O-304

DESCRIPTION:

O-304 (also known as ATX-304) is an investigational small molecule designed to activate AMP-activated protein kinase (AMPK), a central regulator of cellular energy homeostasis. AMPK functions as a metabolic master switch, promoting catabolic pathways that generate ATP (including fatty acid oxidation) while downregulating anabolic pathways such as lipogenesis and cholesterol synthesis. Activation of AMPK has been widely studied in the context of metabolic dysfunction, insulin resistance, and hepatic steatosis.

Preclinical data suggest that O-304 induces a metabolic shift characterized by increased fatty acid oxidation and reduced lipid synthesis. Through AMPK activation, downstream signaling appears to suppress sterol regulatory element-binding proteins (SREBPs) and other lipogenic transcription pathways, while enhancing mitochondrial oxidative metabolism. This metabolic reprogramming promotes lipid utilization rather than storage.

In animal models of metabolic dysfunction, O-304 has demonstrated reductions in whole-body fat mass, circulating cholesterol levels, and hepatic triglyceride accumulation. Additionally, treatment was associated with decreased markers of oxidative stress in metabolic tissues and attenuation of fibrotic signaling pathways within the liver.

Collectively, these findings position O-304 as a metabolic modulator targeting core cellular energy pathways rather than acting as a direct anorectic or stimulant.

PROTOCOL:

Content & Potency: 100mg capsule provided in a quantity of 30 capsules
Suggested dosage: take one capsule daily for 4-8 weeks

Summary of Key Preclinical Study:

Holm et al., JCI Insight, 2025

Title: AMPK activator ATX-304 reduces oxidative stress and improves MASLD via metabolic switching.

In this preclinical study, O-304 was evaluated in murine models of metabolic dysfunction–associated steatotic liver disease (MASLD). Oral administration of O-304 led to significant reductions in whole-body adiposity and circulating cholesterol levels compared with controls.

Histologic and biochemical analyses demonstrated decreased hepatic triglyceride accumulation and improvement in steatosis severity. Treatment also reduced markers associated with hepatic fibrosis and suppressed pro-fibrotic signaling pathways.

Gene expression profiling showed upregulation of fatty acid oxidation pathways and downregulation of lipogenic gene networks, consistent with AMPK pathway activation.

Additionally, hepatic oxidative stress markers were significantly reduced, supporting the proposed mechanism of improved mitochondrial efficiency and metabolic reprogramming.

Holm E, Vermeulen I, Parween S, et al. AMPK activator ATX-304 reduces oxidative stress and improves MASLD via metabolic switching. JCI Insight. 2025;10(7):e179990. doi:10.1172/jci.insight.179990.

Link: https://insight.jci.org/articles/view/179990