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Neuropsychopharmacological effects of *Aronia melanocarpa*: A narrative review

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Summary

Background: *This narrative review examines the neuropsychopharmacological effects of Aronia melanocarpa (black chokeberry), focusing on its potential in the prevention and treatment of neuropsychiatric disorders such as anxiety, depression, and cognitive decline. Subjects and Methods: A comprehensive literature search across Web of Science, Scopus, and Google Scholar identified 29 original studies, based on in vitro, animal, and human research. Results: Findings demonstrated that Aronia melanocarpa, rich in polyphenols like anthocyanins and proanthocyanidins, exerts cognitive-enhancing, anxiolytic-like, and antidepressant-like effects. These outcomes are mediated by mechanisms involving antioxidant activity, modulation of neurotransmitter systems, inhibition of monoamine oxidases, reduction of neuroinflammation, modulation of gut microbiota, and upregulation of brain-derived neurotrophic factor (BDNF). Animal models of Alzheimer's disease and stress-induced disorders, along with human clinical trials, corroborated these effects. Conclusions: The review underscores the therapeutic promise of Aronia melanocarpa nutraceuticals in neuropsychiatric health and highlights the need for further clinical validation.*

Keywords: *Aronia melanocarpa, neuropsychopharmacological effects, review*

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INTRODUCTION

Anxiety and depressive disorders are among the most common mental health conditions and are major contributors to disability due to their chronic nature, elevated risk of secondary mental comorbidities, and reduced life expectancy. According to a report by the World Health Organization, the emergence of COVID-19 has been associated with a 25% increase in the prevalence of depressive and anxiety symptoms, particularly among young people and women (WHO, 2022). Simultaneously, increased life expectancy and advancements in healthcare have inevitably led to a higher incidence of age-related neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease (PD). A bidirectional relationship between neurodegenerative and psychiatric disorders has also been established (Wingo et al., 2022). These findings underscore the importance of prioritizing early preventive strategies in healthcare approaches to neuropsychiatric disorders.

Throughout history, people have used plant-based remedies to treat psychiatric disorders. While modern medicine, especially over the past century, has greatly improved psychiatric care, some believe valuable natural treatments were dismissed too quickly. Many patients still turn to medicinal plants for self-treatment (Babić, 2007). In the last decades, the use of natural compounds has been a widely recognized complementary approach in the prevention or management of psychiatric conditions such as schizophrenia, bipolar affective disorder, anxiety and depression ((Babić D & Babić R, 2009). In particular, polyphenols (PPs) have garnered substantial scientific interest in recent decades. PPs are ubiquitously distributed biologically active plant substances which are categorized in two main classes: flavonoids and non-flavonoids. PPs possess diverse biological activities (antioxidant, anti-inflammatory, antidiabetic, lipid-lowering). A growing body of evidence supports their potential role in the prevention of obesity, diabetes, cardiovascular diseases, malignancies (Stromsnes et al., 2021) and neuropsychiatric disorders (Zekrumah et al., 2023).

Aronia melanocarpa, commonly known as black chokeberry, is a shrub of the *Rosaceae* family, native to North America and cultivated in several European countries. Due to their astringent taste, *Aronia* berries are rarely consumed raw and are more commonly processed into juice, jam, wine, liqueur, or tea. Studies have identified an exceptionally high concentration of polyphenols in chokeberry fruits—particularly proanthocyanidins (oligo- or polymers of monomeric flavonoids from the flavan-3-ol subclass), flavonoids especially from the subclass of anthocyanins, as well as non-flavonoids, presented by

phenolic acids (predominantly chlorogenic and neochlorogenic) (Valcheva-Kuzmanova et al., 2018).

In order to exert effects on the central nervous system (CNS), polyphenols (PPs) need to cross the blood–brain barrier (BBB). Until the early 2000s, a major concern regarding their therapeutic potential was their ability to localize within the brain. The first evidence of central distribution of PPs was reported in 2005, when several blueberry-derived anthocyanins were detected in specific brain regions—including the cerebellum, cortex, hippocampus, and striatum—of blueberry-fed rats. These animals also exhibited improved cognitive performance (Andres-Lacueva et al., 2005). While the systemic effects of polyphenols had been documented prior to this, these findings were the first to suggest their potential neuroprotective properties. Similarly, the ability of *Aronia* anthocyanins and their metabolites to cross the blood–cerebrospinal fluid barrier and reach the brain was confirmed in a sheep model following fruit consumption (Płatosz et al., 2021).

Over the past two decades, there has been a steady increase in the number of studies investigating the central effects of *Aronia melanocarpa* and its bioactive constituents. However, a review synthesizing these findings is currently lacking in the scientific literature. Therefore, the aim of this paper was to summarize the existing evidence on the neuropsychopharmacological effects of Aronia melanocarpa, including the methodologies employed to assess them, key findings and underlying mechanisms, as well as any reported inconsistencies or contradictions.

METHODS

This paper presents a narrative review of the neuropsychopharmacological effects of *Aronia melanocarpa*. A comprehensive search was conducted using the databases Web of Science (WoS), Scopus, and Google Scholar up to February 2025. The following keywords and subject headings were employed: "*Aronia melanocarpa*" OR "*chokeberry*" AND "*anxiolytic*" OR "*depression*" OR "*antidepressant*" OR "*mood*" OR "*memory*" OR "*cognition*" OR "*cognitive*" OR "*behavior*" OR "*behavioral*" OR "*locomotor*" OR "*brain*" OR "*neuroprotection*" OR "*neuroprotective*."

Inclusion criteria consisted of original research articles with study designs including *in vitro* assays, animal studies, and human studies. Review articles and studies considered irrelevant to the topic were excluded.

From the WoS database, 82 records were initially identified, of which 60 were excluded, leaving 16 articles for final analysis. In Scopus, a total of 127 articles were identified. After removing duplicates and applying the exclusion criteria, 3 papers were included in the review process. From Google Scholar, 2150 articles were retrieved using the search terms. After eliminating duplicates and applying the inclusion and exclusion criteria, 10 articles were selected for review.

In total, 29 original articles were thoroughly reviewed and analyzed by two independent reviewers (MR and SVK).

Based on the reviewed literature, the neuropsychopharmacological effects of *Aronia melanocarpa* nutraceuticals were identified in the following areas: cognition enhancement, anxiolytic-like effects, and antidepressant-like effects.

RESULTS

Cognition-enhancing properties

Alzheimer's disease (AD) and dementia remain major medical conditions characterized by progressive cognitive decline and memory loss. AD is associated with the accumulation of amyloid-beta (Aβ) plaques and tau protein in the brain, leading to hippocampal damage that impedes the consolidation of short-term memory into long-term storage. Furthermore, the cholinergic neurotransmitter system, which plays a crucial role in memory formation, is compromised in AD (Lamptey et al., 2022).

The search process yielded fourteen articles in total (12 animal studies and 2 human studies) investigating the impact of *Aronia melanocarpa* on cognition. Different experimental models were employed to assess these effects in animals. The intracerebroventricular injection of Aβ is used to mimic AD by disrupting the cholinergic system, leading to learning and memory deficits (Kim et al., 2016). The muscarinic antagonist scopolamine, when injected intraperitoneally, impairs the cholinergic neurotransmission, induces oxidative stress, and leads to the accumulation of reactive oxygen species (ROS), resulting in memory impairment in rodents (Bunadri et al., 2013). The 5xFAD mouse model incorporates transgenic mice with five mutations (K670N/M671L, V717I, I716V, M146L, and L286V) to induce familial AD (FAD). The combined effect of these mutations triggers rapid disease progression—amyloid accumulation becomes evident after 2 months, and neurodegeneration with neuronal cell loss occurs by 9 months (Oakley et al., 2006). The Senescence Accelerated Mouse Prone 8 (SAMP8)

model displays various pathophysiological characteristics associated with AD, including altered expression of anti-aging factors, oxidative stress, neuroinflammation, Aβ deposition, tau hyperphosphorylation, endoplasmic reticulum stress, dysregulated autophagic activity, and disruption of the intestinal microbiota (Liu et al., 2020). Systemic administration of D-galactose induces brain senescence both *in vitro* and *in vivo* in animals, triggered by mitochondrial dysfunction, oxidative stress, inflammation, apoptosis, and a reduction in brain-derived neurotrophic factor (BDNF) levels. These effects ultimately lead to cognitive decline in the tested subjects (Shwe et al., 2018). Given that research has shown the harmful impact of high-calorie intake on spatial learning and memory (Alemohammad et al., 2022), calorie-dense diets are used in rodent studies to induce cognitive impairment and assess the effects of pharmacological interventions.

The methodologies implemented in the animal studies include: behavioral tests to assess spatial memory, histological and immunohistochemical assays, biochemical and Western blot analyses, cell viability assays, and microbiome analysis.

Lee *et al*. used male ICR mice to assess the cognitive effects of *Aronia melanocarpa* berry extract (AMBE) in a scopolamine-induced memory impairment model (Lee et al., 2016). The test substances—AMBE (administered in two doses: 200 mg/kg and 400 mg/kg) and the anthocyanin cyanidin-3-galactoside (C3Gal, 50 mg/g)—were given daily for four consecutive days prior to the Morris water maze (MWM) test and once before training in the one-way passive avoidance test (PAT). MWM and PAT are employed to evaluate long-term spatial memory. In MWM, rodents are trained to escape opaque water by locating a hidden platform. The time spent in the target quadrant and the escape latency are documented (Morris, 1984). In the PAT, mice explore light and dark compartments, receiving an electric shock in the dark compartment. The latency to enter the dark compartment is measured in subsequent trials (Eagle et al., 2016). Scopolamine injection induced memory impairment, as evidenced by a lack of improvement in escape latency time, increased time spent in the target quadrant in the MWM, and reduced latency time in the PAT. Additionally, scopolamine increased acetylcholinesterase (AChE) activity and reduced the expression of phosphorylated cAMP-response element-binding protein (p-CREB) and BDNF in the hippocampus. Both doses of AMBE and C3Gal counteracted these negative effects (Lee et al., 2016).

Another study employed a D-galactose-induced aging model in mice to investigate the effects of Aronia melanocarpa polysaccharides on cognitive function (Zhao et al., 2021) using eight-arm maze test. The eight-arm maze, also known as the radial arm maze, is a test where animals navigate multiple arms to find food, with only one arm containing a reward. This task measures how quickly animals locate the food and how often they revisit previously explored arms, reflecting their memory ability (Carter & Shieh, 2010). Aging induced by D-galactose led to significant cognitive decline, as demonstrated by increased total distance traveled and prolonged latency time in the eight-arm maze test. Histological analysis revealed a reduction in brain weight, the presence of hemorrhagic spots on the brain surface, and poorly defined structural differentiation. Biochemically, the aging model was characterized by elevated AChE activity and increased oxidative stress, evidenced by elevated malondialdehyde (MDA) levels, reduced superoxide dismutase (SOD) and catalase (CAT) activity, and down-regulation of the antioxidant markers nuclear factor erythroid 2-related factor 2 (Nrf2) and heme oxygenase 1 (HO-1). Furthermore, markers of pyroptosis (gasdermin D, caspase-1, apoptosis-associated speck-like protein containing CARD), apoptosis (increased caspase-3 and Bax; decreased Bcl-2), and inflammation (elevated interleukin-1β, NLRP3 inflammasome, nuclear factor kappa B and IκBα) were significantly upregulated. Aging also altered signaling associated with cellular senescence, as indicated by increased AMP-activated protein kinase (AMPK) and sirtuin 1 (SIRT1) expression and decreased p53 levels. Treatment with *Aronia melanocarpa* polysaccharides significantly attenuated these age-related pathophysiological alterations. Inflammatory responses were suppressed via AMPK-mediated modulation of the NLRP3 inflammasome; oxidative stress was alleviated through activation of the Nrf2/HO-1 pathway; apoptosis was mitigated via regulation of the PI3K/AKT/mTOR signaling cascade; and pyroptotic responses were down-regulated by reducing the expression of key pyroptotic proteins. Additionally, gut microbiota composition was improved, as reflected by an increased relative abundance of *Bacteroides* and a decreased abundance of *Firmicutes* species in the treated group (Zhao et al., 2021).

Another study demonstrated that ultrasonic processing of *Aronia melanocarpa* extract enhanced cognitive function, as evidenced by improved performance in both the MWM and PAT, alongside a 1.46-fold reduction in AChE gene expression in animals treated with the ultrasonically modified extract compared to those receiving the non-processed form (Kim & Lee, 2016). These cognitive improvements were attributed to the increased content of C3Gal in the ultrasonicated extract. Furthermore, fermentation appears to potentiate the neuroprotective effects of *Aronia* extracts. A study by Kim et al. reported that lactic acid-fermented *Aronia melanocarpa* extract

exhibited enhanced radical scavenging activity and more potent anti-cholinesterase effects. These biochemical properties translated into significantly improved MWM and PAT performance in rats (Kim et al., 2015).

Daskalova et al. investigated the neuroprotective effects of *Aronia melanocarpa* fruit juice administered over a period of 105 days in aged rats using the two-way active avoidance test (AAT) (Daskalova et al., 2019). The AAT is a behavioral test in which rats learn to avoid an aversive stimulus by relocating to a different compartment. Initially placed in one of two chambers, the rat is exposed to a conditioned stimulus, such as light or tone, followed by a mild electrical shock. Through repeated trials, the rat learns to associate the conditioned stimulus with the impending shock and moves to the adjacent compartment to avoid discomfort (Jänicke & Coper, 1996). Natural aging was associated with a decline in cognitive function, as evidenced by a reduced number of avoidances in the AAT, diminished density of nerve fibers within the hippocampal perforant pathway, and decreased cholinergic activity. Chronic treatment with *Aronia melanocarpa* fruit juice significantly improved cognitive performance, which was linked to increased fiber density in the perforant pathway and enhanced cholinergic neurotransmission in both the prefrontal cortex and hippocampus (Daskalova et al. 2019).

Hippocampal protection was also demonstrated in a study by Wen et al., which investigated the effects of *Aronia melanocarpa*-derived anthocyanins on Aβ-induced cognitive impairment in Sprague-Dawley rats. Administration of Aβ resulted in significant behavioral deficits, as evidenced by increased escape latency and prolonged time spent in the target quadrant during the MWM test. Histopathological analysis of hippocampal tissue from Aβ-treated animals revealed substantial neuronal damage, including a reduced number of neurons in the CA1 and CA3 regions, disorganized cellular architecture, neuronal degeneration marked by enlarged cell bodies, cytoplasmic shrinkage, compromised structural integrity, and nuclei with atypical oval or triangular shapes. Treatment with anthocyanins ameliorated these neuropathological changes, as demonstrated by improved cognitive performance in the MWM and restoration of hippocampal structural integrity (Wen et al., 2020).

Yamane *et al*. investigated the neuroprotective effects of *Aronia melanocarpa* juice and five distinct fractions from it through both *in vitro* and *in vivo* experiments, employing transgenic 5xFAD mice as a model of Alzheimer's disease (Yamane et al., 2023). The juice was administered over a 12-week period, while non-transgenic mice receiving water *ad libitum* served as the control group. Y-maze test (a variant of the T-maze) was used to evaluate the effects of the juice on the cognitive function. It is a spatial memory test in which rodents are required to alternate between two goal arms based on their natural tendency to explore novel environments. This task assesses spatial working memory by testing the animal's ability to remember which arm was previously visited, without the need for rewards, punishments, or pre-training. Thus, it is a time-efficient and ethical cognitive evaluation tool (d'Isa et al. 2021). In parallel, the juice and its fractions were assessed *in vitro* using the SH-SY5Y human neuroblastoma cell line. The 5xFAD mice exhibited impaired cognitive function, as indicated by reduced percentage of spontaneous alternations in the Y-maze test. Histopathological and biochemical analyses revealed an increased number of Aβ plaques, elevated levels of amyloid-β and tau proteins in the cerebrum, and enhanced δ-secretase activity of the enzyme asparagine endopeptidase, which is involved in the production of amyloid-β peptides. Administration of *Aronia* juice significantly attenuated these pathological alterations and improved all measured outcomes. These *in vivo* findings were corroborated by *in vitro* results, which confirmed both the anti-δ-secretase activity of the juice and, notably, of one of the fractions. Furthermore, cell viability assays demonstrated that the same fraction conferred protection against Aβ-induced cytotoxicity disease (Yamane et al., 2023).

Wen et al. employed the SAMP8 mouse model to investigate the anti-dementia effects of C3Gal, derived from *Aronia melanocarpa*, administered either alone or in combination with the antidiabetic drug metformin. Treatment with metformin and C3Gal significantly improved spatial learning and memory in SAMP8 mice, accompanied by an increased neuronal count and a marked reduction in Aβ aggregation. In addition to cognitive improvements, the combined treatment favorably modulated the metabolic profile, as validated by increased levels of short-chain fatty acids and alcohols, alongside decreased concentrations of indoles, methyl esters, and ketones. These findings suggest a synergistic therapeutic potential of *Aronia*-derived C3Gal and metformin in delaying the progression of Alzheimer's disease (Wen et al., 2021).

Valcheva-Kuzmanova *et al*. conducted a series of experiments to evaluate the effects of *Aronia melanocarpa* fruit juice on spatial memory in rats. An initial study assessed the impact of single oral doses of *Aronia melanocarpa* juice (5 ml/kg and 10 ml/kg) in healthy male rats. While no significant changes in working memory were observed, the juice did not induce any cognitive impairment (Valcheva-Kuzmanova & Zhelyazkova-Savova, 2009). A subsequent study utilized healthy young male Wistar rats to assess memory performance using the AAT.

The juice was administered orally at a dose of 10 ml/kg for either 21 or 30 days. Both treatment durations significantly increased the number of avoidances during the first two training days and on the retention test performed 24 hours after the second training session, with a more pronounced effect observed in the 30-day treatment group (Valcheva-Kuzmanova et al., 2013). In another study, the juice was administered at doses of 2.5, 5.0, and 10.0 ml/kg for 7, 14, 21 and 30 days. A dose-dependent improvement in memory was observed in the PAT, with significant increases in latency time and time spent in the illuminated compartment after 21 and 30 days. Notably, the most pronounced effects were seen at the doses of 5.0 and 10.0 ml/kg during the retention tests (Valcheva-Kuzmanova et al., 2014). More recently, a 2024 study demonstrated that administration of *Aronia* juice for three months at doses of 2.5, 5, and 10 ml/kg improved spatial memory in rats with diet-induced metabolic syndrome (MS) as evidenced by improved discrimination index in the place recognition test (PRT). PRT is a modified version of the novel object recognition test, designed to assess the spatial memory of subjects. Conducted in two sessions, the first being a training one, rats explore two identical, immobile objects for three minutes. After a 30-minute interval, one object is relocated for the test session. The time spent exploring each object is recorded to calculate a discrimination index, which serves as an indicator of spatial memory performance (Abtulov et al., 2024). Collectively, these findings suggest that *Aronia melanocarpa* fruit juice may enhance memory function in rats, particularly with higher doses and prolonged administration.

Two human studies investigating the cognitive effects of *Aronia melanocarpa* were identified. Both studies were conducted on apparently healthy individuals.

The first study was a randomized, double-blind, placebo-controlled trial involving 101 healthy adults with a body mass index (BMI) of 25–35 kg/m². Over a 24-week period, participants were assigned to receive either *Aronia melanocarpa* extract in a capsule form at two different dosages (90 mg or 150 mg) or a placebo (Ahles et al., 2020). Cognitive performance was assessed using the Stroop Color and Word Test, the Grooved Pegboard Test, and the Number Cross-Out Test. The Stroop Color and Word Test consists of three cards: one displaying the names of colors printed in black ink, one showing colored rectangles, and a third showing the names of colors printed in incongruent ink colors. Participants are instructed to quickly and accurately name the ink color on the third card. The Stroop interference score is calculated based on the time difference between completing the second and third cards. A color blindness test is administered prior to testing to ensure valid results (Dennis & Vander, 2010). The Grooved Pegboard Test, used to assess psychomotor activity, requires participants to insert pegs into slotted holes arranged in a random orientation, using both their dominant and non-dominant hands. Performance is scored based on completion time, number of dropped pegs, and number of correctly placed pegs within a 5-minute period (Lohman et al., 2003). The Number Cross-Out Test is a validated assessment of attention in which participants are required to cross out or underline specific numbers from a field of 800 numbers within a 3-minute time limit. Attention is quantified through accuracy (total correct minus total incorrect responses) and diligence (total edited minus total incorrect and missed items). Final scores are adjusted for age to generate percentile rankings (Dekker et al., 2007). No significant improvements were observed in cognitive flexibility, as measured by the Stroop test, following *Aronia* extract supplementation. Similarly, attention scores derived from the Number Cross-Out Test showed no significant time-by-treatment interaction for either the accuracy index (total correct minus total incorrect) or the diligence index (total edited minus total incorrect and missed responses). In contrast, psychomotor performance, as assessed by the Grooved Pegboard Test, demonstrated a significant treatment effect for the dominant hand: participants receiving the 90 mg dose of *Aronia* extract outperformed those in the placebo group. However, no significant differences were observed between the 150 mg and placebo groups, or between the two extract doses. While performance declined over the 24-week period (a significant time effect), a significant interaction was detected for the non-dominant hand; nevertheless, this finding did not remain significant after correction for multiple comparisons. Serum BDNF levels were not significantly altered by *Aronia* supplementation (Ahles et al., 2020). Overall, *Aronia melanocarpa* extract showed potential benefits for psychomotor speed but did not produce measurable improvements in attention or cognitive flexibility.

A randomized, double-blind, placebo-controlled cross-over trial evaluated the cognitive performance of healthy adults with a body mass index (BMI) of 18.5–30.0 kg/m² following one week of *Aronia melanocarpa* extract or placebo supplementation, separated by a two-week washout period (Ahles et al., 2024). Cognitive performance was assessed using the computerized and validated neuropsychological testing system Cambridge Neuropsychological Test Automated Battery (CANTAB) to evaluate attention and psychomotor speed, memory, and executive function. Attention and psychomotor speed are measured using the Five-Choice Reaction Time (RTI) test, which evaluates both reaction and movement times. Memory is assessed using the Delayed Matching

to Sample (DMS) and Paired Associates Learning (PAL) tests, which evaluate accuracy following variable delays and track errors in paired-item recall. Executive function is assessed through the Multitasking Test (MTT)—which measures response latency, incongruency cost, multitasking cost, and errors—and the Spatial Working Memory (SWM) test, which records total errors and strategy scores during a 12-item trial (Cambridge Cognition, 2019). The Motor Screening Test (MOT) was administered first to familiarize participants with the system, followed by RTI, DMS, PAL, MTT, and SWM tasks. The RTI test revealed no significant difference in reaction time between the extract and placebo periods; however, movement time was significantly improved by 4.8% following one week of *Aronia melanocarpa* extract supplementation. In the memory domain, a significant intervention-by-sex interaction was observed for total errors on the PAL test, with women exhibiting fewer errors than men after extract supplementation. No significant main effects were found for the DMS, PAL, MTT, or SWM tasks; however, a significant intervention-by-sex interaction was noted for the MTT incongruency cost, with men demonstrating greater benefit from *Aronia* extract. Furthermore, *Aronia melanocarpa* supplementation significantly increased serum BDNF levels compared to placebo (Ahles et al., 2024). Collectively, these findings suggested that *Aronia melanocarpa* extract administration could improve cognitive performance predominantly affecting psychomotor speed and attention in healthy adults.

Anxiolytic-like properties

Anxiety disorders are characterized by excessive fear and behavioral disturbances that significantly impair daily functioning. These disorders, including generalized anxiety disorder, panic disorder, and social anxiety disorder, arise from complex interactions between genetic, neurobiological, and environmental factors (Penninx et al., 2021). Moreover, anxiety disorders are associated with dysregulation of monoaminergic neurotransmission. Monoamine oxidase (MAO) enzymes—particularly MAO-A—play a crucial role in the metabolism of key neurotransmitters such as serotonin, norepinephrine, and dopamine, which are implicated in anxiety pathophysiology. Genetic and pharmacological studies have demonstrated that altered MAO activity influences anxiety-like behaviors and susceptibility to anxiety disorders (Shih et al., 1999). Despite the availability of effective treatments such as cognitive-behavioral therapy and pharmacotherapy, many patients remain undiagnosed or inadequately treated, particularly in primary care settings (Thibaut, 2017). The high prevalence and frequent comorbidity with other mental health conditions underscore the importance of improved recognition and management strategies (Penninx et al., 2021).

The effects of *Aronia melanocarpa* on the anxiety level were assessed in a total of 9 studies (7 animal and 2 human) in which anxiolytic-like effects were reported. Methods used to evaluate the anxiolytic-like effects include behavioral tests and *in vitro* biochemical essays to determine enzymatic activities.

The first studies demonstrating the anxiolytic-like effect of Aronia melanocarpa were conducted by Valcheva-Kuzmanova *et al*. In a 2009 study, *Aronia* was administered in the form of fruit juice at single doses of 5.0 ml/kg and 10.0 ml/kg to healthy rats. The social interaction test (SIT) was utilized to assess anxiety-like behavior, and the anxiolytic drug diazepam was used as a comparator (Valcheva-Kuzmanova & Zhelyazkova-Savova, 2009). In the SIT, rodents are exposed to an anxiety-provoking environment characterized by bright lighting, an unfamiliar arena, and an unknown conspecific partner. Weight-matched animals are observed for a 5-minute session within a square arena, during which various active social behaviors—such as sniffing, grooming, kicking, and climbing on the partner—are recorded. Passive contact, including sitting or lying next to one another, is not considered as social interaction. The total duration of active social behaviors serves as a measure of the anxiolytic efficacy of the test substance (File & Hyde, 1978). Results showed that both doses of the juice significantly increased the interaction time between unfamiliar partners in the SIT, with effects comparable to those of diazepam (Valcheva-Kuzmanova & Zhelyazkova-Savova, 2009). This effect was further confirmed in a 21-day study in which the juice produced an anxiety-reducing effect at the dose of 5.0 ml/kg (Eftimov & Valcheva-Kuzmanova, 2013).

To determine whether the anxiolytic-like effect depends on duration or dosage, the juice was administered at three different doses (2.5 ml/kg, 5.0 ml/kg, and 10.0 ml/kg) over four time periods (7, 14, 21, or 30 days) in rats and the elevated plus maze (EPM) test was used to assess anxiety (Valcheva-Kuzmanova et al., 2016). The EPM is based on the rodents' innate preference for enclosed, dark spaces as a means of avoiding potential threats. In this test, rats or mice are placed at the center of a four-armed maze, oriented toward an open arm. Their behavior—including entries into open arms and time spent in open versus closed arms—is recorded over a 5-minute period using both a video-tracking system and direct observation. Additional behavioral parameters, such as rearing, head-dipping, and stretched-attend postures, may also

be documented. Increased exploration of the open arms, reflected by longer durations or higher frequency of entries, is interpreted as indicative of anxiolytic-like activity (Walf & Frye, 2007). After administration of 10.0 ml/kg of juice for 21 or 30 days, anxiety-reducing effects were observed as indicated by increased entries into the open arms, longer time spent there, a higher open/total arm entry ratio, and reduced time in the closed arms in the EPM test. (Valcheva-Kuzmanova et al., 2016).

Diet-induced MS in rats is an established model characterized by the development of anxiety-like behaviors and cognitive deficits, particularly impairments in spatial memory (Reyzov et al., 2019). Administration of 2.5 ml/kg of juice was sufficient to antagonize the anxiety-like state induced by MS in another study, with no such effects observed at higher doses (Abtulov et al. 2024).

Ovariectomy (OVX) involves the surgical removal of the ovaries in female animals to induce an estrogen-deficient state, replicating postmenopausal conditions that include both depression-like and anxiety-like behaviors (Grigoryan, 2022). Anxiety induced by OVX was prevented in a dose-dependent manner following administration of the fruit juice over a three-month period (Georgieva et al., 2022). Chlorogenic acid, a polyphenol present in *Aronia melanocarpa* fruits, may contribute to the anxiolytic activity of the juice, as similar effects were observed following its subchronic administration for 14, 21, and 30 days (Valcheva-Kuzmanova et al., 2015).

Tomic et al. evaluated the effects of one-moth unlimited consumption of either *Aronia melanocarpa* juice or juice reconstruct without polyphenols on the anxiety-like state in rats via EPM test on day 32. The effects were compared to placebo and diazepam. *Aronia* juice consumption was associated with significant increases in the time spent in open arms and in the number of open arm entries, with the latter effect being superior to the effect of diazepam. These findings were accompanied by strong *in vitro* inhibitory effect of *Aronia* juice on MAO-A rather than on MAO-B. Analysis of separate polyphenol compounds of the juice showed that only quercetin exerted pronounced MAO-A inhibitory activity (Tomić et al., 2016).

Two human studies evaluated the effect of *Aronia melanocarpa* on the anxiety level. Methods used to evaluate the anxiety level in clinical trials included tests assessing the mood and biochemical tests.

In the first study, overweight or obese participants were enrolled and received capsules containing either 90 mg or 150 mg of *Aronia melanocarpa* extract daily for a duration of six months. Mood was assessed using a visual analogue mood scale. Although no statistically significant, time-by-treatment interactions were observed for mood scores: the treatment effect for sadness and the time effect for anger approached significance, manifested by slightly lower sadness levels following 150 mg extract supplementation compared to placebo, as well as a reduction in anger with prolonged supplementation. However, serum BDNF levels remained unaffected by *Aronia* extract administration (Ahles et al., 2020).

A second study evaluated the effects of short-term (1-week) administration of 750 mg *Aronia melanocarpa* extract on mood scores in young adults. Although no significant changes in mood were observed following extract supplementation, serum BDNF levels were significantly increased compared to placebo (Ahles et al., 2024).

Antidepressant-like properties

Major depressive disorder (MDD) encompasses several cardinal symptoms, such as persistent low mood, diminished interest or pleasure in activities, alterations in body weight and/or appetite, and an elevated risk of suicidal behavior. The development of MDD is influenced by multiple factors, reflecting its multifaceted nature. The hypothalamic-pituitary-adrenal axis dysfunction hypothesis suggests that patients with depression exhibit increased release of hypothalamic corticotropin-releasing hormone, which stimulates the production of downstream hormones, such as adrenocorticotropic hormone and glucocorticoids. This, in turn, reduces levels of sex hormones and BDNF. According to the monoamine hypothesis, the levels of the neurotransmitters serotonin, dopamine, and norepinephrine are reduced in certain brain areas, contributing to the development of depressive symptoms. The inflammatory hypothesis proposes that, in MDD, pro-inflammatory factors (e.g., interleukins and tumor necrosis factor-alpha) as well as reactive oxygen species (ROS) are elevated. Moreover, the activity of MAO, involved in the metabolism of serotonin, dopamine, and norepinephrine, is affected by ROS. Recent studies highlight the importance of the gut-microbiome-brain axis in preventing depressive symptoms through the production of short-chain fatty acids by the microbiota, which reduce gut permeability and inflammation. Finally, genetic and psychosocial factors, as well as structural and functional brain abnormalities, may all be involved in the complex pathophysiology of MDD (Cui et al., 2024).

The effects of *Aronia melanocarpa* on depression-like behavior was evaluated in a total of 6 studies, all performed on animals. Experimental animals were healthy or depressed rats/mice. Depression-like state was induced using corticosterone injections, oral alcohol administration, as well as through OVX (in female rodents) and social isolation of the animals.

Antidepressant-like effects of *Aronia melanocarpa* were documented using behavioral tests, biochemical essays for enzymatic activities and serum levels of neurotrophic factors and pro-oxidants, and microbiota diversity analysis.

In the first studies, the effect of *Aronia melanocarpa* on depression-like behavior was assessed in healthy young male rats. Aronia was administered as fruit juice at doses of 2.5 ml/kg, 5.0 ml/kg, and 10.0 ml/kg for periods of 21 and 30 days and the behavior in the Forced Swim Test (FST) was evaluated (Eftimov & Valcheva-Kuzmanova, 2013). The FST, introduced by Porsolt et al., is used to evaluate the effects of antidepressants in rodents by measuring their immobility in a water-filled container from which they cannot escape. In rats, the procedure involves two exposures (15 minutes and 5 minutes, 24 hours apart, with immobility time recorded during the second test), while in mice, a single 6-minute exposure is used. A decrease in immobility time reflects the antidepressant-like activity of the test substance. (Porsolt et al., 1978). In the above-cited experiment, a significant reduction in immobility time was documented after 21 days of juice administration at doses of 2.5 ml/kg and 10 ml/kg. After 30-days treatment, immobility time was reduced in a dose-dependent manner, with significance reached at the highest dose (Eftimov & Valcheva-Kuzmanova, 2013).

To confirm the antidepressant-like activity of *Aronia*, the same research group evaluated its effect on ethanol-induced depression-like behavior in rats (Valcheva-Kuzmanova et al. 2013b). Alcohol administration has been shown to trigger hippocampal BDNF reduction and depressogenic effects in rats (Hauser et al., 2011). It was administered twice daily for 14 days, with *Aronia* fruit juice provided as a pretreatment 1 hour before each alcohol administration. Results from the FST, conducted on day 15, demonstrated that the juice antagonized the alcohol-induced increase in immobility time, with the greatest effect observed at the lowest juice dose (2.5 ml/kg). Neither alcohol nor the juice affected the levels of the pro-oxidant marker thiobarbituric acid-reactive substances levels in serum or brain homogenates, suggesting that the observed effects may involve non-antioxidant mechanisms (Valcheva-Kuzmanova et al. 2013b).

Social isolation in rodents acts as a strong stressor which disrupts the cognitive functions and induces depression-like behavior (Eftimov et al., 2014). Four weeks of social isolation in individual cages induced a tendency to decrease immobility time in the FST, which was ameliorated by subsequent four-week administration of *Aronia* juice at a dose of 10 ml/kg (Eftimov et al., 2014).

Aronia melanocarpa fruit juice was found to counteract ovariectomy-induced depressive behavior following three months of supplementation following the ovariectomy (Georgieva et al. 2022).

Tomic et al. further confirmed the antidepressant-like effect of the juice and identified inhibition of monoamine oxidase A and B (MAO-A and MAO-B) as a putative mechanism (Tomić et al., 2016).

A study of Liu et al. explores the antidepressant potential of polyphenol extracts from *Aronia melanocarpa* fruits and leaves using a corticosterone-induced mouse model of depression and two behavioral tests – FST and Sucrose Preference Test (SPT) (Liu et al., 2022). Corticosterone-induced depression-like behavior reproduces clinical symptoms of depression after repeated injections, pellet implantation or oral administration (with the drinking water) through hypothalamus-pituitary gland-adrenal gland axis dysfunction and BDNF modulation (Mastoli et al., 2025). The SPT utilizes a two-bottle choice paradigm, in which rats are offered a choice between water and sucrose solution. This approach is widely employed to investigate the effects of stress on anhedonia, with increased preference for the sucrose solution indicating a reduced depression-like state. (Willner et al., 1987). Following extract administration, behavioral improvements were observed through FST and SPT, with leaf-derived extracts demonstrating superior efficacy to fruit-derived ones. Analysis of intestinal microbiota and BDNF levels revealed that the extracts enhanced microbial diversity and increased BDNF expression by 18.23% and 81.39%, respectively (Liu et al., 2022). These findings suggest that *Aronia melanocarpa* polyphenols may alleviate depressive-like behavior by modulating gut microbiota and neurotrophic signaling pathways.

Strengths and limitations of the current evidence

The current body of literature on the neuropsychopharmacological effects of *Aronia melanocarpa* offers several notable strengths. A substantial number of preclinical studies provide consistent evidence supporting cognitive-enhancing, anxiolytic-like, and antidepressant-like effects. These studies employ a variety of well-validated behavioral models—including the MWM, EPM, FST, and SPT—which enhances the reliability of the observed outcomes. Importantly, many investigations extend beyond behavioral endpoints to elucidate underlying molecular and biochemical mechanisms, such as modulation of monoaminergic neurotransmission, inhibition of MAO-A and MAO-B, upregulation of BDNF, reduction of oxidative stress and inflammatory markers, and alterations in gut microbiota composition. Moreover,

multiple studies confirmed the ability of *Aronia* polyphenols, especially anthocyanins, to cross the blood-brain barrier and cerebrospinal fluid barrier, providing pharmacokinetic plausibility for their CNS activity. The use of diverse pathological models—including Alzheimer's disease, ovariectomy-induced estrogen deficiency, MS, and corticosterone-induced depression—adds to the translational relevance and generalizability of the findings. Several studies also demonstrated dose- and time-dependent effects, emphasizing the importance of treatment optimization for achieving beneficial outcomes.

Despite these strengths, several limitations temper the interpretation of the current findings. Clinical evidence remains limited, with only two randomized, double-blind, placebo-controlled trials conducted to date. These studies were performed in healthy adults and did not include participants with diagnosed neuropsychiatric conditions, thus restricting conclusions about clinical efficacy in target patient populations. Furthermore, the reported effects on mood and cognitive performance in humans were modest and inconsistent, with benefits observed primarily in psychomotor speed rather than in attention, memory, or mood regulation. Another limitation involves considerable variability across studies in the type and preparation of *Aronia* products (e.g., fruit juice, dry extract, fermented preparations), dosing regimens, treatment durations, and outcome measures, complicating direct comparisons and meta-analytic synthesis. Standardization of extract composition and polyphenol content is often lacking, which could account for variability in efficacy. In addition, sex-specific responses—though occasionally observed—were not systematically analyzed in most studies, leaving open questions regarding differential effects in males versus females. Finally, the strong emphasis on positive findings across preclinical studies raises concerns about potential publication bias and the underreporting of neutral or negative results.

Overall, while the preclinical evidence is promising and supported by insights into the underlying mechanisms, further well-designed clinical trials are necessary to confirm the therapeutic potential of *Aronia melanocarpa* in neuropsychiatric conditions and to establish standardized guidelines for its use.

CONCLUSIONS

The accumulated evidence highlights *Aronia melanocarpa* as a promising candidate for supporting neuropsychiatric health, particularly in mitigating cognitive decline, anxiety, and depression. Its beneficial effects are likely mediated through antioxidant, anti-inflammatory, neuroprotective, and neurotransmitter-modulating mechanisms. While preclinical studies offer robust support, human trials remain limited and show variable outcomes. Further well-designed clinical research is essential to confirm efficacy and establish optimal dosing strategies.

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