Behavioral And Neurochemical Evaluation of The Antidepressant Activity of Berberine in Rat Models of Depression

Gade Venkateswara[1], G Srinivasa Rao[2], A Vidyadhari[3], Guduru Rajeswari[4]
[1,2,3,4] *Department of Pharmacology, Saastra college of Pharmaceutical Education and Research, Varigonda, T.P. Gudur, S.P.S.R Nellore -524311, Andhra Pradesh*

***Abstract*—Depression is a debilitating psychiatric disorder characterized by persistent sadness, reduced interest in daily activities, impaired cognition, and altered behavioral responses. Despite the availability of several antidepressant medications, many patients experience inadequate therapeutic response and adverse effects. Consequently, there is increasing interest in identifying natural compounds with antidepressant potential. Berberine, an isoquinoline alkaloid isolated from various medicinal plants including Berberis vulgaris, possesses multiple pharmacological properties such as antioxidant, anti-inflammatory, neuroprotective, antimicrobial, and metabolic regulatory activities. The present study was undertaken to evaluate the antidepressant activity of berberine in experimental rat models of depression. Behavioral parameters including Forced Swim Test (FST), Elevated Plus Maze (EPM), Grip Strength Test, and Spontaneous Locomotor Activity were assessed. Oxidative stress markers such as Superoxide Dismutase (SOD), Reduced Glutathione (GSH), and Malondialdehyde (MDA) were estimated in brain tissue homogenates. Berberine treatment significantly reduced immobility time and improved locomotor activity, muscular strength, and cognitive performance. Furthermore, berberine significantly enhanced antioxidant enzyme levels and reduced lipid peroxidation. The findings suggest that berberine exerts significant antidepressant effects through behavioral improvement and attenuation of oxidative stress. Therefore, berberine may represent a promising natural therapeutic alternative for the management of depressive disorders.**

***Index Terms*—Berberine, Depression, Antidepressant Activity, Oxidative Stress, Rat Model, Forced Swim Test, Neuroprotection.**

I. INTRODUCTION

Depression is one of the most prevalent mental health disorders worldwide and represents a major public health concern[1]. According to the World Health Organization, depression affects more than 280 million people globally and contributes substantially to disability-adjusted life years[2]. The disorder is characterized by persistent low mood, loss of interest or pleasure, sleep disturbances, appetite changes, cognitive dysfunction, and suicidal ideation. The pathophysiology of depression is complex and multifactorial, involving alterations in monoaminergic neurotransmission, neuroinflammation, oxidative stress, hypothalamic-pituitary-adrenal axis dysfunction, and impaired neuroplasticity[3-7].

Current antidepressant medications primarily target serotonergic, noradrenergic, and dopaminergic neurotransmitter systems. Although these therapies are clinically effective, approximately one-third of patients fail to achieve complete remission[8]. Furthermore, conventional antidepressants often require prolonged treatment periods before clinical improvement is observed and are associated with adverse effects such as weight gain, sexual dysfunction, gastrointestinal disturbances, and sleep disorders. These limitations have stimulated research into alternative therapeutic agents derived from natural sources[9-12].

Medicinal plants have been utilized for centuries in traditional systems of medicine. Among the bioactive compounds isolated from medicinal plants, berberine has gained significant attention because of its broad spectrum of pharmacological activities. Berberine is a naturally occurring isoquinoline alkaloid present in

species such as Berberis vulgaris, Coptis chinensis, and Hydrastis canadensis. Previous studies have demonstrated its antimicrobial, antidiabetic, cardioprotective, anti-inflammatory, antioxidant, and neuroprotective effects[14-18].

Recent evidence indicates that oxidative stress and neuroinflammation contribute significantly to the development and progression of depression. Increased production of reactive oxygen species leads to neuronal damage, impaired neurotransmission, and disruption of cellular homeostasis. Berberine has been shown to enhance antioxidant defenses, suppress inflammatory mediators, improve mitochondrial function, and regulate neuronal signaling pathways. These properties suggest that berberine may possess considerable antidepressant potential[19].

Therefore, the present study was designed to evaluate the behavioral and neurochemical effects of berberine in experimental models of depression and to investigate its possible mechanism through modulation of oxidative stress markers[20].

II. MATERIALS AND METHODS

Experimental Animals

Adult Wistar albino rats weighing between 150 and 250 g were used for the study. The animals were housed under standard laboratory conditions with a controlled temperature of 25 ± 2°C, relative humidity of 55 ± 5%, and a 12-hour light-dark cycle. Animals had free access to standard pellet diet and water throughout the experimental period. All experimental procedures were performed according to CPCSEA guidelines and were approved by the Institutional Animal Ethics Committee.

Experimental Design

Animals were randomly divided into four groups consisting of six animals each.

Table 1: Experimental Design

Group	Treatment
Group I	Normal Control
Group II	Depressed Control
Group III	Fluoxetine (Standard)
Group IV	Berberine Treatment

Behavioral Evaluation

Behavioral assessment was performed after treatment administration using established experimental models.

Forced Swim Test

The Forced Swim Test is a widely accepted model for screening antidepressant activity. Rats were individually placed in a transparent cylindrical tank containing water. Immobility time was recorded during the observation period. A reduction in immobility time was considered indicative of antidepressant activity.

Elevated Plus Maze

The Elevated Plus Maze was used to evaluate learning and memory. Transfer latency was recorded as the time taken by the animal to move from the open arm to the enclosed arm.

Grip Strength Test

Muscular strength was evaluated using a grip strength apparatus. Improvement in grip strength indicates reversal of depression-associated physical impairment.

Spontaneous Locomotor Activity

Locomotor activity was measured using an actophotometer. Increased locomotor activity reflects improvement in exploratory behavior and motivational status.

III. BIOCHEMICAL EVALUATION

Following completion of behavioral assessments, animals were sacrificed and brain tissues were collected for biochemical estimation.

Table 2: Biochemical Parameters Evaluated

Parameter	Significance
GSH	Major endogenous antioxidant
SOD	Protects against superoxide radicals
MDA	Marker of lipid peroxidation
Total Protein	Indicator of tissue integrity

Reduced glutathione levels were estimated using Ellman's reagent method. Superoxide dismutase activity was determined spectrophotometrically. Malondialdehyde levels were estimated as an index of lipid peroxidation.

IV. RESULTS

The administration of berberine significantly improved behavioral parameters in depressed rats. In the Forced Swim Test, berberine-treated animals exhibited a marked reduction in immobility time compared with depressed control animals, indicating significant antidepressant activity. Similar improvements were observed in locomotor activity and grip strength assessments.

The Elevated Plus Maze test demonstrated improved cognitive performance in berberine-treated animals, as evidenced by a significant decrease in transfer latency. These findings suggest that berberine not only alleviates depressive behavior but also improves memory and learning functions.

Table 3: Summary of Behavioral Effects of Berberine

Parameter	Depressed Control	Berberine Treated
Immobility Time	Increased	Significantly Reduced
Locomotor Activity	Decreased	Increased
Grip Strength	Reduced	Improved
Transfer Latency	Increased	Reduced

Biochemical analysis revealed significant alterations in oxidative stress markers. Berberine treatment significantly increased GSH and SOD levels while reducing MDA concentrations when compared with depressed control animals. These findings indicate enhanced antioxidant defense and reduced oxidative damage.

Table 4: Effect of Berberine on Oxidative Stress Markers

Parameter	Depressed Control	Berberine Group
GSH	Decreased	Increased
SOD	Decreased	Increased
MDA	Increased	Decreased

V. DISCUSSION

The present study demonstrated significant antidepressant activity of berberine in experimental rat models of depression. Behavioral studies revealed that berberine effectively reduced immobility time in the Forced Swim Test, a well-established indicator of antidepressant efficacy. The reduction in immobility suggests a decrease in behavioral despair and an improvement in stress coping ability.

Depression is frequently associated with reduced locomotor activity, muscular weakness, and cognitive impairment. Berberine significantly improved locomotor activity, grip strength, and memory performance, indicating comprehensive neurobehavioral protection. These observations are consistent with previous reports demonstrating the neuroprotective effects of berberine in neurological disorders.

Oxidative stress is increasingly recognized as an important factor in the pathogenesis of depression. Elevated levels of reactive oxygen species can damage neuronal membranes, proteins, and DNA, leading to impaired neurotransmission and neurodegeneration. The significant increase in antioxidant enzymes such as SOD and GSH observed in the present study suggests that berberine enhances endogenous antioxidant defense mechanisms.

The reduction in MDA levels further confirms the ability of berberine to prevent lipid peroxidation and oxidative neuronal damage. Previous studies have reported that berberine activates AMP-activated protein kinase (AMPK), modulates inflammatory pathways, and improves mitochondrial function. These mechanisms collectively contribute to neuronal survival and improved behavioral outcomes.

The antidepressant effect observed in the present investigation may therefore be attributed to the combined antioxidant, anti-inflammatory, and neuroprotective properties of berberine. The results support the growing body of evidence suggesting that natural phytochemicals can provide effective alternatives for the management of depressive disorders.

VI. CONCLUSION

The findings of the present study clearly demonstrate that berberine possesses significant antidepressant activity in experimental rat models of depression. Berberine effectively improved behavioral abnormalities and restored antioxidant defense mechanisms by increasing GSH and SOD levels while reducing MDA concentrations. The study suggests that the antidepressant action of berberine is mediated through attenuation of oxidative stress and enhancement of neuroprotection. Further preclinical

and clinical investigations are required to establish its therapeutic utility in human depression.

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