WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.990
Volume 4, Issue 11, 1196-1206. Research Article ISSN 2277– 7105

ANTIOBESITY POTENTIAL OF *BOERHAAVIA DIFFUSA* ON ANIMAL MODEL OF OBESITY

Charan Singh[*1], Tarun Virmani[1], Jyoti Gupta[1], Reshu Virmani[2], Deepak Gahlawat[3], Geeta[4]

[1]School of Pharmaceutical Sciences, MVN University, Palwal, Haryana, India.

[2]Spectrum Institute of Pharmaceutical Sciences and Research, Plot No 21, Knowledge Park-1, Gautam Buddha Nagar, Uttar Pradesh, India.

[3]Department of Pharmaceutical Technology, NIET, Plot no. 19, Knowledge Park-II, Greater Noida, U.P., India.

[4]CBS College of Pharmacy & Technology, Faridabad, Haryana, India.

Article Received on
26 Aug 2015,

Revised on 15 Sep 2015,
Accepted on 05 Oct 2015

***Correspondence for Author**
Charan Singh
School of Pharmaceutical Sciences, MVN University, Palwal, Haryana, India.

ABSTRACT

Boerhaavia diffusa (Nyctaginaceae) is a well-known medicinal plant in traditional Indian medicine as well as other parts of world. Its various parts and especially roots have been used for gastrointestinal, hepatoprotective, and gynecological indications. In Ayurveda texts, more than 35 formulations of different types contain it as major ingredient. In Ayurveda, BD has been classified as "rasayana" herb which is said to possess properties like anti-aging, reestablishing youth, strengthening life and brain power, and disease prevention, all of which imply that they increase the resistance of the body against any onslaught, in other words, providing hepatoprotection and immunomodulation. The aim of present study was to estimate the ant obesity activity of ethanolic root extract of boerhaavia diffusa. Animals were divided into different group's control, standard, and test group after IAEC approval. Final results of different groups were compared (results of the extract 400 mg/kg) with that of standard drug (Orlistat 10 mg/kg). On the basis of experimental data obtained, it was observed that the root extract showed significant anti-obesity. The result suggests that the ethanolic extract from the whole plant of *Boerhaavia diffusa* exhibited significant anti-obesity activity.

KEYWORDS: *Boerhaavia diffusa*, Orlistat, Antiobesity, Rasayana, Ethanolic.

INTRODUCTION

Obesity epidemic is a leading cause of morbidity and mortality in developing as well as developed countries.[1] Obesity, a global problem, is a multifactorial disorder. The factors are environmental, metabolic and genetic and their interaction with each other regulates the body weight. Imbalance in either of the factors may be responsible for weight gain.[2] Obesity increases the risk of type 2 diabetes, cardiovascular disease, cancer, and premature death.

The strategies to treat obesity involve life-style interventions and pharmacological therapies. Many medications were introduced in for obesity management in past and were withdrawn from the market subsequently.[3,4] Rimonabant, a selective antagonist of cannabinoid type 1 receptor due to safety concerns (psychiatric effects) and Sibutramine, due to it associated potentials to increases BP and pulse rate were withdrawn from the market recently.[5] Currently, Orlistat which is a pancreatic and gastrointestinal tract lipase inhibitor is the only agent approved by Food and Drug Administration for long-term use in obesity. However, it is also associated with gastrointestinal side-effects and questionable efficacy.

Thus, the focus of anti-obesity treatment has shifted toward herbal drugs. The high cost of conventional drugs, relatively high incidence of toxicity and side effects, unavailability of orthodox drugs in many rural areas and clinical limitation, especially in the management of some chronic diseases are some of the risks in case of modern medicine. Hence, Indian traditional herbal medicine, which provides an effective solution without side effects of this possible risk, is preferred here. According to the World Health Organization (WHO), approximately 80% of the world's population currently uses herbal medicines in healing different ailments. Among the estimated 400,000 plant species, only 6% have been studied for biological activity, and about 15% have been investigated phytochemically. This shows a need for planned activity guided Phyto-pharmacological evaluation of herbal drugs.[6]

For present study we have chosen the *Boerhaavia diffusa* plant to evaluate its anti-obesity potential. *Boerhaavia diffusa* (Nyctaginaceae) is one of the most famous medicinal plants in India, where it is widely used in folk medicine. *Boerhaavia diffusa* is an Ayurvedic remedy used traditionally for the treatment of a number of diseases, including those affecting the gastrointestinal tract. In Indian traditional medicine, *Boerhaavia diffusa* (punarnava) roots have been widely used for the treatment of dyspepsia, jaundice, enlargement of spleen, abdominal pain and as an anti-stress agent. In *Charaka Samhita* and *Sushrita Samhita*, it is mentioned that the Ayurvedic preparations made from *punarnava*—namely, *punarnavastaka*

kvath, *punarnava kshar* and *punarnava taila*—were used for the treatment of various ailments such as stomachache, anemia, cough and cold, and used as laxative and expectorant. Many traditional uses of *B.diffusa* as, diuretic, anti-fibrinolytic, anti-bacterial, hepatoprotectant, anti-helmintic, febrifuge, anti-leprotic, anti-asthmatic, anti-scabies, anti-urethritis, anti-convulsant, cardiotonic, immunosuppressant, anti-viral and anti-oxidant, anti-inflammatory, anti-diabetic and anti-cancer, had been validated pharmacologically.

Pharmacological evaluation of the crude ethanolic extract of *B. diffusa* roots has been shown to possess antiproliferative and immunomodulatory properties. Oral administration of *B. diffusa* leaf extract (BLEt) resulted in significant reduction in serum and tissue cholesterol, free fatty acids, phospholipids, and triglycerides.[7]

MATERIALS AND METHODS

Selection of Plant Part and Authentication

Roots of *Boerhaavia diffusa* plant was purchased from Khari Baoli Delhi. The roots were authenticated as *Boerhaavia diffusa* L. root by NISCAIR Delhi (ref. NISCAIR/ RHMD/ Consult/-2012-13/2133/140).

Preparation of Extract

First of all the roots were washed with water to remove the dust and impurities from it. Then they were dried in shade. After drying it was changed into coarsely powdered form. For extraction sufficient quantity of ethanol was taken to submerge the root powder placed in a glass percolator. After standing it about 22 hours at room temperature, the percolate was collected. This process of extraction was repeated for 6 times for complete extraction of plant material. The combined ethanolic extract was evaporated to dryness under reduced pressure at 45^0C. Final drying was done in vacuum to get the extract.[8]

Experimental Animals

Male wistar rats (Animal Facilitation Centre, R.V. Northland Institute, Dadri, Greater Noida) weighing between 190-210 g were used for study. All the animals were 2-3 months old at the start of the study. Total 24 rats were used and they were categorized into four different groups with each group having 6 animals. Study was carried out after approval of CPCSEA.

Housing

All the animals were housed in different clean polyethylene cages under standard laboratory conditions, which were maintained on a 12h light /dark cycle, controlled temperature 25 ± 2^0C and humidity 55%. All the animals had free access of water.

Bedding

Clean paddy sterilized husk bedding was used. Bedding was changed by the investigator every week to maintain proper hygienic conditions.

Drugs and Doses

Standard Drug

Orlistat (*Vyfat)* was purchased from a local pharmacy and were used by dissolving appropriate dose (10mg/kg) in normal saline and given by oral route.[9]

Test Drug

Extract was given 400mg/kg by per oral route.[10]

High Fat Diet

Table No.1 Composition of High Fat Diet[11]

Ingredients	Diet(g/kg)
Powdered NPD	365
Lard	310
Casein	250
Cholesterol	10
Vitamins & mineral mix	60
DL-Methionine	03
Yeast Powder	01
Sodium chloride	01

Study Design

All the animals were divided into four different groups containing 6 animals in each. Group-I was assigned as Control group and kept on Normal diet (no treatment was given), group-II kept on High Fat Diet 20gm/day/rat (Obese), group-III as test group and treated with extract (400mg/kg) + High Fat Diet, while group-IV was assigned as standard group and treated with the HFD and Orlistat (10mg/kg). Animals were acclimatized to laboratory conditions for 7 days before starting the study. All experiments were conducted between 9am to 5pm. Prior approval was given by Institutional animal ethics committee for this study protocol.

Table No. 2 Grouping of Animals.

S. No.	Group name	Treatment	Dose & Route of administration	Duration
1.	Control	No	-------	28 days
2.	Obese	HFD	20gm/day/rat	28 days
3.	Test	HFD + Extract	400mg/kg BW Oral	28 days
4.	Standard	HFD + Orlistat	10mg/kg BW Oral	28 days

Procedure

After acclimatization of animals in lab condition the animals were divided into four groups as shown in above table. Group 1st was kept control and it received normal diet (20gm/day) supplied by golden feed and water *ad libitum* .Group obese, standard and test received the diet and drug as shown in table. The blood was collected on 0, 7, 14, 21 and 28th respectively from retro orbital route in anesthetic condition. Then blood is centrifuged for separation of serum and parameters were estimated. Animals were kept on fasting of 12 hours before blood collection. Daily food intake of every single animal was noted on regular timing and 20gm feed per rat were kept for next day. Body weight, body length was measured at 0, 7, 14, 21 and 28th day.

Statiscal Analysis

All results were are expressed as mean ± SEM. Statiscal analysis was performed using Graph pad prism 5, using Graph pad software. One way ANOVA followed by Dunnett's test was performed.

RESULTS

Effect of ethanolic root extract of *Boerhaavia diffusa* on in obese rats depicted in Table 3 and table 4.

Significant results were there when compared with obese group (increase in weight, BMI. Lee Index and Daily Food intake).

Table No. 3 Effect of *B. Diffusa* Root Extract on Anthropometric Parameters.

Parameters	Normal	Obese	Test	Standard
Increase in Weight in grams	19.2±0.84	133.88±2.39***	89.4±0.99***	55.43±2.46***
BMI	0.4095± 0.00359	0.67583± 0.0092***	0.57533± 0.00907***	0.4785± 0.00337***
LEE Index	0.26±0.0011	0.31133±.00178***	0.29483±.00232***	0.2745±.00072***
Daily Food Intake	15.629±0.173	18.339±0.304***	16.925±0.278**	16.268±0.310^{ns}

The values are mean ±SEM, n=6, When compared with Obese *p<0.05, **p<0.001, ***p<001 (One way ANOVA followed by Dennett's, multiple comparison test).

Finally the lipid profile of all the groups were compared followed by Dennett's, test at $p < 0.05$. Significant differences were observed.

Table No. 4 Effect of *B. Diffusa* Root Extract on Lipid Profile.

Parameters	Normal	Obese	Test	Standard
Total Serum Cholesterol	101.767±0.681	166.02±1.066***	122.83±0.83***	110.833±0.368***
Triglyceride	63.883±0.638	135.33±0.88***	103±0.82***	89.33±1.36***
HDL	31.567±0.279	24.283±0.17***	38.117±0.194***	44.117±0.21***
LDL	56.383±0.247	110.4±0.477***	61.317±0.492***	50.433±0.223***
VLDL	12.983±0.147	30.5±0.216***	22.65±0.41***	20.117±0.108***

The values are mean ±SEM, n=6, When compared with Obese *p<0.05, **p<0.001, ***p<001 (One way ANOVA followed by Dennett's, multiple comparison test.

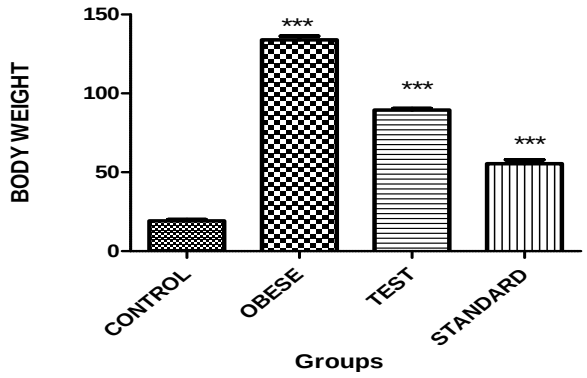

Fig. 1 Effect of *B. diffusa* root extract on increase in Weight.

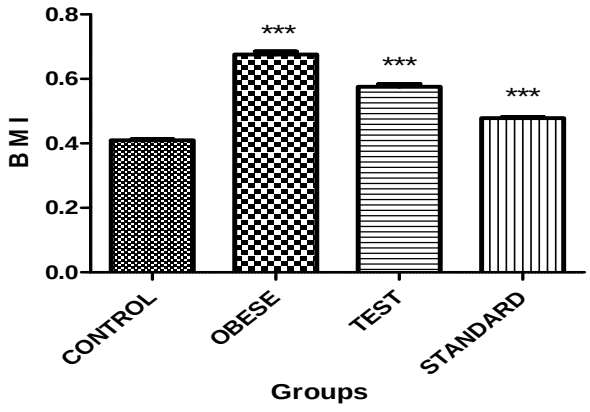

Fig. 2 Effect of *B. diffusa* root extract on body mass index.

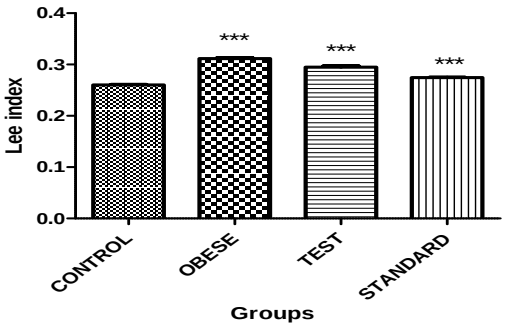

Fig. 3 Effect of *B. diffusa* root extract on Lee index.

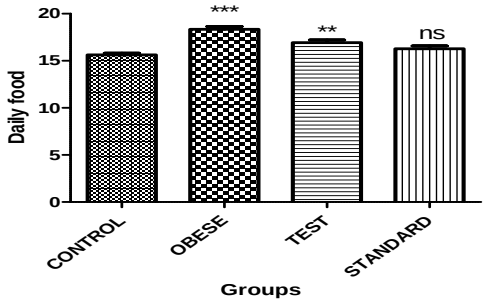

Fig. 4 Effect of *B. diffusa* root extract on daily food intake.

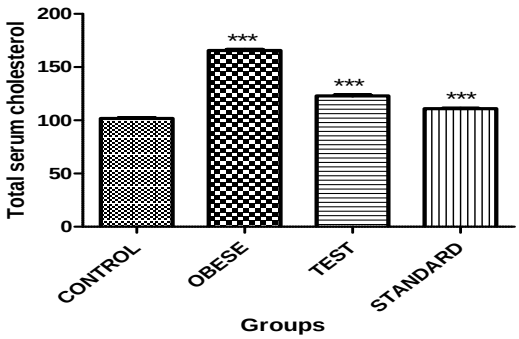

Fig. 5 Effect of *B. diffusa* root extract on Total Serum Cholesterol.

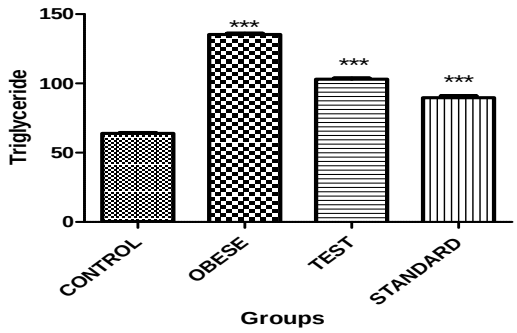

Fig. 6 Effect of *B. diffusa* root extract on Triglycerides level.

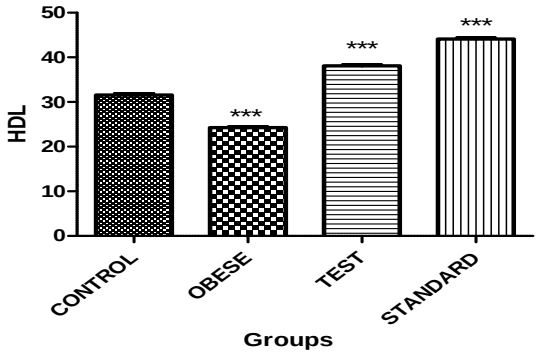

Fig. 7 Effect of *B. diffusa* root extract on HDL level.

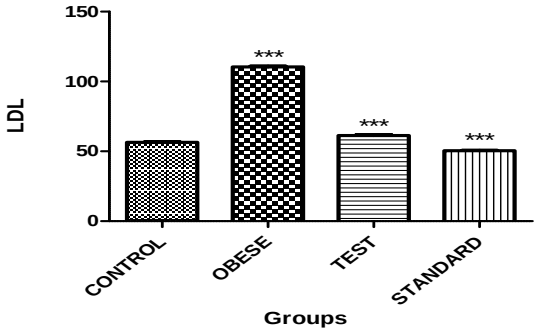

Fig. 8 Effect of *B. diffusa* root extract on LDL level.

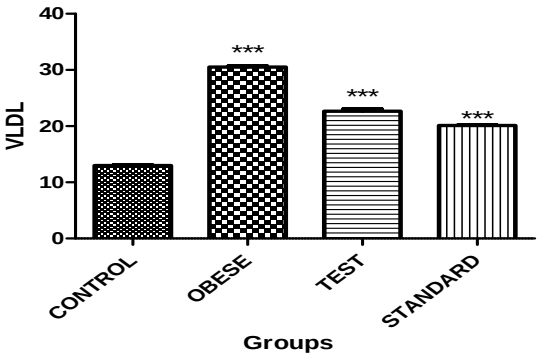

Fig. 9 Effect of *B. diffusa* root extract on VLDL level.

DISCUSSION

Obesity is one of the most widespread metabolic disorders in contemporary society. It is associated with the development of type two diabetes mellitus, coronary heart disease, cancer, respiratory complications and osteoarthritis.[12] Leptin is a hormone secreted by adiposities that provides a negative feedback signal to the brain to decrease energy intake. Deficiency in leptin as well as genetic defects in the leptin receptor are known to cause obesity in mice and have been proposed to play a role in obesity in humans.[13] Obese persons

are at increased risk for developing serious medical conditions such as diabetes mellitus, hypertension and cardiovascular disease, and obese persons are at increased risk of death from cardiovascular disease, diabetes, kidney disease, and cancer.[14] Obesity may induce systemic oxidative stress in accumulated fat is one of the underlying causes of deregulation of adipocytokinase and development of metabolic syndrome.[15]

In the present study the antiobesity activity of *Boerhaavia diffusa* root extract was studied using high fat diet rat model of obesity as they have been reported to bear close resemblance to human obesity. High fat diets have been previously reported to cause obesity in animals as well as humans. Different types of high fats diets are there and they produce obesity according to their composition. The final body weight gains in HFD group were 52.88 % greater than the normal control groups. The food intake of rats in the HFD+BDRE group was significantly lower than the values for the HFD group ($P<0.001$). The phytoconstituents compounds β-sitosterol found in this plant which is structurally similar to cholesterol has been suggested to reduce cholesterol by lowering the level of LDL-cholesterol and cholesterol level decrease significantly in plasma without any side effects.[16]

CONCLUSION

The present study demonstrated that significant reduction in body weight as well as lipid profiles as anti-obese activity and hypolipidemic activity of *Boerhaavia diffusa* root extract in experimental animals supplemented with high fat diets. *Boerhaavia diffusa* root extract ability to reduce the body weight gain could be due to its combined effects on the metabolic and serotonin pathways. The phytoconstituents compounds β-sitosterol found in this plant which is structurally similar to cholesterol has been suggested to reduce cholesterol by lowering the level of LDL-cholesterol and cholesterol level decrease significantly in plasma without any side effects.

Further, there is need to identify the phytoconstituents responsible for the activity and to formulate a polyherbal antiobesity preparation containing *Boerhaavia diffusa* root extract as a main ingredient.

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