Metformin

Metformin Hydrochloride (M2076) is a compound that has been used for its antidiabetic properties for several decades. Metformin is typically used to reduce blood sugar in subjects with type 2 diabetes mellitus. Although the mechanism of action is not well characterized, metformin is known to decrease hepatic glucose production by inhibiting mitochondrial respiration and activating AMPK¹⁻². Metformin also enhances peripheral glucose uptake and increases insulin sensitivity³.

More recently, metformin has come back into the research spotlight for other potential applications. Metformin shows activity in cell and animal models of cancer as well as aging.

In various cancer models, metformin stops cell growth, cancer metastasis, and tumorigenesis; these effects are likely due to its ability to limit mitochondrial oxidative phosphorylation. In primary ovarian cancer cells, metformin induces cell cycle arrest and apoptosis⁴. In cell and animal models of cholangiocarcinoma, metformin limits cell cycle progression, halts cell proliferation, and suppresses growth of xenograft tumors⁵. Analysis of several clinical studies focusing on metformin administration in breast cancer subjects indicates a link between metformin use and lower mortality rates⁶.

New studies suggest that metformin may also slow down the effects of aging. In *Drosophila* intestinal stem cells, metformin inhibits age- and oxidative stress-induced centrosome amplification, limiting stem cell aging⁷. Metformin also targets complex I of the mitochondrial electron transport chain, altering mitochondrial free radical production⁸. In *Caenorhabditis elegans*, metformin administration extends lifespan through the promotion of mitohormesis⁹. Additional publications highlight the connection between inactivation of insulin signaling or caloric restriction -- both of which can be achieved with metformin -- and increased life span¹⁰.

M2076 Metformin Hydrochloride

References:

- 1. Zou MH, Kirkpatrick SS, Davis BJ, et al. J Biol Chem. 2004 Oct 15;279(42):43940-51.
- 2. Andrzejewski S, Gravel SP, Pollak M, et al. Cancer Metab. 2014 Aug 28;2:12.
- 3. Guigas B, Bertrand L, Taleux N, et al. Diabetes. 2006 Apr;55(4):865-74.
- 4. Patel S, Singh N, Kumar L. Asian Pac J Cancer Prev. 2015;16(16):6973-9.
- 5. Fujimori T, Kato K, Fujihara S, et al. Oncol Rep. 2015 Dec;34(6):2987-96.
- 6. Yang T, Yang Y, Liu S. J Breast Cancer. 2015 Sep;18(3):264-70.
- 7. Na HJ, Park JS, Pyo JH, et al. Mech Ageing Dev. 2015 Jul;149:8-18.
- 8. Matsuzaki S, Humphries KM. Biochemistry. 2015 Mar 24;54(11):2011-21.
- 9. De Haes W, Frooninckx L, Van Assche R, et al. Proc Natl Acad Sci U S A. 2014 Jun 17;111(24):E2501-9.
- 10. Anisimov VN. Cell Cycle. 2013 Nov 15;12(22):3483-9.









