

# Brain-Specific Effects of Ambrotose® Products: A Preliminary Animal Study to Investigate Cognitive Benefits Found in Humans

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**BACKGROUND:** Saccharides play important roles in the brain, where they are largely glycoconjugated to proteins or lipids to assist in structural development, synaptogenesis and synaptic transmission. Saccharides can also be a source for energy and neurotransmitter production. There is considerable interest in better understanding the health benefits of orally administered naturally derived polysaccharides and exploring their potential to influence neurologic function and health<sup>1</sup>. A number of clinical studies have demonstrated that intake of a mixed saccharide prebiotic glyconutritional dietary supplement, Ambrotose® complex (AMB), can improve various aspects of learning, memory, and mood in healthy adults.

**OBJECTIVES:** To review the current literature on the cognitive benefits of Ambrotose complex consumption and explore possible mechanisms by which it and a similar formulation enhanced with *Undaria pinnatifida* fucoidans, Advanced Ambrotose® powder (AA), might influence brain function.

**METHODS:** C57BL/6 male mice (5/group) were fed a normal diet and received daily 57.4 mg/kg of Ambrotose

complex or Advanced Ambrotose powder, or water (control) by oral gavage for 28 days. On day 29 animals were sacrificed by CO<sub>2</sub> asphyxiation and the hippocampus and prefrontal cortex were immediately removed and flash frozen in liquid nitrogen. Total RNA was extracted and quantitative RT-PCR was used to measure levels of brain-derived neurotrophic factor (BDNF), interleukin (IL)-6, IL-1 $\beta$ , and tumor necrosis factor (TNF)- $\alpha$  mRNA.

**RESULTS:** Six randomized, double-blind, placebo-controlled human clinical trials indicate that oral intake of Ambrotose® complex exerts positive effects on cognitive function and mood in healthy adults (Table 2). Intake by mice of a dose of Advanced Ambrotose w/w equivalent to the 4 g daily dosage recommendation for adults for 28 days significantly increased gene expression of BDNF in the hippocampus and decreased expression of IL-6 in the cortex (Figure).

**DISCUSSION:** A number of clinical studies suggest that Ambrotose complex shows promise, when taken orally, in supporting neurologic health and function. BDNF is a commonly studied protein associated with a variety of brain functions, including learning, memory, and stress.

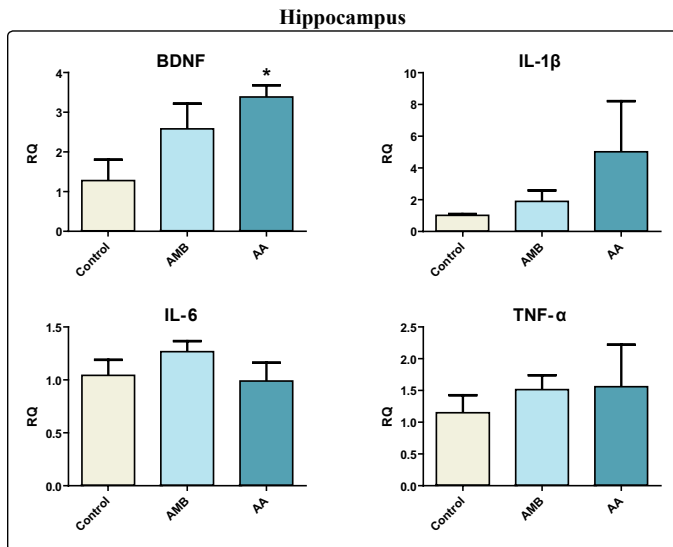
**Table 1. Ambrotose product formulations**

	Aloe vera gel powder	Aloe vera gel extract	Larch arabinogalactan	Gum ghatti	Gum tragacanth	Glucosamine	Undaria pinnatifida
Ambrotose complex powder		✓	✓	✓	✓	✓	
Advanced Ambrotose powder	✓		✓	✓	✓	✓	✓

**Table 2. Ambrotose complex improves cognitive function and mood in healthy adults**

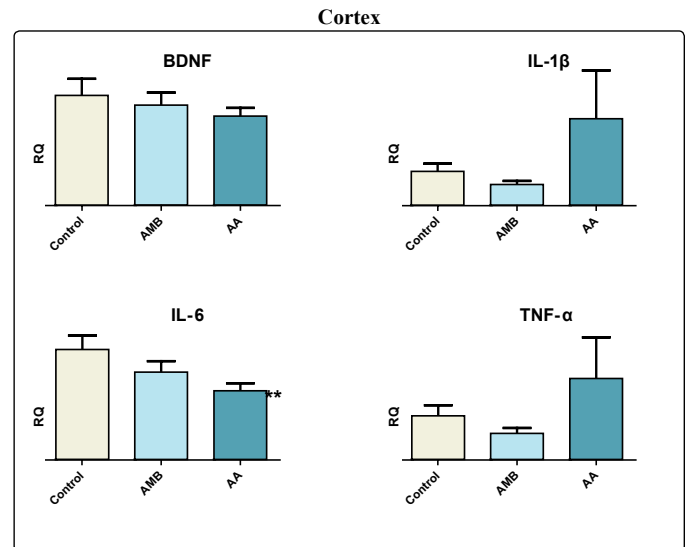
Study design	Population	N	Dose	Duration	Cognitive tests performed	Significant effects	Reference
Randomized, double-blind, placebo-controlled	Healthy middle-aged adults	109	3.6 g/day	12 weeks	Rey Auditory-Verbal Learning Test (RAVLT); Visual Pattern Span Recall; Visual Pattern Span Recognition Reading Span; Computation Span; Stroop; Letter Cancellation; Digit Symbol Coding, Boxes test, Matrix Reasoning & Spot the Word [Wechsler Adult Intelligence Scale III]; POMS; Depression Anxiety and Stress Scale; Perceived Stress Scale-10	Better performance on immediate recall tasks [RAVLT trials 2 & 5] and recognition memory task [RAVLT Recognition]; lower depression-dejection and anger-hostility scores [POMS]	10
		73	4 g	2 hr	RAVLT; Cognitive Demand battery (Serial Threes; Serial Sevens, Rapid Visual Information Processing (RVIP), Visual analogue mental fatigue scale); POMS; Short-form health survey (SF-36); State-trait anxiety questionnaire; Bond-Lader visual analogue scale	Better performance on recognition memory task [RAVLT recognition A & B] and working memory task [Serial Sevens] during mental fatigue. Effects were independent of blood glucose response.	11
		45	7 g	10 min	RAVLT; Self-Ordered Pointing; Digit Span forwards; Digit Span backwards; Matrix Reasoning [Wechsler Adult Intelligence Scale III]	No effects. 25 g glucose also showed no effects.	12
Randomized, double-blind, placebo-controlled, crossover	Healthy college students	30	1 tbsp (approx. 4 g)	45 min	Same-Different visual discrimination; Standard Progressive Matrices; Stroop	Better performance on visual discrimination task [Same-Different]	13
		32	1 tbsp	45 min	Reading Span; Operation Span	Better performance on simple working memory task [Reading span, first session]	13
	Healthy male college students	20	1 tbsp	30 min	EEG recordings during focus on a stationary visual target	Enhanced power in theta, alpha and beta brain wave frequencies associated with attention and arousal	14

## Effects of Ambrotose complex (AMB) and Advanced Ambrotose powder (AA) intake on gene expression in the mouse brain



\* p=0.0326 (Control vs. AA)

\*\* p=0.008 (Control vs. AA)



An increase in BDNF has been shown to be associated with probiotic supplementation<sup>2</sup> and with enhanced learning and memory and elevated mood, particularly in the hippocampus.<sup>3</sup> Specific cytokines are also known to be expressed in the brain. In particular, IL-1 and IL-6 are pro-inflammatory cytokines that have been shown to regulate learning and memory in healthy animals,<sup>4,5</sup> while IL-1  $\beta$ , IL-6, and TNF-alpha are believed to play a pivotal role in "sickness behavior" – when inflammation leads to behavioral changes, including impaired cognitive function and anhedonia.<sup>6</sup> These preliminary study results suggest that clinical improvements in brain function following Ambrotose product intake may be correlated with brain-specific changes in gene expression, particularly that of BDNF and IL-6 in areas of the brain important for regulating learning, memory and mood behaviors.

**CONCLUSIONS:** In previous preclinical studies, Ambrotose complex and Advanced Ambrotose powder have been shown to exert prebiotic effects *in vitro*<sup>7</sup> and modify serum glycosylation profiles in adults.<sup>8,9</sup> The current study suggests that changes in the expression of genes in the brain associated with learning, memory and mood may contribute to the clinically-documented cognitive improvements reported for Ambrotose products. Additional research is needed to confirm these results and to better determine the mechanisms that underlie the cognitive benefits of Ambrotose products.

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