

## **Health Claim Paper**

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I investigated the claim that consumption of ginseng root reduces cognitive decline and risk of Alzheimer's Disease. Alzheimer's Disease occurs when microglia and astrocytes in our brain are continuously activated, which results in the inflammation process that may cause the symptom such as dementia and memory loss (Sawikr Y, et al., 2017). Dietary factors that increase the risk of cognitive decline and Alzheimer's Disease include not only the excess intake of carbohydrates especially fructose, but also a lack of dietary fat and cholesterol, because they will have a negative effect on the metabolism of astrocytes (Seneff S, Wainwright G, Mascitelli L., 2011). Pharmaceutical treatment to Alzheimer's Disease involves some phytochemicals containing polyphenolic and other bioactive substances which are important mediators for the anti-oxidation and anti-inflammation process. Ginseng root, as an important nutraceutical, is widely used in traditional Chinese medicine. It is rich in ginsenoside and gintonin (Kim HJ, Jung SW, Kim SY, et al., 2018), which have various functions such as anti-tumor, anti-inflammatory, antioxidant, and anti-apoptotic properties (Razgonova MP, Veselov VV, Zakharenko AM, et al., 2019). Ginseng root is implicated because it contains abundant bioactive natural substances that have minimum adverse effects on patients, and thus could be linked to its contribution to the prevention and amelioration of Alzheimer's Disease. Generally speaking, Alzheimer's Disease is one the leading diseases of cognitive disorder among elderly people worldwide, which features its chronic and irreversible neurodegeneration. It is estimated by (Centers for Disease Control and Prevention., 2019) that the number of Alzheimer's Disease will reach 14 million by 2060. Diseases associated with Alzheimer's include but are not limited to agitation, depression, wandering, malnutrition and dehydration (Valencia Higuera, 2016). Overall, Alzheimer's Disease severely affects the quality of life and survival rate of the elderly. I believe that the claim about ginseng root is true, and the scientific literature related to this claim is described below.

The first study conducted by (Tan X, Gu J, Zhao B, et al., 2015) in the Journal of Ginseng Research demonstrated that ginseng products are effective in reducing the risk of Alzheimer's Disease and memory loss based on the animal test. The main objective of the study is to assess the possible effect and mechanism of panax ginseng based on rat models mediated by advanced glycation end products, which are harmful compounds formed in Alzheimer's Disease. 80 adult male Sprague-Dawley rats were involved in this study and were randomly separated into eight groups including the control group, Bovine serum albumin (BSA) group, advanced glycation end product (AGE) group, and other groups that combine AGE with anti-RAGE, donepezil, or panax ginseng in different dosage. The drugs were fed for continuous 30 days, and 25 days after the drug intervention, Morris water maze test was given to observe the rats' memory condition. Step-down type passive avoidance test was followed to measure their learning ability. After that, SOD activity and levels of MDA and GSH were measured on 6 rats from each group, while the rest of the rats were used to study the expressions of RAGE and NF-kB which are both important indicators for Alzheimer's

Disease. In this study, they conducted 5 experiments and found that panax ginseng can improve the memory and learning ability among rats with Alzheimer's Disease by inhibiting the RAGE and NF- $\kappa$ B expression in brain. The authors proved this through both behavioral observation and pathological detection. On the positive side, this study succeeded to support the application of ginseng in the treatment of cognitive disorder, especially in Alzheimer's Disease. However, the authors used rats instead of humans and the number of rats they used in the study was quite small. Besides, although they took advantage of HPLC system to detect the compounds of PG extract, they didn't demonstrate which ingredient in panax ginseng is playing a leading role.

The second study implemented by (Lee ST, Chu K, Sim JY, Heo JH, Kim M., 2008) proved the positive effects of ginseng root in the treatment for AD patients in a clinical trial. The main objective of the study is to examine the efficacy of ginseng on a clinical level, based on the previous research in rodent models. 97 AD patients aged from 47-83 years old were initially recruited, which were further separated randomly into control group and ginseng group. No intervention was given to the control group, while patients in ginseng group was provided with 4.5 g/d Korean white ginseng powder for consecutive 12 weeks. After that, patients in ginseng group were observed for additional 12 weeks, and part of them were required to take the dose-response effect test. Evaluation of the patients' cognitive condition was based on Mini mental state examination (MMSE) and Alzheimer disease assessment scales (ADAS), and the authors found that ginseng shows salient features in cognitive improvement among AD patients. The authors proved this by comparing the difference of AD patients' cognitive condition between control group and ginseng group, and by observing the decline of cognitive level in ginseng group when ginseng powder was not provided to them during week 13-24. On the positive side, this study succeeded to conduct ginseng study on a clinical level, which provides guidance for further clinical study about ginseng application on the treatment of Alzheimer's Disease in the future. However, the sample number and test cycle were not adequate enough to construct a linear relationship of dose-response and time-response, which makes it hard to convincingly demonstrate the efficacy of ginseng in cognitive enhancement among AD patients. Besides, placebo was not used in the study, which may also influence the reliability of the conclusion.

The third study was carried out by (Heo JH, Lee ST, Chu K, et al., 2008) and was published in the European Journal of Neurology. This study focused on evaluating the value of Korean red ginseng as an adjuvant treatment method for the amelioration of cognitive function among patients with Alzheimer's Disease. 61 patients aged over 50 years with cognitive impairment due to Alzheimer's Disease were involved in this study and were treated with drugs such as donepezil, galantamine, memantine, or rivastigmine for more than half a year before they received this intervention study. The research team used 6-year-old Korean red ginseng (KRG) root as intervention. Patients were separated into 3 groups. 31 patients were in control group, 15 patients were in low-dose (4.5g) KRG group, and 15 patients were in high-dose (9g) KRG group. Ginseng was administered for consecutive 12 weeks and then stopped for additional 12 weeks. After that, participants' cognitive condition was evaluated through various criteria including ADAS, K-MMSE, and CDR, which covered the periods from week 1 to week

24. The study conducted the experiments above and found significant improvement of cognitive ability in both low-dose and high-dose KRG groups. The authors proved this by assessing the data among those three groups after excluding interference factors such as age and gender. More specifically, the improvement of low-dose and high-dose KRG groups was reflected on the variation of ADAS-cog and CDR value compared with control group. However, according to the ADAS-non-cog and MMSE Score, the low-dose and high-dose KRG group didn't show significant differences in cognitive improvement, which indicated that a higher dosage won't ensure a better effect. On the positive side, this study demonstrated the function of Korean red ginseng in adjuvant treatment for Alzheimer's disease. However, both the sample scale and study duration were insufficient, which will affect the reliability of the study. Besides, the mechanism about how ginseng plays a role in enhancing the cognitive ability was not involved in this study, which makes it less persuasive in explaining the specific function of ginseng on a biological basis.

Taking all the evidence together, all of the three scientific literature supports the claim that consumption of ginseng root reduces cognitive decline and risk of Alzheimer's Disease, which confirms my original statement. The first article demonstrated the function of panax ginseng based on a rat model and explained the mechanism on the perspective of cell biology. The second article applied Korean white ginseng to patients with Alzheimer's Disease and proved the effect of ginseng root in enhancing cognitive ability among AD patients. The third article was able to show the value of Korean red ginseng in adjuvant treatment for Alzheimer's disease by making comparison between different group. Among the three articles, the experiments performed in the first article were the best controlled and valid because the authors considered various factors that may interfere the reliability of the study, so that up to eight groups were assigned to ensure that each reagent or object has corresponding data for analysis. Besides, I admire the variety of the experiments conducted in the first article, which not only included macroscopic observation (Morris water maze test, Step-down type passive avoidance test), but also involves microanalysis (Assays for SOD activity and the content of MDA and GSH, Immunohistochemistry for RAGE and NF-kB expressions), and such diversity makes the whole study topic complete and logically persuasive. Regarding the other two articles, both of them studied ginseng on a clinical level, but they didn't perform well compared with the first article. They didn't explain the mechanism of ginseng acting on human, which makes it less convincing and superficial. In addition, all of the three articles studied ginseng on the pathology perspective, and none of them showed direct evidence or cases that ginseng root is effective among healthy people in reducing cognitive decline and risk of Alzheimer's Disease. However, based on the mechanism that ginseng can act on astrocytes and inhibit RAGE and NF-kB expression in brain, with strong anti-inflammatory and antioxidant ability, as well as a minimum adverse effect mentioned above, dietary intake of ginseng root is regarded as an effective way to reduce cognitive decline and risk of Alzheimer's Disease. I therefore claim that ginseng root can be applied to old people with a high risk of Alzheimer's Disease or cognitive decline, and to AD patients as an adjuvant treatment.

## References:

1. Tan X, Gu J, Zhao B, et al. Ginseng improves cognitive deficit via the RAGE/NF- $\kappa$ B pathway in advanced glycation end product-induced rats. *J Ginseng Res*. 2015;39(2):116–124. doi:10.1016/j.jgr.2014.09.002
2. Lee ST, Chu K, Sim JY, Heo JH, Kim M. Panax ginseng enhances cognitive performance in Alzheimer disease. *Alzheimer Dis Assoc Disord*. 2008;22(3):222–226. doi:10.1097/WAD.0b013e31816c92e6
3. Heo JH, Lee ST, Chu K, et al. An open-label trial of Korean red ginseng as an adjuvant treatment for cognitive impairment in patients with Alzheimer's disease. *Eur J Neurol*. 2008;15(8):865–868. doi:10.1111/j.1468-1331.2008.02157.x
4. Sawikr Y, Yarla NS, Peluso I, Kamal MA, Aliev G, Bishayee A. Neuroinflammation in Alzheimer's Disease: The Preventive and Therapeutic Potential of Polyphenolic Nutraceuticals. *Adv Protein Chem Struct Biol*. 2017;108:33-57. doi: 10.1016/bs.apcsb.2017.02.001. Epub 2017 Mar 22. Review. PubMed PMID: 28427563.
5. Seneff S, Wainwright G, Mascitelli L. Nutrition and Alzheimer's disease: the detrimental role of a high carbohydrate diet. *Eur J Intern Med*. 2011 Apr;22(2):134-40. doi: 10.1016/j.ejim.2010.12.017. Epub 2011 Jan 26. Review. PubMed PMID: 21402242.
6. Kim HJ, Jung SW, Kim SY, et al. Panax ginseng as an adjuvant treatment for Alzheimer's disease. *J Ginseng Res*. 2018;42(4):401–411. doi:10.1016/j.jgr.2017.12.008
7. Razgonova MP, Veselov VV, Zakharenko AM, et al. Panax ginseng components and the pathogenesis of Alzheimer's disease (Review). *Mol Med Rep*. 2019;19(4):2975–2998. doi:10.3892/mmr.2019.9972
8. Alzheimer's Disease. *Centers for Disease Control and Prevention*. <https://www.cdc.gov/aging/aginginfo/alzheimers.html/>. September 20, 2019
9. Valencia Higuera. Complications of Alzheimer's Disease (AD). *Healthline*. <https://www.healthline.com/health/alzheimers-disease-complications>. August 16, 2016