Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Chotosan

Evidence Summary

Chotosan may provide cognitive benefits in vascular dementia. However, evidence from large rigorously designed clinical trials is lacking.

Neuroprotective Benefit: A meta-analysis of clinical trials reported improvements in cognitive functions in vascular dementia patients. Clinical efficacy is less clear in Alzheimer's disease and mild cognitive impairment.

Aging and related health concerns: Chotosan is used clinically to treat headache, vertigo, and other conditions in older people who have high blood pressure and have physical weakness. Antihypertensive effects have also been confirmed in rodent models.

Safety: A meta-analysis in dementia patients reported that chotosan is well tolerated with adverse events including diarrhea, appetite loss, and elevated liver enzymes. Rarely, *Glycyrrhiza radix* can lower K+ levels and increase blood pressure and edema.

Availability: used clinically in Japan	**Dose**: Typical commercial products come in packets of dried herbal extract; each packet contains 2.5 g of dried herbal extract, which is taken orally with every meal (7.5 g/day).	**Herbal components:** Uncariae Uncis Cum Ramulus (hooks and branch of *Uncaria sinensis*), peel of *Citrus unshiu*), tuber of *Pinellia ternata*, root of *Ophiopogon japonicus*, Hoelen (fungus of *Poria cocos*), root of *Panax ginseng*, flower of *Chrysanthemum morifolium*, root and rhizome of *Saposhnikovia divaricata*, root of *Glycyrrhiza uralensis*, Gypsum Fibrosum (CaSO4 2H2O), and rhizome of *Zingiber officinale*
Half-life: varies by compounds/herbs	**BBB**: some compounds are penetrant	
Clinical trials: The largest meta-analysis to date included 3 randomized controlled trials enrolling a total of 219 patients with dementia.	**Observational studies**: No large observational studies of chotosan exist.	

What is it?

Kampo medicine in Japan originates from traditional Chinese medicine, but the Japanese have created a unique system of diagnosis and therapy using a combination of herbs. Kampo medicine is approved by the Ministry of Health, Labor and Welfare and integrated in the Japanese healthcare system; it is covered by health insurance. Kampo medicine uses fixed combinations of herbs with standardized proportions and is under strict manufacturing and safety guidelines similar to those for drugs. More than half of Japanese physicians prescribe Kampo medicines. A Kampo formula is individually selected for each patient on the basis of the diagnostic theory of Kampo medicine, the pattern of symptoms, and the physical constitution of the patient.

Chotosan (釣藤散) is a type of Kampo medicine used clinically to treat headache, vertigo, hot flashes, tinnitus, insomnia, and painful tension of the shoulder in middle-aged and elderly people who have high blood pressure and have physical weakness (Terasawa et al., 1997; Imai et al., 2017). Many of these symptoms are thought to originate from disorders in the cerebrovascular system. Chotosan has been studied in small clinical trials of Alzheimer's disease and vascular dementia (Suzuki et al., 2005; Shimada et al., 1994; Terasawa et al., 1997). Chotosan extracts contain 11 dried medical herbs mixed in the following ratio: Uncariae Uncis Cum Ramulus (3.0 g, hooks and branch of *Uncaria sinensis*), Aurantii

Nobilis pericarpium (3.0 g, peel of *Citrus unshiu*), Pinelliae tuber (3.0 g, tuber of *Pinellia ternata*), Ophiopgonis tuber (3.0 g, root of *Ophiopogon japonicus*), Hoelen (3.0 g, fungus of *Poria cocos*), Ginseng radix (2.0 g, root of *Panax ginseng*), Chrysanthemi flower (2.0 g, flower of *Chrysanthemum morifolium*), Saphoshnikoviae radix (2.0 g, root and rhizome of Saposhnikovia divaricata), Glycyrrhizae radix (1.0 g. root of *Glycyrrhiza uralensis*), Gypsum Fibrosum (5.0 g, CaSO4 2H2O) and Zingiberis rhizoma (1.0 g, rhizome of *Zingiber officinale*).

Mechanisms of action of chotosan for neuroprotection may include antioxidant activity, anti-inflammatory activity, modulation of glutamate signaling, improvement of cerebral blood flow and blood pressure, and restoration of cholinergic functions (Chen et al., 2016; Jiang et al., 2019; Zhao et al., 2012; Watanabe et al., 2003). Uncariae Uncis cum Ramulus is thought to play a particularly important role in the neuroprotective actions of chotosan in dementia (reviewed in Matsumoto et al., 2013).

Neuroprotective Benefit: A meta-analysis of clinical trials reported improvements in cognitive functions in vascular dementia patients. Clinical efficacy is less clear in Alzheimer's disease and mild cognitive impairment.

Types of evidence:

- 1 meta-analysis of randomized controlled trials
- 4 clinical trials
- Numerous laboratory studies

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function:

In a controlled clinical trial of 10 stroke patients with mild cognitive impairment, chotosan treatment (7.5 g daily, orally, between meals; TJ-47, Tsumura & Co., Tokyo, Japan) for 12 weeks significantly improved cognitive scores measured by the MMSE (from 23.8±3.6 to 25.2±4.0; $p<0.05$) and verbal fluency test scores (from 8.3±3.8 to 10.0±3.7 $p<0.05$) compared to baseline (Yamaguchi et al., 2004). There were no effects of chotosan on the Self-Rating Depression scale. The control group showed no significant changes in MMSE, verbal fluency, or the Self-Rating Depression scale. Chotosan treatment significantly shortened the P3 latency to target sounds concurrently with reduced reaction time to the sounds and increased correct response rate. P3 amplitude to novel sounds was enlarged and its

topography shifted from central to frontal brain sites. Study authors speculated that these electrophysiological changes relate to improved attention and decision-making.

Human research to suggest benefits to patients with dementia:

In a meta-analysis of 3 randomized controlled trials including a total of 219 dementia patients, chotosan treatment (TJ-47, Tsumura & Co.; 2.5 g with every meal, 7.5 g daily, orally) for 8-12 weeks resulted in short-term improvement of cognitive function compared to placebo (p=0.03), but there were no effects on global cognition or activities of daily living (Imai et al., 2017). Two trials were in vascular dementia patients, and one trial was in Alzheimer's patients. The 2 studies included a total of 176 patients with vascular dementia and showed that chotosan was more effective than placebo in improving cognitive function (p=0.02), and the magnitude of effect was comparable to that of donepezil for vascular dementia. No significant effect in cognitive function was seen in the study of Alzheimer's patients. Overall, results are inconclusive given the small number of studies and participants included in the meta-analysis.

Described below are the individual clinical trials:

- In a double-blind randomized placebo-controlled trial of 139 patients with vascular dementia, chotosan treatment (2.5 g, 3 times daily, orally; TJ-47; Tsumura & Co.) for 12 weeks was statistically superior to placebo in the global improvement rating, utility rating, global improvement rating of subjective symptoms, global improvement rating of psychiatric symptoms, and global improvement rating of disturbance in daily living activities (Terasawa et al., 1997). Chotosan was statistically superior to placebo in global improvement rating at the 8-week ($p<0.01$) and 12-week ($p<0.001$) time points. Global improvement rating of subjective symptoms was also significantly superior in the chotosan group compared to placebo at 8 weeks ($p<0.05$) and 12 weeks ($p<0.01$). Chotosan showed statistically significant superiority to the placebo group in the improvement rating of "disturbance in daily living activities" at 12 weeks ($p<0.05$). With regards to the revised version of Hasegawa's Dementia Scale (HDS-R), there were no statistical differences between chotosan and placebo groups at any time points. There was also no statistically significant difference between chotosan and placebo groups in the global improvement rating of neurological symptoms at any of the time points. Chotosan was statistically superior to placebo in the global improvement rating of psychiatric symptoms at 4 ($p<0.05$), 8 ($p<0.001$), and 12 weeks ($p<0.001$). Chotosan showed statistical superiority to the placebo in improving "spontaneity of conversation" at 8 weeks, "lack of facial expression" at 8 weeks, "simple arithmetic" at 12 weeks, "global intellectual ability" at 12 weeks, "nocturnal

delirium" at 8 weeks, "sleep disturbance" at 8 weeks and 12 weeks, and "hallucinations or delusion" at 8 weeks and 12 weeks.

- In a randomized placebo-controlled trial of 60 patients with vascular dementia, chotosan treatment (2.5 g, 3 times daily, orally; TJ-47; Tsumura & Co.) for 12 weeks significantly improved the global improvement rating at every time point compared to placebo ($p<0.05$ at 4 weeks, $p<0.01$ at 8 weeks, and $p<0.01$ at 12 weeks)(Shimada et al., 1994). Chotosan was statistically superior to placebo in the global improvement rating of subjective symptoms at each time point ($p<0.05$ at 4 weeks, $p<0.01$ at 8 weeks, and $p<0.01$ at 12 weeks). Chotosan was statistically superior to placebo in the improvement rating of specific subjective symptoms including dizziness or vertigo ($p<0.05$ at 4 weeks), shoulder stiffness ($p<0.05$ at 4 weeks and $p<0.05$ at12 weeks), and palpitation ($p<0.05$ at 12 weeks). There was no statistically significant difference between the chotosan and placebo groups in the global improvement rating of neurological symptoms at any of the evaluation points. Chotosan was statistically inferior to placebo in the improvement rating of urinary incontinence at 8 weeks ($p<0.05$) and 12 weeks ($p<0.05$). Chotosan was statistically superior to placebo in the global improvement rating of psychiatric symptoms at 4 weeks ($p<0.05$), 8 weeks ($p<0.01$) and 12 weeks ($p<0.01$). Chotosan was statistically superior to placebo in the improvement rating of specific psychiatric symptoms including "decline in interest in television or books" at 8 weeks ($p<0.05$) and 12 weeks ($p<0.05$), "lack of facial expression" at 12 weeks ($p<0.05$), and "disorientation" at 4 weeks ($p<0.05$). Chotosan was statistically superior to placebo in the global improvement rating of disturbance in daily living activities at each evaluation point ($p<0.05$ at 4 weeks, $p<0.05$ at 12 weeks). With regards to HDS-R, the chotosan group showed statistically significant improvements at all time points ($p<0.05$ at 4 weeks, $p<0.01$ at 8 weeks, and $p<0.01$ at 12 weeks) compared to baseline. However, there were no differences in HDS-R between chotosan and placebo groups at any of the time points.
- In a double-blind randomized placebo-controlled trial of 30 patients with Alzheimer's disease (13 had mild to moderate Alzheimer's disease, 17 had Alzheimer's disease and cerebrovascular disease), chotosan treatment (2.5 g, 30 minutes before every meal; Tsumura & Co.) for 8 weeks significantly increased cognitive scores (measured by MMSE) compared to baseline values (from 15.5±4.0 to 17.5±4.9 points; $p<0.01$), while no improvement was seen with placebo or with a different Kampo formulation, gosya-jinki-gan (Tsumura & Co.)(Suzuki et al., 2005). Activities of daily living (measured by Barthel Index) also increased significantly compared with baseline values in the chotosan group ($p=0.046$) but not in the gosya-jinki-gan or placebo groups.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:

In a mouse model of Alzheimer's disease (induced by intrahippocampal infusion of Aβ42), chotosan treatment (365 or 750 mg/kg/day) for 3 weeks significantly restored memory impairment (measured by the Morris water maze and Y-maze) and significantly reduced inflammation (reduced TLR-4 and NFkB p65 expression and reduced the release of proinflammatory cytokines, TNF-α and IL-1β in the hippocampus)(Chen et al., 2016). Chotosan treatment also reduced neuronal apoptosis as evidenced by the increased Bcl-2/Bax ratio and decreased activity of pro-apoptotic caspase-3.

In a mouse model of cognitive dysfunction (induced by transient cerebral ischemia), pretreatment with chotosan (750-6000 mg/kg, orally) significantly restored cognitive functions measured by the Morris water maze (Watanabe et al., 2003). Pretreatment with chotoko (*Uncariae Uncis cum Ramulus;* 75-600 mg/kg, orally), an ingredient of chotosan, also prevented the cognitive dysfunction. Both the alkaloid fraction (188 mg/kg, orally) and the phenolic fraction (188 mg/kg, orally) of chotoko (*Uncariae Uncis cum Ramulus*) prevented the ischemia-induced impairment of escape latency on the Morris water maze. Specifically, indole alkaloids, rhynchophylline (10 mg/kg, orally) and geissoschizine methyl ether (10 mg/kg, orally) prevented the cognitive dysfunction. In cell culture studies (NG108-15 cells), chotosan (250-1000 µg/ml), chotoko (*Uncariae Uncis cum Ramulus*; 250-1000 µg/ml), and its phenolic constituents, (-)epicatechin (200 µM) and caffeic acid (200 µM), significantly increased cell viability under H2O2 exposure.

In a rat model of cerebral ischemic injury (induced by common carotid artery occlusion), chotosan treatment (375 or 750 mg/kg/day, orally) for 4 weeks ameliorated memory impairment and neuronal loss (Jiang et al., 2019). Chotosan treatment also significantly reversed reactive oxygen species production, caspase-3 activation, and microglial activation in the hippocampus. Chotosan increased Nrf2 expression and its nuclear translocation, resulting in antioxidant effects. In a mouse model of chronic cerebral hypoperfusion (induced by common carotid artery occlusion), a single administration of chotosan (750 mg/kg, orally) restored spatial memory deficits measured by the Morris water maze (Murakami et al., 2005). Restoration of memory deficits were also observed with uncariae treatment (75 mg/kg, orally), a component of chotosan, but an uncariae-free formulation of chotosan failed to restore cognitive deficits. The effects of chotosan and uncariae were blocked by a selective cholinergic muscarinic M1 antagonist. Daily administration of chotosan or uncariae significantly increased levels of acetylcholine in the cerebral cortex and hippocampus of these mice to levels comparable to sham-operated control mice. These findings suggest that the restoration of spatial memory deficits in this model may be attributable to uncariae and the restorative effects are mediated, in part, by stimulation

of muscarinic M1 receptor. In the same mouse model, chotosan treatment (750 mg/kg/day, orally) improved object discrimination deficits while also restoring mRNA expression of muscarinic M3 and M5 receptors and ChAT in the cerebral cortex (Zhao et al., 2007). This study suggests that the beneficial effects of chotosan on cognitive deficits is through restoring cholinergic functions.

In a rat model of ischemic reperfusion, chotosan treatment significantly prevented delayed neuronal cell death (measured by TUNEL staining) in the hippocampal CA1 region (Dohi et al., 2003). Based on electron spin resonance studies, chotosan inhibited the formation of hydroxyl- and superoxide-radicals.

In a mouse model of accelerated senescence (SAMP8 mice), chotosan treatment (TJ-47, Tsumura & Co., mixed in food at 1%) started at the age of 7 months and continued for 3-5 months improved memory retention measured by the step-through passive avoidance task (Mizushima et al., 2003).

In a mouse model of accelerated senescence with transient ischemic insult (SAMP8 mice with bilateral common carotid artery occlusion), chotosan treatment (750 mg/kg, orally) for 3 weeks significantly ameliorated the cognitive deficits measured by the novel object recognition and Morris water maze (Zhao et al., 2011). Chotosan treatment also restored the marked decreases in neuroplasticity-related proteins (GluN1, CaMKII, CREB, and BDNF) and vasculogenesis/angiogenesis factors (VEGF, VEGF receptor type 2, PDGF-A, and PDGFRα) in the frontal cortex of sham-SAMP8 and carotid artery occluded SAMP8 mice.

In a rat model of juvenile-onset diabetes (induced by streptozotocin injection), chotosan treatment (1,000 mg/kg/day, orally) for 3-7 days restored spatial working memory, measured by spontaneous alternation performance on the Y-maze test (Sasaki-Hamada et al., 2014). Chotosan treatment also restored the enhanced synaptic transmission in this rat model, while concurrently downregulating the overexpressed GluN2B subunit of the NMDA receptor.

In a mouse model of diabetes (db/db mice), chotosan treatment (375-750 mg/kg/day, orally) for 7 weeks ameliorated cognitive deficits measured by the novel object recognition, Y-maze test, and Morris water maze tests (Zhao et al., 2012). Chotosan treatment also reversed the neurochemical and histological changes caused by diabetes, including the restoration of VEGF, VEGF receptor type 2, PDGFB, and PDGF receptor β in the hippocampus. Chotosan treatment also restored cholinergic function, including restoration of expression levels of ChAT, M1 cholinergic receptor, M3 cholinergic receptor, and M5 cholinergic receptor in the hippocampus.

In cell culture studies, chotosan (and other Kampo medicines including hochuekkito, kososan, and ninjinyoeito) increased BDNF levels in the culture media (Nakajima et al., 2021). Additionally, chinpi (citrus unshiu peel), a component of chotosan, also increased BDNF levels in the culture media as well as increased BDNF mRNA expression.

In vitro studies have found that a fraction of chotosan showed protective effects against Aβ25-35-induced neurotoxicity (Wei et al., 2016). Of the various compounds present in chotosan, caffeic acid, chlorogenic acid, 1,5-dicaffeoylquinic acid, 3,5-dicaffeoylquinic acid, and 4,5-dicaffeoylquinic acid (compounds present in *Chrysanthemum morifolium*) had significant neuroprotective effects against Aβ25-35-induced neuronal death. In addition, nobiletin and hesperidin inhibited Aβ42 aggregation. These findings suggest that antioxidative effects may partly mediate the neuroprotective benefits observed with chotosan.

In cell culture (NG108-15 cells), chotosan (5-100 µg/ml) and chotoko (*Uncariae Uncis cum Ramulus*; 5-100 µg/ml) increased the level of glutathione and stimulated the activities of antioxidant enzymes including SOD, catalase, and glutathione peroxidase (GPX)(Mahakunakorn et al., 2005). Of phenolic compounds present in chotosan, epicatechin stimulated catalase, GPX, and glutathione content (but not SOD); quercetin stimulated all, and caffeic acid stimulated SOD activity but had no effects on others. In NG108-15 cells, chotosan, chotoko, and phenolic compounds present in chotoko (epicatechin, caffeic acid, and quercetin) had antioxidant and cytoprotective properties against oxidative damage (Mahakunakorn et al., 2024). Chotosan, chotoko, epicatechin, caffeic acid, and quercetin showed DPPH radical-scavenging activity, inhibitory activities against superoxide anion formation, hydroxyl radical-scavenging activity, and protection against H2O2-induced oxidative damage.

APOE4 interactions:

No clinical or preclinical studies have evaluated whether chotosan has differential effects based on APOE genotype.

Aging and related health concerns: Chotosan is used clinically to treat headache, vertigo, and other conditions in older people who have high blood pressure and have physical weakness. Antihypertensive effects have also been confirmed in rodent models.

Types of evidence:

- 1 retrospective study
- Numerous laboratory studies

Hypertension: IMPROVED

In a retrospective study of 171 patients making a visit to a neurosurgical outpatient division complaining of headache, dizziness, neck stiffness, nausea, head discomfort, etc., many had undiagnosed hypertension and chotosan treatment (2.5 g, twice daily, orally; administered to 50.3% of patients) significantly improved patient outcomes (odds ratio of 3.13)(Kanazawa et al., 2024). The number of improved outcomes was significantly higher in patients prescribed chotosan than in patients given other prescriptions. Chotoko (*Uncariae Uncis cum Ramulus*, an ingredient in chotosan, has a blood pressure-lowering effect.

In a rat model of hypertension (spontaneously hypertensive rats), a single administration of chotosan (500-6000 mg/kg, orally) or chotoko (*Uncariae Uncis cum Ramulus*, 200 mg/kg, orally) produced dose-dependent hypotensive effects without affecting heart rate (Watanabe et al., 2003). No effects of chotosan were seen on blood pressure or heart rate in normotensive Wistar-Kyoto rats.

In a rat model of hypertension (10-11-month-old spontaneously hypertensive rats) experiencing hemorrhagic hypotension, chotosan treatment (0.5-2.0 g/kg/day, orally) for 14 days inhibited the decrease in cerebral blood flow when the perfusion pressure was reduce, but did not alter the baseline values of cerebral blood flow or mean arterial blood pressure (Sugimoto et al., 2000). Treatment with *Uncariae Ramulus et Uncus* (150 mg/kg/day, orally) showed an effect equivalent to that of chotosan. These effects appeared to be mediated in part by activation of the nitric oxide synthase.

Stroke: POTENTIAL IMPROVEMENT BASED ON RODENT MODELS

In a rat model of cerebral stroke (stroke-prone spontaneously hypertensive rats), chotosan (450 mg/kg/day in drinking water; Tsumura & Co.) for 8 weeks caused a decrease in blood pressure (Yang et al., 2002). Chotosan treatment also significantly decreased serum lipid peroxide levels compared to the

control rats. Blood viscosity was not significantly affected by chotosan treatment, but erythrocyte deformability was significantly improved with chotosan compared to the control group. Endothelium-dependent relaxation induced by acetylcholine was significantly increased with chotosan compared to control, while endothelium-independent relaxation was unaffected. Investigators suggested that chotosan may be protective against cerebral vascular injury in susceptible animals.

Lifespan: INCREASED IN A RODENT MODEL OF STROKE

In a rat model of cerebral stroke (stroke-prone spontaneously hypertensive rats), chotosan treatment (150 or 450 mg/kg/day in drinking water) started at 8 weeks of age significantly increased survival times compared to the control group receiving regular drinking water (Shimada et al., 2003). The mean survival times of the control, 150 mg/kg dose chotosan, and 450 mg/kg dose chotosan groups were 122.1, 159.8 and 176.8 days, respectively. Percent survival was also significantly higher for both the 150 mg/kg dose chotosan and 450 mg/kg dose chotosan groups compared to the control ($p<0.05$). The cumulative percent occurrence of neurological and behavioral signs accompanying stroke in the 450 mg/kg dose chotosan group was significantly lower compared to the control group ($p<0.05$). Based on these findings, chotosan appears to prevent the occurrence of stroke and death in this rat model.

Safety: A meta-analysis in dementia patients reported that chotosan is well tolerated with adverse events including diarrhea, appetite loss, and elevated liver enzymes. Rarely, *Glycyrrhiza radix* can lower K+ levels and increase blood pressure and edema.

Types of evidence:

- 1 meta-analysis
- 1 clinical trial
- Numerous reviews

In a meta-analysis of 3 randomized controlled trials including a total of 219 dementia patients, chotosan treatment (TJ-47, Tsumura & Co., Tokyo, Japan; 2.5 g with every meal, 7.5 g daily, orally) for 8-12 weeks did not result in significant differences from placebo with respect to dropouts due to adverse effects (Imai et al., 2017). A few reported adverse events in the chotosan arm included elevated liver enzymes, low serum potassium levels, urticaria, diarrhea, appetite loss, heartburn, and hypertension (Terasawa et al., 1997).

In the double-blind randomized controlled trial in 139 vascular dementia patients, 13 patients withdrew from the study, 8 of whom had complications: cerebral infarction (n=2), cerebral bleeding, pneumonia (n=2), ileus, heart failure, and colitis. Five patients withdrew due to adverse events (urticaria, diarrhea, appetite loss in the chotosan group and liver enzyme elevation and oral bitterness in the placebo group). All of the adverse events were resolved during the course of the trial or after discontinuation of the study drug (Terasawa et al., 1997).

While rarely reported, long-term use of chotosan can produce adverse effects such as hypokalemia and pseudoaldosteronism, which is attributable to *Glycyrrhiza radix*, a component of chotosan. *Glycyrrhiza radix* can lower potassium levels (through accelerated excretion via the renal tubules), leading to increased blood pressure from fluid retention and myopathy (due to low potassium levels).

Drug interactions:

Herb-drug interactions with chotosan have not been well documented. Because of chotosan's known effects on blood pressure and potassium levels, there are potential interactions with antihypertensive medications and diuretics, though specific interactions have not been documented.

Sources and dosing:

Chotosan is available with prescription in Japan and is often in powder form. Chotosan is a type of Kampo medicine that consists of 11 types of dried medicinal herbs mixed in the following ratio: Uncariae Uncis Cum Ramulus (3.0 g, hooks and branch of *Uncaria sinensis*), Aurantii Nobilis pericarpium (3.0 g, peel of *Citrus unshiu*), Pinelliae tuber (3.0 g, tuber of *Pinellia ternata*), Ophiopgonis tuber (3.0 g, root of *Ophiopogon japonicus*), Hoelen (3.0 g, fungus of *Poria cocos*), Ginseng radix (2.0 g, root of *Panax ginseng*), Chrysanthemi flow (2.0 g, flower of *Chrysanthemum morifolium*), Saphoshnikoviae radix (2.0 g, root and rhizome of Saposhnikovia divaricata), Glycyrrhizae radix (1.0 g. root of *Glycyrrhiza uralensis*), Gypsum Fibrosum (5.0 g, $CaSO_4 2H_2O$) and Zingiberis rhizoma (1.0 g, rhizome of *Zingiber officinale*).

Research underway:

There are no ongoing clinical trials testing chotosan for cognitive decline or dementia.

Search terms:

Pubmed, Google: chotosan, 釣藤散

Websites visited for chotosan, :

- Clinicaltrials.gov (0)
- NIH RePORTER (0)
- DrugAge (0)
- Drugs.com (0)
- WebMD.com (0)
- DrugBank.ca (0)