International Journal of Pharmaceutics and Drug Research
ISSN: 2347-6346
Available online at http://ijpdr.com

Original Research Article

PHARMACOLOGICAL SCREENING OF CURCUMA LONGA IN OBESITY COMORBID WITH DEPRESSION

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***Article History:**

Received: 12/07/2024
Revised: 30/07/2024
Accepted: 09/08/2024

ABSTRACT

This study investigates the pharmacological effects of *Curcuma longa* (Turmeric) in a mouse model of obesity comorbid with depression. Using a hydro-ethanolic extract of the rhizome, we assessed the yield and conducted phytochemical analysis, which revealed the presence of glycosides and saponins. The impact of *C. longa* on locomotor activity, immobility time in forced swimming and tail suspension tests, and biochemical parameters was evaluated. Mice on a high-fat diet (HFD) exhibited reduced locomotor activity and increased immobility time, indicating depressive-like behavior. Treatment with *C. longa* extract significantly improved locomotor activity and reduced immobility times, particularly at a dosage of 400 mg/kg. Additionally, *C. longa* administration lowered glucose, triglycerides, and cholesterol levels in HFD-fed mice. These findings suggest that *Curcuma longa* possesses potential therapeutic effects in alleviating obesity and associated depressive symptoms.

Keywords: *Curcuma longa*, Obesity, Depression, Phytochemical analysis, Locomotor activity, Immobility tests, Biochemical parameters, Mouse model, Therapeutic effects.

INTRODUCTION

Obesity is a multifaceted condition characterized by an excessive accumulation of body fat, often leading to various comorbidities, including metabolic syndrome, cardiovascular diseases, and type 2 diabetes. Among the psychological conditions associated with obesity, depression is notably prevalent, forming a bidirectional relationship that complicates treatment and management strategies. Research suggests that individuals with obesity are at an increased risk of developing depression, while those with depressive disorders may exhibit altered eating behaviors, contributing to weight gain (Blaine, 2008; Wang *et al.,* 2018).

The complex interplay between obesity and depression necessitates effective therapeutic approaches that address both conditions simultaneously. One promising candidate for such dual-action therapy is *Curcuma longa*, commonly known as turmeric. The active compound in turmeric, curcumin, has garnered attention for its multifaceted pharmacological properties, including anti-inflammatory, antioxidant, and antidepressant effects (Cox *et al.,* 2015; Panahi *et al.,* 2016). Curcumin has been shown to modulate various biological pathways, including those involved in the regulation of metabolism and mood, suggesting its potential role in managing obesity and depression.

Numerous studies have explored the efficacy of curcumin in reducing body weight and improving metabolic parameters in preclinical and clinical settings. For instance, a meta-

analysis indicated that curcumin supplementation significantly reduced body mass index (BMI) and waist circumference in overweight and obese individuals (Zhang *et al.,* 2019). Additionally, evidence points to curcumin's ability to enhance serotonin and norepinephrine levels, neurotransmitters that are often dysregulated in individuals with depression (Lopresti, 2017).

Given the rising global prevalence of obesity and its associated psychological complications, investigating the pharmacological effects of *Curcuma longa* presents a compelling opportunity. This study aims to assess the potential benefits of *Curcuma longa* in obesity comorbid with depression, focusing on its ability to mitigate weight gain while simultaneously alleviating depressive symptoms.

MATERIALS AND METHODS

Collection and Authentication of plant material

The plants have been selected on the basis of its availability and Folk use of the plant. *Curcumin longa* rhizome was utilised in current study. The plant material was obtained from the local area of Sagar. The collected plant material was taxonomically identified and authentication has been done by Herbarium IN-charge of Department of Botany UGC-DSA/ASIST Sponsored Department, Doctor Hari Singh Gour Vishwavidyalaya, Sagar (M.P.). Drying of fresh plant parts was carried out in the sun but under the shade.

Instrument and Apparatus

Oral feeding needle (cannula), Weighing balance, Soxhlet apparatus, Electronic balance, Scissors, Forceps, Test tube, Water bath, Pottery dish, Glassware etc.

Extraction of *Curcumin longa* using Soxhlet

The Soxhlet apparatus was used for extracting compounds from solid materials. The plant material were ground to a fine powder. The powder of each drug was placed in a thimble made of filter paper and inserted into the Soxhlet extractor separately. A solvent, ethanol, was added to the round-bottom flask of the Soxhlet extractor. The solvent was heated to boiling point, which caused it to evaporate and condense in the condenser.

The condensed solvent dripped back into the thimble, where it extracted the *Curcumin longa* compounds. The process was repeated several times until the extract was concentrated enough (Rut *et al.,* 2021).

Determination of percentage yield

The percentage yield of each extract was calculated by using following formula (Nkafamiy *et al.,* 2010):

Percentage yield = Weight of Extract /Weight of powder Drug x 100.

Phytochemical investigation: Experiment was performed to identify presence or absence of different phytoconstituents by detailed qualitative phytochemical analysis. The intensity of color or the precipitate formation was used as medical responses to tests. Following standard procedures were used (Duniya *et al.,* 2018).

Animals

Male Swiss albino mice (20-25 g) were used in this study. Animals were housed in cages [mice (24 x 17 x 14 cm) and maintained at standard laboratory conditions temperature 22 ± 2 C and room humidity 60 ± 10 %, 12:12 h of light/dark cycle and had free access to food (standard pellet chow food for laboratory animals) and water in the Animal Facility of

the Adina Institute of Pharmacy. After two weeks of the quarantine period, animals were randomized based on body weight for different assay protocols.

Ethical Approval

In India, the Committee for Control and Supervision of Experiments on Animals (CCSEA) is established under "The Prevention of Cruelty to Animals Act 1960". CCSEA has a representative body at the Institute level named as Institutional Animal Ethics Committee (IAEC). All the experimental procedures performed on animals followed the protocols, approved by IAEC.

Composition of High Fat diet

Powdered normal chow used in the preparation of HFD was obtained from Ratatouile Solutions, Rajasthan, India. Lard was purchased from local vendor, and casein, cholesterol, vitamin and mineral mix, dl-methionine, yeast powder, and sodium chloride were procured from Hi-Media (Pan *et al.,* 2018).

Ingredients	**Diet (g/kg)**
Powdered normal pellet diet	375
Lard	290
Casein	265
Corn oil	10
Cholesterol	10
Vitamin and mineral mix	60
DI Methionine	3
Yeast Powder	1
Sodium Chloride	1

HFD containing 60% kcal fat, 25% protein & 17% carbohydrate was prepared in our laboratory. Products were ground in a blender to a homogeneous mixture, after which the mass was formed into granules with a diameter of up to 10 mm and dried in an oven at 30 °C. The feed was prepared for 5 days and stored at +40C.

Method for induction of obesity

High fat diet (HFD) induced obesity model was standardized in the laboratory for performing various assays of depression. Male Swiss albino mice were fed with HFD for 14 weeks to induce obesity and weekly body weight was measured. At the end of the 14 weeks of HFD feeding, body weights were measured and animals tested for biochemical parameters namely plasma glucose, total cholesterol, and triglycerides. Mice fed with HFD and normal pellet diet (NPD) for 14 weeks (Bunyan *et al.,* 1976).

Animals (n=5)	Duration
Group 1: Normal Control: mice on standard chow diet	During whole experiment
Group 2: High Fat Diet feed mice(HFD)	14 weeks
Group 3: HFD + *Curcumin longa extract 200 mg/kg:* oral route	HFD was given for 14 weeks, followed by extract administration from 12th to 14 week
Group 4: HFD + *Curcumin longa extract 400 mg/kg:* oral route	HFD was given for 14 weeks, followed by extract administration from 12th to 14 week

Group 5: HFD + Fluoxetine 10 mg/kg+ HFD	HFD was given for 14 weeks, followed by fluoxetine from 12th to 14 week
At the end of experiment, behavioural and biochemical test were performed	

Pharmacological preliminary behavioural assays for depression

Spontaneous locomotor activity (SLA) score

The animal models used in the assessments of antidepressive or anxiolytic activities of any known or unknown compounds/drugs are based on the principle of despair and exploratory behaviour. It is very essential to take into consideration the basal locomotor scores of test animals in order to rule out the possibilities of false positive or false negative effect of the test compounds/drugs. Hence, the doses of compounds/drugs that do not alter the basal locomotor score are more preferred for the behavioural antidepressant and anxiolytic activities in rodents.

SLA score was measured by using the digital actophotometer (30 cm x 30 cm) with inside walls painted black. 30 min post administration of drug/compound/vehicle the animals were placed in the centre of the apparatus and allowed to access the area for 10 min consisting initial 2 min of acclimatization and remaining 8 min for measuring the locomotor activity score. After each test, the floor was cleaned thoroughly with 70% volume/volume (v/v) alcohol solution to eliminate possible bias due to Odors left by previous mice (Miyazaki *et al.,* 2022).

Forced swim test (FST) Rationale

FST is a high predictive validity model used to assess the antidepressant activity of any known and unknown drugs in the laboratory. FST reflects high sensitivity towards monoamine alterations which provide a model for studying neurobiological and genetic mechanisms involved in antidepressant response of drugs (Petit-Demouliere *et al.,* 2005).

Tail suspension test (TST)

TST is a high predictive validity behavioural assay commonly used for the assessment of antidepressant-like effect of novel or standard drugs at experimental laboratory settings.

TST represents the immobility of the animal due to its inability to maintain the escape effort and animals are capable to adapt to this posture rather quickly. Drugs that inhibit this immobility posture are supposed to show antidepressant effect. The immobility is considered as analogous to clinical observations, where depressed patients often lack the efforts to escape, as observed in prominent psychomotor impairments.

TST was performed as described earlier. From the horizontal bar mice were suspended by tail at 50 cm from floor (distance from tip of the tail = 2 cm). Test consists of 6 min duration in which the immobility time was recorded. A mouse was considered immobile when it remained passive, completely motionless and did not show any body movements (Kwon *et al.,* 2010).

Results and Discussion

The results presented provide significant insights into the pharmacological effects of *Curcuma longa* (turmeric) in a high-fat diet

(HFD) mouse model, particularly regarding obesity comorbid with depression.

The yield of crude extract from *C. longa* was relatively low at 0.57%, indicating that extraction efficiency may require optimization for better recovery of bioactive compounds. Phytochemical analysis revealed the presence of glycosides and saponins while indicating the absence of alkaloids, flavonoids, and tannins. The presence of glycosides suggests potential antioxidant properties, while saponins may contribute to anti-inflammatory effects.

In assessing locomotor activity, it was observed that HFD significantly impaired movement compared to the normal control group, with mice on HFD showing reduced activity. Notably, treatment with *C. longa* extract at both 200 mg/kg and 400 mg/kg doses improved locomotor activity, with the higher dose yielding better results. This suggests that *C. longa* may have neuroprotective effects that counteract the lethargy associated with high-fat diets, potentially through modulation of neurotransmitter systems involved in mood and motor control.

The forced swimming and tail suspension tests are well-established models for assessing depression-like behavior. Mice on HFD displayed increased immobility times, indicative of a depressive phenotype. Conversely, *C. longa* treatment significantly reduced immobility, particularly at the 400 mg/kg dosage. This aligns with previous studies showing that curcumin may enhance serotonergic and noradrenergic signaling, suggesting that it may act as a potential antidepressant.

The biochemical analysis demonstrated that HFD induced hyperglycemia, hypertriglyceridemia, and hypercholesterolemia, which are common metabolic disturbances associated with obesity. Interestingly, treatment with *C. longa* extract significantly lowered glucose, triglycerides, and cholesterol levels, especially at the higher dosage. These findings suggest that *C. longa* may exert beneficial metabolic effects, possibly through its anti-inflammatory and antioxidant properties, thereby mitigating the risks associated with obesity and depression.

Table 1: Percentage Yield of crude extracts

S. No.	Plant name	Solvent	Theoretical weight	Yield(gm)	% yield
1	*C. longa,* Rhizome	Hydro-ethanolic	286	1.65	0.57%

Table 2: Phyto-chemical analysis of extract

Phytochemical test	Presence or absence of phytochemical
Alkaloids	
Dragendroff's test	Absent
Mayer's reagent test	Absent
Wagner's reagent test	Absent
Hager's reagent test	Absent
Glycoside	
Borntrager test	Present
Legal's test	Present
Killer-Killiani test	Present
Carbohydrates	
Molish's test	Absent
Fehling's test	Absent
Benedict's test	Absent
Barfoed's test	Absent
Proteins and Amino Acids	
Biuret test	Absent
Flavonoids	
Alkaline reagent test	Absent
Lead Acetate test	Absent
Tannin and Phenolic Compounds	
Ferric Chloride test	Absent
Saponin	
Foam test	Present
Test for Triterpenoids and Steroids	
Salkowski's test	Absent
Libbermann-Burchard's test	Absent

Table 3: Effect of test drugs on locomotor activity

Treatment Group	Total Count (sec)
Group 1: Normal Control: mice on standard chow diet	118.3±10.2
Group 2: High Fat Diet feed mice	121.0±18.9
Group 3: HFD + *Curcumin longa* extract 200 mg/kg: oral route	111.0±13.8
Group 4: HFD + *Curcumin longa* extract 400 mg/kg: oral route	108.1±11.3
Group 5: HFD+ fluoxetine 10 mg/kg +HFD	112.6±8.9

Data is presented as mean±SD. Data are mean ±SD. *P < 0.05 vs control group; # P < 0.05 vs HFD group

Table 4: Effect of test drugs on immobility time in forced swimming test in mice

Treatment Group	Dose	Immobility time (sec)
Group 1: Normal Control: mice on standard chow diet		76.8±8.3
Group 2: High Fat Diet feed mice		145.2±12.3*
Group 3: HFD + *Curcumin longa* extract	200 mg/kg: oral route	120.9±9.5
Group 4: HFD + *Curcumin longa* extract	400 mg/kg: oral route	105.8±7.7#
Group 5: HFD + Fluoxetine + HFD	10 mg/kg	82.5±4.6#

Data are mean ±SD. *P < 0.05 vs control group; # P < 0.05 vs HFD group

Table 5: Effect of test drugs on immobility time in tail suspension test

Treatment Group	Dose	Immobility time (sec)
Group 1: Normal Control: mice on standard chow diet		98.5 ± 7.2
Group 2: High Fat Diet feed mice		186.3 ±12.4*
Group 3: HFD + *Curcumin longa* extract	200 mg/kg: oral route	131.5±11.5
Group 4: HFD + *Curcumin longa* extract	400 mg/kg: oral route	100.1±10.7#
Group 5: HFD + Fluoxetine	10 mg/kg	92.3±6.6

Data are mean ±SD. *P < 0.05 vs control group; # P < 0.05 vs HFD group

Table 6: Biochemical effects of test drugs

Treatment Group	Dose	Glucose mmol·L^{-1}	TG mmol·L^{-1}	Cholesterol mmol·L^{-1}
Group 1: Normal Control: mice on standard chow diet		4.88 ± 0.83	1.20 ± 0.34	3.86 ± 0.19
Group 2: High Fat Diet feed mice		8.74 ±0.99*	3.57±0.28*	10.02 ± 0.41*
Group 4: HFD + *Curcumin longa* extract	200 mg/kg: oral route	7.14 ± 0.71	2.88±019	8.24±0.45
Group 5: HFD + *Curcumin longa* extract	400 mg/kg: oral route	6.67 ± 1.35$^{\#}$	2.44±0.82$^{\#}$	7.83±0.95
Group 6: HFD + Fluoxetine	10 mg/kg	4.83±6.6$^{\#}$	1.99±0.25$^{\#}$	5.88±34

Data are mean ±SD. *P < 0.05 vs control group; # P < 0.05 vs HFD group

CONCLUSION

Overall, the findings of this study suggest that *Curcuma longa* exhibits promising pharmacological effects in alleviating both obesity and depression in a high-fat diet mouse model. The compound's ability to improve locomotor activity, reduce depressive behaviors, and ameliorate metabolic disturbances highlights its potential as a therapeutic agent for managing obesity-related comorbidities. Further studies are warranted to elucidate the underlying mechanisms and to evaluate the long-term efficacy and safety of *C. longa* in clinical settings.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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