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Depression Still Requires Novel Psychiatric Medication

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Depression is a mood disorder which leads to sadness, emptiness, loss of interest and energy for the patient. Major depressive disorder (MDD) is a widespread disease, with a lifetime prevalence of 15% and an annual incidence of ~7%. It is associated with significant costs in quality of life, loss of work productivity, and a high risk of mortality. Herein, brain chemistry plays an important role in determination and also treatment of depression for individuals (1). Monoamine oxidase (MAO) enzyme is a flavoprotein containing flavin-adenine-dinucleotide localized at the outer mitochondrial membranes of brain, intestinal mucosa, liver and other organs. MAO-A and MAO-B are two isoforms with 70% identical amino acids but with different selective inhibitors and substrate specificities. MAO-A catalyzes biogenic amines deaminations such as dopamine, norepinephrine, adrenaline and serotonin, resulting in the toxic production of hydrogen peroxide, ammonia and aldehydes, which leads to neuronal death. These reactions could yield loss of biogenic amines in the brain and appearing depression. Therefore, regulation and inhibition of the MAO-A activity with antidepressant drugs seems to be the key step in the treatment of depression (2). Current antidepressant therapeutics target aspects of the monoamine neurotransmitter systems (e.g. serotonin and serotonin–norepinephrine reuptake inhibitors (SSRIs and SNRIs) in the brain and are often only partially effective for MDD. Furthermore, these synthetic medications may have adverse effects on human health condition. Hence, it is still necessary to find potential alternative medicines with potent antidepressant efficacy (3). In medicine, there are two main methods of improving the health care provided: seeking new treatment procedures and perfecting (optimizing) the existing ones. Optimization of treatment includes not only practical tools such as therapeutic drug monitoring but also implementation of general trends in the clinical practice. New pharmacological options include new more sophisticated forms of monoaminergic drugs, old drugs rediscovered on the base of a better understanding of pathophysiology of mental illnesses, and drugs aimed at new treatment targets. Phytochemicals derived from herbs are known to decrease the risk of some severe disorders including autoimmune and cardiovascular diseases as well as neurodegenerative diseases. Indeed, popular polyphenols such as curcumin, ferulic acid, proanthocyanidin, quercetin, andresveratrolhaveshown potent anti-inflammatory and antioxidant properties. These phytochemicals repeatedly have demonstrated their neuroprotective effects, strongly suggesting that they can improve the symptoms of depression (4). During the last decade, so many researchers have dedicated their efforts to detect the most effective potent natural products with antidepressant activities, which reveal the importance of herbal natural products

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to be considered as psychoactive drugs. Antidepressant response rates in controlled trials are estimated at ~54% and real-world effectiveness data suggests a somewhat lower rate. Response rates are lower still in patients who have not responded to previous treatment attempts and meaningful advancements will likely come only from identification of mechanistically novel agents.

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