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Editorial

Novel Antidepressant Frontiers: Unlocking the Therapeutic Potential of Plant-Derived Flavonoids

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Depression is one of the most complicated psychiatric disorders, which leads to cognitive impairment and thinking disturbances. This disorder negatively effects the quality of life badly. Major depression contains behavioral and physiological symptoms like depressed mood, highly diminished pleasure in many activities and loss of concentration. According to World Health Organization (WHO) around 350 million persons suffer from depression. Depression will be the second driving cause of disability globally. There are many effective antidepressants available but still there is need to discover novel agents for treatment of this disorder with better efficacy and fewer side effects [1].

Conventional antidepressant drugs ultimately act by increasing monoamine levels at the synaptic cleft by either inhibiting the reuptake of monoamines, inhibiting the enzyme monoamine oxidase, which degrades monoamine neurotransmitters; or interacting with pre- or postsynaptic receptors that regulate monoamine transmitter release and/or neuronal firing rate. It has been proposed that as antidepressant drugs increase extracellular monoamine concentrations, depression might be produced by deficiencies in noradrenaline, 5-HT and dopamine at their receptor sites in the brain. This concept is known as the monoamine depression hypothesis [2].

Although *the* effects of antidepressants on monoamines can be seen soon after administration, it generally takes a few weeks of continued treatment for therapeutic responses to appear. Due to the therapeutic delay of antidepressants, problems involving the neural network's processing of information, rather than chemical disequilibrium might well underlie depression. In fact, conventional antidepressants mediate their effects by increasing Brain-Derived Neurotropic Factor (BDNF) in the forebrain regions, particularly in the hippocampus, making BDNF an essential determinant of antidepressant efficacy. BDNF acts in the brain inducing neuroplasticity, which results in depressive symptom improvements, and it has already been shown that hippocampal neurogenesis is a requirement for the therapeutic effects of antidepressants [3].

Depression pharmacotherapy is costly, though widely prescribed by physicians. However, less than half of the patients treated obtain complete remission through therapy with single antidepressant drugs. Some patients exhibit partial or no remission and some patients display treatment intolerance responses. This emphasizes the need to identify novel classes of antidepressants. The most frequent side effects of these drugs are due to rapid monoamine concentration increases at the receptor sites. These effects could be summarized as increased anxiety, gastrointestinal and sexual problems and decreased alertness. The challenge for such new antidepressants is to achieve fast antidepressant response, broader efficacy, and fewer adverse effects. Additionally, some side effects of anti-depressant and anti-psychotic drugs are related to hematology and biochemical parameters also [4].

Flavonoids extracted from natural plant sources have been reported to possess antidepressant-like effect in many studies [5]. The antidepressant-like effect mechanism of flavonoids is well-defined in rats and it could be the reversal of monoamine neurotransmitter attenuations by 5-HT, NA and DA, and 5-hydroxyindoleacetic acid (5-HIAA), and most probably the regulation of the neurotransmitter receptor expression. According to a recent report, more than 6000 flavonoids are known with diverse pharmacological effects. The

neuroprotective like effect and antitumor action of isolated flavonoid have been recently reported. Flavonoids found in food or medicinal plants must pass the blood-brain barrier, and to achieve this goal they must be absorbed in the digestive tract, and transported by the circulatory system to the brain [6].

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