

## Focusing on Brain Nutrients

### A Scientific & Regulatory Review



By Gene Bruno, MS, MHS

In writing an article on brain nutrients, the choices of potential nutraceuticals for inclusion are almost endless. A partial list includes (in alphabetical order) acetyl-L-carnitine, alpha-GPC, *Bacopa monnieri*, citicoline, DHA, DMAE, *Ginkgo biloba*, gotu kola, huperzine A, L-glutamine, phosphatidylcholine, phosphatidylserine, vinpocetine, vitamin B12 and others. So, how to choose which of them to write about? In order to do justice to the topic, I decided to write about one amino acid, one herb and one vitamin. In this case, phosphatidylserine, ginkgo biloba and vitamin B12.

#### Phosphatidylserine

The phospholipid phosphatidylserine (PS) is active at cell membranes (including synaptic membrane zones) and is a major building block for nerve cells. A significant amount of published clinical research has demonstrated that PS supplementation supports various cognitive parameters.<sup>1</sup>

An example is a double-blind, randomized, controlled study<sup>2</sup> to investigate the effects of PS on the cognitive functions of elderly Japanese subjects with memory complaints. Seventy-eight

elderly people with mild cognitive impairment (50-69 years old) were randomly assigned to take PS (100 mg or 300 mg/day) or placebo for six months. In the subjects with a relatively low score at baseline, the memory scores in the PS-treated groups were significantly increased compared to the baseline, while those of the placebo group remained unchanged. The memory improvements in the PS-treated groups were mostly attributed to the increase in delayed verbal recall, a memory ability attenuated in the earliest stage of dementia.

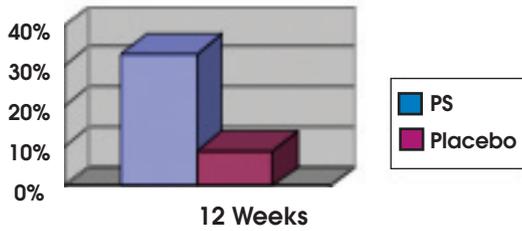
Another double-blind, placebo controlled study<sup>3</sup> assessed the influence of PS on memory and mood in patients aged 60-80 years, and who reported some memory difficulties that were verified by a score of at least 25 out of 30 on the Mini Mental State Test, which screens for cognitive impairment. Seventy-two subjects, randomly assigned to placebo and therapy groups, were treated for three months with 300 mg, PS daily. Results showed a large and statistically significant positive influence of treatment on both memory and mood, whereas influence of placebo was small and non-significant. Components of

memory and cognition that were most improved by the treatment included memorizing information, visual memory, and memorizing numbers. Mood was also influenced. Winter mood changes ("winter blues") did develop in the placebo group but were entirely blocked in those treated with PS.

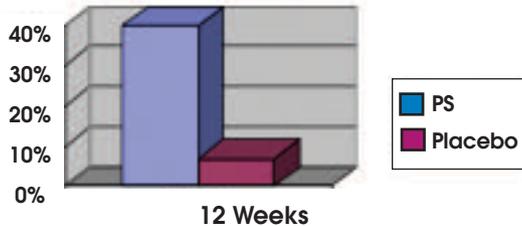
A 12-week, placebo-controlled clinical trial<sup>4</sup> conducted on 50 patients (mean age of 60.5, 52 percent female) with age-related cognitive decline examined the effects of 300 mg of soy derived PS daily. Learning and memory were assessed at three, six, nine and 12 weeks using a clinically relevant computerized neuropsychological test battery. Comparisons with PS and placebo are shown below.

Other controlled trials were also conducted on PS. In each case, the results showed significant improvements in cognitive performance over placebo in patients with cognitive performance issues (300 mg/day),<sup>5</sup> Alzheimer's (300-700 mg/day)<sup>6-8</sup>, and senile dementia (300 mg/day).<sup>9</sup> In addition, research with PS supplementation has also shown improvements in cognitive function in both patients with mild cognitive impairment<sup>10</sup> and mild dementia.<sup>11</sup>

## Remembering names one hour after introduction



## Learning & remembering written information



In laboratory tests on serum samples of patients treated with PS, significant reductions in uric acid and SGPT levels were noted (which may be considered beneficial), and all other serum parameters were unaffected.<sup>12</sup> In addition, PS has a favorable benefit-to-risk profile since, according to researchers, "its benefits are often remarkable, adverse effects from its use are virtually never seen, and its compatibility with most common drugs is established."<sup>13</sup> Most of the research on PS in the treatment of dementias and cognitive dysfunctions indicated an effective daily dosage range of 300-400 mg.<sup>14</sup>

### Ginkgo biloba Extract

The research on *Ginkgo biloba* extract in treating dementias and other cognitive functions is vast. As a matter of fact, there are hundreds of published clinical studies on ginkgo.<sup>15</sup> Consequently, with the exception of a discussion on one clinical trial, it was necessary to limit my presentation of the data to reviews and meta-analyses on the topic. It should be noted that ginkgo is used as a standardized preparation containing 24 percent ginkgo flavonoid glycosides and six percent terpene lactones, in a typical range of 120-240 mg daily, taken in two to three doses.<sup>16</sup>

To begin with, eight randomized, double-blind, placebo-controlled studies on ginkgo extract were systematically reviewed.<sup>17,18</sup> The reviewers concluded

that that ginkgo had modest effects on improving the symptoms of dementia and cerebral insufficiency. Furthermore, they indicated that the improvement was equivalent to therapy with ergoloid mesylates (hydergine).

A meta-analysis<sup>19</sup> included four studies (with a total of 212 subjects in the placebo and ginkgo groups) that met inclusion criteria for adequate clinical design for examining ginkgo's effects on objective measures of cognitive function in patients with Alzheimer's disease. The results were that a significant overall effect in the ginkgo groups was demonstrated that was comparable with the benefits of donepezil (Aricept).

Likewise, a review<sup>20</sup> of studies on ginkgo that lasted at least six months in duration concluded that ginkgo extract was equally effective in mild to moderate Alzheimer's dementia in comparison to second-generation cholinesterase inhibitors. Other research reviews on the use of ginkgo in treating dementia have shown similar beneficial results to those previously discussed.<sup>21</sup> In a controlled trial of ginkgo extract, LeBars et al. (1997) treated 309 patients with mild to moderately severe forms of dementia of the Alzheimer type (DAT) or multi-infarct dementia (MID), using 120 mg/day or placebo. The evaluation of patients took place periodically, up through 52 weeks of therapy. The results indicated that ginkgo extract was capable of stabilizing cognitive performance and social functioning in patients with dementia. These changes were objectively quantifiable and noticeable by caregivers, despite the fact that they were classified as modest.

### Vitamin B12

Vitamin B12 deficiency is frequently associated with neurological problems, including memory loss and dementia.<sup>22</sup> Individuals with Alzheimer's disease often have low levels of vitamin B12 in the blood and/or low cerebrospinal fluid.<sup>23</sup> In fact, vitamin B12 deficiency affects 10-15 percent of adults over the age of 60.<sup>24</sup> According to some researchers, many cases of Alzheimer's dementia are actually missed B12 defi-

ciency cases, and repletion of the vitamin has positive results regardless of other risk factors.<sup>25</sup> In one clinician's experience, replenishment of vitamin B12 can reverse 75 percent of B12 deficiency dementias when discovered early enough.<sup>26</sup> Other research also suggests that dementia caused by vitamin B12 deficiency can be reversed by vitamin treatment, but reversibility seems to be dependent upon the duration of the associated neurologic complications.<sup>27</sup>

In an initial, randomized, controlled study<sup>28</sup> on elderly subjects with increased dementia risk (mild cognitive impairment), researchers showed that treatment with 500 mcg vitamin B12, combined with 800 mcg folic and 20 mg vitamin B6, slowed shrinkage of the whole brain volume by 50 percent over two years. In a follow up study<sup>29</sup>, the same researchers found that the vitamin B12 combination reduced, by as much as seven fold, the cerebral atrophy in those gray matter (GM) regions specifically vulnerable to the Alzheimer's disease process, including the medial temporal lobe.

**A note on vitamin B12 absorption:** The intestinal absorption of B12 is dependent upon its binding with the glycoprotein intrinsic factor (IF), secreted from the parietal cells of the stomach. If the gastric juices of a person lacks IF, then there is little uptake of the vitamin (as little as one percent).<sup>30</sup> This issue can be addressed through the use of a vitamin B12 lozenge, which can be absorbed via the sublingual plexus and buccal cavity, thereby bypassing the issue with IF entirely. The result is a 90 percent increase in serum B12.<sup>31</sup>

### Conclusion

Although there are many nutraceuticals that support brain health, PS, ginkgo and B12 are three very good ones with a history of safe and effective use. **VR**

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## 2013 Retailer of the Year

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study released in July by the Centers for Disease Control and Prevention (CDC), which noted that Aloha State residents 65 years old can expect another 16.2 years of healthy living. But even Hawaiians have their share of health issues. "Our customers have a lot of the usual needs for a good multivitamin, bone support, immune support, digestion (fiber, probiotics, enzymes) and omega-3s," said Wolf. "Unfortunately, as people throughout our nation have reduced healthy lifestyles and gained weight, we see a lot of new customers coming in looking for products that can help support healthier blood pressure, cholesterol, blood sugar and weight loss. And with the modern lifestyle comes a need for stress and mood support, as well as energy and sleep aids.

"Many customers want to try a natural approach and avoid going on medications if possible. We show them what is available to support their body's needs," she added. "We always remind them that these are lifestyle-driven health



issues. Eating a healthy diet, exercising regularly and managing their stress are truly the foundations to good health. We show them what we have that can support or 'supplement' a healthy lifestyle, and offer the best options."

### Island Issues

While Whole Foods Market's arrival to Hawaii posed a steep challenge, one that the store meets with store renovations, customer service and by introduc-

ing new stores in under-served parts of the state, Down to Earth has also had to address major workplace safety issues and workers compensation problems. "We dealt with this by introducing a team member safety program that has been very successful," Fergusson said.

And being located in Hawaii brings geographic obstacles. "We are challenged by shipping problems as getting our orders takes 10 days from order to receipt. It makes it more difficult to receive orders in a timely way, and increases our out-of-stocks," he added.

Despite the challenges, Fergusson said there's more work to be done at Down to Earth. "We will grow and expand, opening more stores in Hawaii and one day possibly the mainland or even internationally." **VR**

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