



# Research Summary: Methylene Blue #4

As featured in Dr. Kenny Mittelstadt's video:  
"Methylene Blue Dosage: More Isn't Better (Safety Guide)"  
Date of Publication: 05/16/2026

## Research Context:

This week's topic explores why methylene blue dosing is often misunderstood, not because people are asking bad questions, but because very different contexts are being collapsed into the same conversation. Emergency IV use, oral supplementation, longevity discussions, and biohacker experimentation are frequently treated as interchangeable, even though the way this compound behaves can change significantly depending on dose, route, and the condition of the system receiving it.

The deeper pattern here is that methylene blue may function less like a simple energy booster and more like a metabolic efficiency tool. That distinction matters because more is not always better. In some cases, increasing the dose may actually create additional stress on the system rather than improve performance.

## Key Findings from the Research:

### Study 1 (PMID 36803299):

Researchers explored how methylene blue influenced brain energy metabolism and oxygen use in both humans and animal models at different doses. The expectation was that increasing the dose would improve brain energy production. Instead, researchers found that higher exposures reduced cerebral blood flow and oxygen utilization in certain situations. This challenged the assumption that more methylene blue automatically creates more benefit. The findings support the concept of hormesis, where smaller amounts may support the system while larger amounts can create additional metabolic stress. This matters because many people approach supplements with a "more is better" mindset, even though the response may depend more on timing, context, and overall system readiness.

### Study 2 (PMID 33206681):

This study examined how different doses of methylene blue affected the gut microbiome and cognitive performance in mice over time. At lower doses, researchers found the microbiome stayed relatively stable and cognitive performance improved or remained intact. At higher doses, they observed noticeable shifts in gut bacterial patterns along with a loss of some of the earlier cognitive benefits. The findings suggest that dose changes the biological environment in meaningful ways. This matters because the gut microbiome helps regulate communication between the brain, immune system, metabolism, and nervous system. The study reinforces the idea that compounds can shift from supportive to stressful depending on dose and the body's ability to adapt.

### Study 3 (PMID 32508596):

Researchers investigated whether low-dose methylene blue could help preserve mitochondrial function and reduce memory impairment during stress conditions. Mitochondria are the energy-producing structures inside cells that help power the brain and body. The study found that low-dose methylene blue helped preserve mitochondrial enzyme activity and supported memory performance. One of the most important findings was that methylene blue did not appear to simply "create" new energy. Instead, it helped maintain the system's existing ability to function more efficiently. This matters because many people assume a poor response means they need a higher dose, when the deeper issue may involve metabolic strain, stress burden, or reduced mitochondrial capacity.



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## Functional Medicine Connections:

Here's how these pieces fit together: your mitochondria do not operate in isolation. They respond to signals coming from your nervous system, hormones, gut health, blood sugar regulation, immune activity, and overall stress load.

This is why two people can take the exact same compound and have completely different experiences. One person may notice clearer thinking or steadier energy at a very small amount. Another may feel overstimulated, anxious, fatigued, or notice no change at all.

That difference may not simply be about "finding the perfect dose." It may reflect differences in metabolic flexibility, recovery capacity, gut integrity, or how much overall stress pressure the system is already carrying. The bigger clue here is that your response itself may contain information. Sometimes the body is not rejecting the compound. Sometimes it is revealing where the system is struggling to adapt.

## Practical Reflections & Takeaways:

Think about the way you typically interpret your body's response to supplements, stimulants, or even lifestyle changes. If something does not seem to "work," is your first instinct to assume you need a higher amount, or could the response be pointing toward a deeper limitation in energy production, recovery, sleep quality, digestion, or overall stress load? Sometimes what looks like resistance is actually useful feedback about the condition of the system underneath.

It may also be worth reflecting on whether your response to things like caffeine, exercise, fasting, or supplements changes depending on the season of life you are in. Many people notice they tolerate certain inputs differently during periods of high stress, poor sleep, illness, overtraining, or burnout. These fluctuations are often treated as random or frustrating inconsistencies, but they may actually reveal important clues about metabolic resilience and the body's current adaptive capacity.

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## References:

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