Methelyne Blue

MB Intro

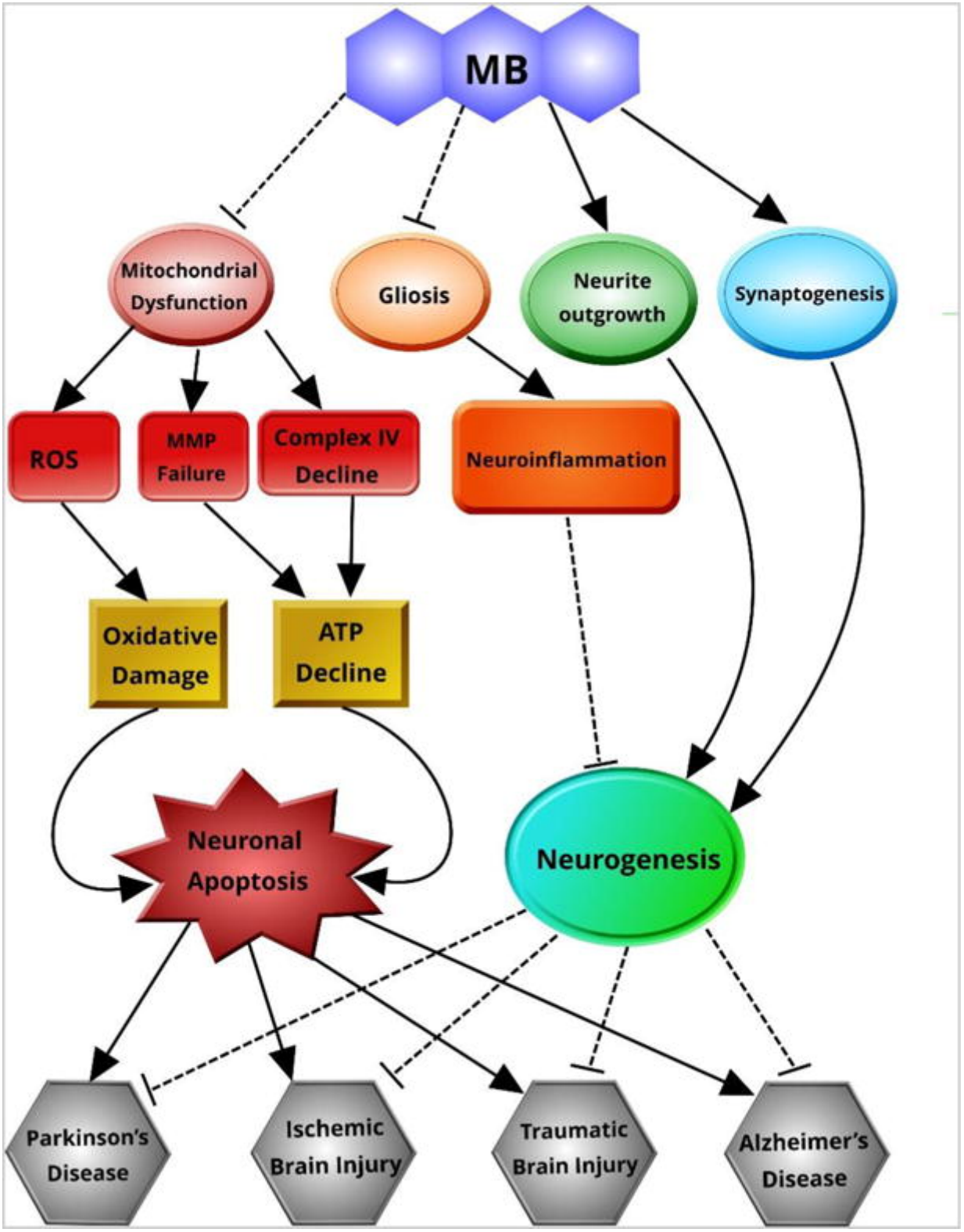
Originally created as a textile dye in 1876, it's now recognised for its role as an alternative electron carrier in mitochondria.

Methylene blue acts as an electron shuttle in the mitochondria, bypassing blocks in the electron transport chain. This helps maintain energy (ATP) production when the normal pathway is impaired.

MB Benifits

Brain Mitochondrial Enhancer

Our brain relies on oxidative metabolism for energy, making proper mitochondrial function crucial for brain health. MB prevents premature brain cell death while supporting energy production and the growth of new neural connections



2 - Cognitive Enhancer

MB is known as a nootropic. It increases ATP production in the brain, providing the energy needed for enhanced brain performance. It's one of the best options for improving attention span, memory, and overall cognition.

The concept of cognitive enhancement via mitochondrial modulation has been investigated increasingly in recent years. The general concept is that by improving mitochondrial function and oxidative defenses, neurons can function with improved efficiency and maintain proper health, improving basal function and stymieing cognitive decline associated with age and neurodegeneration [154]. Early work by Gonzalez-Lima has shown that MB improved spatial memory retention alongside long-lasting mitochondrial respiratory function, mediated through complex IV [26]. The long-term upregulation of CCO may be related to increased H_2O_2 production without superoxide formation, via MB in physiological conditions, leading to upregulation of Nrf2/ARE [135]. In a human study, MB administration increased cerebrovascular reactivity in psychomotor vigilance task and a short-term memory test. This was accompanied with modest improvements in performance on the short-term memory test [155]. These benefits correlated with mitochondrial function are corroborated by experiments showing similarly improved cognition with photobiomodulation, the stimulation of complex IV with transcranial near-infrared laser irradiation [156].

3 - MB Against Infectious Diseases

MB has antimicrobial properties, making it effective against various pathogens (bacterial, viral, and fungal). It also aids in C19 treatment by inhibiting SARS-CoV2 replication.

Table 1

Mechanisms of action of methylene blue (MB) in COVID-19 disease. Abbreviations: ACE2: Angiotensin-converting enzyme 2.

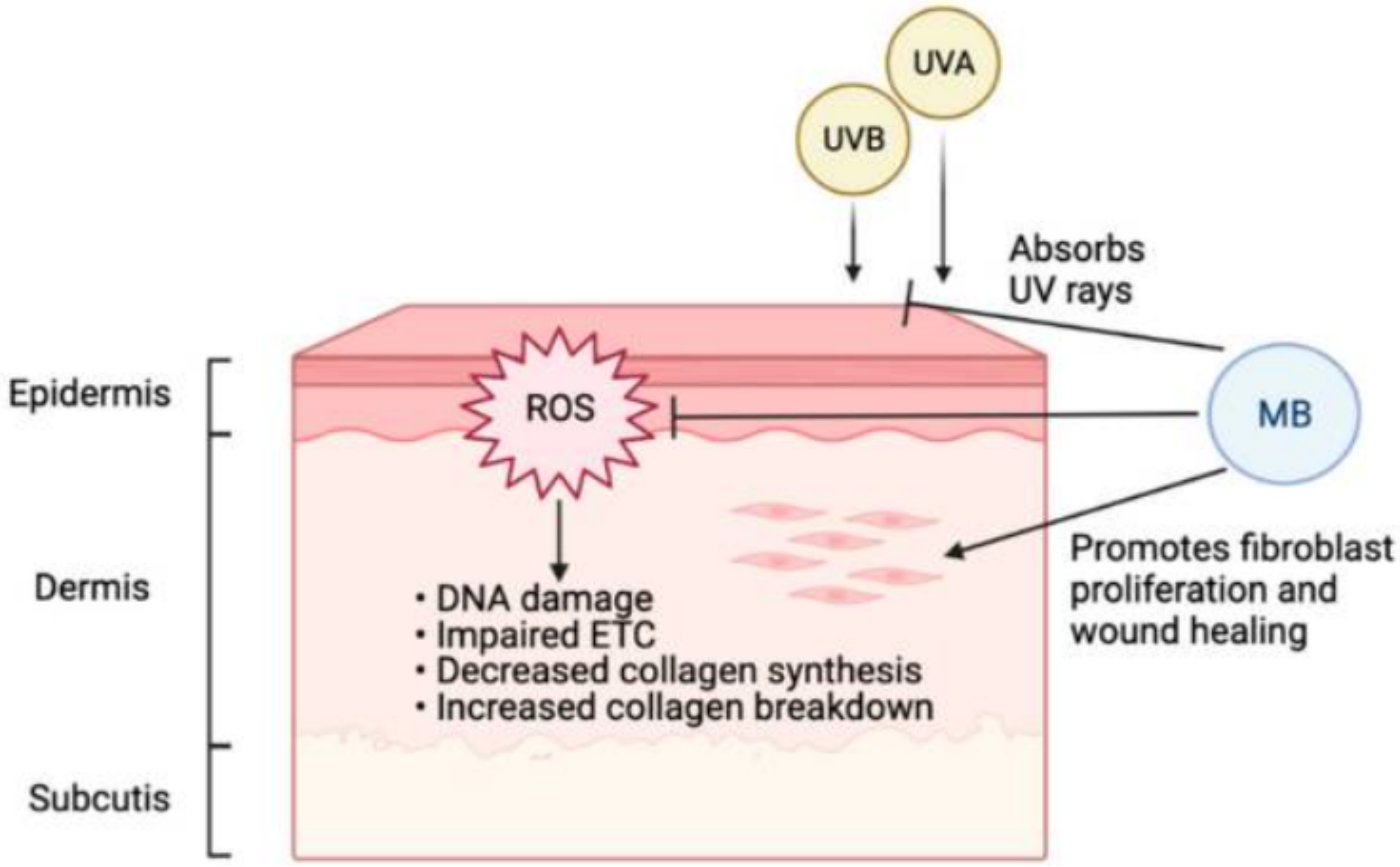
Actions against SARS-CoV-2 Virus	
Reduced Viral Entry	1. Inhibits binding of spike protein to ACE2 receptor 2. Impairs membrane fusion/endocytosis
Reduced Viral Replication	1. Reduces viral uncoating (increases lysosomal pH) 2. Reduces protein translation (increases lysosomal pH) 3. Inhibits RNA dependent RNA polymerase (zinc ionophore)
Photo-Oxidative Viral Inactivation [activation by 660 nm light]	1. Targets viraemia 2. Augments the effects of topical oral/nasal PDI
Reduced Organ Damage	
Reduced Cytopathic Effects	1. Reduced viral replication/protein translation 2. Reduced oxidative stress 3. Reduced cytokine damage
Reduced Hypoxia	1. Improves mitochondrial respiration 2. Rapidly reduces methemoglobinemia 3. Reduces micro-thrombi (reduces platelet aggregation)
Reduced Hyper-Inflammation	1. Inhibits NLRP3 2. Reduces excess nitric oxide/bradykinin activity 3. Scavenger of reactive oxygen/nitrogen species
Broad Spectrum Antimicrobial (Bacterial/Fungal/Other Viruses)	
Reduced Secondary Infections	1. Intrinsic anti-microbial actions 2. Intravascular photo-oxidative anti-microbial actions

4 - MB Delays Skin-Aging

MB has the ability to delay skin aging as well

- Increases cell longevity
- Protects skin from UV exposure
- Accelerates the wound healing process

Additionally, MB's antimicrobial properties are beneficial for skin, too.



5 - MB as Anti-Depressant

MB works as a monoamine oxidase inhibitor (MAOI), increasing serotonin, norepinephrine, and dopamine levels.

Plus, it reduces brain inflammation.

Clinical research shows 15mg/day significantly improved depression symptoms compared to placebo in a controlled trial

> Methylene blue, 15 mg/day, was compared with placebo in treatment of severe depressive illness. The 3-week trial was designed to avoid bias by placebo response and also to avoid observer bias. Improvement in patients receiving methylene blue was significantly greater than in those receiving placebo. Methylene blue at a dose of 15 mg/day appears to be a potent antidepressant, and further clinical evaluation is essential.

Dosage

- Start with 5 drops (2.5 mg) daily, steadily increase to 12 (6 mg) if you respond well
- Up to 15 drops (7.5 mg) if I have a key outcome that I'm taking it for (anti-infection, cognitive enhancement, etc.)
- I have experimented with 15 drops twice per day and seen diminishing returns. (No additional benefits seen)

Consumption

Add MB to fresh orange juice to avoid blue tongue/mouth staining. Other liquids that also work well: Kombucha, raw milk. Be cautious not to spill—it stains. Note: If it does get on your skin, it's always worn off within a day for me

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MB Side effects

Scientific studies have proven MB's cognitive effects and it's antimicrobial powers (it was one of the earliest antimalarial drugs). But here are the risk-factors you should be aware of

1 - The Herxheimer reaction

When MB rapidly kills bacteria, they release endotoxins faster than your body can clear them. This causes temporary inflammatory responses that manifest as "die-off" symptoms.

Understanding the Herxheimer Reaction:

The Herxheimer reaction, also known as Jarisch-Herxheimer reaction, is essentially an acute exacerbation of symptoms that occurs when microorganisms release toxins into the body during the process of being killed off by antibiotics or other antimicrobial agents. It typically manifests as an initial worsening of symptoms, followed by improvement as the body clears the toxins.

The mechanism behind the Herxheimer reaction lies in the rapid destruction of pathogens, which leads to the release of endotoxins or other harmful substances. These toxins can overwhelm the body's detoxification systems, triggering an inflammatory response that exacerbates existing symptoms or causes new ones. Common symptoms of the Herxheimer reaction include fever, chills, headache, muscle aches, and fatigue.

The phenomenon is commonly observed in the treatment of various infections, including Lyme disease, syphilis, and certain bacterial, fungal, and parasitic infections. It is particularly prevalent in conditions where the pathogen burden is high or when aggressive antimicrobial therapy is initiated.

Herxheimer reactions from MB can include:

- Headaches
- Debilitating fatigue
- Nausea
- Brain fog
- Flu-like symptoms
- Muscle aches
- Fever or chills

These symptoms are documented in Lyme disease treatment literature.

2- MB's role as a Monoamine Oxidase Inhibitor (MAOI).

Studies confirm MB is a potent reversible inhibitor of MAO-A, which normally breaks down serotonin and other neurotransmitters. By blocking this enzyme, MB increases serotonin levels.

Methylene blue and serotonin toxicity: inhibition of monoamine oxidase A (MAO A) confirms a theoretical prediction

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Affiliations + expand

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Abstract

Background and purpose: Monoamine oxidase inhibitors (MAOI) are known to cause serotonin toxicity (ST) when administered with selective serotonin reuptake inhibitors (SSRI). Methylene blue (methylthionium chloride, MB), a redox dye in clinical use, has been reported to precipitate ST in patients using SSRI. MB was assessed for MAO inhibition and so for its potential to precipitate ST.

Experimental approach: Inhibition of purified human MAO was quantified using kinetic assays and visible spectral changes to study the interactions of MB with MAO A.

Key results: MB was a potent (tight binding) inhibitor for MAO A. It also inhibited MAO B but at much higher concentration. Interactions of MB with the active site of MAO A were confirmed by its action both as an oxidising substrate and as a one-electron reductant.

Conclusions and implications: MB is a potent reversible inhibitor of MAO A with implications for gut uptake of amines when administered orally. At concentrations reported in the literature after intravenous administration, MAO B would be partially inhibited but MAO A would be completely inhibited. This inhibition of MAO A would be expected to lead to perturbations of 5-hydroxytryptamine metabolism and hence account for ST occurring when administered to patients on SSRI treatment.

This MAOI activity creates a serious danger: combining MB with serotonergic drugs can trigger serotonin syndrome. The FDA has issued explicit warnings about this interaction, citing severe CNS reactions when MB is given to patients on psychiatric medications

FDA Drug Safety Communication: Serious CNS reactions possible when methylene blue is given to patients taking certain psychiatric medications

The FDA has issued new information about this safety issue, see the FDA Drug Safety Communication issued 10-20-2011.

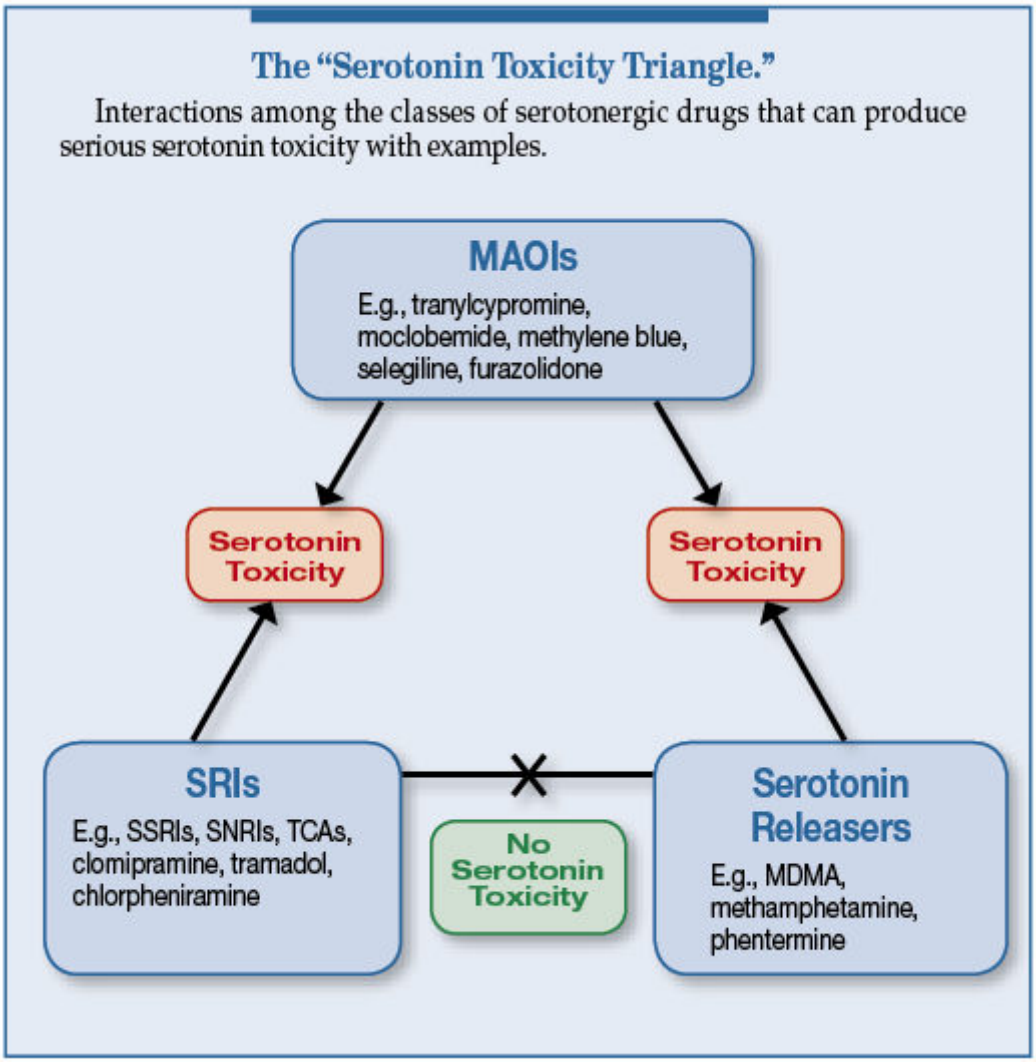
Safety Announcement
Additional Information for Patients
Additional Information for Healthcare Professionals
Data Summary
References

Safety Announcement

[07-26-2011] The U.S. Food and Drug Administration (FDA) has received reports of serious central nervous system (CNS) reactions when the drug methylene blue is given to patients taking psychiatric medications that work through the serotonin system of the brain (serotonergic psychiatric medications). Methylene blue is commonly used in diagnostic procedures and is also used to treat a number of medical conditions (see Facts about methylene blue box). A list of the serotonergic psychiatric medications that can interact with methylene blue can be found here.

Facts about Methylene Blue

- Used to treat methemoglobinemia, vasoplegic syndrome, ifosfamide-induced encephalopathy, cyanide poisoning
- Used as a dye in therapeutic and diagnostic applications
- Is a potent, reversible monoamine oxidase inhibitor (MAOI).



Symptoms of serotonin syndrome include:

- Mental status changes (confusion, agitation)
- Neuromuscular abnormalities (tremor, muscle rigidity)
- Autonomic instability (sweating, fever)
- High blood pressure
- Seizures

Medical literature includes fatal cases.

> Although the exact mechanism of this drug interaction is unknown, methylene blue inhibits the action of monoamine oxidase A—an enzyme responsible for breaking down serotonin in the brain. It is believed that when methylene blue is given to patients taking serotonergic psychiatric medications, high levels of serotonin can build up in the brain, causing toxicity. This is referred to as Serotonin Syndrome. Signs and symptoms of Serotonin Syndrome include mental changes (confusion, hyperactivity, memory problems), muscle twitching, excessive sweating, shivering or shaking, diarrhea, trouble with coordination, and/or fever.

3 - MB with dopaminergic substances.

If MB is combined with L-DOPA, selegiline, or stimulants (Adderall), it can inhibit dopamine breakdown and increase synthesis via mitochondrial effects. This risks dopaminergic overstimulation (agitation, insomnia, paranoia).

4 - MB can turn your brain blue

But only under specific conditions like high doses (>5 mg/kg or >300-400mg/day), chronic use (daily for months/years), IV administration, etc. Most cases are seen in post-mortem studies.

Greenish-blue discoloration of the brain and heart after treatment with methylene blue

Images in Forensics | Published: 17 September 2020

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Abstract

Greenish-blue discoloration of the brain and heart was observed during the autopsy of a 63-year-old woman who had been treated with methylene blue for septic shock following a traffic accident. This "pistachio" or "avatar" discoloration occurs when the colorless metabolite leucomethylene blue is oxidized to methylene blue upon exposure to atmospheric oxygen. Other clinically documented adverse effects of methylene blue include greenish-blue urine and bluish discoloration of the skin and mucosa. In medicine, methylene blue is an inhibitor of nitric oxide synthase and guanylate cyclase with different clinical applications, namely, rapid reversal of circulatory shock that is refractory to fluid administration, inotropic agents, and vasoconstrictors. Postmortem differential diagnosis with putrefaction and hydrogen sulfide poisoning should be made, and forensic pathologists should be aware of methylene blue-related greenish-blue discoloration to avoid unnecessary workup and investigations.

Here are supplements and substances to AVOID with Methylene Blue:

- 5-HTP • L-Tryptophan
- St. John's Wort
- Rhodiola rosea
- SAMe
- SSRIs, SNRIs, TCAs
- Tramadol, dextromethorphan
- L-DOPA (mucuna pruriens)

To minimise die-off reactions if using MB: Start with micro-doses (0.5-1mg) and increase by 0.5mg every 4-5 days Stay hydrated with electrolytes. And don’t forget to take breaks between usage periods.

Who should NOT use Methylene Blue

- Anyone on SSRIs, SNRIs
- Pregnant or breastfeeding women
- Those with G6PD deficiency
- People with severe gut dysfunction or dysbiosis
- Individuals with kidney disease / renal insufficiency

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