

Diapathy

The active ingredients contained in “Diapathy” supplement, can support the characterization “**Prevention of Neuropathic Complication (Retinal, Renal, Cardiac, Vascular) Due to Diabetes**”. Every claim for the ingredients listed below is supported by scientific research results.

How to take:

1-3 capsules per day before a main meal.

Health Benefits

Alpha lipoic acid

Alpha lipoic acid (LA) was first used therapeutically in 1959 in Germany to successfully treat acute liver poisoning, and also has been used to treat other liver pathologies. Shortly thereafter, LA was used to treat diabetes-induced neuropathy, despite the scarcity of information regarding the cause of this condition at that time. It was believed that LA increased glucose utilization in peripheral nerves. However, the report that LA levels are decreased in humans with diabetes and in some patients with polyneuritis and cardiovascular disease likely provided an additional rationale for administering LA to patients with diabetes, (i.e., replacement therapy.) Since then, a number of reports and reviews have suggested alpha lipoic acid as a key ingredient in diabetes-induced polyneuropathy.

Pueraria lobata root extract

Radix *Pueraria lobata* (RP) is the dried root of *Pueraria lobata* (Willd.) Ohwi, which is used traditionally to treat diarrhea, muscle stiffness, thirst, and diabetes in East Asia, and recently was made commercially available as a western dietary supplement. RP is a rich source of isoflavone glucosides and puerarin is the most abundant constituent of RP. Chronic administration of RP extract improved glucose tolerance and decreased fasting plasma glucose levels in ob/ob mice, and that puerarin supplementation reduced body weight gain and lipid levels in liver and serum of high-fat-diet (HFD) fed-induced obese mice. However, the mechanisms responsible for anti-obesity of RP extract or its beneficial effect on glucose metabolism have not been determined.

Vitis vinifera extract

Grape is one of the oldest fruit crops domesticated by humans. The numerous uses of grape in making wine, beverages, jelly, and other products, has made it one of the most economically important plants worldwide. The complex phytochemistry of the berry is characterized by a wide variety of compounds, most of which have been demonstrated to have therapeutic or health promoting properties. Among them, flavonoids are the most abundant and widely studied, and have enjoyed greater attention among grape researchers in the last century. Recent studies have shown that the beneficial health effects promoted by consumption of grape and grape products are attributed to the unique mix of polyphenolic compounds. As the largest group of grape polyphenols, flavonoids are the main candidates considered to have biological properties, including but not limited to antioxidant, anti-inflammatory, anti-cancer, antimicrobial, antiviral, cardioprotective, neuroprotective, and hepatoprotective activities.

Red Korean ginseng

Ginseng roots have been used for over 2,000 years in many Asian countries. *Panax ginseng*, the herbal root of *P. ginseng* Meyer, is also known as *Korean ginseng*. The various forms of ginseng are processed differently for different uses. White ginseng is air-dried, whereas red ginseng is produced by steaming and drying. It has been reported that red ginseng is pharmacologically more active than white ginseng. The difference in the biological activity of red and white ginseng may result from the different chemical constituents produced during processing.

Ginseng has a complex activity profile that includes antioxidant, anti-inflammatory, anti-apoptotic, and immune-stimulatory properties. Overall, ginseng appears to stabilize and balance the entire physiology.

Korean red ginseng was shown in another study to significantly reduce the latency of the P300 component of an evoked potential. This finding suggests that Korean red ginseng can directly modulate cerebro-electrical activity. Kennedy and Scholey similarly suggested that ginseng may be a cognitive enhancer.

Piper nigrum extract

Black pepper (*Piper Nigrum* L.) holds significant health protection potentials due to its antioxidant, antimicrobial and gastro-protective components. Black pepper, with piperine as an active ingredient, demonstrates rich phytochemistry properties that also refer to volatile oils, oleoresins, and alkaloids. Cell-culture studies and clinical trials predicted the role of black pepper against number of maladies. The free-radical scavenging activity of black pepper and its active ingredients might be helpful in chemoprevention and controlling progression of tumor growth. Overall, the key alkaloid component of *Piper nigrum*, assists in cognitive brain functioning, boost nutrient’s absorption and improve gastrointestinal functionality.

Vanadyl sulphate

Vanadium (including vanadyl and vanadate) has been shown to reduce blood glucose level by stimulating glycogenesis, glucose uptake, and metabolism and by inhibiting glucose formation via hepatic gluconeogenesis and glycogenolysis. It has been found that vanadium and vanadium compounds exhibit an insulin-like activity by imitating insulin actions via insulin-receptor tyrosine kinase activation and kinase phosphorylation cascade pathways.

The health claims of the product can be summarized in the table below, including a few indicative bibliography sources. Please note that the sources cited are only a fraction of the research results that corroborate the potential health benefits.

Active Ingredient	Health Protective Claim	Sources
Alpha lipoic acid (LA)	treatment of diabetes-induced neuropathy	1,2
<i>Pueraria lobata</i> root extract	glucose and lipid metabolism, glucose tolerance	3-4
<i>Vitis vinifera</i> extract	Antioxidant, neuroprotective, antiviral, anti-inflammatory, antimicrobial, cardioprotective, hepatoprotective, cognitive function enhancement	5-8
Red Korean ginseng	stabilizing and balancing the entire physiology	9-12
<i>Piper nigrum</i> extract	assistance in cognitive brain functioning	13-14
Vanadyl sulphate	insulin-like activity	15

Bibliography

1. Vallianou N, Evangelopoulos A, Koutalas P. Alpha-lipoic Acid and diabetic neuropathy. *Rev Diabet Stud.* 2009 Winter;6(4):230-6
2. Abubaker SA, Alonazy AM, Abdulrahman A. Effect of Alpha-Lipoic Acid in the Treatment of Diabetic Neuropathy: A Systematic Review. *Cureus.* 2022 Jun 8;14(6):e25750. doi: 10.7759/cureus.25750. PMID: 35812639; PMCID: PMC9264721.
3. Zhang Z., Lam T.N., Zuo Z. Radix puerariae: An overview of its chemistry, pharmacology, pharmacokinetics, and clinical use. *J. Clin. Pharmacol.* 2013;53:787–811. DOI: <https://doi.org/10.1002/jcph.96>
4. Keung W.M., Vallee B.L. Kudzu root: An ancient chinese source of modern antidipsotropic agents. *Phytochemistry.* 1998;47:499–506.
5. Nassiri-Asl M, Hosseinzadeh H. Review of the pharmacological effects of *Vitis vinifera* (Grape) and its bioactive compounds. *Phytother Res.* 2009 Sep;23(9):1197-204. doi: [10.1002/ptr.2761](https://doi.org/10.1002/ptr.2761). PMID: 19140172.
6. Calapai G, Bonina F, Bonina A, Rizza L, Mannucci C, Arcoraci V, Laganà G, Alibrandi A, Pollicino C, Inferrera S, Alecci U. A Randomized, Double-Blinded, Clinical Trial on Effects of a *Vitis vinifera* Extract on Cognitive Function in Healthy Older Adults. *Front Pharmacol.* 2017 Oct 31;8:776. doi: [10.3389/fphar.2017.00776](https://doi.org/10.3389/fphar.2017.00776). PMID: 29163162; PMCID: PMC5671585.
7. Razavi SM, Gholamin S, Eskandari A, Mohsenian N, Ghorbanihaghjo A, Delazar A, Rashtchizadeh N, Keshtkar-Jahromi M, Argani H. Red grape seed extract improves lipid profiles and decreases oxidized low-density lipoprotein in patients with mild hyperlipidemia. *J Med Food.* 2013 Mar;16(3):255-8. doi: [10.1089/jmf.2012.2408](https://doi.org/10.1089/jmf.2012.2408). Epub 2013 Feb 25. PMID: 23437789.
8. Sapwarobol S, Adisakwattana S, Changpeng S, Ratanawachirin W, Tanruttanawong K, Boonyarit W. Postprandial blood glucose response to grape seed extract in healthy participants: A pilot study. *Pharmacogn Mag.* 2012 Jul;8(31):192-6. doi: [10.4103/0973-1296.99283](https://doi.org/10.4103/0973-1296.99283). PMID: 23060692; PMCID: PMC3466453.

9. Xiang YZ, Shang HC, Gao XM, Zhang BL. A comparison of the ancient use of ginseng in traditional Chinese medicine with modern pharmacological experiments and clinical trials. *Phytother Res.* 2008;22:851–858. DOI: [10.1002/ptr.2384](https://doi.org/10.1002/ptr.2384)
10. Yeo HB, Yoon HK, Lee HJ, Kang SG, Jung KY, Kim L. Effects of Korean Red Ginseng on Cognitive and Motor Function: A Double-blind, Randomized, Placebo-controlled Trial. *J Ginseng Res.* 2012 Apr;36(2):190-7. doi: [10.5142/jgr.2012.36.2.190](https://doi.org/10.5142/jgr.2012.36.2.190). PMID: 23717119; PMCID: PMC3659585.
11. Kim TW, Choi HJ, Kim NJ, Kim DH. Anxiolytic-like effects of ginsenosides Rg3 and Rh2 from red ginseng in the elevated plus-maze model. *Planta Med.* 2009;75:836–839.
12. Kennedy DO, Scholey AB. Ginseng: potential for the enhancement of cognitive performance and mood. *Pharmacol Biochem Behav.* 2003;75:687–700.
13. Heerasing Takooree, Muhammad Z. Aumeeruddy, Kannan R.R. Rengasamy, Katharigatta N. Venugopala, Rajesh Jeewon, Gokhan Zengin & Mohamad F. Mahomoodally (2019) A systematic review on black pepper (*Piper nigrum* L.): from folk uses to pharmacological applications, *Critical Reviews in Food Science and Nutrition*, 59:sup1, S210-S243, DOI: <https://doi.org/10.1080/10408398.2019.1565489>
14. Bonetti, Francesco, Gloria Brombo, and Giovanni Zuliani. "Nootropics, functional foods, and dietary patterns for prevention of cognitive decline." *Nutrition and functional foods for healthy aging.* Academic Press, 2017. 211-232.
15. Willsky, G. R., et al. "Effect of vanadium (IV) compounds in the treatment of diabetes: in vivo and in vitro studies with vanadyl sulfate and bis (maltolato) oxovanadium (IV)." *Journal of inorganic biochemistry* 85.1 (2001): 33-42. DOI: [https://doi.org/10.1016/S0162-0134\(00\)00226-9](https://doi.org/10.1016/S0162-0134(00)00226-9)

Data on the toxicity of the product

Pueraria lobate root extract

The mutagenic and antimutagenic activity of the plant extract was evaluated using the Ames test preincubation method S9 for metabolic activation using *Salmonella typhimurium* strains TA98 and TA100 as indicator strains. The cytotoxicity of the extract to the two *S. typhimurium* indicators was evaluated before the mutagenic and antimutagenic tests. The extract at a final concentration of 2.5, 5, 10, or 20 mg/plate exhibited only mild cytotoxic effects. The plant extract at the concentrations of 2.5, 5 and 10 mg/plate in the presence and absence of the S9 mixture were negative in the mutagenic Ames test. In contrast, extract was positive in the antimutagenic Ames test towards either one or both of the tested mutagens 2-(2-furyl)-3-(5-nitro-2-furyl)-acrylamide and benzo(a)pyrene. The absence of mutagenic and the presence of anti-mutagenic activities of the plant extract were confirmed in rec-assays and further supported by a micronucleus test where both plant extracts at doses up to 300 mg/kg body weight (equivalent to 16 g/kg body weight plant tuberous powder) failed to exhibit significant micronucleus formation. The tests confirmed the non-mutagenic but reasonably antimutagenic activities of the plant extract, supporting the current use as safe dietary supplements and cosmetics.

Vitis vinifera

Daily doses used in clinical trials range from 150 to 450 mg. Administration for 12 months of a 100 mg/kg dose did not result in pathological changes.

Red Korean ginseng

Panax ginseng preparations have been used worldwide for many years and so far, no serious adverse events have been reported from clinical trials, epidemiological studies and spontaneous reporting schemes that can be clearly correlated with the ingestion of *Panax ginseng*. Reported adverse effects from clinical trials are mild and mainly gastrointestinal or sleep related, including stomach discomfort, nausea, vomiting, epigastralgia, diarrhoea, constipation, headache, and insomnia. Furthermore, hypersensitivity reactions like urticaria and itching as well as eye burning have been reported. A “Ginseng Abuse

Syndrome” has been described in literature, defined as hypertension together with nervousness, sleeplessness, skin eruptions, edema, and morning diarrhoea after long-term use of daily doses of up to 15 g of “ginseng (-preparations).

Alpha lipoic acid

Alpha-lipoic acid (ALA) (CAS RN 1077-28-7), also referred to as thioctic acid, has been demonstrated to exhibit strong antioxidant properties. In order to test the long-term toxicity of ALA, 180 mg/kg body weight (bw)/day ALA for 24 months was administered. The only notable finding at 180 mg/kg bw daily dosage was a reduction in food intake relative to the controls and a concomitant decrease in body weight. The no-observed-adverse-effect level (NOAEL) is considered to be 60 mg/kg bw/day.

Vanadyl sulphate

Genotoxicity

Vanadyl sulphate was not found to increase the frequency of structural chromosome aberrations in human leukocytes, whereas a significant increase in numerical aberrations, micronuclei, and satellite associations was found. Fluorescence in situ hybridization (FISH) applied to the human lymphocyte micronucleus assay, by means of an alphoid centromere-specific DNA probe, confirmed the aneuploidogenic potentiality of vanadium. Vanadium compounds act mainly as an irritant to the conjunctive and respiratory tract.

This literature overview has been compiled upon request of SAPPARI HEALTH CARE COMPANY[®], regarding specific nutritional supplements health claims. The sources used for this bibliography research are peer-reviewed published scientific data, for each ingredient.

Tsolakou Annia
MSc in Pharmacognosy and Natural Products Chemistry
Research Group of Clinical Pharmacology and Pharmacogenomics
Faculty of Pharmacy, School of Health Sciences
National and Kapodistrian University of Athens