

Memantine

Alzheimer's disease is the most common neurodegenerative disorder and a highly prevalent cause of dementia with aging. Several pathophysiological events are triggered in Alzheimer's disease that ultimately lead to signaling pathway dysfunction, failure of neurotransmission, and neuronal death. **Memantine (M1749)** is used as a treatment to slow the progression of this disease¹.

Several neuroprotective compounds inhibit cholinergic signaling to improve cognitive abilities. Memantine instead acts as a noncompetitive antagonist at NMDA receptors, blocking glutamate signaling². Memantine inhibits prolonged influx of calcium ions from extrasynaptic receptors, lessening neuronal excitotoxicity.

Memantine also interacts with a variety of ligand-gated ion channels such as nicotinic acetylcholine receptors (nAChRs), dopamine receptors, and serotonin receptors³. Most of this activity does not contribute to the effects of memantine on cognitive function, although it may be related to the antidepressant, antitussive, and antinociceptive activities of memantine⁴⁻⁶.

At therapeutic concentrations, memantine promotes synaptic plasticity and preserves or enhances memory in animal models of Alzheimer's disease. Additionally, memantine protects against excitotoxic neurodegeneration. Additional research indicates that memantine suppresses toxicity induced by amyloid- β (A β) plaque formation, potentially inhibiting the production of A β by altering APP processing⁷.

References:

1. Reisberg B, Doody R, Stöffler A, et al. *New Engl. J. Med.* 2003;348(14):1333-41.
2. Cacabelos R, Takeda M, Winblad B. *Int J Geriatr Psychiatry.* 1999 Jan;14(1):3-47.
3. Nakaya K, Nakagawasai O, Arai Y, et al. *Behav Brain Res.* 2011 Mar 17;218(1):165-73.
4. Pringle A, Parsons E, Cowen LG, et al. *J Psychopharmacol.* 2012 Nov;26(11):1417-23.
5. Dicipinigaitis PV, Canning BJ, Garner R, et al. *J Pharmacol Exp Ther.* 2015 Mar;352(3):448-54.
6. Kayser V, Latrémolière A, Hamon M, et al. *Eur J Pain.* 2011 May;15(5):451-8.
7. Colom LV, Castaneda MT, Aleman D, et al. *Neurosci Lett.* 2013 Apr 29;541:54-7.

