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TITLE

MOLECULAR DRUG TARGETS FOR DEVELOPMENT OF ANTIDEPRESSANT DRUGS

Dinesh Dhingra

Pharmacology Division, Department of Pharmaceutical Sciences,

Guru Jambheshwar University of Science and Technology, HISAR-125001 (Haryana), INDIA.

Depression is a heterogeneous mood disorder. The main causes of depression are decreased brain levels of monoamines like noradrenaline, dopamine and serotonin. Therefore, drugs restoring the reduced levels of these monoamines in the brain either by inhibiting monoamine oxidase A or by inhibiting reuptake of these neurotransmitters have been reported to possess antidepressant property. The various other molecular targets for development of antidepressant drugs include nicotinic acetylcholine receptors, glutamate, GABAB, benzodiazepine receptors, neuropeptide Y, neurokinins, corticotropin-releasing factor, neurosteroids, brain-derived neurotrophic factor and cytokines. The relation between nicotine and depression is supported by the fact that transdermal nicotine can improve the mood of depressed patients. Anterior cingulate glutamatergic concentration is found to be significantly decreased in patients of major depression. GABAB receptor antagonism may serve as a basis for the generation of novel antidepressants. Patients on antidepressant drug therapy had decreased serum levels of substance P, thus indicating high levels of substance P in depressed patients. Selective antagonists of the neurokinin NK1, NK2 and NK3 receptors showed antidepressant-like effects. There are a number of studies indicating a hyperactive hypothalamic-pituitary adrenal axis in depressed patients. There is significant elevation of corticotropin-releasing factor concentration in cerebrospinal fluid of patients with major depression. Neurosteroids, particularly allopregnanolone and dehydroepiandrosterone showed antidepressant-like effects. Serum levels of brain-derived neurotrophic factor are decreased in patients of major depression. Alterations in the levels of circulating cytokines such as interleukin 1-beta, interleukin-6, tumor necrosis factor-alpha and interferon-gamma have been linked to a depression.