

Metabolic Effects of Oral Oxaloacetate in Humans – Report 2025

Summary Overview

This document covers the metabolic pathways and physiological effects of orally administered oxaloacetate in humans, focusing on both healthy adults and ME/CFS patients.

1. Effects in Healthy Adults

In healthy individuals, oxaloacetate enhances mitochondrial metabolism, improves NAD⁺/NADH balance, and may support cognitive and mood regulation without major side effects. Studies (Vidoni et al., 2021; Tully et al., 2020) found metabolic and psychological benefits even at moderate doses (200 mg–2 g/day).

2. Effects in ME/CFS Patients

Patients with ME/CFS show significant improvements in fatigue and cognitive symptoms with oxaloacetate supplementation at 1–3 g/day (Cash et al., 2022; 2024). Clinical data confirm dose-dependent efficacy, normalization of mitochondrial activity, and minimal side effects.

3. Key Mechanistic Pathways

- Restores NAD⁺/NADH balance via malate dehydrogenase reaction.
- Enhances mitochondrial biogenesis (PGC-1 α activation).
- Reduces inflammation (NF- κ B downregulation).
- Lowers oxidative stress and ROS.
- Rebalances glycolysis vs oxidative metabolism.
- Activates AMPK, supporting glucose uptake and ATP efficiency.

4. Source Links

- [Cash & Kaufman 2022 – J. Translational Medicine](<https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-022-03488-3>)
- [Cash et al. 2024 – Frontiers in Neurology](<https://www.frontiersin.org/articles/10.3389/fneur.2024.1483876/full>)
- [Tully et al. 2020 – Obstet Gynecol Sci](<https://pubmed.ncbi.nlm.nih.gov/32206660>)
- [Vidoni et al. 2021 – Alzheimers Dement](<https://pubmed.ncbi.nlm.nih.gov/32715609>)
- [Wilkins et al. 2014 – Hum Mol Genet](<https://pubmed.ncbi.nlm.nih.gov/25027327>)
- [Williams et al. 2009 – Aging Cell](<https://pubmed.ncbi.nlm.nih.gov/19751290>)
- [Yin et al. 2024 – FASEB J](<https://pubmed.ncbi.nlm.nih.gov/34877518>)