Glutamate is the principal excitatory neurotransmitter in the brain. Glutamatergic overstimulation may result in neuronal damage, a phenomenon that has been termed, excitotoxicity. Such excitotoxicity ultimately leads to neuronal calcium overload, and has been implicated in neurodegenerative disorders. Glutamate stimulates a number of postsynaptic receptors including NMDA receptor, which has been particularly implicated in memory processes, dementia and in the pathogenesis of neurodegenerative disorders like Alzheimer's disease. Accumulating evidence suggests that excessive glutamatergic stimulation could also be one of the mechanism underlying neurodegeneration in Parkinson's disease as well as in other neurodegenerative diseases such as amyotrophic lateral sclerosis.

Prevalence of Parkinson's disease and Alzheimer's disease increases with age and are associated with chronic, progressive and debilitating conditions. There is impairment of higher mental function, with loss of memory as the cardinal symptom. Aphasia, that is loss of ability to use words; agnosia, that is inability to recognize familiar objects; and apraxia, that is inability to execute complex coordinated movements are some of the symptoms, which are very distressing to patients of Alzheimer's disease. They also constitute a heavy burden on the society as well as health care system. Therefore, there is an ever increasing need for effective pharmacotherapy and recent research efforts have come up with novel therapeutic agents in the treatment of neuro-degenerative diseases. Among these, blockers of glutamate release or of glutamate receptors specifically N-methyl-D-aspartate (NMDA) receptors, have shown considerable importance as potential neuro-protective agents.

**Remacemide**

This drug is a low affinity NMDA channel blocker. It has been recently approved for the treatment of epilepsy. Preliminary studies have shown that the drug could be effective in treatment of Parkinson's disease also, when it is administered concomitantly with dopaminergic agents, such as levodopa. Result from multicentric trials, suggests that it is safe and well tolerated in patients with Parkinson's disease, when used as monotherapy, for a period of 5 weeks. Treatment for longer periods, could produce more benefits.

**Memantine**

It is related to amantadine. Memantine is an uncompetitive NMDA antagonist and functions as a neuroprotective agent. It is being used as an antispastic agent and also in the treatment of dementia. Based on preliminary findings, memantine is being evaluated for its effectiveness in Parkinson's disease. Recent clinical trial in patients with advanced dementia, Alzheimer's disease and vascular dementia suggests therapeutic benefits. Memantine treatment given in a dose of 20 mg once daily, for a period of 28 weeks was found to be useful in reducing the clinical deterioration in moderate to severe Alzheimer's disease, a phase which is associated with distress for patients and burden on the caregivers, and for which currently no other treatment options are available.

**Riluzole**

It is a member of benzothiazole class. Riluzole is an antiglutamate agent, that is already being used for the treatment of amyotrophic lateral sclerosis (ALS). Pharmacological properties include an inhibitory effect on glutamate release, blocking of postsynaptic NMDA and kainate type of glutamate receptors and inhibition of voltage dependent sodium channels. Riluzole exhibited neuroprotective potential in various *in vivo* experimental models of neuronal injury involving excitotoxic mechanism. In *in vitro* tests, riluzole protected the cultured rat motor neurons from the excitotoxic effects of glutamic acid and prevented the death of cortical neurons induced by anoxia. In clinical trials, riluzole showed modest but genuine effects on the survival of patients with ALS.

Although, the magnitude of effect in ALS was small, riluzole still constitutes a significant therapeutic milestone in the treatment of a disease, which is refractory to all previous treatments. It is orally well absorbed and is highly protein bound. It is extensively metabolised by liver. The half life is about 12 h. Recommended dose is 50 mg every 12 h, taken one hour before or two hours after a meal. Riluzole is generally well tolerated, although nausea or diarrhea may occur. Riluzole was found to be well tolerated in patients with Parkinson's disease. Currently, riluzole is being tried in clinical trials to evaluate its effects at early stage of Parkinson's disease, inorder to test its restorative effect. Also, it is being evaluated in patients with fluctuations and dyskinesias.
Newer glutamate antagonists are currently in clinical development and are being tested in Alzheimer’s disease. These include L-701252, LY-235959 and WIN-634802. These agents may also be tested in Parkinson’s disease. Various other agents which are also at different phases of development are LIGA 20, LY-274614 and IX-354740.

**Sources**


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