Endnotes

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Serotonin and suicidal behavior
Ann N Y Acad Sci. 1990;600:476-84; discussion 484-5. doi:10.1111/ j.1749-6632.1990.tb16903.x. PMID: 2252327.

(Authors—Schaller and Mountjoy—are not claiming that the biochemical etiology of suicide is fully understood.)

ABSTRACT: Studies of the brains of suicide victims indicate a decrease in brain stem levels of 5-HT and/or 5-HIAA. There also appears to be a region-specific increase in 5-HT2 receptors, which are post-synaptic and may therefore be elevated in

response to reduced serotonin levels. Because we lack information on how 5-HT2 and other serotonin receptor populations are regulated, the mechanisms underlying these findings remain unclear. If the initial reports of fewer imipramine binding sites prove accurate, it would further suggest involvement of serotonin neurons, specifically at the terminal level. The relationship between suicide attempters and completers is not fully understood; however, studies of attempters, especially those making more lethal attempts, seem to confirm what is observed in the brains of completers. Neuroendocrine and CSF data show evidence of serotonin sub-responsivity and lower CSF 5-HIAA levels. Thus, the overall direction of change is towards a weaker serotonin signal which rather than being due to a primary receptor defect (a possibility that cannot be ruled out but for which there is no current evidence), appears to be due to reduced levels of serotonin release. The causes behind this phenomenon pose a research challenge, and it is clear that reduced serotonin alone cannot account for the timing or nature of suicidal behavior. Future research must explore the roles of other neurotransmitters, which could explain why, in some cases, aggression is directed outward toward others, whereas in other cases it is channeled inward as suicidal behavior. Clarifying the roles of serotonin and related transmitter systems is essential before designing and testing a comprehensive pharmacological treatment plan.

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ABSTRACT: Accumulating evidence supports a psychobiological perspective of suicidal behavior, particularly highlighting the serotonin hypothesis of suicide risk. The initial indication of a link between serotonin and suicide emerged from postmortem brain studies of suicide victims. Current research data point to decreased brain stem levels of serotonin and 5-HIAA, alterations in the presynaptic binding of the ligand 3H-imipramine to serotonin neurons, and a region-specific increase in postsynaptic 5HT2 receptors in the prefrontal cortex of suicide victims. Early CSF studies showed reduced CSF 5-HIAA in patients who had recently attempted suicide, and subsequent investigations involving large cohorts of mood-disorder patients validate the original premise that low CSF 5-HIAA predicts heightened suicide risk following an attempt.

Nonetheless, the clinical applicability of these compelling biological findings in managing suicide risk among psychiatric patients will rely on the outcomes of psychopharmacological treatment research aimed at suicidal behavior.

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Genetics and epigenetics of self-injurious thoughts and behaviors: Systematic review of the suicide literature and methodological considerations

Am J Med Genet B Neuropsychiatr Genet. 2022 Oct;189(7-8):221-246. doi: 10.1002/ajmg.b.32917 Epub 2022 Aug 17. PMID: 35975759.

ABSTRACT: Suicide is a multifaceted and poorly understood clinical outcome, underscoring the urgency of research into its phenomenology and etiology. Epidemiological studies have shown that suicidal behavior is heritable, suggesting that genetic and epigenetic data could function as biomarkers of suicide risk. Here, we comprehensively review the literature on genetic and epigenetic alterations across the spectrum of self-injurious thoughts and behaviors (SITB), encompassing 577 studies focused on genome-wide and epigenome-wide associations, candidate genes (SNP and methylation), noncoding RNAs, and histones. Only limited gene convergence appears across different units of analysis, though pathway analyses implicate nervous system development/function and immunity/inflammation in SITB. We propose directions for future research on the genetic and epigenetic correlates of SITB, emphasizing the importance of measurement considerations.

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ABSTRACT: Depression is a heterogeneous and complex condition with diverse symptoms, and its neurobiological basis remains incompletely understood. At present, there are no validated, easily obtainable, and clinically useful noninvasive

biomarkers or biomarker panels capable of confirming a diagnosis of depression, including its subtypes, or improving diagnostic procedures. Future multimodal preclinical and clinical research, incorporating (epi)genetic, molecular, cellular, imaging, and other studies, is needed to advance our understanding of the roles of monoamines, GABA, the HPA axis, neurotrophins, the metabolome, and the glycome in the development of depression and their potential as diagnostic, prognostic, and treatment-response biomarkers. Such studies should focus on first-episode depression and antidepressant drug-naïve patients with large sample sizes to minimize variability in different biological and clinical parameters.

Currently, a metabolomics study has shown with high precision that a neurometabolite panel consisting of plasma metabolite biomarkers (GABA, dopamine, tyramine, kynurenine) may serve as clinically useful biomarkers of MDD.

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Classics in Chemical Neuroscience: Selegiline, Isocarboxazid, Phenelzine, and Tranylcypromine.
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The prescriber's guide to classic MAO inhibitors (phenelzine, tranylcypromine, isocarboxazid) for treatment-resistant depression.
CNS Spectr. 2023 Aug;28(4):427-440. doi: 10.1017/S1092852922000906. Epub 2022 Jul 15. PMID: 35837681.

ABSTRACT: This article is a clinical guide which discusses the "state-of-the-art" usage of the classic monoamine oxidase inhibitor (MAOI) antidepressants (phenelzine, tranylcypromine, and isocarboxazid) in modern psychiatric practice. It

is intended for all clinicians, including those with limited MAOI prescribing experience. The guide addresses indications, drug-drug interactions, side-effect management, and the safety of various augmentation strategies. A clear, broad consensus (from over 70 international expert endorsers), based on six decades of experience, supports the recommendations presented here. They draw on empirical evidence and expert opinion, establishing a new specialist-consensus standard. The guide provides practical clinical advice, and is the basis for the rational use of these drugs, particularly because it improves and updates knowledge, and corrects the various misconceptions that have hitherto been prominent in the literature, partly due to insufficient knowledge of pharmacology. The guide suggests that MAOIs should be considered in treatment-resistant depression (including melancholic subtypes) and prior to electroconvulsive therapy, taking patient preferences into account. In certain cases, they may be introduced earlier in the treatment sequence than has previously been standard, and should not be seen as a last resort. Indeed, they can be decisively effective when many other treatments have failed. The guide clarifies essential points on co-administrating drugs often mistakenly ruled out (e.g., methylphenidate and some tricyclic antidepressants). It also outlines simple "bridging" methods for transitioning safely from other antidepressants to MAOIs.

18 *List of Monoamine Oxidase Inhibitors. Accessed March 2 2025.* View by: Generic | Brand, Filter by: All conditions Depression, Major Depressive Disorder, Parkinson's Disease

Reviews: phenelzine systemic (Pro)

Brand name: Nardil	8.4	156 reviews tranylcypromine systemic (Pro)
Brand name: Parnate	8.5	126 reviews selegiline systemic (Pro)
Brand names: Eldepryl, Emsam, Zelapar	7.8	68 reviews Isocarboxazid systemic
Brand name: Marplan	9.2	8 reviews

For ratings, users were asked how effective they found the medicine while considering positive/adverse effects and ease of use (1 = not effective, 10 = most effective).

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22 *Treatment-Resistant Mood Disorders 1st Edition*
Jay D. Amsterdam (Editor), Mady Hornig (Editor), Andrew A. Nierenberg (Editor)
Book description: See all formats and editions
Although antidepressants have benefited millions worldwide, a significant number of patients fail to respond or achieve remission. Because limited published information exists for clinicians diagnosing and treating treatment-resistant depression, they are often forced to make challenging decisions based on scarce data. In this volume, the editors and an internationally distinguished team of contributors tackle the issue by providing a critical assessment of all aspects of treatment-resistant depression: causes, epidemiology, comorbidity, evaluation, and treatment. This timely resource will be invaluable to clinicians, neuroscientists, researchers, and graduate students alike.

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Effect of semaglutide on liver enzymes and markers of inflammation in subjects with type 2 diabetes and/or obesity.
Aliment Pharmacol Ther. 2019 Jul;50(2):193-203. doi: 10.1111/apt.15316. Epub 2019 Jun 10. PMID: 31246368; PMCID: PMC6617813.

ABSTRACT: ***Background***: Obesity and type 2 diabetes contribute to non-alcoholic fatty liver disease (NAFLD). Glucagon-like peptide-1 analogues effectively treat both obesity and type 2 diabetes and may have potential for NAFLD management.

Aim: To assess the effect of semaglutide (a glucagon-like peptide-1 analogue) on alanine aminotransferase (ALT) and high-sensitivity C-reactive protein (hsCRP) in individuals at risk for NAFLD.

Methods: Data were analyzed from a 104-week cardiovascular outcomes trial in type 2 diabetes (semaglutide 0.5 or 1.0 mg/week) and a 52-week weight management trial (semaglutide 0.05–0.4 mg/day). Treatment ratios versus placebo were

estimated for ALT (both trials) and hsCRP (weight management trial only) using a mixed model for repeated measurements, with or without adjustment for changes in body weight.

Results: In the weight management trial, 52% of participants (499/957) had elevated baseline ALT (men >30 IU/L; women >19 IU/L). In this subgroup, end-of-treatment ALT was reduced by 6-21% ($p < 0.05$ for doses ≥0.2 mg/day), and hsCRP was reduced by 25-43% compared to placebo ($p < 0.05$ for 0.2 and 0.4 mg/ day). Among these participants, 25-46% achieved normalization of elevated baseline ALT, versus 18% in the placebo group. In the cardiovascular outcomes trial, 41% of participants (1325/3268) had elevated baseline ALT. In this group with elevated ALT, no significant ALT reduction was noted at end-of-treatment for 0.5 mg/week, while a 9% reduction vs placebo was seen for 1.0 mg/week ($P = 0.0024$). Treatment ratios for changes in ALT and hsCRP were not statistically significant after adjustment for weight change.

Conclusions: Semaglutide significantly reduced ALT and hsCRP in clinical trials in subjects with obesity and/or type 2 diabetes.

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ABSTRACT: Monoamine oxidase B (MAO-B) inhibitors are well-established as both monotherapy and as an adjunct to levodopa for managing Parkinson's

disease. Two pivotal insights led to their introduction into this therapeutic domain. The first was Knoll and Magyar's discovery of the unique pharmacological properties of selegiline as a selective MAO-B inhibitor. The second was the original hypothesis by Riederer and Youdim, endorsed by Birkmayer, to evaluate selegiline's impact on Parkinson's patients experiencing on-off phases. In the 1960s, MAO inhibitors were principally explored as potential antidepressants, but Birkmayer observed that combining levodopa with various MAO inhibitors improved akinesia in Parkinson's disease. Unfortunately, serious adverse effects associated with the early non-selective MAO inhibitors curtailed their use. Later research demonstrated that MAO-B, primarily located in glial cells, is integral to dopamine metabolism in the brain. More recent cell and molecular studies have uncovered intriguing characteristics of selegiline, suggesting neuroprotective capabilities and a possible disease-modifying role for MAO-B inhibitors.

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Associate Professor of Psychiatry and Behavioral Sciences, (Major Labs & Translational Neuroscience Incubator) and, by courtesy, of Radiology (Neuroimaging and Neurointervention),

Director, Brain Stimulation Laboratory, Director, Interventional Psychiatry Clinical Research, Department of Psychiatry and Behavioral Sciences, Stanford University
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Personal emails #3.
July 13, 2025

> Kris Newby kindly explained the meaning of each letter in SAINT acronym. The acronym SAINT stands for Stanford Accelerated Intelligent Neuromodulation Therapy, which is an advanced form of transcranial magnetic stimulation (TMS) developed for the treatment of treatment-resistant depression (TRD).

Breakdown of SAINT:

- S — Stanford:
  Refers to Stanford University, where the protocol was developed.
- A — Accelerated:
  Indicates that the treatment is delivered multiple times per day (usually 10 sessions per day over 5 days), as opposed to once daily over several weeks in standard TMS.
- I — Intelligent:
  Refers to the use of functional MRI (fMRI)-guided targeting, specifically personalizing stimulation to a subregion of the left dorsolateral prefrontal cortex (L-DLPFC) that is most anticorrelated with the subgenual anterior cingulate cortex (sgACC), a region implicated in depression.

- N — Neuromodulation:
  Refers to the use of magnetic pulses (similar to TMS) to modulate brain activity in specific neural circuits involved in mood regulation.

- T — Therapy:
  Indicates that this is a therapeutic intervention for major depressive disorder (MDD), particularly in patients who have not responded to conventional treatments.

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ABSTRACT: ***Background***: The treatment of depression has faced obstacles due to the limited efficacy of antidepressant medications and safety concerns with alternative methods. Recent research indicates that multi-watt transcranial near-infrared light therapy (NILT) can effectively address traumatic brain injury (TBI). The present goal is to evaluate multi-watt NILT as a proof-of-concept therapy for depression.

Methods: Thirty-nine consecutive patients treated for TBI between March 2013 and May 2017 contributed depression self-assessment data and/or underwent the Hamilton Depression Rating

Scale. Each participant completed the Quick Inventory of Depression Symptomatology-Self Report (QIDS) both before and after receiving treatment. Patients received multi-Watt NILT using near-infrared lasers (810/980 nm at 8-15 W) applied bilaterally to the forehead and temporal regions for 9-12 minutes each. Pre- and post-treatment scores were compared using paired t-tests.

Results: All participants met QIDS criteria for mild to severe depression, and 69% had previously tried antidepressants. After 16.82 ± 6.26 treatments, 36 of the 39 patients had a robust response (≥50% reduction in QIDS score), and 32 of 39 reached remission (QIDS total ≤5). Overall, QIDS scores declined from 14.10 ± 3.39 to 3.41 ± 3.30 ($p = 6.29 \times 10^{-19}$). Patients who received 12 or fewer treatments showed a reduction from 14.83 ± 2.55 to 4.17 ± 3.93, whereas those receiving 13 or more treatments showed a change from 13.67 ± 3.64 to 3.11 ± 3.14. Among 15 individuals who completed their treatment course in 5.33 ± 1.72 weeks (≤8 weeks), QIDS scores fell from 13.86 ± 3.14 to 4.5 ± 3.94. Suicidal ideation resolved in all but two patients, and some remained in remission for up to 55 months after one course of treatment.

Conclusion: This is the first report of high-powered NILT showing efficacy in treating depression. Multi- Watt NILT demonstrated far greater efficacy and lasting benefits than low-power

(<1 Watt) infrared light. Notably, some patients improved after only four treatments, with depressive symptoms resolving within four weeks in certain cases. These findings suggest that multi-Watt NILT may be a safe, effective, and rapid therapy for depression comorbid with TBI, as well as potentially for primary major depressive disorder. A double-blind, placebo-controlled study is warranted to confirm these proof-of-concept data.

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ABSTRACT: Traumatic brain injury (TBI) is a growing public health concern, affecting both civilians and military personnel. In this review, we discuss treatment options for chronic TBI patients, including pharmaceuticals, nutraceuticals, cognitive therapy, and hyperbaric oxygen therapy. Overall, published data suggest only marginal benefits with prolonged treatment courses. An emerging therapeutic approach is near-infrared (NIR) light, shown to be beneficial in animal models of stroke, spinal cord injury, optic nerve injury, and TBI, as well as in some human trials for stroke and TBI. However, results have been confounded by varying degrees of efficacy and a complex assortment of treatment parameters. Some evidence indicates that low-level NIR diodes often fail to

deliver sufficient radiant energy at the required depth to achieve meaningful clinical outcomes. As part of this review, we present a retrospective case series utilizing a high-power NIR Class IV laser. We observed greater clinical efficacy with higher fluence, contrary to the previously proposed bimodal efficacy model. Ten patients with chronic TBI (average time since injury 9.3 years) received ten treatment sessions over 2 months using a high-power NIR laser (13.2 W/0.89 cm^2 at 810 nm or 9 W/0.89 cm^2 at 810 nm and 980 nm). Headaches, sleep disruptions, cognitive issues, mood dysregulation, anxiety, and irritability all improved. Changes were monitored via depression scales and a novel patient diary system specifically developed for this study. NIR light at 10-15 W and wavelengths of 810 nm and 980 nm can be administered safely and appears effective in alleviating chronic TBI symptoms. We discuss the clinical benefits of infrared phototherapy on mitochondrial function and secondary molecular processes in the context of adequate radiant energy penetration.

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ABSTRACT: Depression is a severe mental disorder affecting 20% of the world's population. Despite their effectiveness, antidepressants often have delayed onset and serious side effects. Seven years ago, we identified spadin (PE 12-28) as a promising endogenous peptide with antidepressant activity. Spadin selectively blocks the TREK-1 channel. Previously, we found that spadin's effect disappeared beyond 7 hours after administration. In order to improve in vivo spadin stability and bioavailability, we screened spadin analogs and derivatives. From the study of spadin

blood degradation products, we designed a 7 amino-acid peptide, PE 22-28. In vitro studies on hTREK-1/HEK cells by using patch-clamp technique, showed that PE 22-28 displayed a better specificity and affinity for TREK-1 channel compared to spadin, IC50 of 0.12 nM vs. 40-60 nM for spadin. In the same conditions, we also pointed out that different modifications of its N or C-terminal ends maintained or abolished TREK-1 channel activity without affecting PE 22-28 affinity. In vivo, the antidepressant properties of PE 22-28 and its derivatives were demonstrated in behavioral models of depression, such as the forced swimming test. Mice treated with spadin-analogs showed a significant reduction of the immobility time. Moreover, in the novelty suppressed feeding test, after a 4-day sub-chronic treatment, PE 22-28 reduced significantly the latency to eat the food pellet. PE 22-28 and its analogs were able to induce neurogenesis after only a 4-day treatment with a prominent effect of the G/A-PE 22-28. On mouse cortical neurons, PE 22-28 and its derivatives enhanced synaptogenesis measured by the increase of PSD-95 expression level. Finally, the action duration of PE 22-28 and its analogs was largely improved in comparison with that of spadin, up to 23 h instead of 7 h. Taken

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ABSTRACT: ***Objective***: Lyme borreliosis is a tick-borne infectious disease that may confer

an increased risk of mental disorders, but previous studies have been hampered by methodological limitations, including small sample sizes. The authors used a nationwide retrospective cohort study design to examine rates of mental disorders following Lyme borreliosis.

Methods: Using Denmark's National Patient Register and the Psychiatric Central Research Register, and including all persons living in Denmark from 1994 through 2016 (N=6,945,837), the authors assessed the risk of mental disorders and suicidal behaviors among all individuals diagnosed with Lyme borreliosis in inpatient and outpatient hospital contacts (N=12,156). Incidence rate ratios (IRRs) were calculated by Poisson regression analyses.

Results: Individuals with Lyme borreliosis had higher rates of any mental disorder (IRR=1.28, 95% CI=1.20, 1.37), of affective disorders (IRR=1.42, 95% CI=1.27, 1.59), of suicide attempts (IRR=2.01, 95% CI=1.58, 2.55), and of death by suicide (IRR=1.75, 95% CI=1.18, 2.58) compared with those without Lyme borreliosis. The 6-month interval after diagnosis was associated with the highest rate of any mental disorder (IRR=1.96, 95% CI=1.53, 2.52), and the first 3 years after

diagnosis was associated with the highest rate of suicide (IRR=2.41, 95% CI=1.25, 4.62). Having more than one episode of Lyme borreliosis was associated with increased incidence rate ratios for mental disorders, affective disorders, and suicide attempts, but not for death by suicide.

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ABSTRACT: Cytomegalovirus (CMV) is a common, neurotropic herpesvirus that can be reactivated by inflammation and cause central nervous system (CNS) disease. We hypothesized that CMV might contribute to the neuroinflammation underlying certain psychiatric disorders by (1) worsening inflammation through anti-viral immune responses and (2) transforming peripheral inflammation into CNS

inflammation. We investigated whether the presence of anti-CMV antibodies in blood correlates with mental illness, suicide, neuroinflammation, and microglial density in the dorsolateral prefrontal cortex (DLPFC) using postmortem samples. Data (n = 114 with schizophrenia; n = 78 with bipolar disorder; n = 87 with depression; n = 85 controls) were acquired from the Stanley Medical Research Institute. DLPFC gene expression data from a subset of 82 samples were categorized into "high" (n = 30), and "low" (n = 52) inflammation groups based on a recursive two-step cluster analysis using expression data for four inflammation-related genes. Measurements of the ratio of non-ramified to ramified microglia, a proxy of microglial activation, were available for a subset of 49 samples. All analyses controlled for age, sex, and ethnicity, as well as postmortem interval, and pH for gene expression and microglial outcomes. CMV seropositivity significantly increased the odds of a mood disorder diagnosis (bipolar disorder: OR = 2.45; major depression: OR = 3.70) and among the psychiatric samples, of suicide (OR = 2.09). Samples in the upper tercile of anti-CMV antibody titers were more likely to be members of the "high" inflammation group (OR = 4.41, an effect driven by schizophrenia and

bipolar disorder samples). CMV-positive samples also showed an increased ratio of non-ramified to ramified microglia in layer I of the DLPFC (Cohen's d = 0.81) as well as a non-significant increase in this ratio for the DLPFC as a whole (d = 0.56). The results raise the possibility that the reactivation of CMV contributes to the neuroinflammation that underlies some cases of psychiatric disorders.

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the virus genome in every nucleated cell of their bodies. This review highlights our current understanding of HHV-6A/B integration and reactivation as well as aspects that should be addressed in the future of this relatively young research area. It forms part of an online symposium on the prevention and therapy of DNA virus infections, dedicated to the memory of Mark Prichard.

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ABSTRACT: Early-life infections and associated neuroinflammation are incriminated in the pathogenesis of various mood disorders. Infection with human roseoloviruses, HHV-6A and HHV-6B, allows viral latency in the central nervous system and other tissues, which can later be activated causing cognitive and behavioral disturbances. Hence, this study was designed to evaluate possible association of HHV-6A and HHV-6B activation with three different groups of psychiatric patients. DNA qPCR, immunofluorescence, and FISH

studies were carried out in post-mortem posterior cerebellum from 50 cases each of bipolar disorder (BPD), schizophrenia, 15 major depressive disorder (MDD), and 50 appropriate control samples obtained from two well-known brain collections (Stanley Medical Research Institute). HHV- 6A and HHV-6B late proteins, indicating active infection, and viral DNA were detected more often ($p < 0.001$ for each virus) in the cerebellum of individuals with MDD and BPD compared to controls. By contrast, these roseolovirus proteins and DNA were less frequently observed in schizophrenia cases. Active HHV-6A and HHV-6B infections were also frequently identified in cerebellar Purkinje cells of BPD and MDD patients. Furthermore, we found a significant association of HHV-6A infection with reduced Purkinje cell size, suggesting virus-mediated abnormal Purkinje cell function in these disorders. Finally, gene expression analysis of cerebellar tissue revealed changes in pathways consistent with a possible inflammatory response to HHV-6A infection. These findings offer molecular evidence supporting a role for active HHV-6A and HHV-6B infection in BPD and MDD.

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ABSTRACT: Viruses are responsible for a variety of human pathogenesis. Owing to the enhancement of the world population, global travel, rapid urbanization, and infectious outbreaks, a critical threat has been generated to public health, as preventive vaccines and antiviral therapy are not available. Herbal medicines and refined natural products have resources for the development of novel antiviral drugs. These natural agents have shed light on preventive vaccine development and antiviral therapies. This review intends to discuss the antiviral activities of plant extracts and some isolated plant natural products based on mainly preclinical (in vitro and in vivo) studies. Twenty medicinal herbs were selected for the discussion, and those are commonly recognized antiviral medicinal plants in Ayurveda (Zingiber officinale, Caesalpinia bonducella, Allium sativum, Glycyrrhiza glabra, Ferula assafoetida, Gymnema sylvestre, Gossypium herbaceum, Phyllanthus niruri, Trachyspermum

ammi, Withania somnifera, Andrographis paniculata, Centella asiatica, Curcuma longa, Woodfordia fruticose, Phyllanthus emblica, Terminalia chebula, Tamarindus indica, Terminalia arjuna, Azadirachta indica, and Ficus religiosa). However, many viruses still lack effective vaccines, and only a handful of antiviral drugs have received clinical approval. Consequently, the development of new antiviral agents remains critically important, and natural products serve as excellent prospects for such innovations. In this review, we outline the antiviral properties of selected plant extracts and some isolated natural compounds from medicinal herbs.

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ABSTRACT: Serotonin transporter (SERT) inhibitors treat depression by elevating extracellular brain 5-hydroxytryptamine (5-HT_Ext). However, only one-third of patients respond adequately, leaving treatment-resistant depression (TRD) as a significant unmet need. Interestingly, pushing 5-HT_Ext levels beyond what a SERT inhibitor alone achieves appears to help address TRD. Adjunctive 5-hydroxytryptophan (5-HTP) can safely raise 5-HT_Ext beyond the effect of a SERT inhibitor in humans, but 5-HTP itself cannot serve as a clinically viable drug due to poor pharmacokinetics. A slow-release (SR) formulation is predicted to overcome these limitations, greatly enhancing its pharmacological action and transforming 5-HTP into a viable clinical treatment. Animal studies support this prediction. Thus, 5-HTP SR adjunct therapy may be an important new avenue for TRD. This review examines the clinical and preclinical evidence for this approach.

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