DTOX CAPS Brain & Balance Complex

Daily dose (DDD): 5 capsules

Daily-dose context:
A daily dose of 5 capsules represents a functional nutritional dosing level which, for most ingredients, approaches or enters the range used in clinical and interventional studies targeting stress, cognitive load, fatigue, and nervous-system support. At this dose, it is appropriate to speak about a biologically relevant effect, not merely "micro-support."

Composition – daily dose (5 capsules)

- **Lion's mane (Hericium erinaceus)** extract 10:1 (30% polysaccharides) – **800 mg**
- **Reishi (Ganoderma lucidum)** extract (30% polysaccharides) – **650 mg**
- **Ashwagandha KSM-66® (Withania somnifera, 5% withanolides) – 300 mg**
- **L-theanine (from green tea, 98%) – 200 mg**
- **Citicoline (CDP-choline) – 400 mg**
- **Phosphatidylserine (20%) – 300 mg**
- **Magnesium bisglycinate (10–12%) – 200 mg**
- **Vitamin C (sodium ascorbate) – 100 mg**
- **L-cysteine hydrochloride – 350 mg**
- **Curcumin (Curcuma longa, 95%) – 25 mg**
- **Piperine (black pepper, 95%) – 5 mg**
- **Saffron (Crocus sativus, 3% safranal) – 30 mg**
- **Pyrroloquinoline quinone (PQQ) – 10 mg**
- **Coenzyme Q10 (98%) – 100 mg**

Neuroprotective and nootropic compounds for brain health (overview of effects and evidence)

Lion's mane (Hericium erinaceus) – 10:1 extract (30% polysaccharides)

Rationale for use:
Lion's mane (Hericium erinaceus) is a medicinal mushroom with pronounced neuroprotective properties. It contains polysaccharides (especially β-glucans) and terpenoids (hericenones, erinacines) that support nerve growth factor (NGF) and thereby stimulate neuronal growth and regeneration. Research indicates that lion's mane extracts improve neurogenesis, memory, and concentration and may protect against neurodegenerative changes. Terpenoid constituents cross the blood–brain barrier and increase NGF levels in the brain, which helps maintain neuronal survival and function. Beyond antioxidant activity (reduction of oxidative stress and inflammation in brain tissue), lion's mane also exerts anti-inflammatory effects—reducing NF-κB activity and pro-inflammatory cytokines, thereby mitigating neuroinflammation.

Clinical evidence:
Several clinical studies have been conducted to date. In a randomized placebo-controlled trial in Japanese patients with mild cognitive impairment (age 50–80), 16 weeks of lion's mane extract led to a significant improvement in cognitive function versus placebo. However, the effect diminished after discontinuation, suggesting that long-term administration may be necessary to maintain benefit. Another pilot study in early Alzheimer's disease suggested improved memory and reduced neuropsychiatric symptoms with regular lion's mane use—likely due to NGF stimulation and suppression of brain inflammation. Findings on mood are also of interest: a small clinical study demonstrated reduced anxiety and improved mood in individuals using lion's mane, likely via neurotrophic and anti-inflammatory effects.

Relevance for cannabis users:
The neuroregenerative activity of lion's mane may also be beneficial for chronic THC users. Long-term cannabis use may reduce receptor density and weaken neuroplasticity; NGF-supporting compounds in lion's mane could help restore neuronal connections and function. Anti-inflammatory and antioxidant effects additionally protect brain cells from oxidative stress associated with smoking cannabis. Although direct studies in cannabis users are lacking, the overall profile of lion's mane (improved memory, concentration, and mood) suggests it could help reduce cognitive deficits and mood discomfort arising from chronic marijuana use. Lion's mane is well tolerated; however, larger clinical trials are needed to confirm these benefits in cannabis users.

Source studies:
The effects described above are supported by numerous preclinical and clinical works that rank H. erinaceus among promising nutraceuticals for cognitive support and neuroprotection. Although current clinical data are limited by small sample sizes, the overall trend is improved cognition (especially memory) in older patients and relief of mild anxiety and depressive symptoms. These findings support the use of lion's mane as an adjunct therapy for dementia prevention and mitigation of cognitive impairment.

Reishi (Ganoderma lucidum) – extract 30% polysaccharides

Rationale for use:
Ganoderma lucidum (reishi) is another medicinal mushroom with significant immunomodulatory and neuroprotective effects. Its polysaccharides (especially β-glucans) act as antioxidants and protect neurons from oxidative damage. In cellular and animal models, polysaccharide extracts of

reishi reduce oxidative-stress–induced neuronal apoptosis—suppressing activation of caspases and pro-apoptotic proteins (Bax, Bim) and increasing anti-apoptotic Bcl-2. Reishi triterpenoids (ganoderic acids) have strong anti-inflammatory effects: they inhibit the NF-κB pathway, reduce TNF-α, IL-6 and other cytokines, and increase expression of the antioxidant enzyme heme oxygenase-1. These mechanisms contribute to protecting neurons from chronic inflammation and oxidative damage involved in the pathogenesis of neurodegenerative diseases. In addition, some reishi constituents may support neurogenesis and cognitive function—for example, reishi polysaccharides in mice with an Alzheimer's model improved memory and increased proliferation of neuronal progenitors in the hippocampus. Reishi is also traditionally considered an "adaptogen" that helps the body cope with stress. Mushroom sterols and peptides in reishi may influence the GABAergic system, which could explain its mild sedative and anxiolytic effects described in traditional medicine.

Clinical and preclinical evidence:
Clinical studies with reishi extracts have shown improvements in subjective well-being and reduced fatigue in older patients. However, the more substantial evidence comes from preclinical findings: in Alzheimer's disease models, reishi improved cognitive performance (e.g., better maze navigation) and protected hippocampal neurons from degeneration. Reishi polysaccharides administered to transgenic Alzheimer's mice reduced amyloid beta deposition in the brain and supported activation of neurotrophic pathways (FGF2/ERK/Akt). In another experiment, reishi improved spatial memory in aging rats, reduced neuroinflammatory markers, and increased antioxidant enzyme levels. These results confirm that Ganoderma lucidum benefits the brain through multiple mechanisms: reducing inflammation and oxidative stress, improving neuronal metabolic function, and preventing apoptosis. Human clinical data in dementia are still preliminary—small studies suggest that reishi extract may mildly improve cognition in Alzheimer's disease, with short-term effects comparable to some standard drugs (e.g., cholinesterase inhibitors). Reishi is generally safe; at high doses, gastrointestinal discomfort or allergic reactions have occurred rarely.

Relevance for cannabis users:
Chronic THC use may induce inflammatory changes and oxidative stress in the brain. Reishi, due to its strong antioxidant and anti-inflammatory effects, may help "counterbalance" these unfavorable influences. Reishi polysaccharides protect neurons against oxidative death and triterpenes suppress inflammatory cytokines, potentially contributing to restoration of homeostasis in the endocannabinoid system under long-term THC burden. Although direct studies are unavailable, it is reasonable to expect that in cannabis users, reishi could mitigate cognitive issues (forgetfulness, reduced concentration) by improving neuronal mitochondrial function and reducing neuroinflammation. Furthermore, the adaptogenic action of reishi may support resilience against stress and anxiety, which is valuable both for the general population and for cannabis users—particularly during THC discontinuation, which is often accompanied by increased stress and restlessness. Overall, Ganoderma lucidum represents a promising dietary supplement for brain nutrition and neuronal protection under burden states.

Ashwagandha (Withania somnifera) KSM-66® – extract 5% withanolides

Rationale for use:
Ashwagandha is a well-known adaptogen with pronounced effects on reducing stress and anxiety and supporting cognitive function. It contains withanolides (steroidal lactones) that act as neuropharmacologically active compounds—mimicking GABAergic effects and modulating cholinergic receptors. In vitro and in vivo studies indicate that ashwagandha behaves as a GABA mimetic and cholinomimetic, supporting calming neuronal activity and improved cognition. Some

ashwagandha metabolites have been found to agonize α7 nicotinic acetylcholine receptors, potentially improving attention and memory. Overall, ashwagandha supports neurotransmitter balance in the brain—raising inhibitory mediators (GABA) and modestly increasing serotonin and dopamine in the limbic system (indirectly via reduced cortisol and inflammation). It has demonstrable anti-stress effects: reducing cortisol levels and alleviating anxiety symptoms. Mechanistically, ashwagandha dampens HPA-axis hyperactivity—reducing excessive ACTH release and adrenal reactivity. It also increases expression of brain-derived neurotrophic factor (BDNF) and supports dendritic growth in experimental models, contributing to neuroplasticity.

Clinical evidence:
Ashwagandha's effects on stress and anxiety are documented in multiple RCTs. A systematic review of 7 clinical studies (n=491) found that ashwagandha extract over 6–8 weeks significantly reduced perceived stress and anxiety (via validated scales) and reduced serum cortisol versus placebo. The strongest effects were observed at doses around ~600 mg/day. More recent studies support these conclusions: for example, a 30-day RCT with NooGandha® (225 or 400 mg/day) in adults with chronic stress reduced anxiety and depression and even appetite, with the 225 mg group showing lower salivary cortisol versus placebo. Another 90-day study (300 mg/day KSM-66) in healthy individuals with high stress demonstrated improved stress scores and sleep quality. Cognitive benefits are also supported: in an 8-week study in older adults (600 mg/day), improvements were observed in memory, executive function, attention, and processing speed. Similarly, in patients with mild cognitive impairment, ashwagandha improved immediate and general memory and executive function. Even in young healthy individuals, an acute effect has been shown—one 400 mg dose improved working memory and sustained attention over 6 hours of testing versus placebo. Meta-analyses thus rank ashwagandha among promising natural anxiolytics and nootropics, comparable in efficacy to common pharmacological agents in milder anxiety/insomnia states, but with better tolerability.

Relevance for cannabis users:
Ashwagandha may be particularly beneficial for individuals who use cannabis, in the context of stress and anxiety reduction. Many cannabis users experience anxiety or insomnia during discontinuation; ashwagandha has demonstrated reductions in anxiety symptoms and improvements in sleep quality, which could mitigate withdrawal-related discomfort. In addition, chronic THC exposure may disrupt stress-axis balance and increase cortisol—ashwagandha normalizes this hormone, contributing to balancing the endocannabinoid system and stress resilience. A potential influence on THC tolerance is also theorized: adaptogenic effects could reduce the perceived need to escalate cannabis doses by stabilizing neurotransmitter networks. Moreover, ashwagandha improves cognitive functions (memory, attention) that may be weakened in regular cannabis users. Finally, withanolides have neuroprotective effects—reducing neuroinflammation and oxidative damage—which may protect the brain from long-term consequences of cannabinoid use. Overall, ashwagandha can be recommended as a supportive measure for improving psychological balance and cognition in cannabis-using patients, with a scientifically documented safety profile and multiple CNS benefits.

Green tea extract – 98% L-theanine

Rationale for use:
L-theanine is an amino acid from green tea with unique psychophysiological effects—inducing relaxation without sedation and improving concentration. Structurally similar to glutamate, theanine acts on glutamatergic receptors in the brain as a partial agonist/antagonist, modulating excitatory transmission. It partly blocks excessive NMDA receptor activation and increases levels of the

inhibitory neurotransmitter GABA. It also affects dopamine and serotonin levels—animal studies show that theanine increases monoamine concentrations in the brain and supports synaptic plasticity in the hippocampus. L-theanine also stimulates alpha brain waves, which correlate with relaxed attention. Overall, it improves the ability to focus, especially when combined with caffeine (a synergistic nootropic effect). Finally, it has neuroprotective effects: lowering stress hormones, increasing BDNF expression, and exhibiting antioxidant activity (protecting neurons from excitotoxicity and improving memory in stressed animals).

Clinical evidence:
L-theanine has been evaluated in several clinical studies in healthy individuals under psychological stress. In a randomized crossover study in 30 healthy adults (200 mg theanine daily for 4 weeks), there was a significant reduction in anxiety symptoms, improved sleep quality, and reduced depression scores compared with placebo. Some cognitive functions also improved—specifically verbal fluency and executive function (better performance on executive tests after theanine). These benefits were most pronounced in individuals with mild cognitive complaints. Other studies confirm that 4–8 weeks of L-theanine supplementation (typically 200–400 mg/day) reduces stress reactivity—for example, in healthy individuals exposed to an acute stressor, theanine reduced cortisol elevation and subjective stress compared with placebo. L-theanine has also shown improvements in attention and processing speed: in one study in middle-aged adults it improved working memory and executive function in tests of cognitive flexibility. Overall, systematic reviews report that theanine supports mental well-being, reduces anxiety, and mildly improves cognition, especially in individuals with higher stress levels. Importantly, theanine does not cause drowsiness or cognitive dulling—on the contrary, it helps maintain attention (in vigilance tests, theanine prevented a decline in reaction speed at the end of the day compared with placebo). This makes it an attractive nutraceutical for managing stress in demanding professions.

Relevance for cannabis users:
Cannabis users may benefit from theanine in several ways. First, theanine reduces anxiety and stress, which may help those who use cannabis for anxiety, or those in whom THC sometimes induces unpleasant anxiety or paranoia. Theanine supplementation could smooth the “edges” of THC euphoria—promoting a calmer, more focused state without impairment. Second, theanine improves sleep quality and circadian rhythm (shortens sleep onset latency and improves sleep continuity), which can be beneficial during cannabis discontinuation, when insomnia often occurs. Third, theanine has neuroprotective action: it attenuates excessive glutamate release and protects neurons from excitotoxic damage. Chronic THC use may lead to some dysregulation of glutamatergic signaling in the brain; theanine helps restore balance by binding to glutamate receptors and modulating their activity. This could theoretically contribute to reduced tolerance—there are indications that substances blocking excessive NMDA receptor stimulation slow the development of tolerance to psychoactive substances. While this has not been clinically tested for THC, the mechanism is plausible. Theanine is very safe (commonly consumed in tea) and therefore represents a suitable harm-reduction support for cannabis users—reducing anxiety, supporting cognitive performance, and protecting the brain from burden.

Citicoline (CDP-choline)

Rationale for use:
Citicoline is a precursor of brain phospholipids and a choline source for acetylcholine synthesis. In the body, CDP-choline breaks down into cytidine (converted to uridine) and choline; these components are reused for phosphatidylcholine formation in neuronal membranes. Citicoline thus improves integrity and function of neuronal membranes, supports repair, and enhances synaptic

plasticity. It also increases acetylcholine synthesis in the hippocampus and neocortex and increases dopamine availability in the corpus striatum. Studies show that citicoline increases levels of several neurotransmitters: norepinephrine (in cortex and hypothalamus), dopamine (in striatum), and serotonin (in cortex and hypothalamus). It also increases expression of the glutamate transporter EAAT2, thereby reducing excessive glutamatergic activity in the brain. This mechanism is important for protection against excitotoxic damage. Overall, citicoline has neuroprotective effects (membrane stabilization, anti-apoptotic action) and nootropic effects (supporting cognitive pathways including cholinergic function).

Clinical evidence:
Citicoline is used in Europe as a medicinal product in stroke and cognitive disorders. A Cochrane meta-analysis in vascular dementia found that citicoline improved cognitive performance compared with placebo and was very well tolerated. In older patients with mild cognitive impairment, citicoline administration resulted in greater improvement in verbal memory than placebo. In post-stroke studies, citicoline improved cognitive function and was more effective at higher doses (2–4 g/day). In neurorehabilitation, results are mixed—e.g., a large trial in traumatic brain injury did not show a significant effect versus placebo, which may be related to study design. In psychiatry and addiction medicine, citicoline has been explored as adjunct therapy: small studies in addictions suggested reduced craving and improved cognition. A noteworthy finding comes from a pilot study in cocaine dependence, where 8 weeks of 1,000 mg citicoline did not significantly reduce cocaine use but had a side effect of reducing concurrent cannabis and alcohol use in the citicoline group. This suggests citicoline may support impulse control and reduce incidental use of other addictive substances. The mechanism may relate to modulation of the dopaminergic system (citicoline increases dopamine release and D2 receptor expression) and improved frontal-lobe function (executive control). Additional pilot RCTs in adolescent marijuana dependence (NAC studies) with citicoline have not yet been published, but by analogy with the cocaine findings, effects on cognitive performance and reduced use frequency are being explored.

Relevance for cannabis users:
Citicoline may offer several potential benefits in chronic cannabis use. Cognitively, it may help alleviate memory and attention deficits linked to long-term THC use by supplying choline for acetylcholine synthesis, thereby improving memory functions often impaired in regular smokers. It also supports restoration of neuronal membranes and synapses, potentially contributing to faster recovery of receptors (e.g., downregulated CB1 receptors) during abstinence. Citicoline's modulation of dopamine and glutamate is also relevant—chronic THC use is often associated with disrupted glutamate homeostasis in the nucleus accumbens; citicoline increases EAAT2 transporter expression and normalizes glutamate transmission, which resembles the effect of N-acetylcysteine used in addiction treatment. This could reduce craving and tolerance to cannabis. Finally, by increasing brain energy metabolism (ATP synthesis in neurons), citicoline can counter "brain fog" and fatigue. Although direct studies of citicoline in THC dependence are limited, the literature suggests it could be a useful adjunct to improve self-control and restore cognitive function in patients attempting to reduce or stop cannabis use. Citicoline is safe, commonly available as a dietary supplement, and thus represents an interesting brain-support option for this population.

Phosphatidylserine – 20% powdered extract

Rationale for use:
Phosphatidylserine (PS) is a phospholipid naturally present in neuronal cell membranes, crucial for membrane fluidity, receptors, and brain signaling. PS supplementation (historically from bovine brain, now from soy) has been shown to improve cognitive function in the aging brain and regulate

stress response. By modulating receptors (e.g., NMDA, AMPA) and ion channels, PS supports efficient synaptic transmission. In older individuals, brain PS levels decline with age, which is associated with memory deterioration; PS supplementation can partially restore these functions. For example, clinical studies from the 1980s–1990s showed that 300 mg PS daily in patients with age-related memory loss improved recall and attention compared to placebo. Modern research has also demonstrated an effect of PS on the stress axis: PS reduces excessive cortisol release in response to stress. In young healthy individuals, PS (400–800 mg/day) significantly reduced cortisol rise during intense physical and mental stress. Specifically, 600 mg PS/day for 10 days reduced cortisol area-under-the-curve during a stress test by ~35% versus placebo. A higher dose of 800 mg reduced peak cortisol during stress by up to 30%. PS thus prevents excessive HPA-axis activation and maintains anabolic–catabolic balance (increasing the testosterone/cortisol ratio). In cognition, PS has also been shown to improve memory and attention under stress. Young people given PS showed better mood and higher accuracy in cognitive tasks during mental stress compared with placebo. Mechanistically, this involves dampening stress hormones and maintaining neurotransmitter balance (PS may increase dopaminergic transmission in the prefrontal cortex and improve acetylcholine signaling).

Clinical evidence:
More than 10 placebo-controlled studies have evaluated phosphatidylserine in cognitive disorders. Most found improvements in memory, attention, and verbal fluency in older adults with age-related memory decline at a dose of 300 mg PS daily for 3–6 months. For example, in one RCT (Jorissen et al.), healthy seniors with memory complaints achieved better results in memory tests than the placebo group. In Alzheimer's disease, results are mixed—some small studies suggested improvements in cognition and behavior in early stages, others did not. The stress-modulating effect was confirmed by Hellhammer's group: in a randomized study, 400 mg PS daily for 6 weeks in healthy young people significantly reduced anxiety and improved mood during exposure to a social stressor (Trier Social Stress Test) versus placebo. Interestingly, the cortisol effect was not linearly dose-dependent—in one study 400 mg had a greater effect on reducing cortisol during mental stress than 600–800 mg, suggesting the optimal mental-health dose may be around 300–400 mg. PS has also been tested in children with ADHD (combined with omega-3), with results suggesting improved attention and reduced hyperactivity. Overall, phosphatidylserine is evaluated as a safe nootropic with demonstrated effects on cognitive aging and as an adaptogen reducing stress load (some authors refer to it as a "nutritional cortisol inhibitor").

Relevance for cannabis users:
Cannabis users may gain dual benefit from phosphatidylserine: cognitive and endocrine. First, PS may improve memory function and mental speed, which can be impaired in heavy THC users. It helps restore synaptic membrane fluidity and thus receptor function (it may support a "reset" of downregulated CB1 receptors in neuronal membranes). Second, PS lowers cortisol and may mitigate the rebound phenomenon after cannabis discontinuation, when stress reactivity is increased. Many users report irritability and stress during abstinence—PS could blunt this and improve mood during that period. Lower cortisol also means reduced risk of anxiety attacks and improved sleep (THC abstinence is accompanied by insomnia, amplified by high evening cortisol; PS could help restore the physiological evening cortisol decline). It can also be speculated that PS might reduce development of THC tolerance—tolerance is partly driven by stress and glutamatergic excitotoxicity from frequent stimulation, and PS attenuates both (protecting neurons from excess glutamate and apoptosis). Finally, PS may help normalize sleep and circadian rhythm disturbances by supporting a healthier daily cortisol profile via HPA-axis modulation. For cannabis patients who often use at night (and may have disrupted REM sleep), PS could support recovery of higher-quality sleep when THC is reduced. Overall, phosphatidylserine is a promising nootropic and nutritional therapy for brain support in this population, with substantial safety and efficacy data in other groups (seniors, athletes, ADHD, etc.).

Magnesium bisglycinate (magnesium chelate, 10–12% Mg)

Rationale for use:
Magnesium is an essential mineral with a key role in the nervous system—it is a cofactor for >300 enzymes and a natural modulator of NMDA receptors. Under physiological conditions, magnesium ions block the NMDA channel, preventing excessive Ca^{2+} influx into neurons and protecting against excitotoxic damage. With magnesium deficiency, neuronal excitability increases, clinically manifesting as nervousness, anxiety, insomnia, and cognitive worsening. Magnesium supplementation in individuals with low Mg status reduces anxiety and improves sleep—a systematic review of 18 studies suggested a beneficial effect on subjective anxiety particularly in people predisposed to anxiety (PMS, hypertension, mild anxiety disorder). Magnesium acts on the psycho-neuro-endocrine axis: it regulates HPA activity (reducing ACTH release and adrenal sensitivity to ACTH), decreases hyperexcitability in limbic circuits (acting as a natural "dampener" of the amygdala), and increases GABA_A receptor function. As a result, magnesium has demonstrable anxiolytic and anti-stress effects. Clinical studies show that magnesium administration (typically 200–400 mg/day elemental magnesium) for 4–8 weeks reduces anxiety and stress scores across populations—for example, women with PMS showed reduced anxiety symptoms and improved mood compared with placebo; in individuals with high stress, magnesium improved subjective well-being and reduced cortisol. Magnesium also improves sleep quality and may have mild antidepressant effects (Mg deficiency is associated with depression). Mechanistically, in depression models magnesium increased BDNF and reduced inflammatory cytokines in the brain. The bisglycinate form is particularly suitable—glycine itself is a calming neurotransmitter, and magnesium bisglycinate chelate is characterized by excellent absorption and minimal gastrointestinal side effects.

Clinical evidence:
Smaller studies exist specifically for magnesium bisglycinate on sleep and anxiety. In general, meta-analyses support magnesium's role in mental health: in randomized studies magnesium significantly improved subjective stress and anxiety in people prone to magnesium insufficiency. Combination with vitamin B6 may further enhance effects (in one study Mg+B6 reduced stress more than Mg alone, although Mg alone was also effective). Regarding cognitive function, magnesium's effect is indirect: specialized forms (e.g., magnesium threonate) have shown memory improvement in older adults by increasing brain magnesium concentration. Standard magnesium bisglycinate is not patented in this way, but in people with low Mg, replenishment may be associated with improved concentration and reduced fatigue. Magnesium also has neuroprotective potential: in neurology, IV magnesium has been used in acute brain ischemia to limit injury (with mixed trial outcomes). Nonetheless, in laboratory models magnesium reduces neuronal apoptosis, suppresses excessive NMDA activation, and reduces glutamate release. Magnesium also strengthens GABA_B receptors and reduces adrenaline release, contributing to neuroprotection. Epidemiological studies suggest low serum magnesium is a risk factor for dementia, whereas adequate magnesium levels may be protective. Overall, magnesium supplementation is considered a simple but effective intervention to improve stress tolerance and potentially cognitive reserve, especially in populations with insufficient dietary magnesium intake (often estimated at ~50–70% in Western countries).

Relevance for cannabis users:
Magnesium has particularly interesting connections in the context of regular cannabis use. It may reduce excitotoxicity and tolerance: research in other drugs (opioids, stimulants) has shown that magnesium can slow tolerance development by acting on NMDA receptors and the dopaminergic system. While direct cannabis research is lacking, THC tolerance mechanisms also involve

glutamatergic pathways and receptor downregulation—magnesium, as an NMDA antagonist and membrane stabilizer, could theoretically slow adaptation to THC and help maintain efficacy at lower doses. Anecdotally, users report that magnesium supplementation reduces the perceived need to escalate cannabis dose, which aligns with these mechanisms. Magnesium may also relieve withdrawal symptoms: after stopping THC, restlessness, muscle tension, irritability, and sleep disturbances are common—symptoms linked to nervous-system hyperexcitability that magnesium can dampen. Magnesium may alleviate insomnia and nervousness during abstinence due to its calming effect (supporting GABA and muscle relaxation). It also protects against oxidative burden associated with smoking: smoke generates free radicals, and chronic THC use may increase reactive metabolites; magnesium activates antioxidant enzymes (SOD, GPx) and reduces lipid peroxidation, protecting neurons and vasculature. Magnesium may also contribute indirectly to endocannabinoid balance: stress reduces endocannabinoid levels, and magnesium reduces the stress cascade, potentially normalizing endocannabinoid signaling. Many cannabis users also have impaired metabolic and sleep profiles—magnesium helps with insulin sensitivity, blood pressure, and sleep, supporting overall health. In summary, magnesium (especially in bisglycinate form) is a simple, safe supplement that may reduce stress, anxiety, insomnia, and potentially tolerance in cannabis users, while protecting the nervous system from long-term burdens.

Sodium ascorbate (vitamin C)

Rationale for use:
Vitamin C is a key antioxidant in the central nervous system and a cofactor in neurotransmitter synthesis. It is present at high concentrations in the brain—participating in norepinephrine synthesis (hydroxylation of dopamine to norepinephrine) and in serotonin synthesis from tryptophan. It also protects neurons from oxidative stress by directly scavenging free radicals and regenerating other antioxidants (e.g., vitamin E). During stress responses, the body uses large amounts of vitamin C—animals capable of synthesizing it dramatically increase vitamin C production under burden. Humans lack this capacity, so supplementation can help balance stress responses. Vitamin C, together with cortisol and adrenaline, forms part of the acute stress response: during adrenal activation, vitamin C is also released into circulation (from the adrenal cortex). In vitamin C deficiency, stress response becomes dysregulated. Ascorbate supplementation may therefore reduce negative stress impacts. Specifically, an RCT by Brody et al. found that 14 days of high-dose vitamin C (2×500 mg sustained release) in healthy volunteers led to lower blood pressure, lower perceived stress, and faster return of cortisol to normal after an acute psychological stressor (public speaking) compared to placebo. Thus, vitamin C blunts excessive cortisol response and subjectively improves stress coping. Additionally, vitamin C supports neurotransmitter balance: adequate vitamin C supports dopamine release (as a cofactor for its release from neurons) and modulates glutamatergic transmission (protecting against excess glutamate). In experimental models, vitamin C increased expression of TrkB receptors (for BDNF), supporting neuroplasticity.

Clinical evidence:
Classic clinical research relates to anxiety and stress: in a public-speaking stress study, individuals taking vitamin C for 2 weeks had a lower cortisol rise and lower blood pressure during the speech compared to placebo, and reported less stress and better mood. Another study in medical students during exam periods found that the vitamin C group had lower anxiety levels and fewer depressive episodes. A meta-analysis on mood suggests a mild antidepressant effect of higher-dose vitamin C in subclinical depression (likely via reduced neuroinflammation and oxidative stress). In seniors with cognitive impairment, lower blood vitamin C levels have been observed; supplementation is being studied as part of combined antioxidant therapy to slow cognitive decline. Vitamin C alone is unlikely to produce dramatic dementia improvement, but in synergy with vitamin E and other

antioxidants, some protection against further deterioration has been observed. Findings are also notable in traumatic brain injury and hemorrhage—vitamin C levels are extremely low and replacement may improve neurological outcomes (vitamin C is administered in some centers, e.g., in subarachnoid hemorrhage, for brain protection). Overall, ascorbate is very safe; mega-doses may cause diarrhea or kidney stones in predisposed individuals.

Relevance for cannabis users:
In chronic cannabis smokers, vitamin C may serve several useful roles. Detoxification and lung protection: smoke (including cannabis smoke) generates free radicals in the lungs; vitamin C neutralizes these radicals and protects lung tissue. Improved antioxidant status also benefits vasculature and the brain—vitamin C reduces oxidative damage to lipids and proteins in the brain, potentially lowering neurodegeneration risk associated with chronic inflammatory burden from smoking. Stress axis: many people use cannabis to cope with stress; paradoxically, chronic use can dysregulate the stress axis (THC can exhaust adrenal responsiveness). Vitamin C helps normalize stress response—reducing excessive cortisol release and acting as a "buffer" during stress. Thus, it may reduce withdrawal-related irritability and restlessness when discontinuing THC. Neurotransmitters: chronic THC sometimes contributes to dopaminergic deficit in reward circuitry (long-term users may show reduced motivation and dysphoria upon stopping). Vitamin C supports dopamine and norepinephrine synthesis, potentially improving mood and motivation in former or reducing users. It also participates in synthesis of the endocannabinoid N-arachidonoyldopamine (NADA)—the mechanism is not fully understood, but sufficient vitamin C may support endocannabinoid balance. Immunity and inflammation: the endocannabinoid system is closely linked to immunity; high-dose vitamin C modulates immune response (reducing inflammatory cytokines such as IL-1β, TNF-α), potentially balancing immune dysregulation associated with chronic smoke exposure. Experimental work shows vitamin C reduced neuroinflammatory marker HMGB1 and inhibited NF-κB activation. For cannabis users, this may mean reduced chronic brain inflammation risk. Overall, vitamin C functions as a universal supportive factor: widely available, safe, and low-cost. In this group, antioxidant and anti-stress vitamin support may meaningfully improve neurological well-being. Therefore, sodium ascorbate is a logical component of a comprehensive brain nutrition formula—enhancing the effects of other compounds (e.g., recycling oxidized vitamin E), protecting neurons, and supporting overall vitality.

L-cysteine hydrochloride (glutathione precursor)

Rationale for use:
L-cysteine is an amino acid required for synthesis of glutathione, the main intracellular antioxidant in the brain. In practice, N-acetylcysteine (NAC) is often used as a supplement because it is better absorbed; however, L-cysteine HCl serves a similar role—providing cysteine for maintaining the glutathione cycle. Higher glutathione means stronger neuronal protection against oxidative stress and detoxification of free radicals and toxins. Beyond antioxidant action, cysteine/NAC has a significant effect on the glutamate system: NAC increases activity of the cystine–glutamate antiporter (system Xc^-) in the brain, which helps normalize disrupted glutamate levels in synaptic spaces. Chronic use of addictive substances (including THC) disrupts this antiporter and leads to accumulation of extrasynaptic glutamate, associated with addictive behavior and craving. NAC can reverse this pathology—normalizing glutamate release in the nucleus accumbens and thereby reducing pathological compulsion to use the drug. NAC also supports expression of EAAT2 glutamate transporters on glia, improving glutamate reuptake. L-cysteine thus functions as a neurochemical stabilizer: increasing glutathione (→ less oxidative damage and neuroinflammation) and modulating neurotransmitter systems (glutamate, dopamine). NAC is also known to reduce dopaminergic sensitization—raising density of mGluR2 glutamate receptors, which dampen

dopamine release in reward circuits and thereby reduce pathological reinforcement of addictive behaviors.

Clinical evidence:
The strongest evidence for cysteine/NAC lies in addiction and impulse-control disorders. A randomized placebo-controlled trial of NAC in cannabis dependence (adolescents and young adults; 8 weeks; 2×1200 mg/day) showed that NAC doubled the odds of abstinence compared with placebo (odds ratio 2.4; p=0.03) when combined with psychosocial therapy. This was a breakthrough result—the first pharmacotherapy to show an effect on marijuana dependence in an RCT. NAC was well tolerated and led to a higher proportion of negative THC urine tests during treatment. After the intervention, the NAC group still showed a trend toward lower use. Another (negative) study in adult cannabis users did not confirm the effect, suggesting NAC may be more effective in younger populations or when combined with motivational therapy. Beyond cannabis: NAC has shown benefit in cocaine dependence, methamphetamine dependence, gambling, and trichotillomania—generally reducing craving and improving impulse control. For example, in cocaine users NAC did not directly reduce use but improved cognitive performance and working memory and increased retention in treatment. In bipolar depression and schizophrenia, NAC improved symptoms in some studies (reduced negative symptoms in schizophrenia, accelerated depression remission). In neurology, NAC has been studied in Parkinson's disease, Alzheimer's disease, and brain injury—with promising but not yet definitive results (improved mitochondrial markers, trends toward slower progression). The main contribution of NAC/cysteine in the brain therefore remains glutathione support and glutamate homeostasis—therapeutically valuable across many neuropsychiatric conditions. L-cysteine HCl itself is not studied separately to the same extent, but given its biological conversion to cysteine in the body, a broadly similar physiological role is assumed.

Relevance for cannabis users:
Here, the relevance of L-cysteine (and especially NAC) is central. Cysteine may influence THC tolerance and receptor recovery: chronic THC reduces CB1 receptor availability, while NAC accelerates normalization of glutamate signaling, potentially shortening the time needed to "reset" receptor pathways during abstinence. This supports faster recovery of sensitivity to natural stimuli and reduces anhedonia during withdrawal. Craving reduction and relapse prevention: NAC demonstrated clinically in adolescents robust craving suppression and higher abstinence rates—patients reported less urge to smoke and had more negative THC tests. By restoring glutamate control in the nucleus accumbens, reward circuitry stabilizes and individuals better resist triggers. NAC can thus be seen as a partial pharmacological support to psychosocial cannabis-dependence treatment. Neuroprotection: smoking cannabis carries oxidative and inflammatory burden; NAC increases glutathione, protecting neurons from toxic smoke metabolites and inflammatory damage, potentially reducing risk of cognitive worsening in long-term misuse. For example, adolescents with cannabis use have described executive-function deficits—NAC has been associated with improved working memory and cognitive flexibility (as suggested by sub-analyses in cocaine studies). Endocannabinoid balance: NAC normalizes not only glutamate, but also stress-related imbalances in dopamine and endocannabinoids. Chronic stress reduces anandamide; NAC reduces stress (antioxidant, anti-inflammatory effects) and may thereby support endocannabinoid system restoration. Overall, cysteine/NAC is among the best-documented compounds supporting cannabis users: reducing craving, helping maintain abstinence, and protecting the brain. Therefore, its inclusion in a nootropic formula aimed at recovery during cannabis reduction or abstinence is justified.

Curcumin (Curcuma longa) – 95% curcuminoids extract

Rationale for use:
Curcumin is a polyphenol from turmeric with potent anti-inflammatory and antioxidant effects. In the CNS, it inhibits several inflammatory pathways—dampening NF-κB activation, lowering pro-inflammatory cytokines (TNF-α, IL-1β, IL-6), and inhibiting COX-2 and iNOS. This protects neurons from chronic inflammation contributing to neurodegeneration. Curcumin also directly scavenges free radicals and increases endogenous antioxidant enzymes (catalase, SOD, glutathione peroxidase). It can cross the blood–brain barrier to a limited extent, and its metabolites accumulate in structures such as hippocampus and amygdala. Experiments show curcumin supports neurogenesis and synaptic plasticity—for example, increasing BDNF levels and improving survival of new hippocampal neurons in stressed animals. It also exhibits anti-amyloid effects—reducing amyloid beta and tau aggregation and supporting microglial clearance. Clinically relevant is its antidepressant action: it modulates neurotransmitter systems (increasing serotonin and dopamine availability via MAO inhibition and inflammatory cytokine reduction) and has shown significant mood improvement vs placebo in several RCTs in depression. Curcumin is thus a multifunctional nutraceutical—simultaneously targeting inflammation, oxidative stress, and neurotrophic signaling.

Clinical evidence:
Curcumin's brain effects have been studied in healthy older adults, mild cognitive impairment, Alzheimer's disease, depression, and more. **Cognitive function:** A systematic review of 12 studies (2024) reported that in 10 of 11 RCTs, bioavailable curcumin forms significantly improved cognitive outcomes vs controls. In healthy older adults without dementia, curcumin improved working memory and mood; one study showed that 4 weeks of curcumin led to ~20% improvement in cognitive performance (memory tests) and reduced "confusion" vs placebo, with benefits maintained at 12 weeks. In people with obesity/prediabetes, curcumin improved verbal memory and processing speed and improved brain blood flow, suggesting benefit for metabolic and vascular brain health. In Alzheimer's disease, a 22-week RCT reported that a turmeric extract (30 mg twice daily) improved cognition similarly to donepezil with fewer adverse effects. A meta-analysis of four RCTs suggests saffron (see later section) and curcumin are among few plant-derived agents showing short-term significant effects on ADAS-cog vs placebo. **Mood/stress:** A meta-analysis of 8 studies concluded curcumin (500–1000 mg/day) significantly improved depressive symptoms short-term, with efficacy comparable to low-dose SSRIs but without their typical adverse effects. Mechanistically, curcumin increases BDNF and reduces inflammatory markers in depressed patients, correlating with symptom relief. **Bioavailability:** Standard curcumin has low absorption, so formulations with piperine or lipid delivery are used; piperine can increase curcumin bioavailability up to 20-fold. Trials showing benefit typically used such enhanced forms (e.g., Longvida®, Meriva®, Theracurmin). Without this, effects may not be achieved (e.g., Ringman et al. found no effect with poorly absorbed curcumin). Curcumin is considered safe; very high doses (>4 g/day) may cause GI discomfort, but doses up to 1 g/day are generally well tolerated.

Relevance for cannabis users:
Chronic THC users may obtain multiple benefits. **Neuroprotection:** Long-term cannabinoid exposure may activate microglia and contribute to neuroinflammation, potentially worsening cognition; curcumin can reduce neuroinflammation and protect synapses. **Antioxidant:** Cannabis smoke contains oxidants; THC metabolism also generates reactive oxygen species; curcumin scavenges radicals and strengthens glutathione systems, reducing oxidative stress in brain and liver. **Mood/anxiety:** During cannabis abstinence, dysphoria, depression, or anxiety often occur; curcumin's mild antidepressant and anxiolytic effects can help stabilize mood. It may also support endocannabinoid-system recovery: there are indications curcumin may raise anandamide by inhibiting FAAH, potentially alleviating withdrawal symptoms similarly to CBD. In mice, curcumin increased CB1 receptor expression in certain brain regions after stress, suggesting potential

restoration of receptor sensitivity. **Cognition:** If cannabis use leads to subjective memory/attention issues, curcumin with piperine may improve cognition (as shown in older adults). Overall, curcumin supports brain health by reducing inflammation, improving mood, and supporting cognition—important for cannabis users seeking harm reduction or recovery. Bioavailability is crucial; in this formula it is supported via piperine.

Black pepper – 25:1 extract (95% piperine)

Rationale for use:
Black pepper extract is rich in piperine, a well-known bioavailability enhancer. Piperine inhibits intestinal and hepatic enzymes (e.g., CYP3A4 and P-glycoprotein), slowing metabolism of co-administered nutraceuticals (such as curcumin) and improving absorption. For example, adding 20 mg piperine can increase curcumin absorption by up to 2000%. In this formulation, black pepper functions as a synergistic bioactivator, potentiating effects of curcumin, PQQ, CoQ10, etc. Beyond pharmacokinetics, piperine also has its own neuropharmacological actions. Experimental studies show antidepressant-like and cognition-enhancing effects: in a rat Alzheimer's model, piperine (5–20 mg/kg) significantly improved memory and reduced hippocampal neurodegeneration, likely via reduced lipid peroxidation and acetylcholinesterase inhibition (increasing acetylcholine availability). Piperine also showed neurotrophic effects in the hippocampus. Other studies indicate piperine improves spatial memory and increases hippocampal neuronal density in models of demyelination and diabetic cognitive impairment. Piperine also has analgesic and anti-inflammatory properties (TRPV1 modulation; reduced NO and PGE_2). Some work suggests piperine inhibits MAO, increasing serotonin and dopamine, potentially explaining observed mood benefits. Additionally, black pepper essential oil contains β-caryophyllene (BCP), a CB2 agonist considered a "dietary cannabinoid" that reduces neuroinflammation and may be anxiolytic without psychoactivity. In extracts standardized to piperine, BCP may be present only in trace amounts; however, whole-pepper extracts may contain terpenes contributing to overall effect.

Clinical and preclinical evidence:
Direct clinical trials of piperine on cognition are limited; it is more often studied in combinations. Preclinical evidence is strong: piperine repeatedly improved memory and reduced pathology in Alzheimer's models (reduced amyloid deposition and tau phosphorylation). In sleep-deprivation models, black pepper extract improved cognition and mood via JAK/STAT3 pathway modulation. Analgesic effects have shown benefit in clinical settings (e.g., piperine patches in arthritis). In depression models, piperine combined with curcumin enhances curcumin's effects via improved bioavailability. Piperine alone shows antidepressant-like activity comparable to imipramine in animal tests, supporting MAO inhibition and monoamine elevation. **Safety:** high doses may irritate the stomach and cause reflux; therefore, extracts typically use 5–10 mg doses that are generally tolerated.

Relevance for cannabis users:
Black pepper is known in cannabis communities as a "trick" for THC over-intoxication—chewing peppercorns or smelling black pepper essential oil is reported to rapidly calm THC-induced anxiety/paranoia. This has a plausible scientific basis: β-caryophyllene activates CB2 receptors and can exert anxiolytic/antipsychotic-like effects via reduced glutamate release and microglial modulation. In this supplement, black pepper provides piperine to improve absorption of curcumin and other lipophilic compounds (PQQ, CoQ10), increasing efficacy. Piperine itself may support cognitive function—if chronic cannabis use impairs memory/attention, anti-AChE effects could strengthen cholinergic transmission and improve memory performance. Its mood-support effects may also help during THC withdrawal-related dysphoria. Black pepper can also support digestion

and nutrient absorption, relevant for users with GI complaints. TRPV1 modulation may relieve headaches and muscle tension that can occur during withdrawal. Overall, black pepper acts as both a catalyst for other ingredients and a contributor of its own neuroprotective and calming effects.

Saffron (Crocus sativus) – extract 3% safranal

Rationale for use:
Saffron is a spice derived from the dried stigmas of Crocus sativus, historically valued for effects on mood and the nervous system. Its main bioactive compounds—safranal (volatile oil) and carotenoids crocins/crocetin—exert antidepressant, anxiolytic, and neuroprotective effects. The antidepressant mechanism primarily involves monoamine modulation: saffron components inhibit reuptake of serotonin, dopamine, and norepinephrine, increasing their synaptic availability similarly to SSRIs/TCAs. It also reduces inflammatory cytokines and increases BDNF, supporting neuroplasticity and mood improvement. Safranal mildly agonizes GABA_A receptors, contributing to anxiolysis and improved sleep. Regarding cognition, saffron shows benefit particularly in neurodegeneration: crocins inhibit amyloid beta and tau aggregation and improve synaptic function. Due to strong antioxidant and anti-inflammatory effects, saffron protects retina and brain from oxidative damage (it has been studied in macular degeneration as well). Traditional Persian medicine described saffron as a "cheering" remedy for melancholy, supported by modern research.

Clinical evidence:
Saffron's antidepressant effects are among the best documented for herbal preparations. A meta-analysis (including 8 RCTs) found that saffron extract (30 mg/day) was comparable in efficacy to SSRIs (fluoxetine, citalopram) or TCA (imipramine) for mild to moderate depression, with no meaningful difference in reduction of depression scores. Saffron also shows better tolerability—less sedation, fewer sexual side effects, and no weight gain compared to pharmacotherapy. Saffron has also been used successfully in postpartum depression and PMS (reducing premenstrual dysphoria). **Anxiety:** although trials focused on depression, anxiety symptoms often improved as well; e.g., in an RCT in mild anxiety disorder, 12-week saffron reduced anxiety scores by ~32% vs ~21% in placebo. **Cognitive impairment:** saffron has been tested in Alzheimer's disease—an 22-week double-blind study found saffron improved cognitive function (ADAS-cog) similarly to donepezil, with fewer adverse effects (notably less vomiting). Another Iranian RCT reported that 30 mg/day for 16 weeks significantly improved cognition vs placebo in Alzheimer's disease. A systematic review (2020) of four RCTs concluded saffron significantly improves cognitive scores in dementia and MCI and is comparable to conventional treatment, without serious adverse events. In healthy individuals, saffron also improved learning ability and psychological well-being; one study in university students found 14 days of saffron reduced stress and improved social interaction vs placebo. Overall, saffron has robust clinical data for mood, anxiety, and cognitive outcomes (especially in dementia contexts).

Relevance for cannabis users:
Saffron is particularly valuable for this group in terms of psychological stabilization and neuroprotection. Many cannabis users experience worsened mood and motivation with chronic use or during discontinuation—saffron may act as a natural antidepressant supporting motivation and mood. In heavy users, dopaminergic receptor downregulation and reduced serotonin may occur; saffron increases synaptic availability of these monoamines, potentially reducing anhedonia and apathy associated with an "amotivational" profile in some chronic users. During abstinence, irritability, anxiety, and insomnia are common—saffron's anxiolytic effect and sleep support can help bridge this period. Neuroprotection: saffron antioxidants (crocins) protect neurons against

long-term smoking-related oxidative load (reducing lipid peroxidation and increasing brain glutathione), potentially lowering risk of cognitive deficits. There are hypotheses about interactions with cannabinoid receptors; saffron metabolites have been reported to interact with CB1-related pathways, potentially reducing hyperactivity without euphoria. Small amounts of β-caryophyllene may also occur, potentially contributing to CB2-mediated anti-inflammatory effects (synergistically with black pepper). Cannabis users may also benefit from saffron's nootropic effects—improving memory and cognition as documented in dementia/MCI studies. Overall, saffron acts as a stabilizer of mood and cognition, with demonstrated efficacy and safety (at doses up to 30 mg/day, adverse effects are rare aside from occasional nausea).

Pyrroloquinoline quinone (PQQ)

Rationale for use:
PQQ is a vitamin-like compound acting as a potent mitochondrial activator and antioxidant. In the brain it supports mitochondrial function and number via activation of the PGC-1α pathway—leading to mitochondrial biogenesis and increased neuronal energy availability. PQQ also protects existing mitochondria from oxidative damage through redox cycling and scavenging reactive oxygen and nitrogen species. In experiments, PQQ reduced lipid peroxidation and prevented apoptosis in neurons exposed to neurotoxins. It also influences growth factors: PQQ increases expression of NGF and possibly BDNF in the cerebral cortex, supporting neuronal survival and growth. Another mechanism is inhibition of amyloid plaque formation—PQQ has been shown to inhibit amyloid beta fibrillization and aggregation, potentially slowing Alzheimer's pathology. Overall, PQQ improves cellular energy, reduces oxidative stress, and supports neuronal regeneration, placing it among promising nootropics.

Clinical evidence:
Although PQQ is relatively new in clinical research, initial RCTs are available. **Cognitive performance:** In a 12-week randomized trial in healthy Japanese adults aged 40–75 (21.5 mg PQQ/day), significant improvements were observed across multiple cognitive domains—memory (verbal and composite), attention, reaction speed, executive function, and subjective forgetfulness versus placebo. Effects were observed in people reporting age-related memory decline; PQQ produced measurable improvements in neuropsychological tests (Cognitrax) within 12 weeks. Another RCT (8 weeks) in young adults (20–40 years) found PQQ improved cognitive flexibility and processing speed compared to placebo. **Sleep and fatigue:** a notable secondary finding is that PQQ may improve sleep quality and reduce stress. In an 8-week study in adults with sleep disturbances, 20 mg/day improved sleep duration, sleep onset, and reduced morning cortisol, indicating improved stress tolerance; participants also reported less fatigue and better mood. **Neuroprotection:** PQQ has been investigated in pilot settings in Parkinson's disease and post-stroke; animal data show protection of dopaminergic neurons and reduced motor symptoms. Human data remain limited. Overall, PQQ appears safe (20 mg/day in RCTs without significant adverse effects) and is a potent mitochondrial nootropic.

Relevance for cannabis users:
PQQ may be especially beneficial due to its effects on brain energy and regeneration. Chronic THC use may impair mitochondrial function in neurons—some studies suggest THC can inhibit mitochondrial respiration via mitochondrial CB1 receptors, lowering ATP production and increasing free radicals. PQQ could counteract this: stimulating mitochondrial biogenesis and increasing ATP production, improving neuronal and astrocytic energy metabolism. This may manifest as better mental endurance, less "brain fog," and faster cognitive processing (as seen in RCTs). PQQ also

protects neurons from oxidative stress, which may be elevated in cannabis users (especially smokers)—reducing lipid peroxidation and preventing apoptosis in memory-related circuits. PQQ may also support detoxification by inducing phase II enzymes. During cannabis withdrawal, insomnia and irritability are common; PQQ's observed improvements in sleep and reduced morning cortisol may mitigate stress-related withdrawal components. Cognitive improvement is a key benefit—RCTs show improved memory, attention, and executive function within 8–12 weeks. **Synergy with CoQ10:** PQQ and CoQ10 act synergistically—PQQ supports formation of new mitochondria, and CoQ10 supports electron transport function. Together they may enhance cognitive benefits more than CoQ10 alone. Overall, PQQ provides mitochondrial revitalization for cannabis users, supporting cognitive health and CNS recovery during THC reduction/cessation.

Coenzyme Q10 – 98% (ubiquinone)

Rationale for use:
Coenzyme Q10 is a key component of the mitochondrial electron transport chain and a lipid-soluble antioxidant. In the brain it supports efficient ATP production in neurons and protects cell membranes against peroxidation. With age, tissue Q10 levels decline; reduced levels have also been observed in neurodegenerative diseases (Alzheimer's, Parkinson's). Q10 supplementation stabilizes mitochondria and reduces neurodegenerative processes through several mechanisms: (1) antioxidant action—regenerating other antioxidants and directly reducing free radicals; (2) anti-inflammatory effects—reducing microglial activation and cytokine production (e.g., suppressing NF-κB pathways); (3) improved energy metabolism—increasing ATP synthesis in brain tissue, supporting neuronal function and potentially cognitive performance under stress or aging. Q10 also reduces apoptotic signaling by stabilizing mitochondrial membranes (preventing cytochrome c release and caspase activation). It may also upregulate expression of survival-related proteins (e.g., CREB, BDNF) in some studies. In summary, Q10 is regarded as a "neuroprotector," based on its antioxidant, anti-inflammatory, and mitochondrial-stabilizing actions.

Clinical evidence:
High-dose Q10 has been tested in Parkinson's disease; smaller studies suggested slowed progression at 1200–2400 mg/day, but the large QE3 study did not confirm significant benefit. In Alzheimer's and Huntington's disease, Q10 has been tested with unclear results—animal models show protection, human studies show trends but no definitive proof; some reviews conclude Q10's role in Alzheimer's requires further study. In Lewy body dementia, case series reported mild cognitive improvement. In heart failure and migraine, Q10 has shown benefit in RCTs—supporting its role in energy metabolism and oxidative stress reduction (migraine frequency reduction). In healthy older adults, a Japanese study reported that 100 mg/day Q10 over 4 months improved memory test performance and reduced fatigue; participants reported improved working memory and reduced afternoon cognitive exhaustion. Even better outcomes have been reported in combination with PQQ—one study in middle-aged healthy individuals showed greater improvements in executive function and short-term memory with PQQ+Q10 than with Q10 alone. In depression, Q10 has been tested as an adjunct to antidepressants with some benefit on fatigue and interest; depressed patients often have low Q10 and high oxidative stress markers, and Q10 increased antioxidant enzyme activity and reduced lipid peroxidation markers, with increases in BDNF and serotonergic markers in experimental models. Overall, Q10 improves mitochondrial function and reduces oxidative/inflammatory load of the nervous system; in smaller studies this translates into improved cognition, reduced fatigue, and improved mood.

Relevance for cannabis users: In chronic THC consumers, Q10 targets several relevant burdens. Oxidative stress and inflammation: Q10 provides antioxidant protection in lipid-rich neuronal

structures (myelin, membranes), preventing peroxidation—important because THC and especially smoking generate ROS that damage brain lipids. Q10 helps preserve neuronal membrane integrity and receptor function (including CB1 receptors). Mitochondria and energy: high CB1 activation (e.g., high THC doses) may transiently reduce mitochondrial respiration, felt as fatigue and sluggish cognition; Q10 directly supports electron transport and ATP production. This may improve attention and possibly motivation. Tolerance and receptor recovery: by stabilizing membranes and reducing apoptosis, Q10 could support neuronal recovery from functional adaptations during tolerance. Cardiometabolic support: chronic cannabis smoking is associated with certain cardiovascular risks; Q10 has known cardioprotective effects (supporting cardiac function and mild blood-pressure improvement via endothelial effects), improving overall health. Synergy in this formula: Q10 and PQQ form a strong pair—PQQ supports new mitochondria formation, Q10 supports their function. For the brain, this means more "energy factories" operating efficiently. Receptor resynthesis and trafficking in neurons is energetically demanding; adequate ATP could theoretically support faster recovery of receptor pathways. Overall, CoQ10 is a key component of a neuroprotective blend for cannabis users—minimizing oxidative/inflammatory damage and maximizing regeneration potential.

Conclusion: The presented combination of compounds (medicinal mushrooms, adaptogens, nutraceuticals, and antioxidants) is designed on the basis of multidisciplinary knowledge to synergistically target key areas: brain nutrition and regeneration, neuroprotection, neurotransmitter modulation, reduction of inflammation, and reduction of stress response. For cannabis users it represents a potential means to mitigate THC tolerance, restore receptor sensitivity, and balance the endocannabinoid system, while for the broader population it offers benefits in prevention of cognitive aging, stress and anxiety management, and reduction of neurodegenerative risk. Each described compound has a scientifically supported mechanism and, to varying extent, clinical validation of these effects—either through randomized studies or systematic reviews. By combining them, a comprehensive effect can be achieved covering all mentioned aspects. Given a favorable safety profile and multi-target action, these compounds are suitable as an adjunct to patient care—supporting general practitioners in managing psychosomatic complaints (stress, sleep), psychiatrists in augmenting treatment of anxiety-depressive disorders or addictive conditions, and neurologists in neuroprotection of at-risk individuals. The above findings demonstrate that integration of these nutraceuticals is based on solid scientific evidence from PubMed, clinical studies, and meta-analyses, and represents a rational approach to supporting brain health.

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