

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.

PM012

Evidence Summary

PM012 is undergoing a phase 2 trial in Alzheimer's patients. Preclinical studies show neuroprotective benefits of PM012, but no peer-reviewed publications exist for studies in humans to date.

Neuroprotective Benefit: In models of Alzheimer's disease and stroke, PM012 appears to have neuroprotective benefits. A phase 2 trial of PM012 is ongoing in Alzheimer's patients.

Aging and related health concerns: While anecdotal evidence suggest that Gugijihwang-tang or its components have anti-aging properties, no studies have tested the PM012 formulation specifically for age-related diseases.

Safety: Safety data of PM012 in humans have not been published in peer-reviewed articles. In rats, the No Observed Adverse Effects Levels of PM012 is 2,000 mg/kg/day.

Availability: not available; under clinical development	Dose: not established	Contents: <i>Corni fructus</i> , <i>Rehmannia radix</i> , <i>Hoelen</i> , <i>Discoreae radix</i> , <i>Mountain cortex radices</i> and <i>Alismatis radix</i>
Half-life: likely varies by compound	BBB: some compounds, such as paeonol, are penetrant	
Clinical trials: No clinical trial results have been published in peer-reviewed articles. An ongoing phase 2 trial is enrolling 312 patients with Alzheimer's disease.	Observational studies: N/A	

What is it?

PM012, also referred to as Gugijihwang-tang, is a standardized herbal formulation based on a traditional Chinese medicine formula named Yukmijihwang-tang. PM012 is composed of *Lycii fructus* (Goji berries; 26.5%), *Rehmannia radix* (Chinese foxglove root; 26.5%), *Corni fructus* (Asiatic dogwood fruit; 13%), *Discoreae radix* (Chinese yam root; 13%), *Hoelen* (Poria mushroom; 7%), *Alismatis radix* (water plantain rhizome; 7%), and *Mountain cortex radices* (root bark of tree peony; 7%) ([Sohn et al., 2012](#)).

PM012 is under clinical development by [Mediforum](#), a biotech company in Seoul, Korea, for the treatment of neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and stroke.

Yukmijihwang-tang has been used in Asia for diabetes mellitus, neurosis, kidney disorders, osteoporosis, immune disorders, and other conditions ([Park et al., 2005](#)). The ancient Chinese herbal medicine textbooks also have noted that Yukmijihwang-tang may have anti-aging effects.

Neuroprotective Benefit: In models of Alzheimer's disease and stroke, PM012 appears to have neuroprotective benefits. A phase 2 trial of PM012 is ongoing in Alzheimer's patients.

Types of evidence:

- 1 clinical trial testing Yukmijihwang-tang
- Numerous laboratory studies



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

There are no clinical trials that have tested the effects of the PM012 formulation on age-related cognitive decline or dementia prevention.

Yukmijihwang-tang contains similar components to PM012: *Rehmannia glutinosa*, *Cornus officinalis*, *Dioscorea batatas*, *Alisma orientale*, *Poria cocos*, and *Paeonia suffruticosa*. In a double-blind randomized controlled trial of 35 university students, Yukmijihwang-tang treatment (2 capsules each containing 650 mg, 3 times daily, orally) for 6 weeks significantly improved cognitive function as measured by the Korean-WAIS (an IQ test including 6 verbal and 5 non-verbal tests) compared to the placebo group ([Park et al., 2005](#)). The difference of the mean K-WAIS summed scores, composed of the digit span and block design scores, before and after the 6 weeks of treatment was significantly greater in the group treated with Yukmijihwang-tang (3.125 ± 0.682) than that of the placebo group (1 ± 0.524) ($p < 0.05$). The treatment also resulted in substantially shorter P300 latency on the event-related potential, suggesting faster speed of information processing.

Human research to suggest benefits to patients with dementia:

No studies of PM012 in dementia patients have been published. A phase 2 double-blind randomized placebo-controlled clinical study appears to be ongoing to explore the optimal dosage of PM012 tablet in Alzheimer's disease ([NCT05811000](#)), but results have not been made available as of September 2025.

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

In a mouse model of Alzheimer's disease (3-month-old 3xTg-AD mice), PM012 treatment (100 or 400 mg/kg, once a week) for 3 months significantly ameliorated memory deficit measured by shortened escape latencies and increased time spent in the target zone of the Morris water maze test ([Ye et al., 2016](#)). PM012 treatment also significantly decreased A β deposits in the hippocampus, up-regulated the expression of the neurotrophic factor BDNF, increased neurogenesis in the hippocampus (measured by BrdU, DCX), and improved glucose uptake in the cortex and hippocampus (measured by FDG-PET) of 3xTg-AD mice.



In another mouse model of Alzheimer's disease (hPS2m transgenic mice with presenilin 2 mutations), PM012 treatment showed significantly ameliorated cognitive function measured by shortened escape latencies and total swimming distance on the Morris water maze compared to the untreated mice ([Sohn et al., 2012](#)). There was no difference in swimming speed between treated and untreated mice.

In a rat model of memory dysfunction (induced by the neurotoxin trimethyltin), Gugijihwang-tang treatment (10 mg/kg, orally) for 2 weeks significantly improved spatial learning and memory function measured by acquisition and retention of the Morris water maze ([Jung et al., 2013](#)). Gugijihwang-tang treatment also significantly improved brain glucose metabolism, measured by FDG-PET.

In a rat model of stroke (middle cerebral artery occlusion), pretreatment with PM012 (50 mg/kg/day, i.p.) for 2 days before stroke significantly reduced brain infarction and improved locomotor activity ([Wu et al., 2023](#)). In the infarcted cortex, PM012 treatment attenuated the expression of inflammatory markers (IBA1, IL6, and CD86), upregulated the anti-inflammatory marker CD206, and suppressed the expression of ER stress and apoptotic genes. In rat primary cortical neuronal cultures, PM012 treatment antagonized the glutamate-mediated neuronal loss as well as the NMDA receptor-mediated calcium influx. Two potential bioactive molecules, paeoniflorin and 5-hydroxymethylfurfural, were identified in the PM012 extract. Overall, PM012 pretreatment reduced neuronal degeneration, activation of microglia, ER stress, apoptosis, and cerebral infarction in stroke models.

In normal rats, treatment with Yukmijihwang-tang derivatives (400 mg/100 g body weight) for 10 days significantly improved memory, as measured by retention on the passive avoidance test ([Rho et al., 2005](#)). Much less benefit was seen with soya lecithin (10 mg/100 g body weight) or ginkgo biloba (2.6 mg/100 g body weight) treatments. Microarray studies showed that Yukmijihwang-tang treatment led to increased expression of proteins involved in neuroprotection, including transthyretin and PEP-19, a neuron-specific protein that inhibits apoptotic processes.

Individual components of PM012 have been shown to exert various neuroprotective effects. Mountain cortex radices restored viability of oxidative stress-exposed PC12 cells by decreasing production of reactive oxygen species and increasing the expression of proteins important for regulating oxidative stress (heme oxygenase and COMT) ([Rho et al., 2005](#)). In rats, treatment with *Rehmannia radix* improved performance on the Morris water maze and step down task, while increasing the expression of hippocampal NGF and c-fos ([Cui et al., 2004](#)). *Lycii fructus* and *Corni fructus* have anti-oxidative effects, and *Lycii fructus*, *Corni fructus*, *Discorea radix*, and Mountain cortex radices have anti-inflammatory effects (reviewed in [Sohn et al., 2012](#)).

APOE4 interactions: Unknown

Aging and related health concerns: While anecdotal evidence suggest that Gugijihwang-tang or its components have anti-aging properties, no studies have tested the PM012 formulation specifically for age-related diseases.

Types of evidence:

- 0 clinical trials
- 0 observational studies
- 0 laboratory studies

PM012 has not been tested in age-related disease models or patients. Yukmijihwang-tang, which is a traditional Chinese medicine formula that is the basis for PM012, has been used in Asia for diabetes mellitus, neurosis, kidney disorders, osteoporosis, immune disorders, and other conditions ([Park et al., 2005](#)). Yukmijihwang-tang contains similar components to PM012: *Rehmannia glutinosa*, *Cornus officinalis*, *Dioscorea batatas*, *Alisma orientale*, *Poria cocos*, and *Paeonia suffruticosa*. The ancient Chinese herbal medicine textbooks also have noted that Yukmijihwang-tang may have anti-aging effects.

Safety: Safety data of PM012 in humans have not been published in peer-reviewed articles. In rats, the No Observed Adverse Effects Levels of PM012 is 2,000 mg/kg/day.

Types of evidence:

- Several laboratory studies

In male and female rats, repeated oral administration of PM012 (up to 2,000 mg/kg/day) over 26 weeks did not cause adverse effects as assessed by clinical signs, mortality, body weight, food and water consumption, ophthalmology, urinalysis, hematology, serum biochemistry, blood clotting time, organ weights and histopathology ([Sohn et al., 2012](#)). There were no statistically significant differences in body weight or food/water consumption between the control and PM012 treatment groups. PM012 treatment did not significantly affect urinary pH, specific gravity, protein, glucose, urea acid, ketone, occult blood, or sediments. No statistically significant differences were seen in hematological parameters, including red blood cells, platelets, white blood cells, neutrophils, lymphocytes, monocytes,



eosinophils, basophils, and large unstained cell counts. There were no significant differences between PM012-treated and control rats on clotting time, hemoglobin distribution weight, hemoglobin, reticulocytes, hematocrit, mean corpuscular volume, red cell distribution width, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and mean platelet volume. There were no significant differences between PM012-treated and control rats on creatine phosphokinase, glucose, total cholesterol, triglycerides, albumin/globulin ration, blood urea nitrogen, creatinine, or inorganic phosphorus.

There was a dose-dependent PM012-induced increase in thymus weight in female (but not male) rats, but the change was judged to be toxicologically insignificant by the investigators ([Sohn et al., 2012](#)). Histological evaluation of the adrenal gland, pituitary gland, prostate gland, kidney, liver, spleen, lung, heart, thymus, thyroid gland, mesenteric and harderian glands did not reveal any pathological changes in the highest PM012 dose group. The No Observed Adverse Effects Levels of PM012 in rats was determined to be 2,000 mg/kg/day for both sexes.

Female mice treated with the 2,000 mg/kg/day dose of PM012 showed significantly increased serum total protein ([Sohn et al., 2012](#)). No statistically significant differences in serum electrolytes such as K⁺ or Cl⁻ were found. Male mice treated with 1,000 mg/kg/day of PM012 showed significantly decreased serum Ca²⁺, while female mice treated with 1,000 mg/kg/day of PM012 had significantly decreased serum Na⁺. There were no significant differences between PM012-treated and control mice on liver function markers, such as AST, ALT, ALP, or bilirubin.

In a mouse model of Alzheimer's disease (3-month-old 3xTg-AD mice), PM012 treatment (100 or 400 mg/kg, once a week) for 3 months had no effect on body weight ([Ye et al., 2016](#)).

Drug interactions: Drug interactions with PM012 have not been documented.

Sources and dosing:

PM012 is under clinical development by [Mediforum](#), a biotech company in Seoul, Korea, for the treatment of neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and stroke.

Dosage has not been established for any indication. An ongoing phase 2 trial in Alzheimer's disease is testing doses ranging from 2,600 mg/day to 5,200 mg/day ([NCT05811000](#)).

Research underway:

A phase 2 double-blind randomized placebo-controlled clinical study appears to be ongoing to explore the optimal dosage of PM012 tablet in 312 patients with Alzheimer's disease ([NCT05811000](#)). Doses proposed to be tested include 2,600 mg/day, 3,900 mg/day, and 5,200 mg/day, combined with donepezil (5 mg). The intervention duration is 12 weeks. Study completion was estimated for August 2024, but no updates have been posted since April 2023.

Search terms:

Pubmed, Google: PM012

Websites visited for PM012:

- [Clinicaltrials.gov](#)
- NIH RePORTER (0)
- Examine.com (0)
- Drugs.com (0)
- WebMD.com (0)
- DrugBank.ca (0)
- Labdoor.com (0)

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If you have suggestions for drugs, drugs-in-development, supplements, nutraceuticals, or food/drink with neuroprotective properties that warrant in-depth reviews by ADDF's Aging and Alzheimer's Prevention Program, please contact INFO@alzdiscovery.org. To view our official ratings, visit [Cognitive Vitality's Rating page](#).