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Research Article

Antidepressant Activity of *Spirulina Platensis* in Models of Depression

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Abstract

Depression is the most common of the affective disorders (disorders of mood rather than disturbances of thought or cognition); it may range from a very mild condition, bordering on normality, to severe (psychotic) depression accompanied by hallucinations and delusions. Worldwide, depression is a major cause of disability and premature death. Unipolar depression is commonly (about 75% of cases) non-familial, clearly associated with stressful life-events and accompanied by symptoms of anxiety and agitation; this type is sometimes termed reactive depression. Other patients (about 25%, sometimes termed endogenous depression) show a familial pattern, unrelated to external stresses, and with a somewhat different symptomatology. This distinction is made clinically, but there is little evidence that antidepressant drugs show significant selectivity between these conditions.

Introduction

The symptoms of depression include emotional and biological components:

- **Emotional symptoms:**
  1. misery, apathy and pessimism
  2. low self-esteem: feelings of guilt, inadequacy and ugliness
  3. indecisiveness, loss of motivation.
- **Biological symptoms:**
  1. retardation of thought and action
  2. loss of libido
  3. sleep disturbance and loss of appetite.

There are two distinct types of depressive syndrome, namely unipolar depression, in which the mood swings are always in the same direction, and bipolar affective disorder, in which depression alternates with mania. Mania is in most respects exactly the opposite, with excessive exuberance, enthusiasm and self-confidence, accompanied by impulsive actions, these signs often being combined with irritability, impatience and aggression, and sometimes with grandiose delusions of the Napoleonic kind. As with depression, the mood and actions are inappropriate to the circumstances.

Bipolar depression, which usually appears in early adult life, is less common and results in oscillating depression and mania over a period of a few weeks. There is a strong hereditary tendency, but no specific gene or genes have been identified either by genetic linkage studies of affected families, or by comparison of affected and non-affected individuals.

Methods

- To study the effect of *SP* on behavior models of depression like forced swim test, tail suspension test.
- To study the effect of *SP* on mechanism based models of depression like 5-HTP induced head twitches, clonidine induced aggression and L-Dopa induced hyperactivity and aggressive behavior.
- To study the effect of *SP* on anti-oxidant levels of brain.

Objective Of The Study

Spirulina platensis (SP) is a type of fresh-water blue-green algae which grows naturally in warm climate countries and has been considered as supplement in human and animal food (Ruiz Flores et al., 2003). The numerous toxicological studies have established its safety for human consumption (Hirahashi et al., 2002). *SP* has anti-oxidant property as it contains Carotenoids and also rich in amino acids like Tryptophan, Phenylalanine, Tyrosine (Jassby, 1983).

Acute Toxicity Study And Gross Behaviour In Rats

Acute toxicity study – up and down procedure – was carried out as per the guidelines set by Organization for Economic Co-operation and Development (OECD).

If animal dies at particular dose, lower dose was given to next animal and if animal survives at a particular dose next higher dose was given for remaining animals. The maximum upper limit dose 2000 mg/kg of *SP* was administered orally to mice. Animals were observed individually after dosing.

Observation included mortality and clinical signs, such as changes in skin fur, eyes and mucous membranes. The effect of *SP* on passivity, grip strength, pain response, stereotypy, vocalization, righting reflex, body weight and water intake was assessed (Lipnic *et al*., 1995). Pilot study was carried out with various doses (50, 100, 200 and 400 mg/kg, per oral route to rats) of *SP*. At doses of 100, 200 and 400 mg/kg, it was active and at 50 mg/kg it was inactive. Based on this observations three different doses (100, 200 and 400 mg/kg) of *SP* were selected in the present studies.

Results

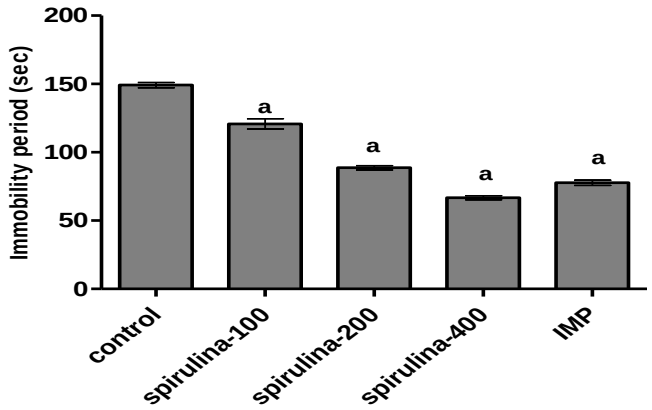
Forced Swim Test (FST)

The results (Table. 1) showed that both *SP* (100, 200 and 400 mg/kg, p.o.) and imipramine (15 mg/kg, i.p.) significantly decreased the duration of immobility time in a dose dependent manner in FST model. Post-hoc analysis showed that the *SP* (100, 200 and 400 mg/kg) and Imipramine (IMP) treated groups were significantly different ($p<0.001$) from the vehicle treated group (Fig. 1).

Group no.	Treatment (dose in mg/kg)	Immobility period (sec) Mean ± SEM
I	Control (0.3% CMC) + FST	149.2±1.905
II	Spirulina (100 mg/kg, p.o.) + FST	120.8±3.781[a]
III	Spirulina (200 mg/kg, p.o.) + FST	88.67±1.647[a]
IV	Spirulina (400 mg/kg, p.o.) + FST	66.67±1.498[a]
V	Imipramine (15 mg/kg, i.p.) + FST	77.67±1.892[a]

Table. 1. Effect of *SP* and imipramine (IMP) on forced swim test (FST) in rats.

Each column represents mean ± S.E.M. of immobility period (sec), n = 6. a = p<0.001 compared to control (One-way ANOVA followed by Student–Newman–Keuls test).



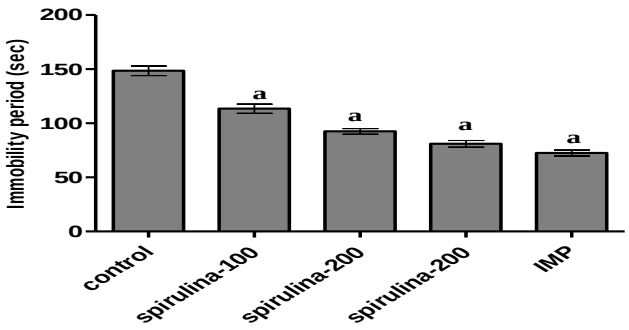
Tail Suspension Test (TST)

The results (Table. 2) showed that both *SP* (100,200,400 mg/kg, p.o.) and imipramine (15 mg/kg, i.p.) significantly decreased the duration of immobility time in a dose dependent manner in TST model. Post-hoc analysis showed that the *SP* (100, 200 and 400 mg/kg) and IMP treated groups were significantly different (p<0.001) from the vehicle treated group (Fig. 2).

Group no.	Treatment (dose in mg/kg)	Immobility period (sec) Mean ± SEM
I	Control (0.3% CMC) + TST	148.5±4.372
II	Spirulina (100 mg/kg, p.o.) + TST	113.5±4.303[a]
III	Spirulina (200 mg/kg, p.o.) + TST	92.5±2.63[a]
IV	Spirulina (400 mg/kg, p.o.) + TST	81±3.011[a]
V	Imipramine (15 mg/kg, i.p.) + TST	72.5±2.754[a]

Table. 2. Effect of *SP* and Imipramine (IMP) on tail suspension test (TST) in mice.

Each column represents mean ± S.E.M. of immobility period (sec), n = 6. a = p<0.001 compared to control (One-way ANOVA followed by Student–Newman–Keuls test).



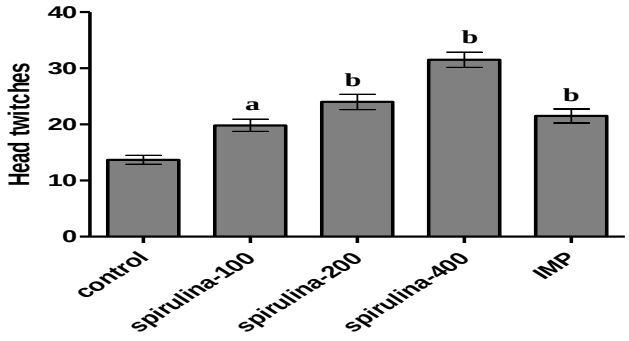
5-HTP induced head twitches in mice

Table.3. illustrates the effect of *SP* and IMP on 5-HTP-induced head twitches in mice. Post-hoc analysis revealed that three doses of *SP* (100, 200 and 400 mg/kg, p<0.01, p<0.001) significantly increased the 5-HTP-induced head twitches in comparison to control group. Further, the dose of 400 mg/kg was more effective than 100, 200 mg/kg. Similarly, IMP treated group showed significant increase (p<0.001) in the 5-HTP-induced head twitches compared to control. However, the effect of 400 mg/kg of *SP* was significantly higher than IMP (p<0.001) (Fig. 3).

Group no.	Treatment (dose in mg/kg)	Head twitches Mean ± SEM
I	Control (0.3% CMC)	13.67±0.8028
II	Spirulina (100 mg/kg, p.o.)	19.83±1.078[a]
III	Spirulina (200 mg/kg, p.o.)	24±1.366[b]
IV	Spirulina (400 mg/kg, p.o.)	31.5±1.335[b]
V	Imipramine (15 mg/kg, i.p.)	21.5±1.258[b]

Table. 3. Effect of *SP* on 5-HTP-induced head twitches in mice.

Each column represents mean ± S.E.M. of number of head twitches, n = 6. a = p<0.01, b = p<0.001 compared to control (One-way ANOVA followed by Student–Newman–Keuls test).



Conclusion

- The results from the present study confirm the antidepressant activity of*Spirulina platensis*, since it reduced the immobility in both FST and TST.
- In the present study, *SP* significantly increased the frequency of 5-HTP induced head twitches, Clonidine induced aggression and L-DOPA induced hyperactivity and aggressive behavior indicating its enhanced activity on serotonergic, noradrenergic and dopaminergic pathways respectively. Our results also confirm the involvement of serotonergic, noradrenergic and dopaminergic pathways in depression.
- Pretreatment with *SP*also significantly increased the levels of SOD and Catalase with simultaneous decrease in LPO levels in rat brain, suggesting its strong antioxidant activity. Since oxidative stress is reported to play an important role in depression, the antioxidant activity of *SP* might be a part of the mechanism for its antidepressant activity.

Results from behavioral experiments indicate that the antidepressant activity of *Spirulin platensis* might be due to the facilitatory effect on serotonergic, noradrenergic and dopaminergic systems apart from the antioxidant activity.

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