# Efficacy of the Constituents of Smart Mind<sup>™</sup> to Enhance Cognitive Performance, Focus and Neuroprotection: Validation through Clinical Trials

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## Introduction

Smart Mind<sup>TM</sup> is dietary supplement system comprised of ingredients selected specifically to support normal, healthy brain function throughout the adult life cycle. In this White Paper the science supporting the entire spectrum of ingredients in the formulation Smart Mind<sup>TM</sup> will be reviewed. Key actives for each ingredient will be identified, information will be provided on the functional effect of these ingredients in reference to the normal structure and function of the central nervous system and the maintenance of brain health, and the effects observed in a series of well designed research studies that have been performed with the three primary active ingredients making up this formulation will be elucidated. We will conclude by validating that the claims proposed for this formulation are sufficiently grounded in evidence-based scientific studies in the literature, which include foundational investigations in both cellular and animal models where appropriate, followed by clinical trials in human subjects.

According to the NIH National Institute on Aging, Alzheimer's Disease currently impacts approximately 5.1 million Americans (https://www.nia.nih.gov/alzheimers) over the age of 65 and is predicted to triple to 13.8 million by 2050 (www.alz.org/facts), making the maintenance of brain health and prevention of age-related deterioration in brain function a pressing public health issue. It is common for individuals to experience a decline in cognitive function as they age, which is often referred to as mild cognitive impairment (MCI) or age-associated memory impairment (AAMI). Individuals with MCI have a gradual memory loss but do not meet the clinical criteria for a formal diagnosis of Alzheimer's disease (AD). It is estimated that the prevalence rate of MCI is 20% of the United States population over the age of 65. <sup>1</sup> It has also been demonstrated that memory and cognition impairments begin to decline at a rate of approximately 10% per decade, starting as early as the 20's.<sup>2</sup> Using neuroimaging technology, research scientists have been able to detect changes in brain function as early as 20 years prior to the onset of detectable Alzheimer's symptoms,<sup>3</sup> demonstrating the importance of adopting a proactive approach in supporting healthy brain function as early in life as possible, given its impact on cognition, mental health and overall wellbeing. This research illustrates that there is a long prodromal phase before the presence of a degenerative disease manifests clinically, providing a window of time where nutrients that

support neuronal growth, synaptic connectivity and density, lipid composition and endogenous antioxidant systems have the potential to significantly attenuate the symptoms associated with brain aging, including MCI and AAMI. Accelerated brain aging is a growing health epidemic that requires a thoughtful, proactive approach adopted early in life, prior to the onset of symptoms of cognitive dysfunction. Nutritional support in the brain health sector is poised for exponential growth, provided that the studies supporting the various approaches to nutritional support, including dietary regimes and dietary supplements, have demonstrated efficacy in validated human clinical trials using the randomized, double-blind, placebo controlled method. To this end, Smart Mind<sup>™</sup> has developed a novel combination of three nutraceutical ingredients, each with an evidence base in the scientific literature and included at the dose demonstrated safe and effective in human clinical trials. Further, these nutraceutical ingredients are sourced from the same suppliers whose materials were utilized in the clinical trials supporting them. Together, these ingredients are provided in a single dietary supplement with the goal of supporting brain function through enhancement of antioxidant systems, promotion of neurogenesis, enhanced neurotransmitter production and stabilization of cell membranes. These nutraceuticals include a proprietary spearmint (Neumentix<sup>TM</sup>) Phenolic Complex K110-42, demonstrated to promote cognitive health and performance through its ability to stimulate neurogenesis and support healthy neurotransmitter function, along with its antioxidant and neuroprotective properties, PhosphatidylSerine (SerinAid®), a phospholipid essential in supporting cellular membrane stability and fluidity, and Thearcine (TeaCrine®), a purine alkaloid isolated from the Camellia assamica var. kucha tealeaf and also a natural constituent of coffee, demonstrated to have both anti-inflammatory and analgesic properties as well as the ability to enhance focus and energy. Taken together, the synergistic impact of these three naturally occurring compounds has the potential to exert significant health promoting effects in the brain.

See Table 1 for the complete list of ingredients and dosages. Listed below, each nutrient is identified and a rationale for providing it in this formulation is given.

## **Background**

## **Key Active Ingredients**

## **Neumentix**<sup>TM</sup>

Neumentix<sup>™</sup> is a proprietary spearmint varietal providing a combination of polyphenols that have been shown to positively impact brain health and cognition through four mechanisms of action, which include enhanced neuroprotection, neurogenesis, acetylcholine production and antioxidant support. Neumentix<sup>TM</sup> has been demonstrated to improve cognitive performance by enhancing working memory and spatial working memory in individuals with age associated memory impairments.<sup>4</sup> These research findings indicate that the metabolites of Neumentix<sup>TM</sup> polyphenols can cross the blood brain barrier. Neumentix<sup>TM</sup> is comprised of a phenolic complex with over 50 polyphenols including rosmarinic acid. salvianolic acid A and B, spearmint extract, lithospermic acid and caftaric acid. There is a substantial body of literature supporting the antioxidant potential of Neumentix<sup>TM</sup> polyphenols rosmarinic acid, salvianolic Acid A and B, and spearmint extract alone or in combination as potent scavengers of free hydroxyl radicals,5,6 in addition to their ability to decrease reactive oxygen species,7-11 prevent lipid peroxidation<sup>12</sup> and enhance antioxidant capacity.<sup>13-15</sup> There are also a significant number of published studies, both in vitro and in vivo, which have examined the effect of the Neumentix<sup>TM</sup> polyphenols rosmarinic acid and salvianolic acid B on the ability to inhibit acetylcholinesterase activity, the enzyme that breaks down acetylcholine in the brain. 12,13,16-18 The inhibition of acetylcholinesterase activity can increase the levels of acetylcholine in the brain, resulting in enhancements in learning and the consolidation of memories. Previous work in a rodent model of accelerated aging (SAMP8) with an aqueous spearmint extract demonstrated improved memory acquisition and retention in T-maze and object recognition, in addition to reductions in oxidative stress in the cortex and hippocampus as compared to controls.<sup>15</sup> Rosmarinic acid and salvianolic acid B have been demonstrated to enhance neurogenesis, through the enhancement of tropic factors including brain derived neurotropic factor (BDNF) and glial derived neurotropic factor (GDNF). 11,19-22 Salvianolic acid A, rosmarinic acid, caftaric acid and lithospermic acid have been shown to enhance cellular viability and survival through the attenuation of apoptotic factors. 8,9,19,23-25

#### **Source**

Neumentix<sup>TM</sup> is a naturally sourced, proprietary phenolic complex consisting of rosmarinic, salvianolic A and B, lithospermic and caftaric acids. These are all non-GMO lines of purpose-grown spearmint.

#### **Structure and Function Claims**

Aging occurs when cellular death from reactive oxygen species occurs at a faster rate than cellular growth. The brain is the most metabolically active organ in the body, causing it to generate a large amount of reactive oxygen species in the process. These reactive oxygen species often get neutralized by the brain's natural antioxidant systems. In a healthy individual these systems operate efficiently, but in an aging individual the reactive oxygen species are often in excess of the antioxidant capacity, resulting in cellular aging. The solution is to incorporate a nutritional supplement specifically to support the brain's antioxidant capacity. The key polyphenols in Neumentix<sup>TM</sup> have been demonstrated to enhance working memory, reduce oxidative stress, increase acetylcholine release by reducing the enzyme activity of acetylcholinesterase, promote neurogenesis through increasing brain derived neurotropic production, and provide cellular neuroprotection.

## Clinical studies with Neumentix<sup>TM</sup>

Fonseca et al.<sup>4</sup> performed a randomized, double-blind, placebo-controlled study to investigate the effects of the spearmint extract blend Neumentix<sup>TM</sup> on cognitive function in n=90 50-70 year old subjects with age-associated memory impairment who received 0mg, 600mg or 900mg of Neumentix<sup>TM</sup> or placebo for 90 days. Cognitive function was assessed at 0, 45 and 90 days using the Cognitive Drug Research assessment tool. Subjects in the 900 mg/day group improved 15% in working memory (p= 0.0469) and 9% in spatial working memory accuracy (0.0456) as compared to placebo. This original research is in a manuscript entitled "Spearmint Extract Improves Working Memory in Men and Women with Age-Associated Memory Impairment" and is under peer-review at the Journal of Alternative and Complementary Medicine.

Neiman et al.<sup>26</sup> performed an open-label pilot study to investigate the effects of an aqueous spearmint extract blend Neumentix<sup>TM</sup> on tolerance, bioavailability and cognitive function in n=11 healthy men and women, 50-70 years of age, with self-reported memory impairment who received 900 mg of Neumentix<sup>TM</sup> for 30 days. Subjects were administered computerized cognitive assessments to measure

memory, reasoning, attention/concentration and planning and blood was drawn at baseline and end of treatment pre and post supplementation time points (0.5 to 4 hours). Consumption of Neumentix<sup>TM</sup> did not impact GI symptoms and tolerability did not differ between baseline and end of treatment. No significant differences in whole blood hematology values were noted. Subjects demonstrated significant improvements in reasoning (p=0.023) and attention and concentration (p=0.002) after 30 days of supplementation. Acute administration showed an improvement in attention and concentration in two tests after 2 hours (p=0.042, p=0.025) and 4 hours (p=0.001, p=0.002).

#### Safety and Efficacy

Preclinical safety studies have been performed in accordance with the Organization for Economic Cooperation and Development<sup>27</sup> and the U.S. Food and Drug Administration's Redbook 200 guidelines<sup>28</sup> on the spearmint extract used in the Nieman et al. tolerability and bioavailability study. A 90-day toxicity study in rodents determined that there was a No Observed Adverse Effect Level (NOAEL) at a dose, which would correspond to 300 mg rosmarinic acid/kg body weight/day.<sup>29</sup> Spearmint extracts are widely used as flavorings and seasonings in foods and have Generally Recognized as Safe (GRAS) status in the United States.<sup>30</sup> In human clinical trials no reported adverse effects were noted by Fonseca et al. at a dose of 900 mg/day for 90 consecutive days.<sup>4</sup> or by Nieman et al. at a dose of 900 mg/day for 30 consecutive days.<sup>26</sup>

## **PhosphatidylSerine**

PhosphatidylSerine (PS) is a fat-soluble phospholipid that is an essential component of cellular membranes, constituting 2-20% of the total phospholipid mass of adult human plasma and intracellular membranes. It is the most abundant phospholipid in the brain and is important in neuronal membrane function, including maintenance of the cellular environment, signal transduction, vesicle release, cell-cell communication and cell growth regulation. PS is also a component of the mitochondrial membrane, as well as myelin, af fatty sheath that insulates the neuron and is essential to the enhanced transmission of electrical impulses. Mitochondria are organelles within the cell which are responsible for cellular energy production. Therefore, a decline in PS production with age impacts cellular energetics and nerve impulse transmission, which can significantly impair multiple aspects of normal brain function including cognition, the consolidation of memories, memory retrieval, focus and energy, language acquisition and problem solving. During the normal aging process the neuronal membrane changes in composition and begins to lose its receptors. This results in compromised neuronal

communication that interferes with the storing of memories, thereby resulting in age-related memory decline. PS has been demonstrated to support the repair of cell membranes, which may help prevent cognitive decline in those with memory impairment.<sup>35</sup> It is believed that exogenous administration of PS may normalize brain lipid content and support the return of neuronal function to a normal state.<sup>36</sup> PS has further been shown to increase acetylcholine, norepinephrine, serotonin and dopamine levels in human and animal models with Alzheimer's disease (AD).<sup>37,38</sup> PS minimizes age-related neuronal dendrite loss and atrophy of cholinergic neurons.<sup>37,38</sup> The body can synthesize PS but it is mostly obtained through the diet as a component of fish, soy, cabbage and white beans.

Dietary supplementation with phosphatidylserine has been demonstrated to be effective for age-related decline in mental function,<sup>39</sup> <sup>40</sup> impact on cellular and neuronal activity,<sup>41,42</sup> attention deficit-hyperactivity disorder (ADHD),<sup>43</sup> depression,<sup>44</sup> exercise performance<sup>45</sup> and stress management.<sup>46</sup> Clinical trials demonstrate it improves attention, arousal and memory in aging people with cognitive deterioration.<sup>36,47</sup>

#### Source

SerinAid® PhosphatidylSerine is plant-based and derived from soybean lecithin.

### **Structure and Function Claims**

Based on the research literature, the physiological benefits of PS include increased fluidity of cell membranes, increased cholinergic neurotransmission, decreased loss of dendritic connections, increased cell membrane ATPase activity, improved physiological activity of acetylcholinesterase and tyrosine hydroxylase enzymes in the brain, up-regulation of antioxidant activities, and an increased resistance to proapoptotic stimuli.<sup>48,49</sup> This results in the reported functional benefits of improved performance in established parameters of mood,<sup>44,50</sup> attention,<sup>43</sup> cognition and memory <sup>35-37,44,47,51</sup> including short and long-term storage and retrieval of memories.<sup>47</sup>

### **Human Clinical Studies with Phosphatidylserine**

There is a robust body of evidence demonstrating the efficacy of PS in enhancing attention in children, as well as cognition in individuals with MCI or serious cognitive decline, including those with Alzheimer's disease (AD). While there is evidence in the literature dating as far back as 1985 demonstrating the efficacy of PS on age-dependent memory dysfunction,<sup>52</sup> there are also much more recent clinical trials demonstrating the efficacy of oral supplementation with PS to impact attention, executive function,

cognition and mental flexibility. In 2015 Zhang et al. 48 investigated the effect of PS on the memory of n=57 patients with AD who were given conventional AD treatment and were administered 300mg/day of PS or placebo for 20 weeks. Patient memory, as assessed by the semantic memory test before and after treatment demonstrated an increase in memory in the PS group, specifically in vocabulary and picture scores. In 2014 Hirayama et al. 43 performed a randomized, double-blind, placebo-controlled trial demonstrating the efficacy of PS on attention and cognition in n=36 children with attention deficit hyperactivity disorder (ADHD) who received 200 mg/day of PS or placebo for 2 months. PS significantly improved short-term auditory memory, inattention and impulsivity, symptoms that are associated with ADHD. In 2013 Richter et al. 40 investigated the safety and efficacy of PS on the cognitive function of n=30 elderly volunteers with memory complaints who took 300mg/day of PS for 12 weeks. PS significantly increased memory recognition, memory recall, executive function and mental flexibility. In 2010 Kato-Kataoka et al.<sup>53</sup> published a double-blind, randomized controlled study to investigate the effects of PS on the cognitive function of n=78 elderly Japanese subjects with MCI who were randomly assigned to take 300 mg/day of PS or placebo for 6 months. The memory scores in PS treated groups were significantly increased as compared to baseline. Taken together these results demonstrate that oral administration of PS can improve memory, vocabulary skills, ability to recall words and attention as well as an ability to attenuate cognitive decline in memory impaired individuals.

### **Bioavailability**

Oral PS is highly bioavailable in humans as was demonstrated in a QEEG study in healthy volunteers,<sup>54</sup> and readily crosses the blood brain barrier.<sup>54</sup>

#### Safety and Efficacy

The safety of dietary supplementation with PS has been demonstrated in many human clinical trials <sup>37,47,53-57</sup> and the FDA has recognized the safety of daily dietary supplementation up to 300 mg of PS. <sup>49,58</sup>

## Theacrine

Theacrine is a naturally occurring purine alkaloid, which is found in foods, including kucha tea (*Camellia assamica variant kucha*), Cupuacu fruit (*Theobroma grandiflorum*) and various coffee species (*Coffea*). It is structurally similar to caffeine and has been demonstrated to exert its effects at the adenosine and dopamine receptors<sup>59</sup> which modulates attention, vigilance, arousal and motor activity.<sup>60</sup> It has been demonstrated to have a sedative properties as observed in a mouse model,<sup>61</sup> suggesting that it does not

result in central nervous system arousal as does caffeine. Further support for this was demonstrated in a human clinical trial by Taylor et al.<sup>62</sup> where the authors' reported no evidence of an enhanced tachyphylactic response that is common to neuroactive agents, including caffeine, following 8 weeks of 300mg TeaCrine® daily.

#### Source

TeaCrine® is produced from kucha tea (Camellia assamica variant kucha).

#### **Structure and Function Claims**

Theacrine has been demonstrated to have anti-inflammatory, antidepressant, sedative, anti-fatigue, analgesic and neuro-locomotor properties in animals. <sup>59,61,63-65</sup> It has been demonstrated to increase energy, enhance focus, attention, concentration, mood and motivational arousal in humans. <sup>62,66,67</sup>

#### **Animal studies with Theacrine**

The two animal studies listed below highlight its effects on central fatigue and locomotion and provide insight on the molecular mechanisms underlying these effects.

Li et al.<sup>65</sup> used a rodent model of stress (restraint stress, which is a form of psychological stress) investigating the effects of theacrine on central fatigue related neurotransmitters in the brain and the subsequent impact on learning and memory. They found that theacrine ameliorated learning and memory impairments caused by central fatigue as measured by the Morris Water Maze, suggesting that the ability of theacrine to manipulate monoamine neurotransmitters, including 5-HTP and dopamine, and the regulation of brain glucose metabolism may result in the anti-fatigue effect observed in their study.

Feduccia et al.<sup>59</sup> used a rodent behavioral model to investigate the effects of theacrine on locomotor activity and demonstrated that theacrine enhanced locomotor activity in rats in a dose-dependent manner without sensitization or tolerance following chronic exposure, beyond what would be expected from caffeine. Furthermore, they demonstrated that theacrine acts as an adenosine receptor antagonist and that it exerts its effects in the nucleus accumbens.

#### **Human Clinical studies with TeaCrine®**

Presently, there is a limited amount of human research on theacrine (TeaCrine®), with two published clinical trials that investigated its effects on energy, mood and cognitive performance. A third clinical study on safety and efficacy of theacrine is listed in the following section.

In a study by Kuhman et al.,<sup>66</sup> the effects of theacrine (Teacrine<sup>TM</sup>, 150 mg) plus caffeine (150 mg) as compared to caffeine only (150 mg) and placebo were investigated on three different days, separated by one week in N=20 healthy male and female subjects. Assessments of energy, mood and cognitive performance were obtained before, and for up to 4 hours after ingestion of the assigned condition. No effect was observed on cognitive performance (trail making test, digit symbol substitution test, and reaction time); however, subjective feelings of focus, energy were improved with corresponding decreases in grogginess in the theacrine plus caffeine condition only. This study demonstrated that while theacrine and caffeine has no impact on cognitive performance, it has a statistically significant impact on subjective feelings related to energy and mood.

In a study by Ziegenfuss et al.,<sup>67</sup> an open label dose-response study was performed in 9 healthy adults, at both 200 mg (n=6) and 400 mg (n=3) of TeaCrine® daily. Assessments of cognitive performance, along with changes in psychometric parameters, gas exchange and vital signs were collected before, 1hr, 4hr and 6hr after ingestion daily for 7 consecutive days. Subjective changes in energy, focus and concentration as measured by the 150-mm anchored visual analog scale (VAS) were increased at both doses, with no dose-response effect observed. This was followed by a randomized, double blind, placebo-controlled crossover trial in N=15 healthy subjects administered a single 200 mg dose of TeaCrine® and placebo. Assessments of physical and mental energy, gas exchange and hemodynamic parameters were collected before, 1hr, 2hr and 3hr after ingestion. After a single dose, significant effects of group x time interaction were observed for energy, fatigue and concentration. No changes were observed in resting heart rate, gas exchange or hemodynamics. No side effects were noted.

### **Safety and Efficacy**

The safety and efficacy of the dietary supplement Teacrine<sup>TM</sup> or TeaCrine<sup>®</sup> has been demonstrated in three human clinical trials with no adverse reactions concerning oral supplementation.<sup>62,66,67</sup> The longest of these studies was performed by Taylor et al. who specifically investigated the safety of TeaCrine<sup>®</sup> after 8 weeks of continuous use in N=60 subjects who ingested doses of 200mg and 300mg.<sup>62</sup> All values for clinical safety markers (heart rate, blood pressure, lipid profiles, hematologic blood counts,

biomarkers of liver, kidney and immune function) fell within normal limits and there was no evidence of an enhanced tachyphylactic response that is common to neuroactive agents, including caffeine. This study also demonstrated a non-habituation response.

The preliminary research in animal and human studies demonstrates the clinical efficacy and safety TeaCrine®. Continued work performing longitudinal studies is needed. Additional human clinical trials are currently being performed at Rutgers University and the University of Memphis.

### **Conclusions**

In conclusion, the combination of nutrients in Smart Mind<sup>TM</sup> (Neumentix<sup>TM</sup> Phenolic Complex K110-42, SerinAid® PhosphatidylSerine and TeaCrine®) results in a nootropic which contains nutrients that have all been clinically tested in humans, demonstrated to be safe and effective, and are all gluten-free and non-GMO sourced. PhosphatidylSerine has the strongest evidence base, spanning decades and demonstrating its efficacy as a brain support nutrient impacting multiple parameters of cognitive function in individuals with MCI and AAMI. The active polyphenolic constituents in Neumentix<sup>TM</sup> have established a strong evidence base using *in vitro* and *in vivo* models demonstrating their efficacy in supporting antioxidant capacity, supporting healthy neurotransmission through enhancing acetylcholine, increasing neurogenesis and improving cellular viability. While TeaCrine® and Neumentix<sup>TM</sup> have a more limited research history due to their more recent introduction into the market, both have published human clinical trials in the peer reviewed literature demonstrating the safety and efficacy of these natural ingredients for the support of focus and cognition.

One of the primary strengths of the Smart Mind<sup>TM</sup> blend is that each ingredient is sourced from the ingredient suppliers whose materials were used in some or all of the cited clinical trials and included, in the case of the two primary nootropic actives, at the dosages published in those human clinical trials. Neumentix<sup>TM</sup> was included at a dose of 900mg from the same source that was used by Fonesca, et al., <sup>4</sup> demonstrating its efficacy on working memory in healthy individuals with age associated memory impairment. SerinAid® PhosphatidylSerine was included at 300 mg, which is consistent with a majority of the human clinical trials in healthy individuals with age associated memory impairments, thereby demonstrating its efficacy in preserving learning skills, memory, concentration and other mental capacities. TeaCrine® was included at a dose of 200 mg, which a the dose that falls well within the safety profile of dosages up to 300 mg/day continuously for 8 weeks as reported by Taylor et al.<sup>62</sup> with the aim of enhancing attentiveness, alertness, energy and focus as reported by Kuhman et al.<sup>66</sup> and

## Ziegenfuss et al.<sup>67</sup>

In closing, Smart Mind<sup>TM</sup> is a naturally sourced brain support dietary supplement that delivers the primary functional ingredients at levels that have been demonstrated to be clinically effective in research studies focused on a maintaining and/or improving a variety of brain health parameters, including multiple aspects of memory. The cognitive health benefits of Smart Mind<sup>TM</sup> are further supported by a novel caffeine-like alkaloid that supports multiple additional aspects of normal brain function without the negative effects typically associated with caffeine.

Future studies demonstrating the clinical efficacy of the Smart Mind formulation in supporting cognition and brain function, including QEEG Brain Mapping studies, will be performed.

Table 1. Smart Mind (3 Capsules)

Ingredients	Dose
Neumentix <sup>™</sup> Phenolic Complex K110-42†	900 mg
Phosphatidylserine	300 mg
TeaCrine <sup>®</sup>	200 mg
Other Ingredients††	

<sup>†</sup> Rosmarinic acid, salvianolic A and B, lithospermic and caftaric acid

## About the author

Kristen Willeumier, Ph.D., is a highly respected neuroscientist with established expertise and clinical experience in demonstrating the efficacy of nutraceuticals using brain-imaging technologies. She was the Director of Research for the Clinical Neuroimaging Department at the Amen Clinics and performed clinical studies across a wide variety of areas including SPECT imaging in clinical practice, traumatic brain injury, suicide, obesity, gender differences in brain function, brain rehabilitation, clinical outcomes and nutraceuticals. Dr. Willeumier has 44 peer-reviewed publications in the field of neuroscience, is professionally associated with the Society for Neuroscience and frequently presents her work in academia and business settings, in addition to National and International scientific conferences. Dr. Willeumier received a B.A. in Psychology from Boston College, two M.S. degrees in Physiological Science and Neurobiology, respectively, and a Ph.D. in Neurobiology from David Geffen School of Medicine at UCLA. She completed Predoctoral training and a Postdoctoral Fellowship in Neurology from Cedars Sinai Medical Center in Los Angeles, CA. She was the recipient of an NIH NRSA Fellowship Award from the National Institute of Mental Health to study the molecular mechanisms underlying Parkinson's disease. She has published articles in notable neuroscience journals including the Journal of Neuroscience, the

<sup>††</sup>Enzyme stabilized rice bran, rice hulls

<sup>††</sup> Shell ingredients (vegetarian): gelatin, glycerin, purified water

Journal of Alzheimer's Disease, PLOS One, Nature Obesity and Nature Translational Psychiatry.

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