



***Andrographis Paniculata* in Depression: A Review of its Pharmacological and Antidepressant-Like Effects**

Charumathi S^{*1}, Karthika S², Deepika V³, Eniyavan S⁴, Vimalya S⁵

^{1,2,3,4,5} M. Pharm Scholar, Department of Pharmacology, Sri Vijay Vidyalaya College of Pharmacy, Dharmapuri-636807, Tamil Nadu, India. Affiliated to Tamil Nadu Dr. M.G.R. Medical University, Guindy, Chennai - 600 032, Tamil Nadu, India.

ABSTRACT

Depression is a common mental health disorder that can affect mood, interest, motivation, sleep, appetite, cognition and daily functioning. Its development involves several interacting biological processes, including changes in neurotransmission, stress responses, inflammation, oxidative balance and neuroplasticity. Although antidepressant medicines are available, continued research into medicinal plants has increased because many plants contain several biologically active compounds. *Andrographis paniculata* (Burm. f.) Wall. ex Nees is a medicinal plant belonging to the family Acanthaceae and is commonly known as Kalmegh or the king of bitters. It contains several phytochemical groups, with diterpenoid lactones such as andrographolide being among its best-studied constituents. Previous experimental studies have reported antioxidant, anti-inflammatory, immunomodulatory and other pharmacological activities of *A. paniculata* and its constituents. Studies related to depression have also reported antidepressant-like effects in experimental animals, particularly with andrographolide and leaf preparations. These findings have been associated with behavioral changes as well as biological pathways involving BDNF signaling, neurogenesis, inflammation and autophagy. This review presents the basic features of depression, the botanical and phytochemical profile of *A. paniculata*, its major pharmacological activities relevant to depression, and the published preclinical evidence for its antidepressant-like activity. Together, the available findings provide a useful overview of the pharmacological basis for continued interest in *A. paniculata* in depression research.

Keywords: Depression; *Andrographis paniculata*; Kalmegh; andrographolide; antidepressant-like activity; pharmacological activity; phytochemistry; preclinical evidence.

1. Introduction

Depression is a clinically important disorder that affects a person's mood, interest, motivation, thinking, sleep, appetite, energy and ability to perform daily activities. It is different from the normal changes in mood that occur in everyday life. During a depressive episode, a person may experience persistent low mood or loss of interest or pleasure, along with symptoms such as poor concentration, low self-worth, hopelessness, sleep disturbance, changes in appetite or weight, fatigue and thoughts of death or suicide [1]. The severity of depression can vary from mild to severe, and some individuals may experience repeated episodes [1]. Depression affects people across different stages of life and has an important effect on individuals, families and society. The World Health Organization has reported that approximately 322 million people worldwide were living with depression in 2023, representing about 5.2% of adults globally [1]. The disorder may interfere with education, employment, relationships and normal daily activities. Therefore, depression is not only a condition involving mood but also an important public health concern [1,2].

The causes of depression are complex. There is a complex interplay between biological, psychological, and social factors. Stressful life events, bereavement, trauma, social difficulties and some physical illnesses may increase vulnerability. Genetic factors, changes in stress responses and changes in brain signaling may also contribute [1,2]. For this reason, depression cannot be explained by a single cause or a single biochemical change. Several biological mechanisms have been studied in relation to depression. Changes in serotonin, noradrenaline and dopamine signaling have traditionally been important in understanding antidepressant action. However, current understanding also includes stress-related changes, inflammation, oxidative imbalance, brain-derived neurotrophic factor (BDNF) signaling and changes in neuroplasticity [3-6]. These processes may influence one another. For example, long-term stress can affect stress-axis regulation and inflammatory responses, while oxidative and inflammatory changes may influence neuronal signaling and plasticity [4-6].

Treatment of depression may include psychological interventions and antidepressant medicines, including selective serotonin reuptake inhibitors such as fluoxetine [1]. However, differences in treatment response and the complex biological nature of depression have encouraged investigation of additional pharmacological approaches. Medicinal plants are of interest because they contain multiple compounds that may act on more than one biological pathway. Among such plants, *Andrographis paniculata* has received considerable attention for its wide range of pharmacological activities [7-10].

2. *Andrographis paniculata*: Botanical and Plant Profile

2.1 Botanical identity and classification

Andrographis paniculata (Burm. f.) Wall. ex Nees belongs to the family Acanthaceae. It is an annual, erect and branched herb. The plant is commonly known as Kalmegh and is also widely referred to as the king of bitters because of its very bitter taste [7,8].

2.2 Distribution and habitat

A. paniculata is native to the Indian subcontinent and Sri Lanka and is widely distributed in South and Southeast Asia [7,8]. It is an important medicinal plant in several Asian traditional medicine systems and is cultivated and collected for medicinal use.

2.3 Morphological features

The plant generally has a slender, erect and branched stem with narrow, lance-shaped leaves. It produces small white flowers with slightly purple markings on the top of the flowers. The leaves and other aerial parts are commonly used as medicinal plant material [7,8]. The distinctly bitter taste is one of the characteristic features of the plant.

2.4 Common names and traditional use

The most commonly used name is Kalmegh, while king of bitters is a widely used English name. *A. paniculata* has a long history of traditional use in Asian medicine. Reported traditional applications include fever, common cold, digestive complaints and inflammatory or infectious conditions [7-9]. These traditional uses have encouraged further pharmacological investigation of the plant.



Figure:1 *Andrographis paniculata* plant

2.5 Phytochemical profile

A. paniculata contains a variety of secondary metabolites. The major and best-known group is the ent-labdane diterpenoid lactones, which includes andrographolide and neoandrographolide. Flavonoids, flavonoid glycosides, quinic-acid derivatives, xanthenes and other compounds have also been reported [7,8].

Andrographolide is the most extensively studied constituent of *A. paniculata* and is generally considered an important bioactive diterpenoid of the plant. Several pharmacological effects reported for the plant have been investigated in relation to andrographolide, including antioxidant, anti-inflammatory and immunomodulatory activities [8-10]. The amount and type of phytochemicals may vary with the plant part, geographical origin, season, harvesting stage and preparation method [7,8].

3. Pharmacological Activities Relevant to Depression

A. paniculata has been studied for a broad range of pharmacological activities. These include antioxidant, anti-inflammatory, immunomodulatory, hepatoprotective, antimicrobial, antidiabetic and other activities [7-10]. Among these, antioxidant, anti-inflammatory and neuronal effects are particularly relevant when considering the biological processes associated with depression.

3.1 Antioxidant activity

Antioxidant activity has been reported for *A. paniculata* and its constituents in different experimental systems [7-10]. This is relevant because oxidative imbalance has been discussed as one of the biological processes associated with depression. Changes in reactive oxygen species and antioxidant defenses may interact with inflammation, neuronal signaling and neuroplasticity [6]. However, antioxidant activity alone does not establish antidepressant activity. It is more meaningful when considered together with behavioral and other biological findings from experimental studies.

3.2 Anti-inflammatory activity

Inflammatory signaling is another process that has been studied in relation to depression. *A. paniculata*, especially andrographolide, has shown anti-inflammatory effects in experimental studies. These effects include modulation of NF- κ B-related signaling and inflammatory mediators [9,10]. Such findings are relevant because inflammatory pathways can interact with brain signaling and neuronal function.

3.3 Neurotrophic and neuronal effects

Neurotrophic signaling is important for neuronal survival, synaptic function and plasticity. Experimental research with andrographolide has reported changes in hippocampal BDNF signaling and neurogenesis along with antidepressant-like behavioral effects [11]. These findings provide a direct connection between a constituent of *A. paniculata* and biological processes that are relevant to depression research.

3.4 Other pharmacological activities

The plant has also been investigated for hepatoprotective, antimicrobial, antidiabetic, immunomodulatory and other activities [7-10]. These findings show the broad pharmacological profile of *A. paniculata*. Although these activities are not direct evidence of antidepressant action, they help explain why the plant has been extensively investigated as a medicinal plant.

4. Antidepressant-Like Activity of *Andrographis paniculata*

The depression-related evidence for *A. paniculata* comes from experimental studies using leaf preparations as well as studies using the isolated constituent andrographolide. These studies have used behavioral models such as the forced swim test (FST), tail suspension test (TST) and chronic unpredictable mild stress (CUMS) model. Such tests are used to assess antidepressant-like behavioral responses in experimental animals and should not be considered diagnostic tests for human depression.

Patil and colleagues studied ethanolic extract and fractions of *A. paniculata* leaves in rats using the FST and TST. Reduced immobility was reported following treatment with the plant preparations, supporting antidepressant-like activity under the conditions of that study [12]. This finding provides direct experimental evidence that a leaf preparation of *A. paniculata* can influence depression-related behavioral measures.

Zhang et al. investigated andrographolide in mice using the FST, TST and CUMS model. The study reported antidepressant-like effects and also associated these behavioral findings with hippocampal BDNF signaling and neurogenesis [11]. This is important because the study connected a behavioral response with biological changes relevant to neuronal plasticity.

Another experimental study reported that andrographolide improved depressive-like behaviors in mice exposed to CUMS. The findings were associated with changes in inflammatory signaling involving NF- κ B and NLRP3-related pathways and with autophagy-related changes [13]. These findings suggest that the reported antidepressant-like effects may involve more than one biological pathway.

More recent research has also investigated methanol leaf extract of *A. paniculata* in mice and reported antidepressant-like and other neuropharmacological effects, together with antioxidant and mechanistic findings [14]. Thus, evidence from different experimental studies consistently supports interest in *A. paniculata* and its constituents as subjects of preclinical depression research.

Taken together, the published studies show that the antidepressant-related evidence for *A. paniculata* is not based on a single experiment or a single proposed mechanism. Behavioral findings have been reported with leaf preparations and andrographolide, while additional studies have associated these effects with BDNF-related signaling, neurogenesis, inflammatory pathways, autophagy and antioxidant-related changes [11-14]. This combination of behavioral and biological evidence provides a broader understanding of the plant's reported antidepressant-like activity.

5. Overall Pharmacological Evidence

When the available literature is considered as a whole, *A. paniculata* shows a broad pharmacological profile with several activities that are relevant to the biological processes involved in depression. Antioxidant activity relates to redox balance, anti-inflammatory activity relates to inflammatory signaling, and neurotrophic effects relate to neuronal survival and plasticity. In addition to these supporting activities, experimental studies have directly reported antidepressant-like behavioral effects of *A. paniculata* leaf preparations and andrographolide [11-14].

The evidence also shows that different studies have examined different preparations, doses, animal models and experimental conditions. Therefore, findings from an isolated compound, a particular leaf preparation or another plant preparation should be interpreted according to the conditions under which they were obtained. The studies are complementary rather than identical, and together they provide a useful picture of the current preclinical evidence.

An important feature of the available evidence is the relationship between behavioral and biological findings. Behavioral tests provide functional evidence of antidepressant-like effects, while biochemical and tissue-level observations can provide additional information about associated biological changes. This combined approach is useful for understanding the pharmacological actions reported for *A. paniculata* in experimental depression research.

6. Conclusion

Andrographis paniculata is a medicinal plant belonging to the family Acanthaceae with a well-described botanical and phytochemical profile. Its major constituents, particularly andrographolide, have been studied for several pharmacological activities including antioxidant and anti-inflammatory effects. These activities are relevant to biological processes associated with depression. More importantly, published preclinical studies have reported antidepressant-like effects of *A. paniculata* leaf preparations and andrographolide in experimental animal models. Behavioral findings have also been associated with BDNF signaling, neurogenesis, inflammatory pathways, autophagy and antioxidant-related changes. Overall, the available literature provides preclinical evidence supporting the antidepressant-like activity of *A. paniculata* and gives a pharmacological basis for continued study of the plant in depression-related research. These findings should be interpreted as experimental evidence and should not be directly considered proof of clinical antidepressant efficacy in humans.

7. References

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