



Benzodiazepine Derivatives with Reduced Side Effects for Treatment of Neuropathic Pain

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Overview

Neuropathic pain encompasses a wide range of painful conditions of diverse origins, including diabetic neuropathy, post herpetic neuralgia, post-surgical nerve injuries and many others. Currently there are five approved drugs on the market to treat the diversity of neuropathic pain conditions; however, they are not effective for all patients and may have adverse side effects.

The Invention

Researchers at the University of Wisconsin-Milwaukee have developed new benzodiazepine derivatives useful in the treatment of neuropathic pain with reduced sedative and ataxic effects. GABA is the major inhibitory neurotransmitter in the central nervous system. Non-selective benzodiazepine drugs, such as valium, act by enhancing the inhibitory effects of GABA at GABAA receptors in the CNS. These drugs broadly target GABAA receptors containing $\alpha 1$, $\alpha 2$, $\alpha 3$, or $\alpha 5$ subunits.

Recently, it was discovered that the various effects of non-selective benzodiazepines are specifically mediated through certain a subunit-containing GABAA receptor populations in the brain. $\alpha 1$ -containing GABAA receptors control sedation, whereas the anti-anxiety and anti-pain activity works mainly through $\alpha 2$ and $\alpha 3$ receptors. $\alpha 5$ receptors play critical roles in learning and memory consolidation.

The inventors of this technology have produced GABAA receptor agonists specific for $\alpha 2$ and $\alpha 3$ receptors. Because the compounds do not affect $\alpha 1$ receptors, they have significant neuropathic pain protection without sedative and ataxic effects. In addition, the compounds are anxiolytic and anti-convulsant. The inventors are carrying out pre-clinical testing of these compounds by conducting *in vitro* studies and animal studies in rats, mice and monkeys. These compounds were found to have significant neuropathic pain protection in mice and rats without causing sedation, muscle relaxation or ataxic effect.

Key Benefits

- Significant neuropathic pain protection
- Anxiolytic and anti-convulsant
- Reduced sedative, hypnotic, muscle relaxant and ataxic effects

Stage of Development

Lead Compound Developed

Tech Fields

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