Avens Publishing Group

J Nutri Health
March 2026 Vol.:9, Issue:1

Open Access Research Article

Journal of Nutrition and Health

Evaluation of Acute and Sustained Cognitive Effects of a Grape and Blueberry Polyphenol-Rich Extract in Healthy 7-12 Years Old Children: A Home-Based, Real-World Consumer Study

Ilona Gille, Emmanuelle Arnaud*, Maïté Jeanroy, Benoit Lemaire and David Gaudout

Activ'Inside, Beychac-et-Caillau, France

***Address for Correspondence**
Emmanuelle Arnaud, Activ'Inside, Beychac-et-Caillau, France, Email: e.arnaud@activinside.com

Submission: 03 February, 2026
Accepted: 10 March, 2026
Published: 14 March, 2026

Keywords: Cognition; Executive function; Polyphenols; Children; Open study; Memophenol™

Abstract

Background: Executive functions such as attention, working memory, and emotional regulation undergo rapid development during school age, a period marked by increasing academic demands. This creates a specific need to support cognitive efficiency in children, whose regulatory capacities are still maturing. Polyphenol-rich nutritional interventions have previously shown benefits on executive processes in adults, but evidence in younger children remains limited, justifying investigation in this age group.

Objectives: This open trial aimed to evaluate both the acute and chronic effects of daily supplementation with Memophenol™ on cognitive performances in children under real- world conditions.

Methods: A 28-day medically supervised real-world open trial was conducted in 41 healthy children (aged 7–12 years) from Singapore. Participants daily consumed one red-berry flavored stick powder containing a polyphenols-rich extract from grape and blueberry (150 mg of Memophenol™), each morning with breakfast. Children's cognitive performance was assessed using the CogniFit Kids digital platform at four points (D0, D0+2h, D14, D28). Parents assessed their child's behavioral and executive functions using an adapted version of the validated BRIEF-2 questionnaire (D0, D14, D28), followed by a satisfaction survey at D28.

Results: Children's cognitive performance improved significantly by +9.5% 2 hours after Memophenol™ intake compared to baseline, as well as by +13.9% after 14 days, and +17.1% after 28 days of supplementation ($p < 0.001$). Executive function, as assessed by the BRIEF-2 Global Executive Composite (GEC), decreased by –8.3% and –12.9%, respectively after 14 and 28 days of supplementation ($p < 0.001$), reflecting better overall executive control. In addition, improvements in the Behavior Regulation (–11.5%), Emotion Regulation (–14.4%), and Cognitive Regulation (–12.8%) indices were observed after 28 days. Parents reported noticeable improvements in attention (63%) and overall efficacy (66%). The formulation was well tolerated.

Conclusions: These preliminary findings suggest that daily intake of 150 mg Memophenol™ may improve cognitive functions in children, with both acute and cumulative benefits after 28 days, observed in a real-world setting. The formulation demonstrated good safety and acceptability, supporting its potential as a natural strategy to enhance cognitive functions and behavioral regulation in school-aged children. These results highlight the potential of polyphenol supplementation to support learning performance and behavioral regulation in children under high academic demand. However, given the absence of a control group and the potential for expectancy and learning effects, these results should be interpreted with caution. Further randomized, controlled, and blinded studies are warranted to confirm these promising effects.

Introduction

The school-age period is marked by rapid neurodevelopment and the maturation of core executive functions such as attention, working memory, reasoning, and emotional regulation. These cognitive processes are essential for learning efficiency, behavioral self-regulation, and adaptation to increasingly demanding educational environments [1,2].

In Asia, academic pressure has become a significant societal concern. Students from Singapore and Japan have high expectations of their own academic achievement but perceive that they are unable to attain those standards. In addition to academic stress arising from self-expectations, Asian adolescents also experience academic stress arising from the need to excel academically to fulfill parental expectations and to avoid the loss of face. [3]. Alarmingly, recent data show that self-harm behaviors are increasingly common among young people in Singapore, with one in four youths reporting having engaged in non-suicidal self-injury (NSSI) at least once [4]. Media have also reported extreme cases, such as a child being hospitalized after spending 14 consecutive hours on homework [5].

This intense pressure drives many parents to seek solutions to support their children's cognitive performance and emotional well-being. In Singapore, a substantial proportion of families invest in academic enrichment resources such as private tuition, reflecting the strong societal emphasis placed on scholastic achievement [6]. Some parents also turn to digital cognitive training tools or nutritional

ISSN: 2469-4185

supplements, although the efficacy and safety of these interventions remain variable and are often debated in the scientific literature [7,8].

In recent years, polyphenols – naturally occurring compounds found in fruits, vegetables, tea, and wine – have attracted considerable interest due to their potential to enhance cognitive performance and brain health [9]. Beyond their classical antioxidant properties, polyphenol- rich foods and extracts, such as those derived from tea, grapes, blueberries, and cocoa, have been suggested to modulate cognitive performance through multiple complementary mechanisms. These mechanisms include acute effects on endothelial function and cerebral blood flow via nitric oxide-related pathways, as well as longer-term effects on neuroinflammation and/or synaptic plasticity [10]. Such mechanisms may contribute to improvements in several cognitive domains, notably memory, attention, and executive functions, in healthy adults and older individuals. Consistent with these mechanistic hypotheses, randomized controlled trials have investigated a range of polyphenol-rich foods and extracts in relation to cognitive outcomes. Cocoa flavanols are among the most extensively studied polyphenol sources in human cognition research. Acute and short-term randomized controlled trials in adults have suggested an association between the consumption of flavanol-rich cocoa and changes in neurovascular markers and brain function, as well as, in some contexts, improvements in cognitive performance. For example, cocoa flavanols have been associated with increased task-related brain activation measured by fMRI in healthy young adults [11] and with enhanced cerebral perfusion in older adults in a placebo-controlled crossover design [12]. More broadly, reviews synthesizing intervention trials conclude that cocoa-derived flavanols represent a polyphenol source with overall favorable effects on cognition [13]. Within this broader landscape, and of particular relevance here, randomized controlled trials have shown that supplementation with flavonoid-rich blueberry or grape extracts can lead to improvements on certain tests of working memory, information-processing speed, and/or verbal learning in adults, although the magnitude and reproducibility of effects vary according to populations, doses, matrices, and outcome measures [14,15].

In this context, there is a growing interest in evidence-based nutritional interventions, such as polyphenol-rich extracts, to support cognitive development in children. Clinical reviews indicate that several nutritional strategies, may influence cognitive development and cognitive performance in school-aged children. For instance, the landmark review by Bryan et al. synthesizes evidence linking specific nutrients to cognitive development and cognitive performance in children [16]. While most clinical evidence on polyphenols and cognition comes from studies conducted in adults and older individuals, these promising findings have prompted investigations into whether similar cognitive benefits might be observed in younger populations, such as children and adolescents. To date, only a limited number of randomized controlled trials have been conducted in this population. For example, a study by Whyte et al. assessed the acute effects of a wild blueberry drink in 7- to 10-year-old children and reported improvements in memory and attention tasks shortly after consumption [17]. Similarly, a randomized trial by Barfoot et al. demonstrated that daily supplementation with blueberry powder over 4 weeks led to enhanced executive function and verbal memory in school-aged children [18]. Other study by Whyte et al. showed that polyphenols from blueberry powder consumption enhance executive function such as reaction time [19].

While current findings are promising, there is a need for larger, well-controlled studies to confirm the cognitive benefits of polyphenol supplementation in children and to better understand the underlying mechanisms. Our study aims to address these gaps by evaluating the effects of Memophenol™, a standardized grape and blueberry polyphenol extract, in a larger cohort of school-aged children, using robust cognitive endpoints and a longer intervention period. Memophenol™ is a patented formulation (WO/2017/072219 and WO/2020/104533) developed by Activ'Inside (Beychac et Caillau, France) that combines standardized grape and wild blueberry extracts). Clinical studies in both young and older adults have demonstrated that Memophenol™ supplementation can improve memory, learning, and executive functions, with measurable effects observed as early as 90 minutes post-intake and sustained benefits after six months of continuous use [20-22]. In addition to these cognitive benefits, preclinical and clinical data indicate that Memophenol™ stimulates neurogenesis, and improves synaptic plasticity, all of which are key mechanisms underlying cognitive performance [23-25]. Building on these findings, the present real-world open study was designed to assess whether these cognitive benefits could also be observed in a younger population. Specifically, we evaluated the effects of a 28-day supplementation with 150 mg of Memophenol™ on cognitive performance and executive function in healthy school-aged children living in Singapore.

Materials and Methods

Study design and participants

This real-world open trial was conducted under medical supervision by Syres-Asia (Singapore), a sensory and consumer research institute specializing in consumer testing for efficacy and tolerance, in Singapore between July 6th and August 2nd, 2025. The study aimed to evaluate the efficacy and tolerance of a dietary supplement containing Memophenol™ in healthy school-aged children. Participants were recruited from the SYRES Singapore database of panelists, using a combination of phone screening and an online questionnaire to ensure completeness of information.

Eligible participants were Chinese children aged 7 to 12 years, with a balanced ratio between the 7-9 and 10-12 age groups and an equal gender distribution. Children had to be declared healthy by their parents or legal guardians, with no diagnosis of ADHD, autism, or other neurological disorders, and no food allergies or dietary restrictions. They could not have participated in any market research activity in the past three months. Both children and parents had to agree to comply with the study instructions, including daily consumption of a fruit-flavored stick supplement at breakfast for 28 days, and completion of cognitive and satisfaction questionnaires at specified timepoints. Children were also required to complete online cognitive mini-games (Cognifit Kids platform) at four key timepoints under standardized conditions at home.

Exclusion criteria included any diagnosed neurological condition such as ADHD, autism, or learning disabilities, as well as chronic disease, food allergy, ongoing medication or food supplement use, and participation in another clinical or open trial within the previous

ISSN: 2469-4185

three months. Refusal to comply with study instructions or the product use protocol also led to exclusion.

The intervention period lasted 28 days, during which each child consumed one red berry- flavored stick containing Memophenol™ dissolved in water at breakfast every day. Assessments were conducted at four timepoints: baseline (D0, before the first intake), two hours after the first intake (D0+2h, to assess acute effects), day 14 (D14), and day 28 (D28). The two-hour post-intake assessment (D0+2h) was specifically chosen based on published pharmacokinetic data indicating that the peak plasma concentration of key polyphenolic compounds, such as flavanol monomers ((−)-epicatechin and (+)-catechin), typically occurs within 1-2 hours after oral administration [26,27]. This timing was selected to coincide with the expected maximal bioavailability of the active compounds and to optimize the detection of any acute cognitive effects. At each timepoint, children completed online cognitive mini- games using the Cognifit Kids platform under standardized home conditions, while parents completed the BRIEF-2 executive function questionnaire at D0, D14, and D28, as well as a satisfaction questionnaire at D28. All children were instructed to maintain their usual diet and physical activity throughout the study, and medical supervision was available for safety monitoring.

A total of 52 children were enrolled, and 41 completed the study per protocol and were included in the analysis. The final sample consisted of 21 girls and 20 boys, with a mean age of 9.5 years, all of Chinese ethnicity, living in Singapore, with no allergies or neurological conditions, and regular breakfast habits.

Intervention

The intervention consisted of a red-berry–flavored powder stick containing 150 mg of Memophenol™, which is a proprietary polyphenol-rich extract made from whole grape (Vitis vinifera L.) and blueberry (Vaccinium spp.) extracts. Each stick was dissolved in a glass of water and consumed at breakfast every day for a 28-day period. Memophenol™ contains at least 75% total polyphenols measured as catechin equivalents, at least 43% total flavonoids including flavan-3-ols, flavonols, and anthocyanins, at least 20% flavan-3-ols monomers, at least 22% flavan-3-ols oligomers with a degree of polymerization less than or equal to four, at least 0.10% anthocyanins including malvidin-3-glucoside, and at least 300 ppm stilbenes including resveratrol.

The selected dosage of 150 mg was determined based on two main criteria, the first being published clinical data assessing the efficacy of polyphenol- and anthocyanin-rich food intake in children, which indicate that similar amounts are found in dietary interventions using blueberries, mulberry powder, or polyphenol-rich supplements, and the second being extrapolation from previous clinical studies in adults, with the dose adjusted according to body weight and established safety margins for daily intake. This approach resulted in a target range of approximately 102 to 164 mg for children aged 7 to 12 years, and the 150 mg dose was chosen to align with both efficacy data and international safety recommendations.

Children were instructed not to consume polyphenol-rich foods such as grape, berries, cocoa, and tea during breakfast throughout the intervention period, and each participant received at home a doypack containing 30 sticks. According to the Memophenol™ specification sheet, the product complies with international regulations regarding contaminants such as heavy metals, polycyclic aromatic hydrocarbons, and pesticides, as well as microbiological safety.

Cognitive assessment

Cognitive performance was assessed using the CogniFit Kids digital platform (CogniFit Inc., Tel Aviv, Israel [28]), a computerized cognitive testing tool specifically adapted for children. The assessments were conducted at four time points: at baseline (D0), two hours after the first intake (D0+2h), and after 14 (D14) and 28 (D28) days of supplementation. The CogniFit Kids platform was accessed online from the participants' homes, under the supervision of a parent or legal guardian to ensure standardized testing conditions and minimize distractions. Each cognitive session lasted approximately 15 to 20 minutes and included a battery of six interactive mini-games designed to evaluate key cognitive domains relevant to school-aged children. The tasks assessed attention, working memory, processing speed, cognitive flexibility, inhibition, and reasoning abilities, in accordance with validated neuropsychological models [29,30]. The platform automatically calculated individual scores for each cognitive domain, as well as a global cognitive performance index, by aggregating performance metrics such as accuracy, reaction time, and task completion. These scores were standardized according to age-appropriate normative data provided by CogniFit, allowing for the monitoring of cognitive changes over the course of the intervention [30,31].

Executive functions were evaluated using the standardized and validated BRIEF-2 (Behavior Rating Inventory of Executive Function, Second Edition) parental questionnaire [32], which was administered in an English-adapted version suitable for the Singaporean context. Parents completed the questionnaire at baseline (D0), day 14 (D14), and day 28 (D28) of supplementation. The BRIEF-2 consists of 63 items and explores three main executive function domains: behavioral regulation, emotional regulation, and cognitive regulation, as perceived in daily life situations. Each item is rated on a three-point Likert scale (Never, Sometimes, Often), and the responses are used to calculate composite scores for each domain as well as a global executive function score. Higher scores indicate greater executive dysfunction. The BRIEF-2 is widely used in both clinical and research settings for the assessment of executive functions in children and has demonstrated robust psychometric properties [33]. The use of the English version ensured that parents could accurately and independently report on their child's executive functioning in a language they were comfortable with.

Satisfaction, Tolerability and compliance

At the end of the study, parents completed a satisfaction and acceptability questionnaire regarding perceived changes in their children's attention, concentration, memory, and overall well-being. In addition to the satisfaction and acceptability questionnaire, a medical assessor supervised the study to collect any adverse events.

Statistical analysis

Baseline demographic variables (sex, age) were described. Categorical data were summarized as percentages, while continuous

ISSN: 2469-4185

variables were reported as mean ± standard deviation (SD). Differences in Cognifit Z-scores (mean) and BRIEF-2 scores (mean) between baseline (D0) and follow-up (D+2h, D14 and D28) were analyzed using two-tailed paired Student's t-tests, and a two-sided P value < 0.05 was considered statistically significant. Statistical analyses were performed using Excel (Microsoft Corporation) with the Analysis ToolPak add-in.

Results

Participant characteristics

The selection of study participants followed a multi-step process, Children aged 7 to 12 years, of both sexes (male and female), were eligible for participation and children with a diagnosed neurological disease were excluded from the study. Initially, 670 potentially eligible children were identified from the database. After applying inclusion and exclusion criteria, 52 participants were enrolled in the study. During the course of the trial, 11 participants were excluded due to non-compliance with study instructions, resulting in a final sample of 41 children who completed the study.

Cognifit tests

Cognitive improvements assessed with Cognifit tests were evident as early as two hours following the first intake of Memophenol™ (Table 1). The Global Cognitive Score (Z score) increased significantly by +9.5% at D0+2h ($p < 0.001$), indicating an acute enhancement of cognitive processing efficiency and attentional control. Continued supplementation further amplified this effect, reaching +13.9% after 14 days and +17.1% after 28 days ($p < 0.001$), demonstrating both rapid and sustained benefits on global cognitive functioning (Figure 1).

Analysis of individual cognitive subdomains confirmed that improvements were broad and not limited to a single process. Significant increases were observed across multiple domains, including memory (+22.9%) and perception (+29.8%), which represented the strongest increases. Reasoning also improved substantially (+14.5%), whereas attention (+9.1%) and coordination (+6.3%) showed moderate but consistent enhancement over the 28-day period (Figure 2).

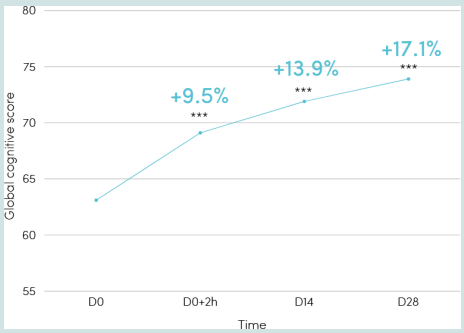

Figure 1: Evolution of the Global cognitive score (Z score) after Memophenol™ intake ***p<0.001

Table 1: Cognifit Z scores (Mean and SD) and evolution after Memophenol™ supplementation (as %)

Cognitive areas	Cognitive skills	Z-Scores (Mean, SD)				% change from D0		
		D0	D0+2h	D14	D28	D0+2h	D14	D28
Global score		63.1 (21.4)	69.1(19.6)***	71.9 (18.6)***	73.9 (17.3)***	**9.5%**	**13.9%**	**17.1%**
Attention	Focused Attention	79.7(27.8)	77.1 (26.3)	75.4 (28.6)*	74 (28.5)*	-3.3%	**-5.38%**	**-7.25%**
	Inhibition	58.3 (35.1)	61.6 (30.6)	69.3 (28.6)*	69.2 (26.6)**	5.56%	**18.77%**	**18.6%**
	Divided Attention	64.2 (28.5)	70 (25)*	72.7 (25.7)**	71.1 (28.1)	**9.08%**	**13.3%**	10.71%
	Updating	64.7 (29.4)	73.1 (24.1)***	75.5 (25.2)***	74 (25)**	**13.04%**	**16.7%**	**14.4%**
Coordination	Hand-eye Coordination	64.8 (28)	63.7 (31.5)	64.6 (28.1)	65 (27.9)	-1.73%	-0.34%	0.23%
	Response Time	73.6 (26.6)	78.9 (24.3)**	77.2 (25)*	78.1 (24.9)*	**7.12%**	**4.87%**	**6.1%**
Memory	Short-Term Memory	65 (27.9)	71 (26.7)	71.9 (26.1)*	75.1 (25.2)*	9.27%	**10.66%**	**15.57%**
	Visual Short- Term Memory	64.9 (25.5)	66.5 (26.3)	66.7 (26.9)	70.8 (26.7)	2.48%	2.9%	9.18%
	Phonological Short-term Memory	61.2 (32.5)	71 (25.8)*	73.5 (23.9)**	78.2 (23.8)**	**16.03%**	**20.18%**	**27.83%**
	Contextual Memory	52.6 (27.5)	64.8 (27.4)***	71.4 (23.3)***	73.9 (25.3)***	**23.23%**	**35.65%**	**40.43%**
	Non-verbal Memory	66.3 (25.4)	70.8 (25.7)	72.2 (24)	76.3 (23.4)**	6.77%	8.9%	**15.08%**
	Naming	64.2 (26.8)	72.7 (25.3)***	73.8 (24.1)***	74.1 (24.1)***	**13.3%**	**14.94%**	**15.51%**
	Working Memory	55.9 (28.6)	65.1 (27.2)***	71.8 (23.3)***	76.3 (21.7)***	**16.59%**	**28.46%**	**36.62%**
Perception	Visual Perception	50.5 (31.3)	60.6 (30.6)**	62.9 (28.9)***	67.8 (27.3)***	**19.94%**	**24.48%**	**34.23%**
	Spatial Perception	63.3 (28)	70.8 (27.8)	74.7 (24.7)**	82.1 (19.3)***	11.71%	**17.91%**	**29.65%**
	Auditory perception	52.5 (29.2)	60.8 (30.8)*	67.3 (24.4)***	70.3 (28.3)***	**15.85%**	**28.21%**	**33.97%**
	Estimation	60.5 (28.2)	69.8 (24.7)**	78.1 (20.2)***	80.1 (22.8)***	**14.45%**	**29.12%**	**32.51%**
	Visual Scanning	73.5 (30.1)	73.9 (28.2)	73.5 (30.7)	74.3 (28.6)	0.56%	0.07%	1.2%
	Recognition	49.7 (30.9)	61.6 (30)**	68.3 (25.7)***	73 (25.8)***	**23.95%**	**37.44%**	**46.91%**
Reasoning	Shifting	67.9 (28.6)	73.3 (25.9)**	76.7 (24.9)***	76.6 (24.7)**	**8.01%**	**12.97%**	**12.75%**
	Planning	63.5 (29.8)	68.2 (27.1)	72.1 (26.5)*	78.3 (23.6)**	7.53%	**13.68%**	**23.37%**
	Processing Speed	72 (27.4)	79.6 (24.2)***	77.8 (24)**	77.3 (23.3)*	**10.5%**	**7.99%**	**7.38%**

Values are expressed as mean Z-scores (SD). Bold values indicate significant difference vs baseline ($p < 0.05$).*p<0.05, **p<0.01, ***p<0.001.

ISSN: 2469-4185

The detailed evolution of each cognitive skill, as assessed by the CogniFit Kids platform, is presented in Table 1. Most sub-scores demonstrated progressive improvement over time, particularly in contextual memory (+40.4%, $p < 0.001$), working memory (+36.6%, $p < 0.001$), and visual perception (+34.2%, $p < 0.001$). These results underline a global enhancement of higher-order cognitive abilities related to attention Brief-A Scores

Behavioral and emotional regulation, assessed via the BRIEF-2 parental questionnaire, also improved significantly compared to baseline during the 28-day supplementation (Table 2). The Global Executive Composite (GEC) decreased by -8.3% at D14 and -12.9% at D28 (both $p < 0.001$), reflecting better overall executive control of children.

All three sub-indices followed this trend: the Behavior Regulation Index (BRI) declined by –11.5%, the Emotion Regulation Index (ERI) by -14.4%, and the Cognitive Regulation Index (CRI) by -12.8% (all $p < 0.001$). These consistent decreases indicate marked improvements in behavioral flexibility, emotional stability, and cognitive organization – key dimensions of executive functioning essential for classroom attention and learning adaptability.

Collectively, these findings confirm that Memophenol™ supplementation was associated with enhanced self-monitoring, emotional control, and cognitive regulation in children, consistently with the objective improvements measured through the digital cognitive tasks.

Parental feedback and satisfaction

At D28, 63% of parents reported noticeable improvement in their child's attention, while 66% perceived the supplementation as globally effective and 61% expressed their intention to continue or purchase the product.

These high levels of satisfaction demonstrate strong acceptability and perceived benefit, suggesting that the cognitive and behavioral changes were both observable and meaningful in daily life contexts.

Tolerability and compliance

Compliance throughout the 28-day intervention was excellent, with 80.5% of participants completing the entire supplementation period without missing a single dose, and 19.5% forgetting to take the supplement 1 or 2 times. Only one mild and transient gastrointestinal event (2.4%) was reported on Day 1, which resolved spontaneously without treatment discontinuation. Overall tolerability reached 97.6%, confirming the product's safety and suitability for pediatric use (Table 3).

The high adherence rate, coupled with positive parental feedback, reinforces the acceptability of Memophenol™ in real-world conditions and supports its feasibility for long- term use in children.

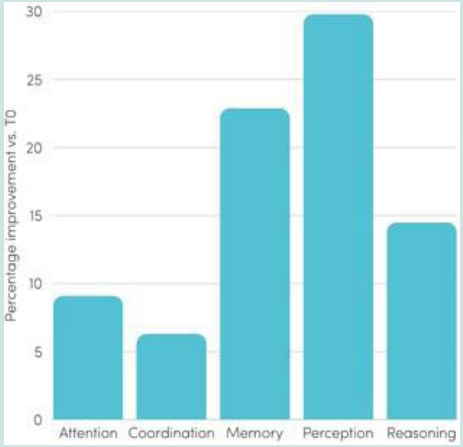

Figure 2: Percentages of improvement in cognitive subdomains after a 28-day Memophenol™ intake vs. T0

Discussion

This real-world open trial provides new evidence that daily supplementation with 150mg Memophenol™ significantly enhances both cognitive and executive functions in school-aged Singapore children aged 7-12 years. Notably, improvements were observed as early as two hours after intake, a timing that was deliberately chosen based on pharmacokinetic data indicating that the key polyphenolic compounds in Memophenol™, such as (−)-epicatechin and (+)-catechin, reach their peak plasma concentrations (Tmax) within 1-2 hours after oral ingestion [26,27]. These flavanol monomers are rapidly absorbed in the small intestine, undergo extensive phase II metabolism (glucuronidation, sulfation, methylation), and their conjugated metabolites are detectable in plasma and urine shortly after intake. This acute bioavailability likely underlies the rapid neuromodulatory effects observed in our study [24].

In line with this, Bensalem et al. demonstrated that supplementation with Memophenol™ led to a marked increase in the urinary excretion of specific polyphenol metabolites, including (+)-catechin, (−)-epicatechin, B-type procyanidin dimers, and their conjugated forms, as early as after the first dose and sustained over 6 months [20]. The progressive increase in performance over 28 days demonstrates the cumulative benefit of sustained supplementation,

Table 3: Tolerability of Memophenol™

Parameter	Observation	% of participants
Compliance	Completed full 28 days	95
Adverse events	Mild transient abdominal pain (Day 1)	2.4
Overall tolerability	Excellent	97.6

Table 2: BRIEF-2 scores (Mean (SD)) and evolution of scores after Memophenol™ supplementation (as %)

Parameter	Baseline (D0)	14 days (D14)	28 days (D28)	% change at D14 vs. D0	% change at D28 vs. D0
Global Executive Composite (GEC)	106.7 (20.2)	97.8 (20.5)***	92.9 (20.0)***	**–8.3%**	**–12.9%**
Behavior Regulation Index (BRI)	20.8 (4.8)	19.4 (4.7)**	18.4 (4.5)**	**–6.7%**	**–11.5%**
Emotion Regulation Index (ERI)	27.0 (4.9)	24.6 (5.2)***	23.1 (5.2)***	**–8.9%**	**–14.4%**
Cognitive Regulation Index (CRI)	58.8 (12.4)	53.8 (12.2)***	51.3 (11.8)***	**–8.5%**	**–12.8%**

Values are expressed as mean (SD). Bold values indicate significant improvement vs baseline ($p < 0.05$). **p<0.01, ***p<0.001.

ISSN: 2469-4185

extending previous findings from adult and elderly populations to a younger age group. The observed acute effects are consistent with the rapid action of flavanol monomers on neurovascular and neurometabolic pathways [36,37]. Previous human studies have demonstrated that Memophenol™ can enhance attentional control and information processing speed within 90 minutes post-intake [21], and other polyphenol-rich interventions (e.g., flavanol-rich cocoa beverages, grape-derived polyphenol drinks) have been shown to acutely enhance cerebral perfusion and oxygen availability, thereby improving attentional control and information processing speed within 1-2 hours post- intake [38]. Thus, the fast cognitive response observed in children after Memophenol™ intake in our study is consistent with these pharmacokinetic and mechanistic findings, and may operate through similar polyphenol-driven pathways shared across flavonoid-rich products. This pattern aligns with mechanistic frameworks summarized in clinical reviews, which highlight improvements in endothelial function and hemodynamic responses as plausible proximal drivers of rapid changes in cognitive efficiency (e.g., processing speed and attentional control), while acknowledging that not all acute trials show benefits depending on the cognitive endpoints and the intervention dose/matrix [35].

In the present study, acute improvements in the Global Cognitive Score (+9.5% after 2 hours) were accompanied by early changes in executive regulation as perceived by parents. Because the Global Cognitive Score is a Z-score normalized to a reference population, these results indicate that children moved from slightly above or around average baseline performance toward higher-than-average levels after supplementation. According to Cognifit normative guidelines, a Z-score improvement of this magnitude reflects a meaningful shift relative to age-matched cognitive norms, supporting the real-world relevance of the effect. The longer- term improvements observed after 14 and 28 days (+13.9% and +17.1%, respectively) likely reflect a progressive neuroadaptive response induced by repeated exposure to polyphenols, including enhanced synaptic plasticity and antioxidant protection within hippocampal and prefrontal circuits. These results may be explained by the mechanisms described by Bensalem et al. [23-25], who demonstrated in aged mice that Memophenol™ promotes hippocampal neurogenesis and synaptic connectivity, leading to measurable gains in learning and memory. Similarly, clinical trials in older adults with mild cognitive impairment [22] and in healthy students under cognitive load [21] have reported significant improvements in attention, working memory, and learning efficiency following supplementation with Memophenol™. The consistent direction of effects across these studies strengthens the hypothesis that the ingredient acts on conserved pathways of neuronal signaling across different life stages.

Beyond cognitive enhancement, the significant reduction in BRIEF-2 indices (GEC: –12.9%, $p < 0.001$) highlights the impact of supplementation on self-regulatory abilities. Improvements in emotion regulation (–14.4%) and behavior regulation (–11.5%) suggest a broader influence of Memophenol™ on executive domains that integrate cognitive, emotional, and social functioning. These effects are particularly relevant in academic contexts where attention, self-control, and emotional stability strongly influence learning outcomes and well- being. Importantly, the formulation was well tolerated, with no adverse effects reported other than one mild, transient gastrointestinal event. This excellent safety profile aligns with previous clinical data [20-22] in both young and older adults, confirming that Memophenol™ supplementation at a daily dose of 150 mg is safe and acceptable for pediatric use. This is also consistent with broader clinical trial evidence suggesting that polyphenol-rich interventions are generally safe and well tolerated across a wide range of doses and durations, with no consistent signal of excess adverse effects compared with controls [34].

Beyond its combination of an acute (2h)) and a short-term (14-28 days) assessment, this study presents several strengths. First, it combines objective cognitive assessments with subjective parental feedback, providing a comprehensive evaluation of the product's effects. Second, the real-life setting enhances the ecological validity and relevance of the findings for end-users. Third, the longitudinal design allows for the monitoring of individual changes over time.

Nevertheless, some limitations should be acknowledged. First, the repeated administration of the CogniFit Kids battery may have induced a potential learning effect, notably in healthy kids, potentially inflating cognitive scores independently of the intervention. Second, the lack of a control group prevents us from attributing the observed improvements solely to the intervention, as natural maturation or external factors cannot be ruled out. Third, the absence of a double-blind design may have introduced expectation or observer bias, particularly in subjective parental feedback. Additionally, the study population consisted exclusively of healthy children living in Singapore, which may limit the generalizability of the results to other socio-educational contexts. Taken together, these limitations suggest that the observed effects should be interpreted with caution, and further randomized, controlled, and blinded studies are warranted to confirm these preliminary findings.

Conclusion

This real-world open trial provides preliminary evidence that daily supplementation with 150 mg of a Grape and Wild Blueberry Polyphenol-Rich Extract (Memophenol™) may significantly enhance cognitive performance and executive functioning in healthy school-aged children aged 7-12 years old from Singapore. Improvements were detectable as early as two hours after intake and continued to increase over 28 days, suggesting a combination of rapid, exposure-driven effects and cumulative benefits with repeated supplementation. The rapid onset is consistent with previously reported acute cognitive effects of Memophenol™ in healthy young adults under sustained cognitive demand [21]. The continued improvement across the 14–28-day period also fits with prior Memophenol™ findings in older cohorts, including randomized controlled trials showing benefits on information-processing speed, learning-related measures, and executive-function indices (e.g., BRIEF-A) in adults with mild cognitive impairment [22] as well as cognitive support in healthy older adults [20], highlighting its potential as a natural and safe nutritional strategy to help school-aged children sustain attention in the classroom, strengthen day-to-day executive skills (e.g., working memory, attention, etc.), and support learning efficiency and behavioral self-regulation when facing homework load, exams, and the routine cognitive demands of school life.

ISSN: 2469-4185

Notably, the agreement between objective task-based performance (CogniFit) and real-life executive-function evaluations (BRIEF-2 and parental feedback) supports the robustness and practical relevance of the observed changes, suggesting they may extend beyond a single assessment method and translate to everyday self-regulation. However, because this study was open-label and lacked a control group, the results should be considered exploratory; well-powered randomized, double-blind, placebo-controlled pediatric trials incorporating biochemical endpoints are needed.

Funding and Conflicts of Interest

Funding: This study was funded by Activ'Inside (Beychac-et-Caillau, France). The sponsor provided the study material Memophenol™ and covered operational costs but had no role in data collection, statistical analysis, or interpretation of the results.

Conflict of Interest: All authors are full-time employees of Activ'Inside. This affiliation did not influence the design, analysis, or interpretation of the study results.

Acknowledgements: The authors thank the Syres team (Dr David Tan, Marion Bousquet, and Séverine Freyssinet) for clinical supervision and coordination of the study, as well as the participating families for their time and commitment.

References

1. Diamond A (2013) Executive functions. Annu Rev Psychol 64:135-168.
2. Best JR, Miller PH (2010) A developmental perspective on executive function. Child Dev.81:1641-1660.
3. Ang RP, Klassen RM, Chong WH, Huan VS, Wong IYF, Yeo LS, et al. (2009) Cross-cultural invariance of the Academic Expectations Stress Inventory: adolescent samples from Canada and Singapore. J Adolesc. 32:1225-1237.
4. The Straits Times. "1 in 4 young people in Singapore has engaged in self-injury without suicidal intent: Study" 2025.
5. The Straits Times. "Child hospitalised after 14 hours of homework." 2023.
6. Tan C (2017) Private supplementary tutoring and parentocracy in Singapore. Interchange.48: 315-329.
7. Diamond A, Lee K (2011) Interventions shown to aid executive function development in children 4 to 12 years old. Science 333: 959-964.
8. Bryan J, Osendarp S, Hughes D, Calvaresi E, Baghurst K, et al. (2004) Nutrients for cognitive development in school-aged children. Nutr Rev 62: 295-306.
9. Godos, Justyna, Carota G, Caruso G, Micek A, Toral ET, Giampieri F, et al. (2025) « Molecular mechanisms underlying the neuroprotective effects of polyphenols: implications for cognitive function ». EXCLI Journal 24: 1262-1294.
10. Rendeiro C, Rhodes JS, Spencer JPE (2015) « The Mechanisms of Action of Flavonoids in the Brain: Direct versus Indirect Effects ». Neurochemistry International 89: 126-139.
11. Francis ST, Head K, Morris PG, Macdonald IA (2006) « The Effect of Flavanol-Rich Cocoa on the fMRI Response to a Cognitive Task in Healthy Young People ». Journal of Cardiovascular Pharmacology, 47: S215-220.
12. Sorond, FA, Lipstiz LA, Hollenberg NK, LI Fisher ND et al. (2008) « Cerebral blood flow response to flavanol-rich cocoa in healthy elderly humans ». Neuropsychiatric Disease and Treatment 4: 433-440.
13. Martín, MA, Goya M, Teresa SDP (2020) « Effect of Cocoa and Cocoa Products on Cognitive Performance in Young Adults ». Nutrients 12: 3691.
14. Spencer JPE (2010) The impact of fruit flavonoids on memory and cognition. British Journal of Nutrition 104: S40-S47.
15. Lamport DJ, Lawton CL, Merat N, Jamson S, Dye L, et al. (2012) Concord grape juice, cognitive function, and driving performance: a 12-wk, placebo-controlled, randomized crossover trial in mothers of preteen children. American Journal of Clinical Nutrition, 95: 1260-1268.
16. Bryan, Janet, et al. (2004) « Nutrients for Cognitive Development in School-Aged Children ». Nutrition Reviews 62: 295-306.
17. Whyte AR, Williams CM (2015) Effects of a single dose of a flavonoid-rich blueberry drink on memory in 8- to 10-year-old children. Nutrition. 31: 531-534.
18. Barfoot KL, May G, Lamport DJ, Ricketts J, Riddell PM, et al. (2019) The effects of acute wild blueberry supplementation on the cognition of 7–10-year-old schoolchildren. Eur J Nutr 58: 2911-2920.
19. Whyte RA, Schafer S, Williams CM (2017) « The Effect of Cognitive Demand on Performance of an Executive Function Task Following Wild Blueberry Supplementation in 7 to 10 Years Old Children ». Food & Function 8: 4129-38.
20. Bensalem J, Gaudout D, Servant L, Calon F, Pallet V, et al. (2018) A polyphenol-rich grape and blueberry extract improves age-related cognitive decline in healthy older adults: A randomized, double-blind, placebo-controlled trial. J Gerontol A Biol Sci Med Sci 73: 1364-1373.
21. Philip P, Sagaspe P, Taillard J, Mandon C, Constants J, et al. (2019) Acute intake of a grape and blueberry polyphenol- rich extract (Memophenol™) ameliorates cognitive performance in healthy young adults during a sustained cognitive effort. Antioxidants 8: 650.
22. Lopresti AL, Smith SJ, Pouchieu C, Pourtau L, Gaudout D, et al. (2023) Effects of a polyphenol-rich grape and blueberry extract (Memophenol™) on cognitive function in older adults with mild cognitive impairment: A randomized, double-blind, placebo-controlled study. Front Psychol 14: 1144231.
23. Bensalem J, Servant L, Gaudout D, Pallet V, Layé S, et al. (2019) Polyphenols from Grape and Blueberry Improve Episodic Memory in Healthy Elderly with Lower Level of Memory Performance: A Bicentric Double-Blind, Randomized, Placebo-Controlled Clinical Study. J Gerontol A Biol Sci Med Sci. 74: 996-1007.
24. Dudonné S, Bensalem J, Gaudout D, et al. (2016) Combined administration of grape and blueberry polyphenols enhances their bioavailability and neuroprotective potential in mice. Food Funct 7: 3737-3749.
25. Bensalem J, Dudonné S, Gaudout D, Servant L, Calon F, et al. (2018) Polyphenol-rich extract from grape and blueberry prevents cognitive decline and improves neuronal function in aged mice. J Nutr Sci. 7: e19.
26. Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L (2004) Polyphenols: food sources and bioavailability. Am J Clin Nutr 79: 727-747.
27. Ottaviani JI, Borges G, Momma TY, Spencer JPE, Keen CL, et al. (2016) The metabolome of 2-14C-epicatechin in humans: implications for the assessment of efficacy, safety, and mechanisms of action of polyphenolic bioactives. Sci Rep 6: 29034.
28. CogniFit Inc. CogniFit Kids User Manual (2022).
29. Tuerk C, Saha T, Bouchard MF, Booji L, (2023) Computerized Cognitive Test Batteries for Children and Adolescents-A Scoping Review of Tools for Lab- and Web-Based Settings From 2000 to 2021. Arch Clin Neuropsychol 38: 1683-1710.
30. Polurde V, Hrabok M, Sherman EMS, Brooks BL (2017) Validity of a Computerized Cognitive Battery in Children and Adolescents with Neurological Diagnoses. Arch Clin Neuropsychol 33: 247-253.
31. CogniFit Science. Normative Data and Scoring Algorithms. Available at: cognifit.com/science.
32. Dodzik P (2017) Behavior Rating Inventory of Executive Function, Second Edition Gerard A. Gioia, Peter K. Isquith, Steven C. Guy, and Lauren Kenworthy Journal of Pediatric Neuropsychology 3: 227-231.
33. Isquith PK, Roth RM, Gioia GA (2016) Contribution of rating scales to

ISSN: 2469-4185

the assessment of executive functions in children and adolescents. Appl Neuropsychol Child 5:125-132.

34. Isquith PK, Roth RM, Gioia GA (2016) Contribution of rating scales to the assessment of executive functions in children and adolescents. Appl Neuropsychol Child 5:125-132.

35. Yang W, Cui K, Zhao J, Zeng Z, Song R, et al. (2019) « Effect of Polyphenols on Cognitive Function: Evidence from Population-based Studies and Clinical Trials ». The Journal of Nutrition, Health & Aging, 25: 1190-204.

36. Ammar A, Trabelsi K, Boukhirs O, Bouaziz B, Muller P, et al. (2020) Effects of Polyphenol-Rich Interventions on Cognition and Brain Health in Healthy Young and Middle-Aged Adults: Systematic Review and Meta- Analysis ». Journal of Clinical Medicine 9: 1598.

37. Sorond FA, Lipsitz LA, Hollenberg NK, Fisher ND (2008) Cerebral blood flow response to flavanol-rich cocoa in healthy elderly humans. Neuropsychiatr Dis Treat. 4: 433- 440.

38. Francis ST, Head K, Morris PG, Macdonald IA (2006) The effect of flavanol-rich cocoa on the fMRI response to a cognitive task in healthy young people. J Cardiovasc Pharmacol. 2; S215-S220.

39. Lamport DJ, Pal D, Moutsiana C, Field DT, Williams CM et al. (2016) The effect of flavanol-rich cocoa on cerebral perfusion in healthy older adults during conscious resting state: a placebo controlled, crossover, acute trial. Randomized Controlled Trial 232: 3227-3234.