Clear Skies: Neuroprotective Potential of Methylene Blue, N-Acetyl Cysteine, NMN, and Ginkgo biloba

Abstract

Brain health is increasingly recognized as a vital component of overall human health and longevity. This paper explores the neuroprotective and anti-aging potential of a supplement formulary—Clear Skies—which combines methylene blue, N-acetyl cysteine (NAC), nicotinamide mononucleotide (NMN), and Ginkgo biloba extract. Drawing upon clinical trials, preclinical studies, and mechanistic insights, we highlight the synergistic properties of these compounds in enhancing cognition, preventing neurodegeneration, and mitigating oxidative stress.

Introduction

The World Health Organization (2022) defines brain health as the ability to achieve one's full potential across the life span, regardless of disease presence. Despite its importance, brain health is often overlooked compared to cardiovascular or metabolic health. Lifestyle modifications and nutraceutical supplementation represent promising strategies, with research suggesting up to 40% of dementia cases may be preventable. The Clear Skies formulation integrates four compounds with emerging evidence for neuroprotection: methylene blue, NAC, NMN, and Ginkgo biloba.

Methylene Blue: Mechanisms and Therapeutic Applications

Methylene blue (MB) functions primarily by reducing Fe3+ in hemoglobin back to Fe2+, restoring oxygen transport. It also inhibits nitric oxide synthase and guanylate cyclase, improving vascular tone and oxygen delivery. Additionally, MB enhances mitochondrial function by bypassing Complex I/III, mitigating oxidative stress, and increasing ATP production. Clinical and Preclinical Applications: - Alzheimer's disease (AD): Randomized controlled trials demonstrate MB improves cognition and reduces amyloid-beta plaque burden. - Parkinson's disease (PD): Preclinical data show MB ameliorates motor deficits and oxidative damage. - COVID-19 management: MB has been repurposed as a dual antioxidant and cytokine suppressor, improving oxygen saturation in hospitalized patients. - Anti-aging potential: MB delays cellular senescence, enhances mitochondrial respiration, and shows skin anti-aging effects.

N-Acetyl Cysteine (NAC)

NAC is a precursor to glutathione, acting as a potent antioxidant and free radical scavenger. It modulates oxidative stress implicated in AD, PD, and amyotrophic lateral sclerosis (ALS). Studies also support NAC in reducing mucus accumulation in respiratory disease.

Nicotinamide Mononucleotide (NMN)

NMN is a nucleotide derived from ribose and nicotinamide and serves as a direct precursor to NAD+, a critical coenzyme for energy metabolism, DNA repair, and cellular signaling. Age-related declines in NAD+ contribute to mitochondrial dysfunction, insulin resistance, and accelerated aging. Supplementation with NMN has been shown to restore NAD+ levels, extend lifespan in animal models, and improve cardiometabolic function.

Ginkgo biloba

Extracts of Ginkgo biloba are widely studied for cognitive enhancement. Randomized controlled trials have demonstrated improvements in memory, attention, and quality of life in dementia patients. Its mechanisms include antioxidant activity, anti-inflammatory effects, and improved cerebral blood flow.

Synergistic Effects of the Clear Skies Formulary

The integration of MB, NAC, NMN, and Ginkgo biloba represents a holistic approach to brain health: - MB enhances mitochondrial respiration. - NAC and NMN mitigate oxidative stress and improve metabolic resilience. - Ginkgo biloba supports cognitive performance through antioxidant and vascular mechanisms. Together, they address both immediate cognitive function and long-term neuroprotection.

Conclusion

Brain health is central to human longevity, yet remains underemphasized. Evidence supports the neuroprotective roles of MB, NAC, NMN, and Ginkgo biloba. The Clear Skies supplement represents a novel, multi-targeted strategy for enhancing cognition, preventing neurodegenerative decline, and promoting healthy aging. Future clinical trials are warranted to establish efficacy and safety in long-term use.

References

1. Ginimuge, P. R., & Jyothi, S. D. (2010). Methylene blue: Revisited. Journal of Anaesthesiology Clinical Pharmacology, 26(4), 517–520. https://doi.org/10.4103/0970-9185.73408 2. Hashmi, M. U., et al. (2023). Exploring methylene blue and its derivatives in Alzheimer's treatment: A comprehensive review of randomized control trials. Cureus, 15(10), e46732. https://doi.org/10.7759/cureus.46732 3. Dabholkar, N., et al. (2021). Repurposing methylene blue in COVID-19 management: Mechanistic aspects and clinical investigations. Biomedicine & Pharmacotherapy, 142, 112023. https://doi.org/10.1016/j.biopha.2021.112023 4. Mokhtari, V., et al. (2017). A review on various uses of N-acetyl cysteine. Cell Journal, 19(1), 11–17. https://doi.org/10.22074/cellj.2016.4872 5. Freeberg, K. A., et al. (2023). Dietary supplementation with NAD+-boosting compounds in humans: Current knowledge and future directions. The Journals of Gerontology: Series A, 78(12), 2435–2448.

https://doi.org/10.1093/gerona/glad106 6. Nguyen, T., & Alzahrani, T. (2025). Ginkgo biloba. In StatPearls. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK541024/ 7. Le Bars, P. L., et al. (1997). A placebo-controlled, double-blind, randomized trial of an extract of Ginkgo biloba for dementia. JAMA, 278(16), 1327–1332. https://doi.org/10.1001/jama.278.16.1327 8. World Health Organization. (2022). Optimizing brain health across the life course: WHO position paper. Geneva: WHO.