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A Comparative Study of Antidepresant Activity of Aqueous Extract of Curcuma Longa With Fluoxetine in Experimental Animals (Albino Rats)

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ABSTRACT

Introduction -Depression belongs to the heterogenous group of mental disorders characterized by extreme exaggerations and disturbance of mood, which adversely affect cognition and psychomotor functions. It results from abnormal brain mechanisms functionally deficient monoaminergic (noradrenaline and/or 5-hydroxytryptamine) transmission in the central nervous system.Aims and Objectives- To evaluate comparatively the Anti- depressant activity of Curcuma longa (Haldi or Turmeric) and Berberis aristata (Daru haridra) albino rats after inducing experimental depression using different methods. Materials and methods - The antidepressant activity of aqueous extract of curcuma longa was screened by tail suspension method and the forced swimming test and compared with the control and standard drug (fluoxetine) for two weeks. Group1- were kept as control.Group 2- were treated with fluoxetine in a dose of 14mg/kg/day as standard drug for one week.Group 3,4 and 5- were given aqueous extract of curcuma longa orally in three graded doses 100,200 and 400mg/kg/day respectively for two weeks. Results -Curcuma longa exhibits antidepressant activity depicted by reduction in the immobility time when compared to the control group. The onset of action was after few days according to the dose of the test drugs following their administration. The effect is comparable with that of standard drug fluoxetine which seem to be due to the presence of various phytochemical constituents like Curcuminoids: mixture of curcumin (diferuloylmethane), monodexmethoxycurcumin and bisdesmethoxycurcumin and which is believed to be due to by inhibiting MAO A , exhibiting immunostimulatory activity ,inhibiting TNF-a induced expression of ICAM-1,VCAM-1 and E-selectin on human umbilical vein endothelial cells and Th1cytokine profile in CD49/T cells by suppressing interleukin-12 production in macrophages. Conclusion –curcuma longa has significant antidepressant activity demonstrated by tail suspension and forced swimming test compared to the test drug.

KEYWORDS Curcuma longa; Antidepressant activity; Immobility; MAO A; MAO B

Introduction

Mood disturbance is characterized by a disturbance in the regulation of mood, behaviour and affect. Mood disorder is subdivided into Depressive disorders, Bipolar disorders and Depression in association with medical illness or alcohol and substance abuse(1). Depression belongs to the heterogenous group of mental disorders characterized by extreme exaggerations and disturbance of mood, which adversely affect cognition and psychomotor functions. It results from abnormal brain mechanisms functionally deficient monoaminergic (noradrenaline and/or 5-hydroxytryptamine) transmission in the central nervous system.(2)

Approximately 15% of the population experiences a major depressive episode at some point in life. Depression in general remains associated with high disability and societal cost; in the Global Burden of disease study conducted by the World Health Organization, unipolar major depression is ranked fourth in percentage of disability-adjusted life years and was projected to rank second in the year 2020.(4)

Numerous treatment modalities are used currently to combat the mood disorders. At present, there are several types of antidepressants used in clinical practice, including tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors

(SSRIs), selective reversible inhibitors of monoamine oxidase A (RIMAs), and specific serotonin–norepinephrine reuptake inhibitors (SNRIs) and atypical antidepressants. Inspite of the introduction of these drugs depression continues to be a major problem, therefore, considerable efforts are being invested in the discovery of better drugs for the treatment of depression. (5)

There are numerous traditional medicinal plants which possess antidepressant activity(6,7,8). Curcuma longa is commonly used indigineous plant which possess antidepressant activity and is much(9). So the present study has been designed to compare the antidepressant activity of aqueous extract of curcuma longa with the standard drug fluoxetine in experimental animals (albino rats) by various methods.(10)

Material and Methods

The present study was conducted on adult albino rats weighing 150-200 gm after taking approval from the Institutional Animal Ethical Committee (IAEC) according to the guidelines for the purpose of control and supervision of experiments on animals (CPCSEA). The animals were housed individually in standard polypropylene cages and kept under controlled room temperature (24± 2˚C) in a 12 h lightdark cycle, given standard laboratory diet and water ad libitum and acclimatized to the laboratory conditions at least one day prior to the behavioral experiments. All the experiments were carried out between 12:00 to 16:00 h. The food was withdrawn 12 h before the experiments. Each animal was used only once. The animal handling was performed according to the Good Laboratory Practice (GLP) guidelines. The animals were equally divided into 5 groups (6 animals in each group).

Group1- were kept as control.

Group 2- were treated with fluoxetine in a dose of 14mg/kg/day as standard drug for one week.

Group 3,4 and 5- were given aqueous extract of curcuma longa orally in three graded doses 100,200 and 400mg/kg/day respectively for two weeks.

The antidepressant like activity of curcuma longa, berberis aristata and fluoxetine was evaluated by forced swimming test (FST)(11) and tail suspension test (TST)(12).

The results were statistically analyzed using unpaired Student's t test and and presented as mean ± SEM. P values were calculated referring to appropriate tables.

Preparation of extracts

The rhizomes of C. longa L. (Zingiberaceae) were purchased from Bhartiya ayurvedic pharmacy, Delhi. The air-dried rhizomes of C. longa (100g) were extracted with 2 litres of hot water for 2 h. The procedure was repeated twice. The extracts were filtered and then concentrated with decoction method and then this final solution of each was preserved in refrigerator. A fresh solution was prepared from time to time according to the requirement. We obtained the water extract of C. longa. Dose of curcuma longa was calculated by using data from ancient Chinese medicine.

Results

Effects of the aqueous extract of C. longa on the duration of immobility time in the rat tail suspension test:

Effects of oral administration of the aqueous extract Of C. longa and fluoxetine solution on the duration of immobility in the rat tail suspension test were shown in Table 1.The extract showed no any change after 1 day treatment, and had the tendency to reduce the immobility time after 7-day treatment. After a 14-day treatment, the extracts at the doses of 100, 200 and 400 mg/kg significantly decreased the duration of immobility in a dose-dependent manner. However, the reference antidepressant fluoxetine at the dose of 14 mg/200g resulted in significant reduction. The effects of C.Longa at the dose of 400 mg/kg appeared to be more potent than that of fluoxetine on 14-day treatment in the study.

TABLE-1

Comparative Effects of the aqueous extract of curcuma longa with the control group (normal saline) on the duration of immobility in the rat tail suspension test (mean ± S.E.M.) (n=6)

Drugs	Dose	Immobility time in seconds(mean±SEM)		
		Day 1	Day 7	Day 14
Control (normal saline)	0.9%	45.30±0.29	43.34±0.80	44.10±0.53
Standard drug (Fluoxetine)	14mg/kg	41.22±0.56***/###	25.40±0.22***/###	11.30±0.26***
Curcuma longa	100 mg/kg	44.40±0.49	41.30±0.56	35.70±0.31***
	200 mg/kg	43.10±0.42**	37.32±0.40***	26.50±0.54***
	400 mg/kg	43.00±0.42**	25.32±0.31***	8.86±0.33***/###

*/# P<0.05(not significant); **/##P<0.01(significant); ***/###P<0.001(highly significant. * - For comparison of curcuma longa with the control group. # - For comparison of curcuma longa with the standard drug.

Effects of the aqueous extract of C. longa on the duration of immobility time in the rat forced swimming test:

Effects of oral administration of the aqueous extract Of C. longa and fluoxetine solution on the duration of immobility in the rat forced swimming test were shown in Table-2. The extract showed no any change after 1 day treatment. The extract at the dose of 400 mg/kg exhibited to show significant immobility reduction after 7-day treatment. The extracts at doses of 140, 280 and 560 mg/kg significantly decreased the duration of immobility in a dose-dependent manner, resulting in 53.2, 63.1 and 69.7% immobility reduction after 14-day treatment, respectively. Fluoxetine at the dose of 20 mg/kg significantly produced a time-dependent immobility reduction. The effect of C. longa at the dose of 400mg/kg appeared to be more potent than that of fluoxetine after 14-day treatment.

TABLE - 2

Comparative effects of the aqueous extract of Curcuma Longa with the standard group(fluoxetine) and the control group on the duration of immobility in the rat forced swimming test (mean ± S.E.M.)(n=6)

Drugs	Dose	Immobility time in seconds(mean±SEM)		
		Day 1	Day 7	Day 14
Control (normal saline)	0.9%(1ml/200g)	42.76±0.34	39.65±0.55	40.43±0.22
Standard drug (Fluoxetine)	14mg/kg	41±0.11	23.45±0.13###	10.65±0.11###

Curcuma longa	100 mg/kg	40.15±0.50**	37.6±0.42	29.51±0.37***
	200 mg/kg	39.98±0.43**	39.98±0.43***	22.9±0.17***
	400 mg/kg	39.1±0.22***	22.15±0.56***/###	8.11±0.17***/###

*/# P<0.05(not significant); **/##P<0.01(significant); ***/###P<0.001(highly significant. * - For comparison of curcuma longa with the control group. # - For comparison of curcuma longa with the standard drug.

DISCUSSION

The present study demonstrated the antidepressant-like effect of curcuminoids, an alkaloid obtained from C.longa, in the forced swim and tail-suspension tests in experimental animals. Curcuma longa has a long history of medicinal usage in both the Ayurvedha and Siddha systems of medicine. It has been reported to possess multiple pharmacological effects. Recent reports have elucidated its role in various central nervous system related disorders(9).

Forced swimming test and tail-suspension tests are considered relatively quick and simple to predict antidepressant activity of drugs (13). In the present study, curcuma longa decreased the immobility period in both the forced swim and tail-suspension tests. However, the effect was dose-dependent. The present study suggests that aqueous extract of curcuma longa poses antidepressant activity which can be attributed to the presence of various phytochemical constituents like Curcuminoids: mixture of curcumin (major constituent exhibited a wide range of biologic activities ,monodexmethoxycurcumin and bisdesmethoxycurcumin). It has also been reported that the antidepressant activity of aqueous extract of curcuma longa may be due to the inhibition of MAO activity in mouse whole brain in a dose dependent manner(14), however, only the extract at a dose upto 560mg/kg exhibited to have the MAO B inhibitory activity. MAO is an important enzyme in the metabolism of a wide range of monoamine neurotransmitters, including adrenaline, noradrenaline, dopamine, and 5-hydroxytryptamine. MAO exists in two isoforms, A and B. MAO A is more important than MAO B in the metabolism of the major neurotransmitter monoamines. MAO A inhibitors have been accepted to treat depression(15,16). These findings suggested that antidepressant effects of C. longa in animal models of immobility tests may be related to the inhibitory activity of MAO, especially to that of MAO A.

It has also been reported in other study that major depression is associated with dysfunction of immunity(17,18). A variety of immune parameters such as mitogen response, natural killer cell activity and T-cell subpopulations were in relation to depression. C. longa exhibited to have immunostimulatory activity (19), inhibiting TNF-a induced expression of ICAM-1,V-CAM-1 and E-selectin on human umbilical vein endothelial cells (20) and Th1cytokine profile in CD49/T cells by suppressing interleukin-12 production in macrophages (21). Although the relevance of these psychoimmune relationships remain in question. From clinical studies evidences showed that patients with depression could exploit their immune system for suicide (18). It is, therefore, suggested that C. longa may have as a possible therapeutic and protective use in the immune-associated depression. Additional study of the depressant mechanism and related active constituents are in progress.

It has been seen that the extract of curcuma longa had a great antioxidant property (22) and oxidative stress play an important role in the pathogenesis of depression. So its antidepressant effect may be related to its antioxidant property.

Our study suggest that curcuma longa have good antidepressant effect which is comparable to standard drug (fluoxetine). Species variations can be present and further studies are required for their efficacy in human beings. However, the exact mechanism of action for the antidepressant effect cannot be ascertained and further studies are required.

Conclusion

From the analysis of generated data the aqueous extract of curcuma longa has significant antidepressant activity which was demonstrated by tail suspension test and forced swimming test and are dose dependent and significantly compared to the control group and the standard group.

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