



Literature Review of Antidepressant Activity of Garlic in Animal Models

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(Received: 16 January 2025

Revised: 20 February 2025

Accepted: 20 March 2025)

KEYWORDS

Garlic,
Anti-depressant
activity,
animal models.

ABSTRACT:

Introduction: Garlic (*Allium sativum*) has been a subject of interest in the field of mental health due to its potential therapeutic properties. The plant's rich composition of bioactive compounds, including organic sulfides, saponins, and phenolic compounds, has prompted researchers to investigate its efficacy in treating various conditions, including depression. While conventional antidepressant medications like Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin Noradrenaline Reuptake Inhibitors are widely prescribed, their limited success rates have led to the exploration of alternative treatments. **Objectives:** The hypothesis linking chronic inflammation to neurotransmitter depletion and subsequent depression has opened new avenues for research, with garlic's anti-inflammatory properties making it a promising candidate for investigation. Recent studies have focused on evaluating garlic's antidepressant activity through comprehensive literature reviews and experimental models. **Methods:** Electronic databases such as PubMed, Scopus, Google Scholar, and Web of Science is utilized to gather relevant information published between 2020 and 2024. The search strategy employed specific terms related to garlic's antidepressant properties and its pharmacological activity in animal models. **Results:** This approach aims to consolidate current knowledge on garlic's potential as an alternative or complementary treatment for depression, particularly in light of its anti-inflammatory compounds like ajoene and dimethyl trisulfide. **Conclusion:** The findings from these studies may contribute to a better understanding of garlic's role in mental health and potentially lead to the development of novel therapeutic strategies for depression management.

1. Introduction

Garlic has been used for centuries in traditional medicine and is known to have antioxidant, anti-inflammatory, and antimicrobial properties. The effects of garlic on cardiovascular health, metabolic disorders, cancer, and immune function were examined¹. The plant's rich bioactive compounds, including sulphides, saponins, and phenolic compounds has prompted many researchers to investigate its efficacy in treating various conditions, including depression. Major depressive disorder is commonly known as depression in which patients suffer with wide range of clinical symptoms². According to the

search results, the number of people suffering from depression worldwide surpassed 300 million as of 2018³. Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin Noradrenaline Reuptake Inhibitors are the pharmacological group of drugs administered for depression⁴. But Study reveals that 30% of patients do not respond to these drugs henceforth proposed a new alternate hypothesis that depression might be due to chronic inflammation⁵. A systemic and meta-analysis involving more than 13000 patients showed the results of elevated CRP in more than quarter of the participants⁶. Another study confirmed the increased levels of



Interlukins and Tumor Necrosis Factor in the patients suffering from depression⁷. The hypothesis linking chronic inflammation to neurotransmitter depletion and subsequent depression has opened new avenues for research, with garlic's anti-inflammatory properties making it a promising candidate for investigation. Electronic databases such as PubMed, Scopus, Google Scholar, and Web of Science is utilized to gather relevant information published between 2020 and 2024. The search strategy employed specific terms related to garlic's antidepressant properties and its pharmacological activity in animal models. This approach aims to consolidate current knowledge on garlic's potential as an alternative or complementary treatment for depression, particularly in light of its anti-inflammatory compounds like ajoene and dimethyl trisulfide⁸. The findings from these studies may contribute to a better understanding of garlic's role in mental health and potentially lead to the development of novel therapeutic strategies for depression management.

Antidepressant Activity of Garlic in Animal Models

Ruiz-Sánchez E et al.⁹ investigated the antidepressant-like effects and antioxidant properties of S-allyl cysteine (SAC), a garlic compound, in mice. The researchers used the Porsolt forced swim test (FST) to evaluate antidepressant-like responses, and analyzed oxidative stress markers in the midbrain, prefrontal cortex, and hippocampus. SAC (120 mg/kg) attenuated immobility scores in the FST, indicating an antidepressant-like effect. This effect was associated with decreased oxidative stress, as shown by reduced lipid peroxidation and increased manganese-superoxide dismutase (Mn-SOD) activity in the hippocampus. The findings suggest that SAC exerts an antidepressant-like effect that is partly mediated by its antioxidant properties.

Mshelia, P et al.¹⁰ investigated the effects of chronic administration of aqueous-methanol extract of garlic (*Allium sativum*) and enriched environment on mice models of depression. The study found that both garlic extract and enriched environment helped mitigate depressive disorders in the mice. Garlic extract and enriched environment improved depressive-like behaviors in the mice, as measured by the forced swimming test, tail suspension test, and sucrose preference test. It also modulated biochemical markers associated with depression, including increasing

antioxidant levels (SOD, GPx) and brain-derived neurotrophic factor (BDNF), while decreasing lipid peroxidation (MDA) and the pro-inflammatory cytokine TNF- α . Finally the study suggests that a conducive environment and garlic extract could be useful in the management of depression.

Rahmani, G et al.¹¹ investigated the effects of garlic (*Allium sativum*) on anxiety- and depression-related behaviors as well as brain oxidative stress in streptozotocin (STZ)-induced diabetic rats. The results showed that garlic treatment (0.5 g/kg) improved anxiety- and depressive-like behaviors in the diabetic rats compared to the diabetic control group. Furthermore, garlic administration (0.5 g/kg) attenuated malondialdehyde (MDA) levels and enhanced superoxide dismutase (SOD) and glutathione peroxidase (GPx) activities in the brain. These findings suggest that garlic can alleviate anxiety and depression in diabetic rats potentially by reducing brain oxidative stress.

The study by Bai X, et al.¹² investigated the anxiolytic and antidepressant effects of two hydrogen sulfide (H₂S) donors, diallyl disulfide (DADS) and GYY4137, in mice with chronic neuropathic pain induced by sciatic nerve injury. The researchers investigated the modulatory role of these drugs on the inflammatory, apoptotic, and oxidative processes implicated in the development of the affective disorders associated with neuropathic pain. The results showed that DADS and GYY4137 had anxiolytic, antidepressant, and antinociceptive properties during neuropathic pain by inhibiting microglial activation and the upregulation of PI3K/p-Akt and BAX in the amygdala and/or periaqueductal gray matter. Both treatments also normalized and/or activated the endogenous antioxidant system. These findings suggest that the therapeutic properties of DADS and GYY4137 may result from the inhibition of the inflammatory, apoptotic, and oxidative responses in key brain regions involved in the modulation of neuropathic pain and associated affective disorders.

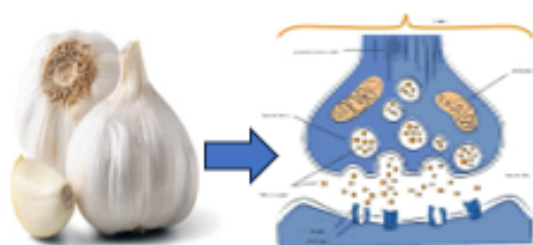
Wei X et al.¹³ showed in their study that acute administration of diallyl disulfide (DADS) can prevent and reverse lipopolysaccharide (LPS)-induced depression-like behaviors in mice. The study found that DADS was effective in ameliorating the depression-like behaviors induced by LPS, and its effects were comparable to those of the antidepressant drug



imipramine. The proposed mechanism involves the regulation of neuroinflammation and oxidative-nitrosative stress.

Huang YJ et al.¹⁴ found that garlic essential oil (GEO) and its active constituent diallyl disulfide (DADS) can ameliorate depression-like behaviors in an unpredictable chronic mild stress (UCMS) animal model. The researchers investigated the potential mechanisms and found that GEO modulated the brain NLRP3 inflammasome pathway and influenced the gut barrier and microbiota, which may contribute to the antidepressant-like effects. The study suggests that garlic essential oil could be a promising natural therapeutic approach for the management of depression.

Mechanism of action of garlic compounds



Garlic extract inhibits MAO-A and MAO-B levels, and through interaction with adrenergic, dopaminergic, serotonergic and GABAergic systems and exhibits antidepressant activity

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