Methylene Blue

BY David Tomen Leave a Comment

Methylene Blue boosts mitochondrial energy, is anti-aging, and improves mood and memory

Methylene Blue (methylthioninium chloride) is a synthetic compound used as a nootropic to increase memory, mood and longevity.

Soon after Methylene Blue was synthesized as a textile dye in the late 1800's, it became the first synthetic drug to be used in humans. It was used for the treatment of malaria.

In the early 20th century, psychiatrists were using Methylene Blue in the experimental treatment of schizophrenia.[i]

Methylene Blue is currently being studied as potential therapy for *mild cognitive impairment*, *Alzheimer's* and *Parkinson's* disease, and other neurodegenerative disorders. *All sharing a common problem with mitochondrial function*.

Your brain's neurons rely almost entirely on mitochondria-derived energy. Failure of mitochondrial function can affect the rest of your body. But it's particularly detrimental to your brain.

This is where Methylene Blue steps in as possibly one of the most important anti-aging and neurological disease preventing nootropics we have available today.

As a nootropic, *Methylene Blue* quickly crosses the blood-brain barrier. It *improves mitochondrial efficiency and respiration, acts as an antioxidant, and increases brain cell lifespan. Resulting in improved memory and mood*.

Here we'll dive into over 140 years of research on how Methylene Blue helps your brain.

Methylene Blue helps:

- **Neurotransmitters**: Methylene Blue inhibits *monoamine oxidase* and *acetylcholinesterase* activity which increases levels of *catecholamines* and *acetylcholine*. And boosts *serotonin* and *norepinephrine* affecting anxiety, depression and memory.
- **Mitochondrial Energy**: Methylene Blue assists *brain cell respiration* by increasing oxygen. And donating electrons to the *electron transport chain* within mitochondria. This same process is used to create *ATP* within mitochondria from the food you eat. So

MB contributes to this energy-production process in place of the nutrients you get from your food. Increasing cellular energy positively effects mood and memory.

- **Neuroprotectant**: Methylene Blue is a potent antioxidant. *Reactive oxygen species* are produced inside mitochondria. The first free radical that is formed inside a cell is *superoxide*. MB will bind to superoxide and reduce it to water. It stops the oxidative cascade at its very beginning. Before it gets a chance to do damage.

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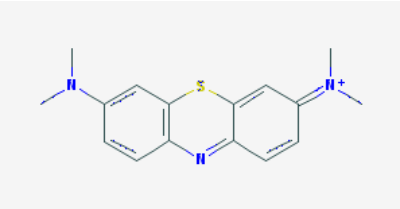
Overview

Methylene Blue (methylthioninium chloride) was first synthesized in 1876 by German chemist *Heinrich Caro* at BASF as an aniline-based dye for cotton staining.

In 1891, German physician and Noble Prize recipient *Paul Ehrlich* pioneered the use of *Methylene Blue* for the treatment of malaria. [ii]



Methylene Blue

Ehrlich discovered that when MB was injected into animals in the lab, it would *quickly concentrate in the brain*. And had an uncanny ability to selectively target diseased tissues in the body.

It was Ehrlich who coined the term "*Magic Bullet*" for this unique action displayed by Methylene Blue. A term still in use today.

Methylene Blue has since been used to treat dementia, in cancer chemotherapy, malaria, methemoglobinemia, urinary tract infections, cyanide and carbon monoxide poisoning.[iii]

As a nootropic, Methylene Blue is used to enhance mitochondrial function, increase cerebral blood flow, and acts as an antidepressant.

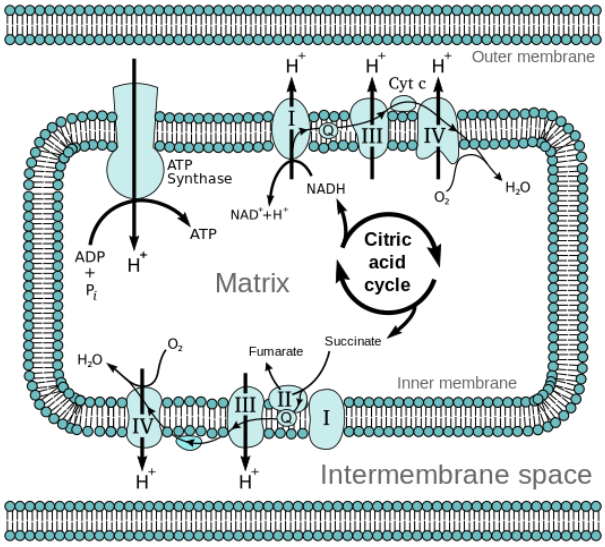
How does Methylene Blue work in the brain?

Methylene Blue boosts brain health and function in several ways. But two in particular stand out.

1. **Methylene Blue improves memory.** Unlike other nootropics which often work by increasing neurotransmitter synthesis and neural signaling, MB improves memory by increasing brain cell respiration. Or how the brain cell utilizes oxygen.

Studies show dramatic increases of cellular oxygen consumption and glucose uptake when using Methylene Blue. MB increases *$CMRO_2$ (cerebral metabolic rate)* through increased activity in the mitochondrial *electron transport chain*.

Methylene Blue functions as an *alternative electron carrier* in the *electron transport chain* in mitochondria. It accepts electrons from ***NADH*** and transfers them to *cytochrome c*.[iv]



Cytochrome complex (cytochrome c) is a component of the *electron transport chain* in mitochondria. Playing a role in apoptosis and as an antioxidant.

Methylene Blue also stimulates *glucose metabolism*. Taken together, increases in *$CMRO_2$* and *glucose uptake* means that *MB elevates oxygen consumption which helps glucose increase ATP production*.

Increases in ATP production provides more cellular energy for better overall brain function including cognition, mood and memory.

2. **Methylene Blue is an antioxidant.** MB has a unique mechanism of action that is fundamentally different from traditional antioxidants. During cellular respiration, the first free radical formed inside a cell is *superoxide (O_2)*.

Methylene Blue binds to *superoxide* and reduces it to water. It *stops the oxidative cascade at its very beginning. Before it gets a chance to do damage*.[v]

So think of Methylene Blue as having a unique dual property. First, it increases cellular energy production which normally leads to oxidative stress. And second, it *eliminates this oxidative stress*. Making it a *metabolic enhancer and an antioxidant*.

Researchers tested Methylene Blue in animal models of neurological disease. First, researchers used rotenone (a potent pesticide) which causes severe dopamine depletion in the part of the brain associated with Parkinson's.

Methylene Blue rescued brain cell mitochondria from the damaging effects of this toxin. By *donating electrons* in the *electron transport chain* broken by rotenone. Essentially *bypassing the broken transport chain with donated electrons as an alternative electron carrier*.

Methylene Blue also countered *cerebral ischemia reperfusion* damage. The tissue damage caused when blood supply returns to tissue after a lack of oxygen from a stroke. And can occur with *Traumatic Brain Injury*. MB accomplished this by *rerouting mitochondrial electron transfer*.

And Methylene Blue dramatically countered the behavioral, neurochemical, and neuropathological impairment found in Parkinson's disease.[vi]

How things go bad

As we live life, our brain chemistry and metabolism changes.

↓ Mitochondrial energy levels decline

↓ Attention, memory and mental agility decline

↓ Tau proteins and amyloid plaques clog the brain

↓ Free radicals damage brain cell mitochondria

↓ Cerebral blood flow declines

All of these changes can happen at any age. And are a product of the food we eat, what we drink, lifestyle habits, the air we breathe and more.

So Methylene Blue can help for age-related cognitive decline, as well as a student looking to do better in school. By boosting brain cell mitochondria energy production levels. And improving cerebral blood flow.

Methylene Blue benefits

Low dose Methylene Blue supplementation provides memory enhancing effects in animals and humans. It works as an *antidepressant*, is *anti-aging*, helps *dementia, Huntington's* and *Alzheimer's*.

Methylene Blue increases low blood pressure, improves cognition in healthy people, *boosts mitochondrial function*, is *anti-microbial*, can help *eliminate fear* and even *slow skin aging*.

Methylene Blue boosts acetylcholine

Research shows that *Methylene Blue* is an *acetylcholinesterase inhibitor* with a preference for *muscarinic acetylcholine receptors*. Meaning MB prevents the breakdown of acetylcholine and making more available in your brain.[vii]

Methylene Blue is an antidepressant

Methylene Blue is a *monoamine oxidase inhibitor (MAOI)*. It inhibits MAO-A more than MAO-B, but inhibits both at large doses.[viii]

One study in 1987 showed that 15 mg per day of *Methylene Blue was a potent antidepressant in those with severe depression*.[ix]

Another study with 31 Bipolar Disorder patients compared 300 mg per day of Methylene Blue with 15 mg per day. The patients were also on lithium treatment. The study showed that the 300 mg dose of Methylene Blue was a "*useful addition to lithium in the long-term treatment of manic-depressive psychosis*". And patients *were significantly less depressed*.[x]

Methylene Blue resists Alzheimer's Disease

Alzheimer's disease and other forms of dementia are associated with a buildup of the protein *Tau*. Clinical trials show that *Methylene Blue inhibits Tau formation*. And is under consideration as a treatment for Alzheimer's.[xi]

Methylene Blue has an inhibitory action on the cGMP pathway, and affects other molecular events closely related to the progression of Alzheimer's.

Methylene Blue boosts neuron resistance to the formation of amyloid plaques and neurofibrillary tangles. And helps *repair impairments in mitochondrial function and cellular metabolism*.

Research also shows that cholinergic, serotonergic and glutamatergic systems all play important roles in the development of Alzheimer's and other cognitive disorders. Methylene Blue provides beneficial effects in mediating these pathways.[xii]

This is particularly significant because most existing treatments for Alzheimer's can only prevent the disease *before it is diagnosed*. But *Methylene Blue shows promise in delaying the effects of Alzheimer's and dementia after it is diagnosed*.

Methylene Blue is anti-aging

Research shows that *Methylene Blue is an effective anti-aging nootropic*. MB increases ***mitochondrial complex IV*** by 30%, enhances *cellular oxygen consumption by 37-70%*, increases ***heme synthesis***, and reverses ***premature senescence*** caused by H_2O_2 or cadmium.

Methylene Blue is considered a *redox agent*. Meaning it cycles between oxidized and reduced forms. This cycling by *MB helps block oxidant production in brain cell mitochondria*.[xiii]

Mitochondrial complex IV is the last enzyme in the respiratory *electron transport chain* in mitochondria. The last step in synthesizing *ATP*. Your cellular source of energy.

Iron (heme) is an essential element and participates in *oxygen transport, DNA synthesis* and *electron transport*. ***Heme synthesis*** begins in *mitochondria*. Every cell requires heme to function properly. [xiv]

Senescence or *biological aging* is the gradual deterioration of cellular function. And is caused by *telomere shortening* that triggers *DNA damage* in response to *reactive oxygen species, hydrogen peroxide (H_2O_2), cadmium* and other toxins. Methylene Blue helps prevent ***premature senescence*** or premature cell death.

Methylene Blue improves memory

Animal studies have shown that *a single low dose of Methylene Blue enhances long-term contextual memory*. This type of memory is the conscious recall of the source and circumstances of a specific memory.

Other studies show that Methylene Blue in low doses taken *after* the event helps memory retention of the event. A study done with rats revealed why this works.

In this study, rats received 1 mg/kg of MB *post*-training for 3 days. The researchers then measured *cytochrome c oxidation* in participants brains. The idea was to determine if an increase in metabolic energy was behind the memory enhancing qualities of MB.

The study found that *in the Methylene Blue treated group, brain cytochrome oxidase activity was 70% higher than in the placebo-treated group*.

The findings suggest that *repeated post-training supplementation of Methylene Blue improves memory consolidation*. And this memory boost is due to the *increased metabolic capacity* in brain regions that require more energy during *discrimination learning*.[xv]

How does Methylene Blue *feel*?

Methylene Blue as a nootropic will likely feel different than any other supplement you've ever tried.

When reading or studying, once you're done, you should feel like you fully understand the subject material. And you'll be able to use what you learned in the future.

Methylene Blue seems to facilitate a full understanding of something on the first try.

Many neurohackers report the biggest nootropic effect they experience with Methylene Blue is "*after the fact learning*". You take in the information. And it's like your brain sorts through the material. Then stores it in a form you can easily access later.

Methylene Blue has this uncanny ability to rewire your brain to *forget about any negative associations you have of a situation*. And *only retains the positive aspects of that memory*.

Some report that *Methylene Blue makes you "feel young again"*. It eliminates *social anxiety*. You'll feel focused and more confident.

Workouts seem easier because *you have more energy*. Your mitochondria are energized. And you may find that recovery from workouts is easier.

Methylene Blue helps eliminate stress. So you have more energy in any situation with a relaxed state of mind.

And one recurring theme from many is *improved sleep while using Methylene Blue*.

Methylene Blue Clinical Research

Research into *Methylene Blue* for its therapeutic value goes back to the late 1800's. But it's only in the last couple of decades that scientists have been able to decode exactly how Methylene Blue works in the brain. All the way down to the molecular level in mitochondria.

A study in 2017 found that Alzheimer's Disease could be caused by more than the accumulation of *amyloid beta* in the brain. The scientists looked into the two main components that produce energy in cells.

1. Glycolysis is the mechanism used to convert glucose into fuel within mitochondria.
2. Creating this fuel in mitochondria uses oxygen in a process called mitochondrial respiration.

The researchers found that *as the brain ages, mitochondrial metabolism deteriorates*. Resulting in a reduction in the molecules needed for energy production. And possibly the main culprit behind many neurological diseases including Alzheimer's and Parkinson's.[xvi]

A study conducted at *Children's Hospital Oakland Research Institute* may have found the solution to this mitochondrial energy problem in brain cells.

The researchers found that *Methylene Blue can prevent or slow the decline of mitochondrial function*.

One of the key aspects of Alzheimer's is mitochondrial dysfunction. Specifically complex IV dysfunction. And this is where Methylene Blue steps in.

The study found that *Methylene Blue enhances complex IV in mitochondria. It increases oxygen consumption. And it reverses premature cell death*.

The researchers concluded that *Methylene Blue may be useful to delay mitochondrial dysfunction with aging and the decrease in complex IV in Alzheimer's disease*.[xvii]

Methylene Blue Improves Memory

26 healthy volunteers aged 22 – 62 participated in a double-blind, randomized, placebo-controlled clinical trial. Purpose of the study was to measure the effects of *Methylene Blue on working memory and sustained attention*.

Study results showed that *a single low-dose of Methylene Blue resulted in an increase in short-term memory* ability. In an area of the brain associated with the senses and visual processing.

Timothy Duong, Ph.D., the study author concluded *Methylene Blue showed promise "in healthy aging, cognitive impairment, dementia and other conditions that might benefit from drug-induced memory enhancement"*.[xviii]

Another study published in the *American Journal of Psychiatry* tested *fear extinction (elimination of fear)* and *contextual memory*. Both are forms of *long-term memory*.

In this study, participants received either Methylene Blue or a placebo *after* being placed in a small dark chamber for a couple of minutes to address their fear.

One month later, *participants that had used Methylene Blue had less retained fear* than those given a placebo. The study authors concluded, "*Methylene Blue enhances memory and the retention of fear extinction*". [xix]

Methylene Blue helps Bipolar Disorder

Increasing evidence shows that *Bipolar Disorder* may be a progressive condition. Dealing with bipolar symptoms long-term can result in deterioration of the cortex and less gray matter.

A study at *Dalhousie University* in Halifax compared the effectiveness of lamotrigine (Lamictal®) along with daily supplementation of either 195 mg or 15 mg of Methylene Blue in patients with *Bipolar Disorder*.

Patients took a dose (Lamictal and either 195 mg or 15 mg of Methylene Blue) for three months. Then switched to the other dose for 3 months. The team found that *bipolar participants had reduced depression and anxiety when taking the higher dose of Methylene Blue* compared to when they were on the lower dose.

Several Bipolar Disorder patients in the study chose to continue using Methylene Blue after the study concluded.[xx]

Methylene Blue Recommended Dosage

Recommended *safe doses based on clinical studies with animals and humans* ranges from 0.5 – 4 mg/kg. So a 90 kg (200 lb.) body weight translates to 45 – 360 mg of Methylene Blue.

45 mg of Methylene Blue is a safe starting dose. But 360 mg of MB is much too high in my opinion even if you're 200 lbs.

The bottom line is there is no true recommended dose for Methylene Blue. My recommendation is start with the lowest dose of 0.5 mg/kg and see how you react.

Methylene Blue is *water-soluble* so you don't need to take it with a meal, or healthy fat like some nootropics.

Methylene Blue has a half-life of about 5 hours. So you can dose twice a day.

Methylene Blue is famous for *turning urine blue*. But for most neurohackers, your urine will only stain blue at doses roughly exceeding 500 mcg. Some recommend preventing blue urine by *mixing Methylene Blue with ascorbic acid* for 3 hours before taking it.

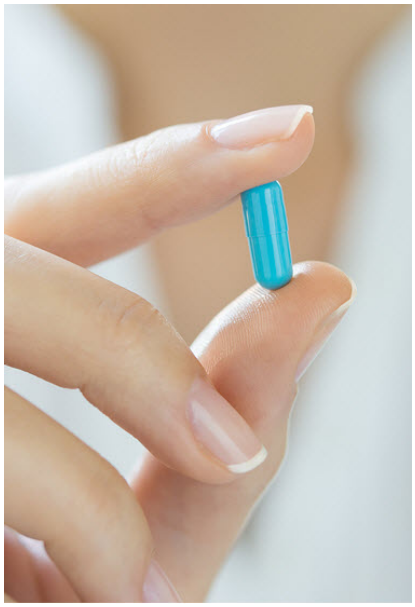
Methylene Blue is also available as a doctor-administered injection for therapeutic use. Typically used to treat diseases like malaria or with anti-cancer therapy.

Methylene Blue Side Effects

Methylene Blue shows a hormetic dose-response, with opposite effects at low and high doses.

In other words, *lower doses of Methylene Blue work well as a nootropic*. But *high doses do not* because MB can potentially "steal" electrons away from the *electron transport chain*. Disrupting the redox balance and acting as a pro-oxidant (instead of an antioxidant).[xxi]

Adverse effects of Methylene Blue also come from chemical impurity. *Even pharmaceutical (USP) grade Methylene Blue can contain impurities like arsenic, aluminum, cadmium, mercury and lead*.



At low doses, these contaminants are not that big of a problem. But higher doses will result in the accumulation of these toxins in your cells.

Side effects with Methylene Blue are rare when doses are under 2 mg/kg. But can include stomach pain, chest pain, dizziness, headache, sweating, confusion, high blood pressure, shortness of breath, accelerated heartbeat, tremor, skin turning blue, urine turning blue or green, reduction of red blood cells, or jaundice (only reported in infants).

Monoamine Oxidase (MAOI) inhibition becomes a big problem at around 2 mg/kg of Methylene Blue. So if you are using antidepressants or antianxiety medications that affect dopamine or serotonin, you should NOT use Methylene Blue. Because using Methylene Blue with one of these medications could cause a *hypertensive crisis* or *Serotonin Syndrome*.

This includes SSRI's and MAOI's such as citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, zimelidine, bupropion, buspirone, clomipramine, mirtazapine and venlafaxine.

Do not use Methylene Blue if you are pregnant or breast-feeding.

Where to buy Methylene Blue

Methylene Blue is sold as a liquid, and in crystalline powder form.

Industrial-grade and *chemical-grade* Methylene Blue is sold as a dye or stain. And can consist of more than 8% – 11% of various contaminants. And *should NOT be used as a nootropic*.

Only *pharmaceutical (USP) grade Methylene Blue* should be used as a nootropic. Ask for a *Certificate of Analysis* which should include the amount of contaminants such as arsenic, aluminum, cadmium, mercury and lead.

I recommend ***CZTL Methylene Blue*** due to their robust testing program. They ship in 1 gram containers of powder with dosage and mixing instructions in each shipment. Along with a ***Certificate of Analysis (CofA)*** verifying the purity of the *Methylene Blue* you get from them.

Nootropics Expert Recommendation

Methylene Blue 0.5 – 4 mg/kg of body weight per day

I recommend using Methylene Blue as a nootropic supplement.

Your body ***does not*** make Methylene Blue on its own. So to get its benefits you must take it as a supplement.

Methylene Blue is especially helpful for those dealing with anxiety and depression.

Methylene Blue is also particularly useful to students and executives who want to boost cognition, learning and memory.

Methylene Blue is a fast-acting nootropic that can also help prevent brain mitochondrial degeneration. Providing potential as

an anti-aging nootropic.

Methylene Blue donates electrons in the *electron transport chain* in your mitochondria. So experienced neurohackers suggest avoiding *CoQ-10* or *idebenone* when using MB because it seems to make Methylene Blue much less effective. Remember earlier in this review when I said the too much Methylene Blue can be counter-productive. The same applies here.

Idebenone is an Alzheimer's drug that has some nootropic benefit. But it works similar to Methylene Blue because it acts as a transporter in the *electron transport chain* in mitochondria. Possibly potentiating Methylene Blue.

I recommend ***CZTL Methylene Blue***

REFERENCES

Wondering Where to Start? There's a Nootropic For That...

Get "Secrets of the Optimized Brain," 92 nootropics to help you plan your Nootropic Stack when you sign up for my newsletter: