ENERGY & STRESS



Available in 60 capsules



Aid mental focus & performance



Minimise effects of stress

GINSENG 5 EXHAUSTION RELIEF

- · Minimise the effects of mental and physical stress
- Improve the body's ability to deal with stress
- Assist mental focus and physical performance
- Support the immune system during times of stress

KEY FORMULA FEATURES

- Combines five different types of ginseng in a well-rounded formula to support concentration, relieve stress symptoms, and maintain physical
- Panax quinquefolius and Panax ginseng improve cognition and mental function.
- Withania improves sleep and promotes physical and mental wellbeing.
- Eleutherococcus senticosus and Panax notoginseng support healthy immune system function during times of stress.



Improve body's ability to deal with stress



Improve vitality



Support immune system during stress

INGREDIENTS:

Each capsule contains:

Eleutherococcus senticosus, dry root, rhizome and stem extract	150mg
from dry root, rhizome and stem (Siberian ginseng)	1.5g
Withania somnifera, dry root extract	100mg
from dry root (Indian ginseng)	1g
Panax ginseng, dry root and rhizome extract	100mg
from dry root and rhizome (Korean ginseng)	1g
Panax notoginseng, dry root and rhizome extract	100mg
from dry root and rhizome (Chinese ginseng)	1g
Panax quinquefolius, dry root extract	100mg
from dry root (American ginseng)	1g

PROFESSIONAL PRESCRIBING GUIDELINES Directions for use (Adult):

Ginseng 5 Exhaustion Relief	{◯} Morning	{○} Lunchtime
Instructions: Take 1 capsule twice daily.	\Diamond	\Diamond
Dosing tip	Ginseng may cause insomnia if taken at night. Counsel patient on appropriate dosing time.	

Or as directed by a healthcare professional.

HCP COUNSELLING QUESTIONS & PRESCRIBING TIPS

When should I take Ethical Nutrients Ginseng 5 Exhaustion Relief?

Panax ginseng can promote wakefulness and is hence best not taken in the evening. We recommend to take this product with breakfast and with lunch

How quickly will this product work?

Each person is different but studies show positive results with ginseng can occur within 24 hours from first use and continues to have an effect with long term use.

Do I need to take this product with food?

While Ethical Nutrients Ginseng 5 Exhaustion Relief can be taken with or without food, some people can experience gastrointestinal upset when taking herbs on an empty stomach. This side effect is reduced when they are taken with food.

Not all cautions, contraindications and warnings are listed. For full details and references, see Metagenics Pharmacy Academy, or contact Clinical Support.

Warnings: None

Cautions - Moderate level:

Aspirin: Ginseng may increase the absorption of aspirin and vice versa. This means blood levels of both herb and medicine may be raised by 50-75%. Use caution and

monitor blood levels of aspirin during concurrent use. $\label{lem:monosuppressants:} \mbox{Withania,} \mbox{3,4,5 Korean ginseng,} \mbox{6,7 Siberian ginseng,} \mbox{8,9 and}$ American ginseng,^{7,10} may stimulate immune function and therefore might decrease the effectiveness of immunosuppressant drugs. Caution should be exercised when used concurrently in patients taking immunosuppressants.

Loop diuretics (bumetanide, etacrynic acid, and furosemide): Ginseng may have a nephrotoxic effect involving the loop of Henle and therefore reduce the diuretic effects of loop diuretics.^{11,12} Monitor patients during concurrent use.

Nifedipine: Korean ginseng has been shown to increase the plasma concentration of this calcium channel blocker in healthy subjects.^{6,8} This may cause an increase in the blood pressure lowing activity of nifedipine, therefore monitor blood pressure in patients if combining.

Thyroxine/Levothyroxine: Withania may add to the effects of thyroid medication. An in vivo study reported that daily administration of withania enhanced serum thyroxine concentrations.^{4,5,13}This effect may be beneficial, however patients' TSH levels need to be closely monitored.

Warfarin: Use with caution and monitor international normalised ratio (INR) in patients

- American ginseng may have anticoagulant actions.
 - Co-administration with warfarin may lead to a decrease in the INR and a decrease in plasma levels of warfarin. 10,1
- This anticoagulant medication is metabolised by cytochrome P450 1A2, and has a narrow therapeutic range. 16,17,18 Ginseng alters the activity of this enzyme, 15 which theoretically may change the drug's therapeutic effect.

Contraindications:

 $\textbf{Allergy and hypersensitivity:} \ \text{Avoid if sensitive to the Solanaceae family of plants.} ^{5,13}$ **Imatinib:** Ginseng may inhibit the CYP3A4-mediated metabolism of imatinib, resulting in increased serum concentration and toxicity of imatinib. Acute lobular hepatitis has been documented in one patient with concurrent use. 11 Avoid coadministration

Pregnancy: Caution: There is conflicting evidence about the safety of ingredients in this product during pregnancy.

Breastfeeding: Limited/unavailable research. A review did not identify any concerns for use during breastfeeding, 5,7,10,14,20,21,22 however safety has not been conclusively established.

Children: Limited/unavailable research. A review did not identify any concerns for use in children, 4,6,7,10 however safety has not been conclusively established.

Free from: Wheat, dairy, lactose, eggs, nuts, yeast, salt,

No added: Artificial flavours, colours, or preservatives.



ENERGY & STRESS

CUSTOMER PRESENTATION

- · Looking to reduce the symptoms of stress
- Feeling mentally drained and looking to improve focus, clarity and concentration
- Tired and fatigued due to stress

THE NEED FOR STRESS SUPPORT

Modern life is busy with little time to rest and recharge. Increased mental and physical stress can take its toll on the body, involving multiple body systems, leading to poor sleep, low vitality, and increased susceptibility to illnes 23

The stress response involves interactions between specific areas of the brain and the adrenal glands. This relationship is known as the Hypothalamic-pituitary-adrenal (HPA) axis, the result of which is the release of stress hormones, adrenaline, and cortisol (Figure 1).

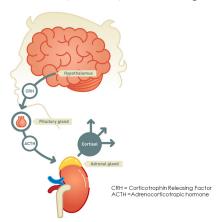


Figure 1: The Hypothalamus-Pituitary-Adrenal (HPA) Axis. 26

This response is essential for protection and survival, but overstimulation of the HPA axis can lead to physical symptoms such as low mood, increased susceptibility to illness, and eventual exhaustion. ²³ Improving the body's resilience to daily life stressors may assist in maintaining the homeostasis of the HPA axis and therefore support the overall health of the mind and body. Herbs known as adaptogens can help the body to adapt and build this resilience. The ingredients in Ethical Nutrients Ginseng 5 Exhaustion Relief are adaptogenic herbs.

CLINICAL FEATURES: MINIMISE THE EFFECTS OF STRESS

Ginseng has a long history of use, dating as far back as 5000 years. ²⁴ It is revered in Traditional Chinese Medicine for its ability to treat fatigue and invigorate the vital energy of the body known as 'chi'. ²⁵ In more recent times this traditional use has been supported by research conducted as both human and animal studies that have demonstrated how different varieties of ginseng are able to regulate the function of the HPA axis, ²⁶ calm the body, reduce the stress response, and increase mental stamina (Figure 2). ²⁷

The mechanisms behind the beneficial effects of ginseng on the HPA axis have indicated that ginseng can improve blood cortisol levels and modulate glucocorticoid receptor levels in both the prefrontal cortex of the brain, and the hippocampus. ²⁵ Ginsenosides (the active constituents in ginseng) may support mood during times of stress via upregulating the expression of neurotrophic factors such as Brain-Derived Neurotrophic Factor (BDNF) expression of which is deceased in chronic stress and has, in turn, been linked to poor cognition and memory, as well as altered mood states. ²⁸

IMPROVE ENERGY AND STAMINA

Ginseng is known for its ability to improve energy and stamina. In support of this are the findings from a 2022 systematic review and meta-analysis which concluded that ingestion of *Panax ginseng* is significantly effective in improving exercise endurance in healthy adults (p=0.01). 29

Panax ginseng is not only supportive of physical energy but may improve mental stamina too, as highlighted in a randomised, double-blind, placebocontrolled, and parallel designed trial. Administration of either 1g or 2g per day of Panax ginseng for four weeks significantly improved mental

fatigue compared with the placebo group (p<0.01). General fatigue was significantly improved in the group taking 2g per day (p<0.05) as was blood levels of reactive oxygen species (p<0.05). The anti-fatigue actions of ginseng, may therefore be in part related to its antioxidant properties.

Ginseng may also improve energy by improving blood glucose levels. In a study of 27 healthy volunteers, participants were given one of four treatments – placebo, ginseng alone, ginseng and glucose, or glucose alone. Those who were given 200mg of *Panax ginseng* alone showed significantly reduced blood glucose levels compared to placebo, as soon as one hour after ginseng ingestion (p=0.046). In the same study, ginseng also significantly improved extended cognitive performance over time compared to placebo (p=0.005). Interestingly, a similar response was seen in the glucose-only group, though the results in the ginseng group were more statistically significant, highlighting the benefits of ginseng over sugar as a "quick fix" to mental fatigue. The support of the study of the support of the s

IMPROVED SLEEP

One of the obvious causes of fatigue is poor sleep. Ginseng may improve sleep both indirectly via counteracting the effects of stress, and directly by promoting a restful night's sleep. Withania somnifera, or Ashwagandha has been used in traditional Ayurvedic medicine to improve physical and mental performance. The favourable effects of Ashwagandha on sleep occur via regulation of the HPA axis and stress hormones including cortisol as demonstrated in a study assessing 58 participants who received 250mg of Ashwagandha or placebo daily for eight weeks. Participants in the treatment group reported a significant reduction in perceived stress scale scores (p<0.05), as well as lowered serum cortisol (p<0.05) and improvements in sleep quality (p<0.05).

A 2021 systematic review and meta-analysis revealed that Ashwagandha significantly improved overall sleep quality compared to placebo (p<0.001). Specific improvements were seen in sleep onset latency (p<0.0001) and total sleep time (p=0.0002). Importantly, many of the studies included were for extended duration, showing Ashwagandha's suitability for use over eight weeks duration. 33

IMMUNE SUPPORT DURING TIMES OF STRESS

Prolonged stress may increase the susceptibility to illness over time, however multiple studies as well as traditional literature has shown that different ginseng species are able to favourably modulate many aspects of immune function.

For example, *Panax ginseng* was shown to increase several immune markers in a group of 40 healthy volunteers who took 100mg, twice a day.³⁴ Whilst a significant improvement was seen at four weeks (p<0.05), this was more significant at week eight (p<0.001), highlighting long-term efficacy. In a 2021 review, *Eleutherococcus senticosus*, was found to reduce the incidence of colds and respiratory illness when taken prophylactically for a month compared to a control group.³⁵ Khanal et al also identified several active constituents of Ashwagandha as immune boosting and demonstrating anti-viral properties.³⁶ Further to this, *Panax notoginseng* and *Panax quinquefolius* appear to have immune enhancing activities including upregulation of natural killer cells³⁷ and the modulation of cortisol production,³⁸ suggesting their suitability for recovery from long-term illness.



Figure 2: Ways ginseng can support the HPA axis.





REFERENCES

- Panax notoginseng. In: Natural Medicines Database [database on the Internet]. Stockton (CA): Therapeutic Research Faculty; 1995-2021 [updated 2021 July 9; cited 2021 Dec 21]. Available from: www.naturalmedicines.therapeuticresearch.com. Subscription required to view
- ² Panax notoginseng. In: IM Gateway [database on the internet]. Unity Health Proprietary Limited; 2001-2021 [cited 2021 Dec 21]. Available from: http://www.imgateway.net/ page.jsp?p_name=InteractionsDatabase subscription required to view.
- ³ Davis L, Kuttan G. Effect of Withania somnifera on cyclophosphamide-induced urotoxicity. Cancer Lett. 2000 Jan 1;148(1):9-17.

 ⁴ Ashwagandha. In: Natural Medicines Comprehensive Database [database on the Internet]. Stockton (CA): Therapeutic Research Faculty; 1995-2018 [updated 2017 Oct 31; cited 2018 Mar 7]. Available from: https://naturalmedicines.therapeuticresearch.com . Subscription required to view.

 5 Braun L, Cohen M. Herbs and natural supplements: an evidence-based guide. 4th ed. Vol 2. Sydney (AU): Elsevier/Churchill Livingstone; 2015. p. 1192-4.
- ⁶ Panax ginseng. In: Natural Medicines Comprehensive Database [database on the Internet]. Stockton (CA): Therapeutic Research Faculty; 1995-2018 [updated 2018 Aug 16; cited 2018 Oct 29]. Available from: http://www.naturaldatabase.com. Subscription required to view.
- ⁷ Skidmore-Roth L. Mosby's handbook of herbs & natural supplements. 4th ed. St Louis (MO): Mosby Elsevier; 2010. p. 294-7
- Braun L, Cohen M. Herbs and natural supplements: an evidence-based quide. 4th ed. Vol 2. Sydney (AU): Elsevier/Churchill Livingstone; 2015. p. 453-62.
- 9 Siberian ginseng. In: Natural Medicines Comprehensive Database [database on the Internet]. Stockton (CA): Therapeutic Research Faculty; 1995-2018 [updated 2018 Aug 16; cited 2018 Oct 26]. Available from: http://www.naturaldatabase.com. Subscription required to view.
- ¹⁰ American Ginseng. In. Natural Medicines Comprehensive Database [database on the Internet]. Stockton (CA): Therapeutic Research Faculty; 1995-2008 [cited 2018 Sept 7]. Available from: http://www.naturaldatabase.com. subscription required to view.
- MIMs Online [Internet]. St Leonards (NSW): MIMs Australia Pty Ltd.; c2017. Panax notoginseng interaction checker: [cited 2021 Dec 21]. Available from: https://www.emims. com.au/. subscription review to view.
- 12 Harkness R, Bratman S. Mosby's handbook of drug-herb and drug-supplement interactions. St Louis (MO): Mosby Inc.; 2003. p. 128.
- 13 Fetrow CW, Avila JR. Professionals handbook of complementary and alternative medicines. 3rd ed. Philadelphia (PA): Lippincott Williams & Wilkins; 2004. p. 58-60.
- ¹⁴ Gardner Z, McGuffin M. Botanical safety handbook. 2nd ed. Botan Raton (FL): CRC Press; 2013. p. 623-6.
- 15 Warfarin [Internet]. Drugbank; 2017 [updated 2021 March 11; cited 2017 Oct 26]. Available from: https://www.drugbank.ca/drugs/DB00682.
- ¹⁶ Yu L. Quality and bioequivalence standards for narrow therapeutic index drugs. 2011 [cited 2017 May 18]. Available from: https://www.fda.gov/downloads/drugs/ $\underline{development approval process/how drugs are developed and approved/approval applications/abbreviated new drug application and agenerics/ucm 292676, pdf.$
- 7 Snyder BD, Polasek TM, Doogue MP. Drug interactions: principles and practice. Aust Prescr. 2012 Jun 1;35(3):85.
- 18 Liang BA, Mackey TK, Lovett KM. Illegal "no prescription" internet access to narrow therapeutic index drugs. Clin Ther. 2013 May; 35(5):694-700. Available from doi: 10.1016/j. clinthera.2013.03.019.
- 19 Liu R, et al. Effects of Panax notoginseng saponins on the activities of CYP1A2, CYP2C9, CYP2D6 and CYP3A4 in rats in vivo. Phytother Res. 2012 Aug; 26(8):1113-8. Available from doi: 10.1002/ptr.3688.
- ²⁰ Skidmore-Roth L. Mosby's handbook of herbs & natural supplements. 4th ed. St Louis (MO): Mosby Elsevier; 2010. p. 566.
- ²¹ Mills S, Bone K. The essential guide to herbal safety. Philadelphia (PA): Elsevier/Churchill Livingstone; 2005. p. 578.
- ²² Gardner Z, McGuffin M. Botanical safety handbook. 2nd ed. Boca Raton (FL): CRC Press; 2013. p 935-8.
- 23 Yaribeygi H, et al. The impact of stress on body function: A review. EXCLI J. 2017 Jul 21; 16:1057-1072. Available from doi: 10.17179/excli2017-480
- ²⁴ Mancuso C, Santangelo R. Food Chem. Toxicol. 2017 Sep;107(Pt A):362-372. Available from doi: 10.1016/j.fct.2017.07.019.
- 25 Jin Y, et al. Mechanisms of Panax ginseng action as an antidepressant. Cell Prolif. 2019 Nov;52(6): e12696. Available from doi: 10.1111/cpr.12696.
- ²⁶ Lee S, Rhee DK. J. Ginseng Res. 2017 Oct;41(4):589-594. Available from doi: 10.1016/j.jgr.2017.01.010.
- ²⁷ Flagg AJ. Traditional and Current Use of Ginseng. Nurs Clin North Am. 2021 Mar;56(1):109-121. Available from doi: 10.1016/j.cnur.2020.10.011.
- 28 Miranda M, et al. Brain-Derived Neurotrophic Factor: a Key Molecule for Memory in the Healthy and Pathological Brain. Front. Cell. Neurosci. 2019; 13:363. Available from doi: 10.3389/fncel.2019.00363
- 29 Ikeuchi S, et al. Exploratory Systematic Review and Meta-Analysis of Panax Genus Plant Ingestion Evaluation in Exercise Endurance2022;14(6):1185. Available from doi: 10.3390/nu14061185.
- 30 Kim HG, et al. Antifatigue Effects of Panax ginseng C.A. Meyer: A Randomised, Double-Blind, Placebo-Controlled Trial. PLoS One. 2013;8(4): e61271. Available from doi: 10.1371/journal.pone.0061271.
- 31 Reay JL, Kennedy DO, Scholey AB. Effects of Panax ginseng, consumed with and without glucose, on blood glucose levels and cognitive performance during sustained mentally demanding' tasks. J Psychopharmacol. 2006 Nov; 20(6):771-81. Available from doi: 10.1177/0269881106061516.
- 32 Salve J, et al. Adaptogenic and Anxiolytic Effects of Ashwagandha Root Extract in Healthy Adults: A Double-blind, Randomized, Placebo-controlled Clinical Study. Cureus. 2019 Dec 25;11(12): e6466. Available from doi: 10.7759/cureus.6466.
- 33 Cheah KL, et al. Effect of Ashwagandha (Withania somnifera) extract on sleep: A systematic review and meta-analysis. PLoS One. 2021 Sep 24;16(9):e0257843. Available from doi: 10.1371/journal.pone.0257843.
- 34 Scaglione F, et al. Immunomodulatory effects of two extracts of Panax ginseng C.A. Meyer Drugs Exp Clin Res. 1990;16(10):537-42. PMID: 2100737.
- as Gerontakos S, et al. Findings of Russian literature on the clinical application of Eleutherococcus senticosus (Rupr. & Maxim.): A narrative review. J Ethnopharmacol. 2021 Oct 5;278:114274. Available from doi: 10.1016/j.jep.2021.114274.
- ³⁶ Khanal P, et al. Withanolides from Withania somnifera as an immunity booster and their therapeutic options against COVID-19. J Biomol Struct Dyn. 2022 Aug;40(12):5295-5308. Available from doi: 10.1080/07391102.2020.1869588.
- ³⁷ Choi JG, et al. Protective Effect of Panax notoginseng Root Water Extract against Influenza A Virus Infection by Enhancing Antiviral Interferon-Mediated Immune Responses and Natural Killer Cell Activity. Front Immunol. 2017 Nov 13;8:1542. Available from doi: 10.3389/fimmu.2017.01542.
- 38 Arring NM, et al. Ginseng as a Treatment for Fatigue: A Systematic Review. J Altern Complement Med. 2018 Jul;24(7):624-633. Available from doi: 10.1089/acm.2017.0361.