L-4-chlorokynurenine

National Cancer Institute

Source

National Cancer Institute. L-4-chlorokynurenine. NCI Thesaurus. Code C118314.

An orally bioavailable, blood brain barrier (BBB) penetrating, chlorinated analog of the endogenous neuromodulator kynurenic acid and prodrug of 7-chlorokynurenic acid (7-Cl-KYNA), a N-methyl-D-aspartate receptor (NMDA-R) antagonist at the glycine-coagonist (GlyB) site, with potential anti-hyperalgesic, neuroprotective and anti-epileptic activities. Unlike 7-Cl-KYNA, L-4-chlorokynurenine, upon oral administration, crosses the BBB and is enzymatically converted, through transamination, within activated astrocytes located at sites of injury in the central nervous system (CNS) to its active metabolite, 7-Cl-KYNA, which allows for high levels of this active metabolite at these specific sites. In turn, 7-Cl-KYNA selectively binds to and blocks the GlyB site within the NMDA receptors. This inhibits both NMDA-R overstimulation by the excitatory neurotransmitter glutamate and NMDA-R-mediated excitotoxicity, which prevents neuronal damage and induces analgesia. In addition, another metabolite, 4-chloro-3-hydroxyanthranilic acid, inhibits the synthesis of quinolinic acid, an endogenous NMDA receptor agonist, thereby further preventing excitotoxic damage. Compared to conventional NMDA-R antagonists, NMDA-R GlyB-specific antagonists appear to have fewer side effects.