LETTER TO THE EDITOR

Magic mushrooms and mood: Exploring psilocybin as a depression treatment

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Dear Editor, In view of ongoing global research on mental health, especially Major Depressive Disorder, we would like to draw attention to a psychedelic substance, Psilocybin, which has been emerging as a viable treatment option for MDD. Psilocybin is a psychedelic compound derived from certain mushrooms that acts on Serotonergic receptors (primarily 5HT-2A). Psychedelic substances have psychological effects, i.e., hallucinations, euphoria, and altered perception.[1] Studies have demonstrated their effectiveness in the treatment of disorders like 'Major Depressive Disorder (MDD)', and 'Treatment-Resistant Depression'. Recently, the FDA gave 'breakthrough' therapy status to a psilocybin treatment developed by London-based biotechnology company 'Compass Pathways Ltd' as stated in.[2]

World Health Organization (WHO) statistics from 2023 revealed that approximately 280 million people worldwide are living with depression. While MDD was ranked as the third most common cause of disease burden worldwide, WHO has predicted that it will be the number one cause by 2030. MDD is defined as a persistent sad/depressed mood, appetite, sleep changes, feelings of guilt, and anhedonia for at least 2 weeks. Despite advancements in understanding the pathophysiology of depression and the discovery of novel antidepressants, only 60-70% of people respond to the treatment.[3]

Psilocybin, also known as 4 phosphoryloxy-N, N dimethyltryptamine (4PO-DMT), is a naturally occurring psychedelic compound found in numerous species of mushrooms. Psilocybin acts as a serotonergic agonist on 5HT receptors, primarily 5HT2A.[2] It also has indirect effects on dopaminergic and glutamatergic neurotransmission and promotes neuroplasticity. It has significant effects on various plasma neurotrophic, immunological (IL-1β, IL-6, TNF-α CRP, and Eosinophils), and neuroendocrine markers (regulate Hypothalamic-Pituitary-Adrenal axis) that are disrupted in MDD.[4]

It increases the release of neurotrophic factors, thereby promoting neuronal regeneration, and decreases the release of above mentioned neuroinflammatory markers. It may help alleviate anxiety and depression by reducing threat sensitivityin the visual cortex and by calming the overactive default mode linked with negative thoughts.[5]

Recent clinical trials show that Psilocybin produces improvement in anxiety and depression symptoms for extended periods and improves quality of life. The most common side effects noted were minor elevations in blood pressure and headaches with rare episodes of paranoia and anxiety.[5]

A prospective 12-month follow-up study supported durable and long-lasting effects of psilocybin and improvements in clinician-based depression scale GRID-HAMD and patient-rated measures of depression BID-II and QID (depression assessment questionnaires).[6]

Another very recent systematic review supports that Psilocybin alleviates depression by enhancing brain flexibility and improving emotional processing and connection with self and others.[7]

In conclusion, Pakistan should explore psilocybin as a potential treatment option for MDD. We encourage the initiation of local clinical trials and develop a regulatory framework to make this treatment option possible. While worldwide research shows positive results, this effort could offer new hope for the treatment of depression.

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