Improve Memory Loss, Protect Brain Neuronal Cells

SILK FIBROIN “BF-7”

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Memory and other cognitive losses associated with aging can concern people approaching their golden years. While aging brings the benefits of wisdom and experience, it is also sometimes associated with reduced mental acuity, brain-processing, and short-term recall of faces, names, numbers, and words – symptoms we refer to as “senior moments.”

In more extreme cases, cognitive decline may manifest itself as dementia, possibly as Alzheimer’s disease. Many people believe that cognitive decline is a natural consequence of aging.

Memory lapses and other signs of reduced brain power are not inevitable, nor are they necessarily early symptoms of Alzheimer’s disease. When cognition (the ability to think, perceive, remember, and reason) declines enough to handicap daily activities, a person may suffer from dementia. Dementia is not a disease in-and-of itself; rather, it describes symptoms which accompany a disease such as Alzheimer’s.

While dementia may be due to age-related factors, it may also result temporarily, among other reasons, from depression, side-effects of some medications, chronic alcoholism, and medical conditions such as low thyroid function, kidney or liver disorders, Vitamin B12 deficiency, and elevated homocysteine levels.
Alzheimer’s disease, an irreversible, progressive brain disorder which extinguishes memory and thinking skills, currently affects between 2.4 and 4.5 million Americans. Characterized by amyloid plaques and neurofibrillary tangles in the brain, as well as loss of connections between, and subsequent death of, nerve cells, Alzheimer’s causes brain shrinkage.

People usually begin displaying forgetfulness, a hallmark symptom of Alzheimer’s, after the age of 60. Whatever the ultimate cause of Alzheimer’s disease may be, the symptoms of the disease arise when neurons that are damaged or destroyed by free radicals (generated by inflammation) fail to function. Such symptoms manifest between 10-20 years after the initial brain damage. Limiting brain damage, then, should be key to preventing Alzheimer’s disease.

Memory loss worries many of us as we get older...
Finding new ways to slow memory loss could produce astounding results. For example, if the onset of Alzheimer's could be delayed in today's population by an average of just one year, there would be about 210,000 fewer people with Alzheimer's 10 years from now. And that would produce a cost savings of $10 Billion.

"The problem with prescription drugs is that they're extremely expensive and often have limited effectiveness during a short window of time," says Evangeline Lausier, MD, assistant clinical professor in medicine, Duke Integrative Medicine, Duke University Medical Center in Durham, N.C.

**Prevention is Key...**
SILK FIBROIN “BF-7”
Silk Fibroin is an insoluble protein created by spiders, the larvae of Bombyx mori, other Moth genera such as Antheraea, Cricula, Samia and Gonometa, and numerous other insects.

**Silk in its raw state consists of two main proteins, sericin and fibroin**, fibroin being the structural center of the silk, and sericin being the sticky material surrounding it.

*Bombyx mori* Cocoon

Cocoon Silk

Silk Sericin

Silk Fibroin
Proven Effects of Silk Fibroin “BF-7”

Proven to be effective in many clinical applications:

- Memory enhancing effect has been scientifically proven by multiple published studies
- Prevents memory loss and dementia of senior people
- Increases cognitive functions
- Highly recommended for students and adults for preparing examination, and seniors who worry about brain health
- Protects brain neuronal cells

2. BF-7 Improved Memory Function and Protected Neuron from Oxidative Stress

3. The Effect of BF-7 on the Ischemia-induced Learning and Memory Deficits
   The Korean J. Anat. 38(2), 181~188, 2005

4. The Role of BF-7 on Enhancement of Memory and Cognitive Function
   The Korean J. Anat. 37(6), 519~527, 2004

5. Memory enhancing effects of silk fibroin derived peptides in scopolamine treated mice

6. The role of BF-7 on neuroprotection and enhancement of cognitive function

7. The improvement of learning and memory ability of normal persons by BF-7

8. Brain Factor-7 Extracted from Bombyx mori Enhances Cognition and Attention in Normal Children
   J Med Food 12(3) 2009, 643-648
SILK FIBROIN “BF-7”
Human neuroblastoma cell test
**BF-7**

**Effect of BF-7 on Aβ-induced neuronal cell death**

* Aβ (Amyloid-beta): Induces neuronal cell death

Treatment with BF-7 alone had no effect on the cell viability although a combination of Aβ and BF-7 was found to block 20% of the cell death induced by Aβ.

* BF-7 attenuated the decreased cell viability induced by Aβ.

*BF-7 attenuated the decreased cell viability induced by Aβ.*

BF-7
Inhibit the apoptotic cell death induced by Aβ

*Morphological assessment of apoptosis by phase-contrast and fluorescence microscopy.

BF-7 treatment prior to Aβ was found to block the morphologic and apoptotic characteristics observed when the cells were exposed to Aβ alone.

Source: Korean J Physiol and Pharmacol 8:173-179 (2004) – Fig. 2.
Inhibitory role on ROS generation by Aβ

*ROS are the main factor that causes oxidative stress, which results in cytotoxicity. The level of DCF fluorescence is an indicator of ROS production.

The intensity of DCF fluorescence showed significant, above seven-fold increases, than those in untreated cells. These results implicate involvement of ROS in Aβ-induced apoptosis and antioxidant effect of BF-7 in SKN-SH cells.

Source: Korean J Physiol and Pharmacol 8:173-179 (2004) – Fig. 3.
Effect of BF-7 on Aβ-induced caspase-3 activity

Although Aβ increased the caspase-3 activity by up to two times, a pretreatment with either BF-7 or zVADfmk, a pancaspase inhibitor attenuated the Aβ-induced caspase-3 activity by either one half or abolished the activity completely, respectively.

* Caspases are real executors leading to apoptosis, the attenuating caspase activation would be pivotal role of BF-7 for protecting neuronal cell.

Source: Korean J Physiol and Pharmacol 8:173-179 (2004) – Fig. 4.
SILK FIBROIN “BF-7”
Animal test
As cognitive function is decreased, the concentration of acetylcholine is reduced. Our result showed that the acetylcholine concentration, in the brain from the rat treated with beta amyloid(Aβ), was reduced by 45% compared with placebo group.

Interestingly, the acetylcholine concentration was recovered by BF-7. Treatment with 5mg/kg and 10 mg/kg of BF-7 increased the acetylcholine level to 78% and 80% compared to control, respectively.

Source: Korean J Physiol and Pharmacol 8:307-312 (2004) – Fig. 5.
Abnormal blood supply to brain, such as ischemia induced neuronal damages, can lead to dementia. To check whether or not BF-7 attenuated the ischemic damage, BF-7 (10 mg/kg) was orally treated for 7 days, once a day.

To evaluate the learning and memory of the rat, 8-arm maze test was conducted.

The increase in working memory errors induced by ischemia was significantly reduced by BF-7.

These results suggest that BF-7 attenuated ischemia-induced object recognition deficits.

Source: The Korean J. Anat. 38(2), 181~188, 2005 – Fig. 4.
BF-7

‘Passive avoidance test’ to evaluate the learning and memory

Scopolamine
- Induces significant memory impairment

Passive Avoidance Test
- Fear-aggravated test used to evaluate learning and memory in rodent models of CNS disorders.
- Subjects learn to avoid an environment in which an aversive stimulus (such as a foot-shock) was previously delivered.
- The latency to pass the gate in order to avoid the stimulus is used as an indicator of learning and memory.

In the passive avoidance test, BF-7 increased the latency of reaction times in learning and short memory retrieval tests. These findings suggest that BF-7 improves learning and memory processes and has a cognition-enhancing effect.

Source: The Korean J. Anat. 37(6), 519~527, 2004 – Fig. 2.
SILK FIBROIN “BF-7”
Human clinical trial
BF-7 Clinical Trial I
Preventing/improving effects of BF-7 against Dementia

<table>
<thead>
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<tr>
<td>30</td>
<td>60 yrs +</td>
<td>400mg of BF-7 (200mg, 2 times)</td>
<td>3 weeks</td>
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Result 1.

* ADAS-cog-K
General clinical test for evaluating symptoms of dementia, including learning and memory, understanding, sense, concentration, awareness, verbal, and movements.

Intake of BF-7 greatly improved the symptoms. More positive effect was represented in the more severe cases, as shown in Result 1. (lower point less than around 10 represents Normal. So, the reduction of the point means improvement)

Source: The Korean J. Anat. 37(6), 519~527, 2004
BF-7 Clinical Trial I
Preventing/improving effects of BF-7 against Dementia

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Result 2.

* MMSE-K
Another method for checking the states of Dementia. Learning and Memory, Caution, Concentration, Calculation, Verbal and Cognitions of time/space were evaluated in this test.

Intake of the BF-7 greatly improved the symptoms of the elders. The more positive effect was represented in the more severe cases, as shown in Result 2. (higher than 24 point represents Normal and lower than 17 point represents severe dementia. So, the increase of the point means improvement)

Source: The Korean J. Anat. 37(6), 519~527, 2004 – Fig. 5.
Enhancing Memory and Concentration Power by BF-7

**BF-7 Clinical Trial II**

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<th>Subject No.</th>
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<td>98</td>
<td>19~64 yrs</td>
<td>200mg or 400mg of BF-7</td>
<td>3 weeks</td>
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**Result 1.**

The memory index MQ, which is the most direct reflective index of memorization ability.

The average MQ of all 98 subjects was around 105. Interestingly, the average MQ was significantly increased to 126.6 after intake of BF-7 for 3 weeks, but not in placebo group.

The MQ score was significantly increased in a dose dependent manner. This results represent that BF-7 enhances memorization ability effectively.

*Enhanced memory quotient (MQ) by BF-7*

Source: Korean J Physiol and Pharmacol 8:307-312 (2004) – Fig. 1.a
BF-7 Clinical Trial II
Enhancing Memory and Concentration Power by BF-7

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Result 2.

Administration of BF-7 significantly increased the number of memorized words compared to placebo in a dose-dependent manner (Fig. a). It was shown that BF-7 was effective for maintaining memory, as the memory maintenance index was increased from 53.2% to 61.3% after intake of BF-7 for 3 weeks, but not in the placebo group (Fig. b).

Source: Korean J Physiol and Pharmacol 8:307-312 (2004) – Fig. 4.
BF-7 Clinical Trial II
Enhancing Memory and Concentration Power by BF-7

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Result 3.

Memory recall efficiency, which is the reflective index of efficiency to memorize something, indicates how much and how precisely one recalls preserved memory. The higher ranked percentage represents better efficiency.

As shown in the figure, the memory recall efficiency score was significantly increased from 31% to 58.9% and 41.5% to 66.5% by intake of 200 mg/day and 400 mg/day of BF-7 for 3 weeks, respectively, but not in placebo case (Fig. 2).

Source: Korean J Physiol and Pharmacol 8:307-312 (2004) – Fig. 2.
BF-7 Clinical Trial II
Enhancing Memory and Concentration Power by BF-7

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Result 4.

The Intelligence Quotient and Memory Quotient consensus score is the direct reflective index of relationship between intelligence quotient and memory quotient. The higher ranked % represents better memory ability compared with intelligence quotient.

As shown in figure, the IQ and MQ consensus score was significantly enhanced from 52.9% to 78.9% and 52.5% to 91.1% after intake of BF-7 200mg/day and 400mg/day for 3 weeks, respectively. The scores were increased in a dose-dependent manner and there is no change in placebo group.

Positive role of BF-7 on intelligence quotient/memory relationship

Source: Korean J Physiol and Pharmacol 8:307-312 (2004) – Fig. 3.
BF-7 Clinical Trial III
Enhancing Cognition and Attention by BF-7

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<td>46</td>
<td>BF-7 group (9.9±1.18 yrs)</td>
<td>400mg of BF-7 (200mg, 2 times)</td>
<td>16 weeks</td>
</tr>
<tr>
<td></td>
<td>placebo (9.8±1.03 yrs)</td>
<td></td>
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Result 1.

The improvement of response time by BF-7

The response times before BF-7 treatment (96.7 seconds) and after 16 weeks (74.8 seconds) are shown in Fig. A. The response time was significantly improved, by 23% with BF-7 treatment (Fig. B). BF-7 significantly reduced the time to conduct the task.

Source: J Med Food 12(3) 2009, 643-648 – Fig. 1.
BF-7 Clinical Trial III
Enhancing Cognition and Attention by BF-7

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Result 2.

**Enhancement of accuracy by BF-7**

The CTT-2 error in the BF-7 group was greatly reduced from 2.17 to 1.22 (Fig. A). These results indicate that the error rate was decreased by around 43%. In other words, the accuracy rate in the BF-7 group was improved significantly (Fig. B).

Source: J Med Food 12(3) 2009, 643-648 – Fig. 2.
## BF-7 Clinical Trial IV

**Rey-Kim Test and Number Memorizing test of K-WAIS**

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<td>30: BF-7 group</td>
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<td><strong>DBE</strong>: BF-7 400mg + DHA 132mg + EPA 206mg</td>
<td>30 days</td>
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<td>10: placebo group</td>
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### Effects of BF-7 on learning and short term memory activity

The average MQ score was significantly increased to about 122 after intake of DBE for a month, but not in placebo cases (Fig. A). To investigate if DBE can help with the ability to memorize something, the number of how many times one should repeat learning to memorize something (learning gradient test) was calculated. The learning gradient was declined from 47% to 18% at DBE treated case. This result represents that DBE was of significant help to enhance learning efficiency (Fig. B).

*Source: Korean J Physiol and Pharmacol 8:173-179 (2004) – Fig. 5, A,B*
BF-7 Clinical Trial IV
Rey-Kim Test and Number Memorizing test of K-WAIS

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**Effects of BF-7 on learning and short term memory activity**

The DBE was effective for prolonging of memory, as the memory preservation index was increased from 58% to 72% (Fig. C). To evaluate how much DBE exerted positive role on the attention and short-term memory, DBE was addressed to a part of IQ test (K-WAIS), memory and recall multiple numbers in order and in reversed order. With one month treatment of DBE, epoke-making score was improved significantly from 21 to 24 (Fig. D). The result represents that DBE is very effective on enhancing short-term memory and attentive concentration.

*Source: Korean J Physiol and Pharmacol 8:173-179 (2004) – Fig. 5. C,D*
BF-7 Summary

- BF-7 development was initiated as Korea government’s national research project involving multiple universities including Seoul National University, Chung-Ang University and National Institute of Agricultural Science Technology, spanning multiple years.

- The significant neuroprotective and learning/memory enhancement effects of BF-7 were proved by multiple published preclinical/clinical studies.

- The safety of BF-7 was certified from Korean Food and Drug Administration.

- The human studies showed it is fast-acting – 3 weeks.

- The potential market is not only for the elderly, but also for students who are having memory problems which in turn interfere with formation of efficient study habits, as well as for other young/middle aged people at workplaces who could use the extra help in memory retention.

- Patent(PCT)-pending
If you have any questions or need more information, please feel free to contact us.

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