

SIBELIUS[™]

: SAGE

Pioneering the development of Old English Sage

MEMORY | FOCUS | ATTENTION | RECALL | MENTAL ACUITY



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Sibelius™: Sage - Ancient Botanical with Modern Applications for Cognitive Support

Before getting started, sit back, relax, take a deep breath, and have a serving of Sibelius™: Sage. Why? Because in the next **15-30 minutes** you will most likely begin to feel its effects. It may seem strange to start a white paper with such a silly request, but many say the **experience** is better than the presentation. Taking this little challenge will help you better understand the impact Sibelius™: Sage can have on an individual, product line, or business. What will you feel? Most people comment on **feeling more alert or focused**, while others comment on feeling "sharper". Granted, these are testimonies which do not make for an excellent white paper, but in the end, Sibelius™: Sage has the research to back up what you are feeling. The following will dig into the background in the area of focus and concentration and the role Sibelius™: Sage will play, and the **clinical research** to back up what you may be feeling.

History of Sage

Before delving deeper into the science behind Sibelius™: Sage, it is beneficial to take a quick peek into the history of sage. Like many natural ingredients marketed these days, it was the historical use of botanicals by indigenous people that made modern scientists look into "what makes them tick." The same can be said about Sage. The genus *Salvia*, commonly known as sage, is the largest member of *the Lamiaceae* or mint family containing over 900 species throughout the world.ⁱ Many species of *Salvia*, including *Salvia officinalis* (common sage), are native to the Mediterranean region and some of the *Salvia* species have been used worldwide as flavoring spices as well as traditional herbal medicine.

Dating back to over 4000 years, Ancient Egyptians believed it helped with infertility.ⁱⁱ Sage has a longstanding reputation as traditional herbal remedies used by ancient Greek and Roman, Ayurvedic, Native American and Chinese folk medicines. Sage possesses well-known carminative, antispasmodic, antiseptic, astringent, and antihidrotic properties.ⁱⁱⁱ For centuries, the botanical has been used for conditions such as pain relief, oxidative stress, inflammation, hot flashes, digestive problems, gas, bloating, elevated blood fats, cognitive performance, and memory.^{iv}

Of the last of these historical benefits, the impact on cognitive performance primarily in the areas of concentration and focus appears to be the leading area of "Focus" in the realm of the scientific community. Why? Perhaps because of the sudden rise in consumer interest in dealing with family struggles with dementia or maybe the demand to stay sharp or focused at work and school. This is where Sibelius™: Sage shines!

Inside the Numbers: Who is Impacted by Decreased Focus and Concentration?

Before digging into the clinical applications of Sibelius™: Sage, it is essential to look inside the numbers with regards to consumer wants and needs in relation to brain health and cognitive or focus help.

- ❖ One in nine Americans aged 45 and older say they are experiencing thinking declines.
- ❖ Among those aged 45 and older who were living alone, 14% said they were suffering from declines in mental function.^v
- ❖ Approximately 30 million adults, the majority of who are men under the age of 50 years, take supplements for brain health.^{vi}
- ❖ The estimated number of people with dementia will increase from 47 million in 2015 to more than 140 million in 2050.^{vii}

- **Attention spans have shrunk by 50% over the past decade.**

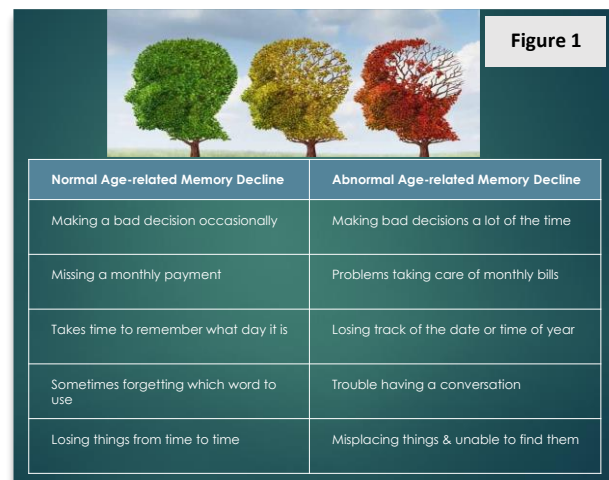
Vitafoods Insider has expanded the reach of cognitive health products to ALL demographics. In a recent publication, it stated, “Cognitive health products are not limited to aging consumers looking to prevent cognitive decline; consumers across the demographics are increasingly interested in natural ingredients for brain health. Interest in supplements for cognition rose by 93 percent from 2017 in the United States and growth is only expected to continue as aging consumers, in particular, prioritize their health.”^{viii}

If those numbers don’t speak to the importance of focus and concentration, then this study on concentration drives home the importance of improved concentration in youth. The study was conducted with over 1,000 children in New Zealand by psychology and neuroscience professors at Duke University. The study tested children born in 1972 and 1973 regularly for eight years, measuring their ability to pay attention and to ignore distractions. Then, the researchers tracked those same children down at the age of 32 to see how well they fared in life. The *ability to concentrate was the strongest predictor of success*. The ability to concentrate was considered more important than IQ or the socio-economic status of the family you grew up in for determining career success, financial success, and health.^{ix}

What does age-related memory decline look like?

As we age, subtle changes in memory occur naturally as part of the aging process. However, sometimes these changes occur sooner than expected or come on faster than we wish. In **figure 1** below, we see the difference between what is normal and what is considered abnormal memory decline.

We can see from the chart that there is a dramatic difference between what is considered “normal” and “abnormal” memory decline. There are multiple memory processes, including **learning new information, recalling information, and recognizing familiar information**. Each of these processes can get disrupted, leading to the experience of forgetting.



The Science with Sage in General

Before we dive into the details on why Sibelius™: Sage stands above the rest, we need to take a closer look at the science done with sage (*Salvia officinalis*) in general concerning safety and efficacy for cognitive health.

Generally speaking, researchers have been primarily researching two types of sage, *S. officinalis*, and *lavandulaefolia*. In the paper published in CNS Neuroscience & Therapeutics titled “*Systematic Review of Clinical Trials Assessing Pharmacological Properties of Salvia Species on Memory, Cognitive Impairment and Alzheimer’s Disease*”, researchers summarized published clinical trials assessing the effectiveness and safety of both *Salvia officinalis* and *Salvia lavandulaefolia* in the enhancement of cognitive performance in

healthy subjects and neurodegenerative illnesses. Six of the studies reviewed involved healthy individuals and their effects on cognitive performance. The results showed that they exert beneficial effects by enhancing cognitive performance. This same review though pointed out that there were methodological issues, differences in herbal preparations (extracts, oils, use of raw material) and lack of details on herbal products used.^x *This last point regarding the preparations is a key component when we discuss Sibelius™ Sage.*

Two studies in particular focused on the same strain of sage (known as *Salvia officinalis*) as Sibelius™: Sage. The first titled “Effects of Cholinesterase Inhibiting Sage (*Salvia officinalis*) on Mood, Anxiety and Performance on a Psychological Stressor Battery” evaluated the use of dried sage in either 300mg or 600mg doses compared to placebo. The results showed improved mood and cognitive performance following the administration of **single doses** to healthy young participants.^{xi}

In the second study titled “*Salvia officinalis* extract in the treatment of patients with mild to moderate Alzheimer’s disease: a double blind, randomized and placebo-controlled trial”, the participants in this 16-week trial 60 drops of sage extract once daily. The results showed that the sage extract produced significant better outcome on cognitive functions than placebo.^{xii}

We will dig deeper into the science specific to Sibelius™: Sage later in this paper and for now we



can see that this amazing medicinal plant packs plenty of power in the areas around cognitive health.

Sibelius™: Sage stands above the rest

Not all sage products are the same.

As the researchers mentioned above, the differences in herbal preparations i.e., extracts, oils, use of raw material played a role in the studies outcomes. This is one of the areas in which Sibelius™: Sage stands out. Sibelius™: Sage is a unique and specific extract of the sage species *Salvia officinalis*. Sibelius™: Sage extract is derived from a non-GMO certified European herb source. All production, including harvesting, is carried out accordingly to defined protocols with **full traceability** of the crop at every stage of production. Sibelius™: Sage has a unique profile when analyzed by NMR spectroscopy and pattern recognition. The chemical fingerprint of the extract can in fact be differentiated from other sources. This means different varieties of *Salvia officinalis* grown under the same conditions, and even the same variety of *Salvia officinalis* grown at the same location but harvested at a different time **do not** present the same activity under analysis.

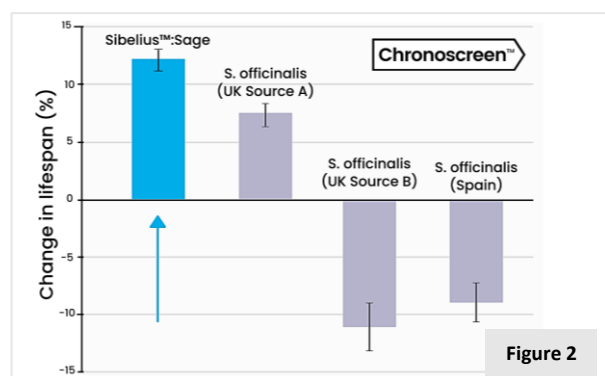
Unique and Specific Extraction, Growing Region & Harvesting

Sibelius™: Sage was developed using Sibelius’ patented **Chronoscreen™** platform, a powerful screening tool for the discovery, evaluation, and monitoring of biologically active natural products. The technology is used to **identify the best sources for existing ingredients**. It drills down past the usual measures of purity and potency; it looks at the actual activity offered from a particular botanical source. Chronoscreen™ utilizes the roundworm, *Caenorhabditis elegans* (*C. elegans*), a whole organism model commonly used in

biomedical research with many physiological similarities to humans including a digestive and nervous system. The platform measures the lifespan in populations of *C. elegans* and their responses to different nutraceutical ingredients.

Extension of lifespan on Chronoscreen™ indicates that the tested ingredient had a beneficial effect on the regulation of cellular ageing and therefore may have a delayed onset of age-related conditions in the worm.

In **figure 2** you will see the difference in biological activity between sage from other sources and regions and Sibelius™: Sage.



Sibelius™: Sage has a unique chemical fingerprint and superior biological activity as compared to other sage extracts.

The Proof is in the Science

Earlier, we saw the general research using *Salvia officinalis* and its impact on many areas of cognitive health. Now we need to take a look at the **science specific to Sibelius™: Sage**. There are multiple clinical studies substantiating the safety and efficacy of Sibelius™: Sage. One study completed with 20 healthy volunteers (65-90-year-old) taking either 167mg or 333mg showed a significant improvement in cognitive performance within 1-hour of treatment. This included the improvement

of secondary memory, recognition, and recall, accuracy, and speed of attention.

Another recent study found some amazing results as well using Sibelius™: Sage extract and its use with young adults. The study was a randomized, double-blind, and placebo-controlled trial with a total of 72-participants ages 12-14 and 18-25. Participants took either placebo, 150mg, or 300mg single dose. The results showed improvements in word recall, short-term episodic memory, and improved ability to focus. Keep in mind that these improvements were also seen after 1-single-dose. No safety concerns or adverse effects were noticed in either age group.

Lastly, a study published in March of 2021 in the Journal of Ethnopharmacology evaluated the effect of sage on decreasing the pro-inflammatory markers mostly in human adipocytes. Chronic, low-grade inflammation is recognized as a major risk factor in the development of many age-related chronic conditions, including reduced brain health. This study showed Sibelius™: Sage reduced ACM-induced inflammation effect which the researchers believed “might be used as a preventive treatment for late-life cognitive impairment related to low-grade chronic inflammation associated with obesity.”

Where to begin when formulating for Success with Sibelius™: Sage

Sibelius™: Sage extract is available in two formats; a dried granulated powder suitable for capsules and tablets, and a water-dispersible micronized powder for novel delivery formats, such as beverages (including carbonated drinks), powders, gummies, jellies and functional foods.

The water dispersible powder was developed by milling the sage to a finer grain. The two formats

do not present any chemical difference and the bioactive composition is the same.

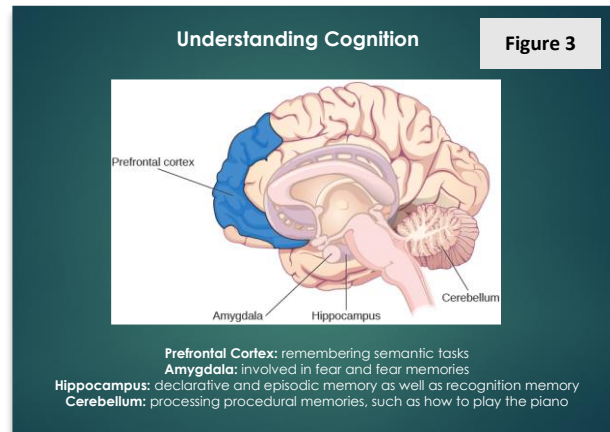
Granted, Sibelius™: Sage as a stand-alone ingredient has amazing benefits for consumers, yet the potential to combine it with other unique nutraceuticals will make for a finished product rise above the rest. Below you will find my formula for “**Formulating for Success**”. In order to formulate for success, two of the key areas to start with are understanding the root causes of a condition and knowing the mechanism of action of each nutraceutical ingredient. By knowing the possible root causes of a condition, we can then use the known mechanism(s) of action to create a combination of ingredients to yield the best results. In my **recent presentation** for Natural Products Insider, this concept was exhibited. Before we dive into this concept, let’s take a closer look at the known **mechanisms of action** of Sibelius™: Sage.

One of the essential questions needing to be addressed is the potential mechanism of action of Sibelius™: Sage. To date, researchers have identified at least **six areas** which influence physiological pathways; amyloid-β peptide, cholinergic activity, neurotrophic, anti-inflammatory, anxiolytic/anti-depressive, and antioxidant.^{xiii} One of the primary areas of focus is its impact on neurotransmitters. Sage extracts have been shown to inhibit the action of acetylcholinesterase; the enzyme that breaks down the neurotransmitter acetylcholine. Acetylcholine is found in the brain in areas associated with attention, memory, and motivation.

As mentioned above, sage has been shown to possess antioxidant, anti-inflammatory, and estrogenic properties. Hormonal imbalance, inflammation, and oxidative stress may all contribute to decreased cognitive function.

5-step Process for Successful Formulating with Sibelius™: Sage

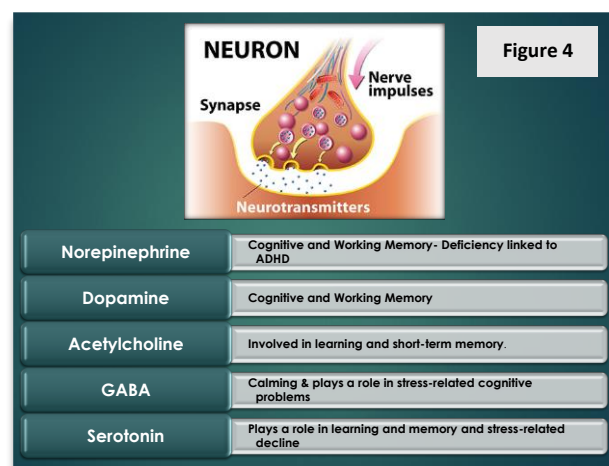
1. Understanding Cognition



When we discuss cognition, we are talking about four areas of the brain; prefrontal cortex, amygdala, hippocampus and cerebellum. We can see in **figure 3** what role each of these play in cognition.

2. Neurotransmitters and Cognition

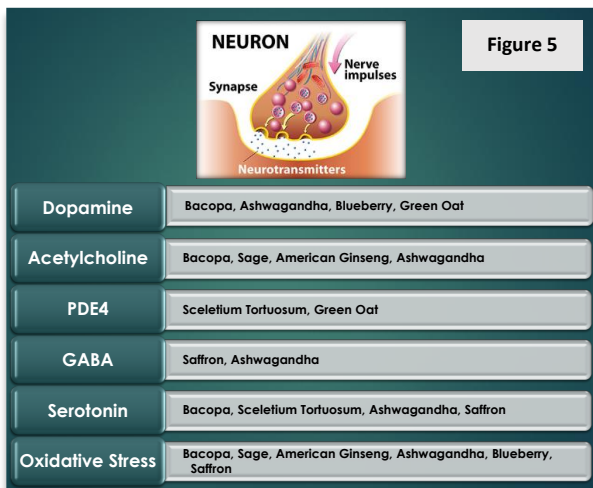
There are five neurotransmitters which play an active role in cognition. We can see in **figure 4** below how they impact cognition. Understanding which neurotransmitter impacts the areas of cognition we wish to influence is important when looking for “synergistic” nutraceuticals to combine.



We need to look for multiple pathways or better stated mechanisms of action to formulate a product with the best efficacy. Impacting multiple neurotransmitters will provide this effect.

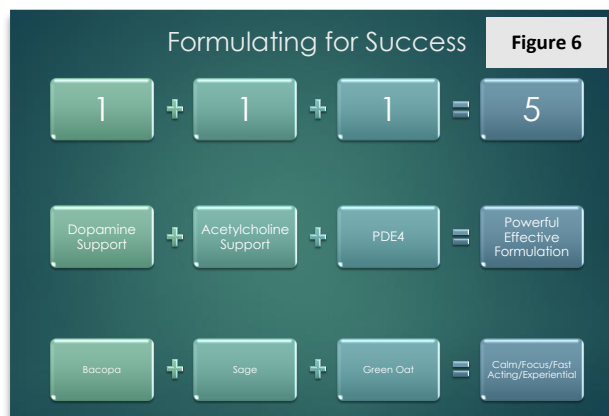
3. What Botanicals Impact Neurotransmitters

As mentioned above, understanding the impact of specific neurotransmitters on cognition and then finding a nutraceutical to fit into that area is critical. **Figure 5** shows examples of botanicals and their impact on different neurotransmitters.



4. Implied Synergy

Lastly, we need to put the pieces of the puzzle together. **Figure 6** gives a great example of how this can be achieved using Sibelius™: Sage.



5. Addressing Pill Fatigue

Pill fatigue is a real thing. Consumers are tired of popping pills which opens the door for innovation. By paying strict attention to using **innovative delivery methods** and dosage forms will open up more opportunities for consumer use and loyalty. Other than traditional capsules and tablets (pill fatigue), there are several different methods to deliver your formulation. Some of the more popular areas are gummies, film strips, beverages, shots, and powders (stick packs, sachets, effervescent, pods, etc.) and functional foods. This is where Sibelius™: Sage rises to the top again. It is available in multiple formats including granulated and micronized. This makes Sibelius™: Sage a viable match for a wide range of delivery formats including gummies, beverages, shots, powders (stick packs, sachets, effervescent, etc.) and functional foods. With its low single-dose effectiveness, it becomes a perfect match for your formulating needs.

Conclusion

Face it; there aren't many ingredients in the natural botanical extract market that can provide documented effects in a short period of time. With **consumers becoming savvy** with regards to science and the desire to "feel" the result, Sibelius™: Sage is an excellent addition to any product line either as a "stand-alone" ingredient or when combined with other ingredients that offer either nutritional brain health benefits such as choline and serine or with other botanicals which possess differing mechanisms of action.

About the author



David Foreman is a pharmacist, author and media personality known internationally as, “The Herbal Pharmacist.” His background in both pharmacy and natural medicine puts David in an elite class of health experts who can teach integrative medicine practices. David’s focus is to help all to achieve the health and vitality they seek by teaching his 4-Pillars of Health: Diet, Exercise, Spirituality and Supplements. David is also highly sought for his abilities as a science engineer by helping companies connect their science to their sales and marketing teams. David is a graduate of the University of South Carolina College of Pharmacy, currently serves on Organic & Natural Health Association’s Scientific Advisory Board and is author of, “4 Pillars of Health: Heart Disease.”

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