetylcholine, a brain neurotransmitter whose main function is the transmission of nerve impulses, so it is of capital importance for proper nerve conduction <sup>(47)</sup>.

**INOSITOL:** This is necessary for healthy nerve cells, and together with choline, is responsible for the creation of neurotransmitters. Inositol intervenes in the chemical balance between copper and zinc in nerve cells. A lack of this vitamin can lead to excess copper, which is responsible for the onset of numerous nervous system problems: anguish, insomnia, nervousness, stress and depression <sup>(48,49)</sup>.

**PABA (PARA-AMINOBENZOIC ACID):** PABA (para-aminobenzoic acid) influences the efficacy and formation of folic acid by stimulating the formation of determined intestinal bacteria. It can increase vitality since it increases the oxygen supply to tissues and collaborates in red blood cell formation. A deficiency of this cofactor can cause fatigue, irritability, depression and nervousness <sup>(50)</sup>.

---

#### References:

- 1) "L-theanine. Monograph." *Altern Med Rev* 10 (2005): 136-138.
- 2) Kimura, Kenta, et al. "L-Theanine reduces psychological and physiological stress responses." *Biological psychology* 74.1 (2007): 39-45.
- 3) World Health Organization. "Radix Withaniae." WHO Monographs on Selected Medicinal Plants 4 (2009): 373-391.
- 4) Singh, Ram Harsh, K. Narsimhamurthy, and Girish Singh. "Neuronutrient impact of Ayurvedic Rasayana therapy in brain aging." *Biogerontology* 9.6 (2008): 369-374.
- 5) Bhattacharya, S. K., and A. V. Muruganandam. "Adaptogenic activity of *Withania somnifera*: an experimental study using a rat model of chronic stress." *Pharmacology Biochemistry and Behavior* 75.3 (2003): 547-555.
- 6) Witania. Consultado en abril 2011. Disponible en [www.fitoterapia.net](http://www.fitoterapia.net).
- 7) Bhattacharyya, D., et al. "Controlled programmed trial of *Ocimum sanctum* leaf on generalized anxiety disorders." *Nepal Med Coll J* 10.3 (2008): 176-179.
- 8) Prakash, P., and Neelu Gupta. "Therapeutic uses of *Ocimum sanctum* Linn (Tulsi) with a note on eugenol and its pharmacological actions: a short review." *Indian journal of physiology and pharmacology* 49.2 (2005): 125.
- 9) Oat herb. List of German Commission E Monographs (Phytotherapy). Published May 5, 1988.
- 10) Cañigueral, Salvador, Roser Vila, and Max Wichtl, eds. *Plantas medicinales y drogas vegetales para infusión y tisana: un manual de base científica para Farmacéuticos y Médicos*. OEMF Internacional, 1998.
- 11) Giménez, Noeli Muñoz, and Elena Mora Corberá. "Fitoterapia del insomnio: consejos desde la farmacia." *Offarm: farmacia y sociedad* 27.10 (2008): 94-101.
- 12) García, D., C. Navarro, and T. Ortega. "Plantas medicinales para el insomnio: Centro de investigación sobre fitoterapia." *Complutense: Infito* 1 (2008): 53-93.
- 13) Pasiflora. Consultado en abril 2011. Disponible en [www.fitoterapia.net](http://www.fitoterapia.net).
- 14) Panossian, Alexander, G. Wikman, and Jerome Sarris. "Rosenroot (*Rhodiola rosea*): traditional use, chemical composition, pharmacology and clinical efficacy." *Phytomedicine* 17.7 (2010): 481-493.
- 15) Panossian, Alexander, and Georg Wikman. "Evidence-based efficacy of adaptogens in fatigue, and molecular mechanisms related to their stress-protective activity." *Current clinical pharmacology* 4.3 (2009): 198-219.
- 16) Olsson, Erik MG, Bo von Schéele, and Alexander G. Panossian. "A randomised, double-blind, placebo-controlled, parallel-group study of the standardised extract shr-5 of the roots of *Rhodiola rosea* in the treatment of subjects with stress-related fatigue." *Planta medica* 75.02 (2009): 105-112.
- 17) Walker, Thomas B., and Robert A. Robergs. "Does *Rhodiola rosea* possess ergogenic properties?." *International journal of sport nutrition and exercise metabolism* 16.3 (2006): 305-315.
- 18) Kelly, Gregory S. "*Rhodiola rosea*: a possible plant adaptogen." *Alternative medicine review* 6.3 (2001): 293-293.
- 19) Spasov, A. A., et al. "A double-blind, placebo-controlled pilot study of the stimulating and adaptogenic effect of *Rhodiola rosea* SHR-5 extract on the fatigue of students caused by stress during an examination period with a repeated low-dose regimen." *Phytomedicine* 7.2 (2000): 85-89.
- 20) Shevtsov, V. A., et al. "A randomized trial of two different doses of a SHR-5 *Rhodiola rosea* extract versus placebo and control of capacity for mental work." *Phytomedicine* 10.2-3 (2003): 95-105.
- 21) Darbinyan, V., et al. "*Rhodiola rosea* in stress induced fatigue—a double blind cross-over study of a standardized extract SHR-5 with a repeated low-dose regimen on the mental performance of healthy physicians during night duty." *Phytomedicine* 7.5 (2000): 365-371.
- 22) Shao, Bao-Mei, et al. "A study on the immune receptors for polysaccharides from the roots of *Astragalus membranaceus*, a Chinese medicinal herb." *Biochemical and biophysical research communications* 320.4 (2004): 1103-1111.
- 23) Park, Hyun-Jung, et al. "The effects of *Astragalus membranaceus* on repeated restraint stress-induced biochemical and behavioral responses." *The Korean Journal of Physiology & Pharmacology* 13.4 (2009): 315-319.

- 24) "Cortex Phellodendron. Monographs on selected medicinal plants." World Health Organization (WHO) 4 (2005): 244-257.
- 25) Felodendron. Consultado en abril 2011. Disponible en [www.fitoterapia.net](http://www.fitoterapia.net).
- 26) Peng, Wen-Huang, et al. "Anxiolytic effect of berberine on exploratory activity of the mouse in two experimental anxiety models: interaction with drugs acting at 5-HT receptors." *Life Sciences* 75.20 (2004): 2451-2462.
- 27) "Fructus Zizyphi. Monographs on selected medicinal plants." World Health Organization (WHO) 3 (2001): 359-369.
- 28) Kalman, Douglas S., et al. "Effect of a proprietary Magnolia and Phellodendron extract on stress levels in healthy women: a pilot, double-blind, placebo-controlled clinical trial." *Nutrition Journal* 7.1 (2008): 11.
- 29) Garrison, Robert, and Walter G. Chambliss. "Effect of a proprietary Magnolia and Phellodendron extract on weight management: a pilot, double-blind, placebo-controlled clinical trial." *Alternative therapies in health and medicine* 12.1 (2006): 50-55.
- 30) Kuribara, Hisashi, et al. "The anxiolytic effect of two oriental herbal drugs in Japan attributed to honokiol from magnolia bark." *Journal of pharmacy and pharmacology* 52.11 (2000): 1425-1429.
- 31) Ai, Jinglu, Xiaomei Wang, and Mogens Nielsen. "Honokiol and magnolol selectively interact with GABAA receptor subtypes in vitro." *Pharmacology* 63.1 (2001): 34-41.
- 32) Seifert, John G., et al. "The role of ribose on oxidative stress during hypoxic exercise: a pilot study." *Journal of medicinal food* 12.3 (2009): 690-693.
- 33) Teitelbaum, Jacob E., Clarence Johnson, and John St Cyr. "The use of D-ribose in chronic fatigue syndrome and fibromyalgia: a pilot study." *Journal of Alternative & Complementary Medicine* 12.9 (2006): 857-862.
- 34) Omran, Heyder, et al. "D-Ribose improves diastolic function and quality of life in congestive heart failure patients: a prospective feasibility study." *European journal of heart failure* 5.5 (2003): 615-619.
- 35) Vitaminas del complejo B. Consultado en abril 2011. Disponible en [www.botanical-online.com](http://www.botanical-online.com).
- 36) Serrano, Salvador Giménez. "Vitaminas, componentes esenciales." *Farmacia profesional* 16.6 (2002): 62-67.
- 37) Benton, David, Rebecca Griffiths, and Jurg Haller. "Thiamine supplementation mood and cognitive functioning." *Psychopharmacology* 129.1 (1997): 66-71.
- 38) Tao, Lingwei, et al. "Dietary Intake of Riboflavin and Unsaturated Fatty Acid Can Improve the Multi-Domain Cognitive Function in Middle-Aged and Elderly Populations: A 2-Year Prospective Cohort Study." *Frontiers in aging neuroscience* 11 (2019): 226.
- 39) Knopp, Robert H. "Evaluating niacin in its various forms." *The American journal of cardiology* 86.12 (2000): 51-56.
- 40) Garg, Aakash, et al. "Role of niacin in current clinical practice: a systematic review." *The American journal of medicine* 130.2 (2017): 173-187.
- 41) Tahiliani, Arun G., and Cathy J. Beinlich. "Pantothenic acid in health and disease." *Vitamins & Hormones*. Vol. 46. Academic Press, 1991. 165-228.
- 42) Williams, Anna-leila, et al. "The role for vitamin B-6 as treatment for depression: a systematic review." *Family Practice* 22.5 (2005): 532-537.
- 43) McCarty, M. F. "High-dose pyridoxine as an 'anti-stress' strategy." *Medical Hypotheses* 54.5 (2000): 803-807.
- 44) Lucock, Mark. "Folic acid: nutritional biochemistry, molecular biology, and role in disease processes." *Molecular genetics and metabolism* 71.1-2 (2000): 121-138.
- 45) Kelly, Gregory S. "Nutritional and botanical interventions to assist with the adaptation to stress." *Alternative medicine review: a journal of clinical therapeutic* 4.4 (1999): 249.
- 46) Gupta, J. K., and Qureshi Shaiba Sana. "Potential benefits of methylcobalamin: A review." *Austin J Pharmacol Ther* 3.3 (2015): 1076.
- 47) Leermakers, Elisabeth TM, et al. "Effects of choline on health across the life course: a systematic review." *Nutrition reviews* 73.8 (2015): 500-522.
- 48) Levine, Joseph, et al. "Double-blind, controlled trial of inositol treatment of depression." *The American journal of psychiatry* 152.5 (1995): 792.
- 49) Mukai, Tomohiko, et al. "A meta-analysis of inositol for depression and anxiety disorders." *Human Psychopharmacology: Clinical and Experimental* 29.1 (2014): 55-63.
- 50) Rossi, Maddalena, Alberto Amaretti, and Stefano Raimondi. "Folate production by probiotic bacteria." *Nutrients* 3.1 (2011): 118-134.