

Publication

Reboxetine: a pharmacologically potent, selective, and specific norepinephrine reuptake inhibitor.

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Abstract

BACKGROUND:

Reboxetine is a potent antidepressant, with efficacy comparable to that of imipramine, desipramine, and fluoxetine, and has improved side-effect profile. The basis of its efficacy and improved tolerability is sought through studies of reboxetine in a number of pharmacological models of depression.

METHODS:

Pharmacological selectivity for uptake systems was defined by uptake and binding assays for the three monoamine uptake sites. Specificity was determined in 39 different receptor and 6 enzyme assays. In vivo selectivity was defined by measurement of neuronal firing rates in the locus coeruleus, dorsal raphe, and substantia nigra. Reserpine-induced blepharospasm and hypothermia, clonidine-induced hypothermia, defined reboxetine's in vivo pharmacology. Reboxetine's antidepressant potential was evaluated behaviorally by the tail-suspension test, forced swimming, and the DRL72 operant responding test.

RESULTS:

Reboxetine is a potent, selective, and specific norepinephrine reuptake inhibitor (selective NRI) as determined by both in vitro and in vivo measurements. Unlike desipramine or imipramine, reboxetine has weak affinity ($K_i > 1,000$ nmol/L) for muscarinic, histaminergic H1, adrenergic alpha1, and dopaminergic D2 receptors. In vivo action of reboxetine is entirely consistent with the pharmacological action of an antidepressant with preferential action at the norepinephrine reuptake site. Reboxetine showed an antidepressant profile in all tests of antidepressant activity used. Significant decreases in immobility were observed in the tail suspension test and behavioral despair test. Increased efficiency in responding was observed in the DRL72 test.

CONCLUSIONS:

Reboxetine is a potent, selective, and specific noradrenergic reuptake inhibitor. It has a superior pharmacological selectivity to existing tricyclic antidepressants and selective serotonin reuptake inhibitors when tested in a large number of in vitro and in vivo systems. Given the pharmacological profile, reboxetine is expected to be a selective and potent tool for psychopharmacological research. The use of reboxetine in the clinic will also help clarify the role norepinephrine plays in depression.