CALBIOCHEM®

10394 Pacific Center Court
San Diego, CA 92121
(619) 450-9600

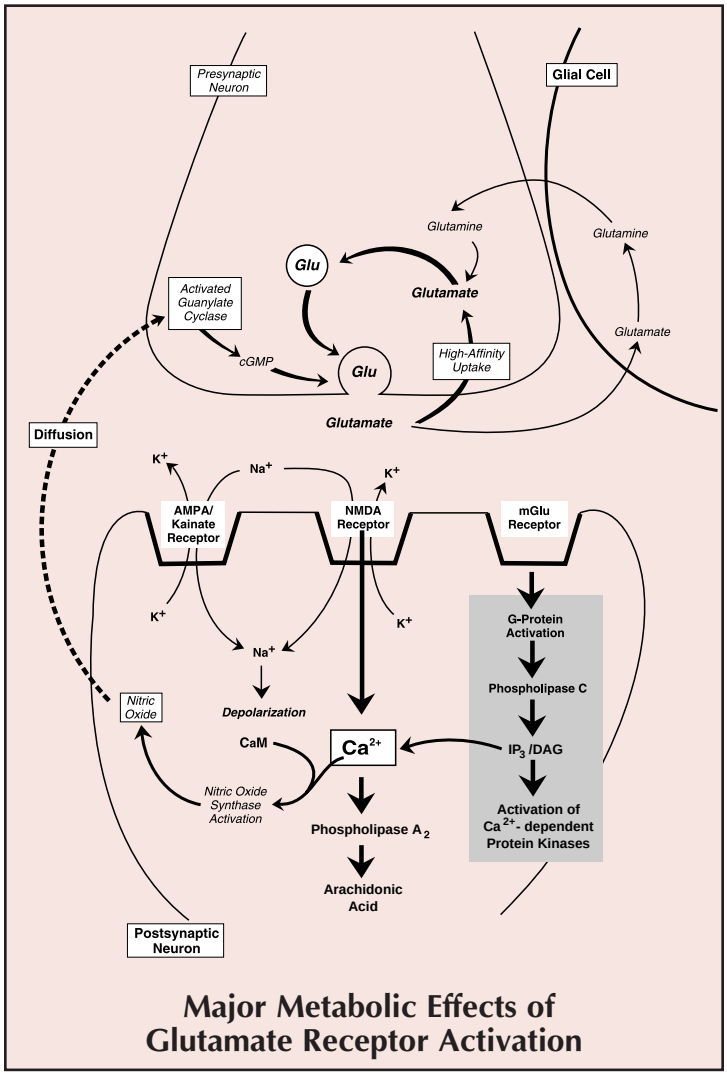
Customer Service: (800) 854-3417
Technical Service: (800) 628-8470
Fax: (800) 776-0999

EXCITOTOXIC GLUTAMATE ANALOGS

Glutamate and related excitatory amino acids are released by about 40% of the synapses in the mammalian brain.[1-3] The excitatory effect of glutamate and its analogs is caused by the activation of glutamate receptors that directly gate ion channels.[4-6] They are known as NMDA (N-methyl-D-aspartic acid), AMPA (α-amino-3-hydroxy-5-methyl-isoxazole-4-propionate), and kainate receptors. Glutamate is also known to activate a metabotropic receptor that couples a GTP-binding protein to intracellular second messengers[7-9] and leads to the activation of phospholipase C.[8]

The release of glutamate from the presynaptic neuron is mediated by a Ca^{2+}-dependent exocytosis process.[10] Glutamate is rapidly cleared from the synaptic cleft by a combination of high affinity transport system and a slow diffusion into the neighboring glial cells.[11] The figure on the right highlights the major effects of glutamate receptor activation and mechanisms involved in the clearance of glutamate from the synaptic cleft.

Excitotoxic effects of glutamate analogs are primarily achieved through the activation of the ionotropic receptors.[1,12] The NMDA receptor complex is permeable to Na^+, K^+ and Ca^{2+} in a voltage-dependent manner. AMPA and kainate receptors have also been shown to form channels for Ca^{2+}.[13] The Ca^{2+}-mediated effects, resulting from the over-stimulation of ionotropic glutamate receptors, particularly the NMDA receptors, have been implicated in neuronal degeneration. NMDA receptors have also been implicated in long-term potentiation and neuronal plasticity.[14-16] They also play a major role in regulating the number of nerve cells during development by contributing to cell death via their excitotoxic action.[12]



Major Metabolic Effects of Glutamate Receptor Activation

Cited References:

1. Coyle, J.T., and Puttfarcken, P. 1993. *Science* **262**, 689.
2. Fonnum, F. 1984. *J. Neurochem.* **42**, 1.
3. Masood, K., et al. 1994. *Mol. Pharmacol.* **45**, 324.
4. Katsuwada, T., et al. 1992. *Nature* **358**, 36.
5. Dumuis, A., et al. 1988. *Nature* **336**, 68.
6. Krizaj, D., et al. 1994. *J. Neurosci.* **14**, 5661.
7. McBain, C. J., et al. 1994. *J. Neurosci.* **14**, 4433.
8. Miller, R.J., et al. 1991. *Trends Pharmacol. Sci.* **12**, 365.
9. Guerineau, N.C., et al. 1994. *J. Physiol.* **474**, 27.
10. Nadler, J.V., et al. 1977. *J. Neurochem.* **29**, 279.
11. Shank, R.P., and Aprison, M.H. 1979. *J. Neurochem.* **28**, 1189.
12. Bahn, S., et al. 1994. *J. Neurosci.* **14**, 5525.
13. Wisden, W., and Seeberg, P.H. 1993. *Curr. Opin. Neurobiol.* **3**, 291.
14. Buller, A.L., et al. 1994. *J. Neurosci.* **14**, 5471.
15. Mohaghan, D.T., et al. 1989. *Annu. Rev. Pharmacol. Toxicol.* **29**, 365.
16. Smirnova, T., et al. 1993. *Science* **262**, 433.

GLUTAMATE RECEPTOR AGONISTS

1-Aminocyclopropane-1-carboxylic Acid. A potent and selective agonist of the glycine modulatory site of NMDA receptor complex. Mimics the effects of glycine on the NMDA receptor ion channel. M.W. 101.1.

Cat. No. 149101-Y 250 mg, 1 g, 5 g

DL-2-Amino-4-phosphonobutyric Acid. A phosphonic acid analog of DL-glutamic acid that does not appear to inhibit Ca^{2+} channels. M.W. 183.1.

Cat. No. 165303-Y 250 mg, 1 g

(±)-*trans*-Azetidine-2,4-dicarboxylic Acid. An activator of the metabotropic glutamate receptor. May be useful in studying the structural differences in the G-protein linked metabotropic receptor subtypes. M.W. 145.1.

Cat. No. 194320-Y 500 µg

Domoic Acid. A structural analog of kainic acid that has excitant potency exceeding that of kainic and glutamic acid for postsynaptic excitation. Its binding to the receptor causes continuous stimulation of nerve cells leading to depletion of energy, cellular edema and death. M.W. 311.3.

Cat. No. 324378-Y 1 mg

EDAC, HCl. A water-soluble carbodiimide that can be used to modify NMDA receptors resulting in reduced MK-801 binding. Also modifies opioid receptors resulting in reduction in bremazocine-binding sites. Useful for conjugating haptens to proteins and polypeptides. M.W. 191.7.

Cat. No. 341006-Y 5 g, 25 g

L-Glutamic Acid. A potent exitatory amino acid. About 20% of the synapses in mammalian brain utilize glutamate as a neurotransmitter. M.W. 147.1.

Cat. No. 3510-Y 100 g, 1 kg

Caged Glutamic Acid. A water-soluble photolabile derivative of glutamic acid that is biologically inactive until photolyzed. Useful in studies involving instantaneous and controlled release of neurotransmitter in isolated cell systems. Extinction coefficient (347 nm, H_2O): 5700 M^{-1} cm^{-1}.

Cat. No. 351015-Y 5 mg

Ibotenic Acid, *Amanita* sp. A structural analog of glutamate and a potent glutamate agonist and neurotoxin. Binds to NMDA receptors. M.W. 158.1.

Cat. No. 401008-Y 1 mg

N-Methyl-D-aspartic Acid (NMDA). An excitatory amino acid analog that acts as a selective agonist for glutamate receptor regulating Ca^{2+} channel. Mediates synaptic transmission and neural plasticity and is involved in long-terrm potentiation, ischemia and neuronal death. M.W. 147.1.

Cat. No. 454575-Y 100 mg

Quisqualic Acid. A potent glutamate analog and vertebrate neurotoxin that acts at AMPA receptors and facilitates the entry of Na^+. M.W. 189.1.

Cat. No. 551900-Y 1 mg

GLUTAMATE RECEPTOR ANTAGONISTS

DL-2-Amino-3-phosphonopropionic Acid. A glutamate metabotropic receptor antagonist. A phosphonic acid analog of DL-aspartic acid. M.W. 169.1.

Cat. No. 165307-Y 250 mg

Conantokin, G, *Conus geographus*. A non-competitive NMDA receptor antagonist that interacts with the glutamate binding site. This antagonistic activity is attributed to non-competitive inhibition of polyamine responses. Also known as "sleeper peptide." M.W. 2264.2.

Cat. No. 234550-Y 50 µg

Conantokin T, *Conus tulipa*. A potent NMDA receptor antagonist. Its antagonistic activity is attributed to non-competitive inhibition of polyamine responses. Also known as "sleeper peptide". M.W. 2683.8.

Cat. No. 234555-Y 50 µg

DL-*threo*-β-Hydroxyaspartic Acid. An amino acid derivative that blocks the uptake of glutamate. A constituent of polypeptide antibiotic cinnamycin. M.W. 149.1.

Cat. No. 390185-Y 10 mg

Joro Spider Toxin JSTX-3, *Nephlia clavata*. Synthetic spider toxin that selectively and irreversibly blocks excitatory postsynaptic potentials without affecting the inhibitory potentials. Selectively inhibits glutamate potentials by blocking quisqualate-sensitive glutamate receptors. M.W. 565.7.

Cat. No. 420102-Y 100 µg

(+)-MK 801 Maleate. A highly potent, selective and non-competitive NMDA receptor antagonist that acts by binding to a site located within the NMDA associated ion channel thus preventing Ca^{2+} flux. M.W. 337.4.

Cat. No. 475878-Y 10 mg

Pentamidine Isethionate. An NMDA receptor antagonist and a neuroprotective agent in vitro. Inhibits neuronal nitric oxide synthase and acts as an uncoupler of oxidative phosphorylation. M.W. 592.7.

Cat. No. 516345-Y 100 mg

Spermine, Tetrahydrochloride. A biogenic polyamine that is essential for growth of normal and neoplastic tissues. Binds to the polyamine modulatory site of the NMDA receptor, attenuating both NMDA and quisqualate-mediated responses in vivo. M.W. 348.3.

Cat. No. 5677-Y 5 g

Please call our Technical Service Department or your local sales office for more information on these products.

Australia
Calbiochem-Novabiochem Pty
Tel (02) 318 0322
Fax (02) 319 2440
calbiochem_novabiochem@compuserve.com

Great Britain
Calbiochem-Novabiochem (UK) Ltd
Tel (0115) 943 0840
Fax (0115) 943 0951
customer.service@cnuk.co.uk

Japan
Calbiochem-Novabiochem Japan
Tel (03) 5443 0281
Fax (03) 5443 0271

USA & Canada
Calbiochem-Novabiochem Corp.
Tel (800) 854-3417
Fax (800) 776-0999
technical@calbiochem.com

Germany
Calbiochem-Novabiochem GmbH
Tel (06196) 63955
Fax (06196) 62361
customer.service@calbiochem-novabiochem.de

For additional information, contact your local Calbiochem-Novabiochem sales office.

CB0521-1197
Printed on recycled paper.