

What is Bluenesse®?

Bluenesse® is a high quality, sustainable, natural food ingredient, which is able to improve cognitive performance while helping to cope with stress.

It is a special *Melissa officinalis* (L.) extract, an annual edible herb native to Europe. Traditionally lemon balm extract is used for relaxation.

In vitro and human studies demonstrated that Bluenesse® combines the traditional calming and mood enhancing effects with beneficial effects to support cognitive performance, particularly alertness and memory.

Bluenesse® is scientifically proven, IP protected and approved to be used in dietary supplements and foods.

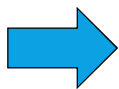


Bluenesse® – Science

Several studies have been carried out using the proprietary *Melissa officinalis* extract to investigate the effects on cognitive performance:

1. Pilot and pharmacokinetic human study
2. Three nutritional human studies to confirm effects of lemon balm in food matrices
3. Three *in vitro* studies to investigate mode of actions related to cognition and mood
 - a. Effects of Bluenesse® on Muscarinic M1 receptor
 - b. Effects of Bluenesse® on Monoamine oxidase B (MAO B) enzyme
 - c. Effects of Bluenesse® on Phosphodiesterase (PDE4) enzyme

Study facts and results are summarized within the leaflet.



**Bluenesse® significantly improves
cognition, mood and the ability to cope with stress**

Bluenesse® helps to support...

- ✿ cognitive performance
- ✿ to cope with stress
- ✿ to relax and sleep
- ✿ nootropic benefits
- ✿ Work-Life-Balance

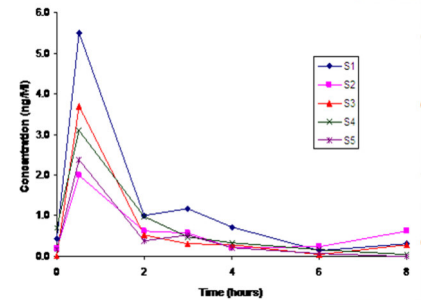
These statements have not been evaluated by FDA and EFSA.

The product is not intended to diagnose, treat or cure any disease.

1. Pilot and pharmacokinetic human study

The results of the single blind pilot study with 5 volunteers showed that supplementation with Bluenesse® supports cognitive performance.

Bluenesse® was absorbed within 0.5-1h in the plasma and eliminated after approx. 5h (see figure of pharmacokinetic study on the right). This indicates a quick onset of effects and that also multiple intake per day is safe.



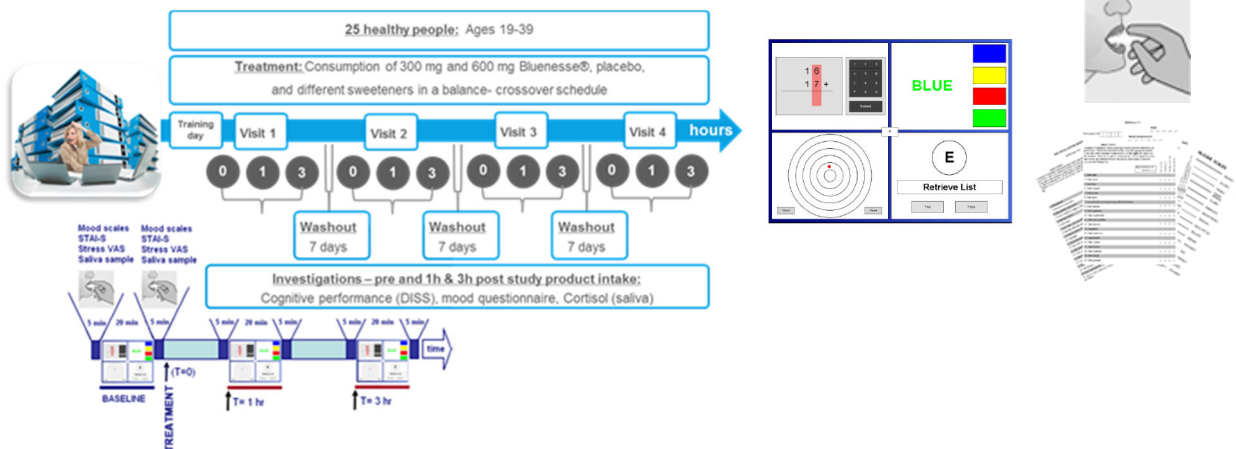
A. Scholey, et al., "Anti-Stress Effects of Lemon Balm-Containing Foods," *Nutrients*, 6, 4805-4821 (2014)

2. Human studies to investigate effects on cognition, mood & stress

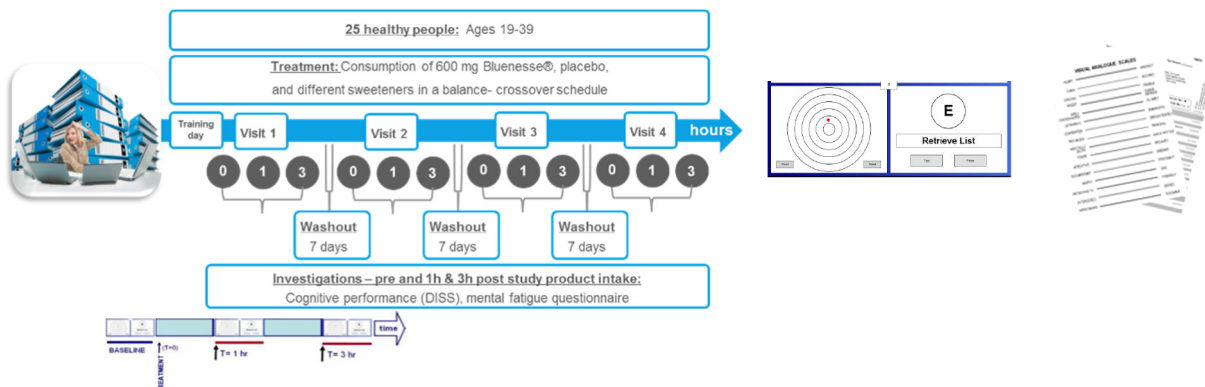
Study facts:

- 25 healthy people, ages 18-39, 8 male and 17 female, non-smoker
- Intake 300 mg or 600 mg lemon balm extract once during study days or placebo
- Study product: water-based drink, yoghurt-based drink and fruit bar
- General population, focusing in students
- The study was conducted by Brain Institute, Swinburne University, Australia

Water drink & yoghurt-based drink study – flow chart:



Fruit bar study – flow chart:



A. Scholey, et al., "Anti-Stress Effects of Lemon Balm-Containing Foods," *Nutrients*, 6, 4805-4821 (2014)

A. Scholey, et al., "Investigation of a Melissa officinalis special extract on Cognition II, Human study - Lemon balm extract administered in confectionary bars," *Agrofood Industry hi-tech* (2015)

Placebo formulations/ Sweetener systems:

Within the studies three different sweetener systems were investigated, applied to the Bluenesse® as well as to the placebo study products; natural fruit sweetener, artificial sweetener and sugar.

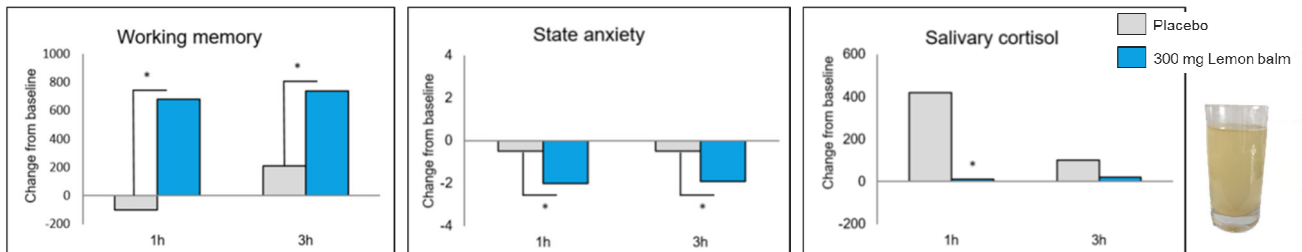
Artificial sweetener had a negative impact on cognitive performance, in the absence of sugar, as also described in literature.

The sugar and the natural fruit sweetener had no significant effects to improve cognitive performance.

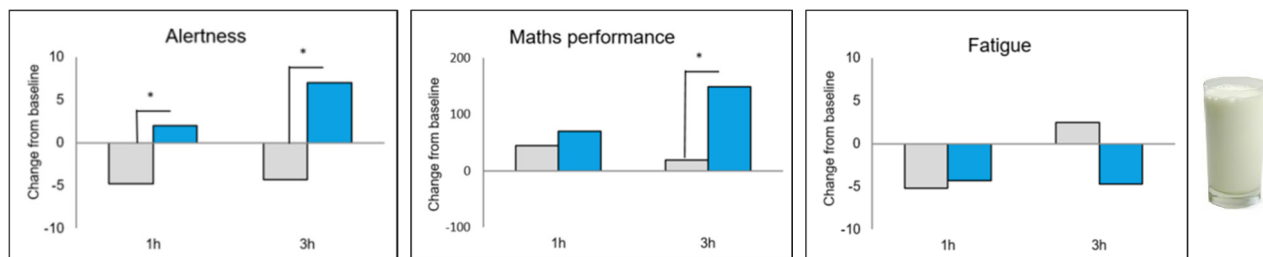
Significant study results – water & yoghurt-based drink:

Two dosages, 300 mg and 600 mg Bluenesse® were studied. 300 mg Bluenesse® was identified to be the effective dosage. 600 mg did not lead to better results.

In the following part, the results for 300 mg Bluenesse® using the natural fruit sweetener system for the Bluenesse® as well as for the placebo study product are summarized.

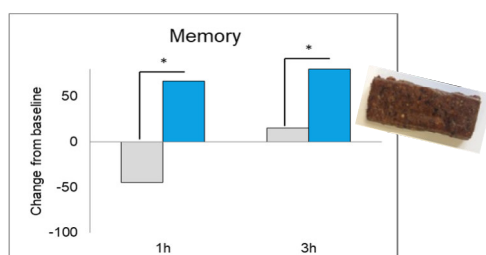


Results showed a significant improvement of working memory and reduction of anxiety, 1 and 3h after Bluenesse® intake. Cortisol, a stress marker, was significantly decreased after 1h. Results confirm, that Bluenesse® can be taken on demand.



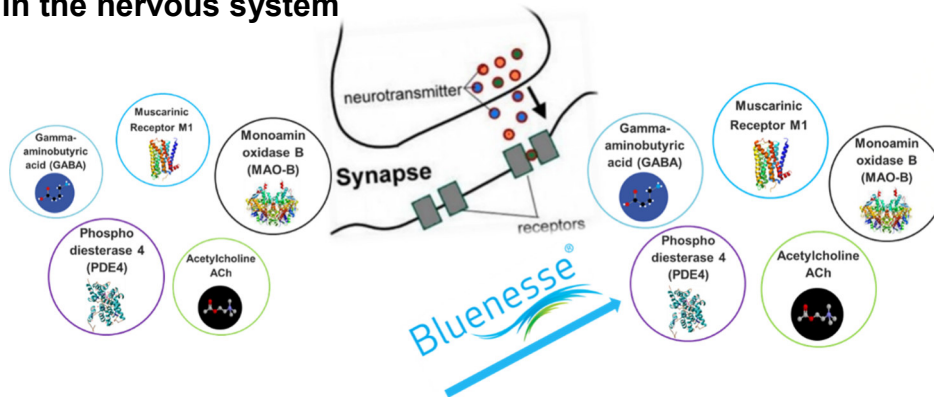
Results demonstrated a significant improvement of alertness 1 and 3h after Bluenesse® intake. In addition, mathematic processing and fatigue were improved after 3h. The bioavailability of Bluenesse® in dairy formulations seems to be slower than in water, still delivering effects on demand.

Significant study results – fruit bar:



Results showed a significant improvement of memory 1 and 3h after 600 mg Bluenesse® intake. In this study only 600 mg Bluenesse® was investigated, assuming that the bioavailability in fruit bars is limited.

🌱 **Bluenesse® optimizes concentration and activity of messenger substances and receptors in the nervous system**

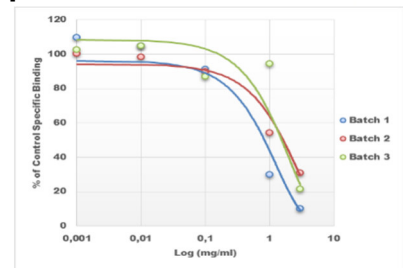


3.a. *In vitro* study to explore binding to Muscarinic M1 receptor

The effect on cognitive performance of Bluenesse® has been investigated by measuring M1 receptor binding properties

🌱 Results show that Bluenesse® has M1 receptor affinity

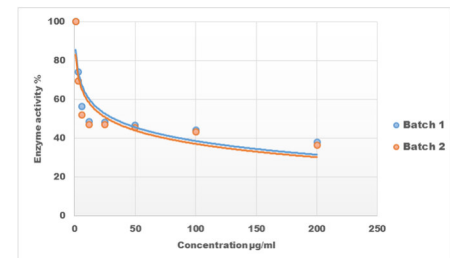
S. Buchwald-Werner et al., "Investigation of a Melissa officinalis special extract on Cognition I, In vitro study on muscarinic properties," Agrofood Industry hi-tech (2015)



3.b. *In vitro* study to test Monoamine oxidase B inhibiting effects

The effects on cognitive performance and mood of Bluenesse® have been investigated by measuring inhibition of MAO B

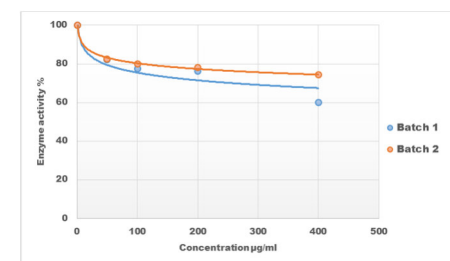
🌱 Results showed that Bluenesse® inhibits MAO B



3.c. *In vitro* study to test Phosphodiesterase (PDE4) inhibiting effects

The effects on cognitive performance and memory of Bluenesse® have been investigated by measuring inhibition of PDE4

🌱 Results showed that Bluenesse® inhibits PDE4



Acetylcholine (ACh) and Gamma-aminobutyric acid (GABA)

Rosmarinic acid is a known GABA transaminase and acetylcholine esterase inhibitor

- 🌱 Higher concentrations of GABA are supporting a calm mood
- 🌱 Elevated acetylcholine levels are improving memory and cognition