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Evaluation of antiobesity activity of *Fucus vesiculosus*

Vishnu Priya Korukanti, Himabindu Ponnam[1], Butchi Raju Akondi

Department of Pharmacology, St. Peters Institute of Pharmaceutical Sciences, Hanamkonda, Warangal, Andhra Pradesh, India, [1]Drug Standardization (Ext.) Unit, Hyderabad, Andhra Pradesh, India

Address for correspondence: Dr. Butchi Raju Akondi, Department of Pharmacology, St. Peter's Institute of Pharmaceutical Sciences, Hanamkonda - 506 001, Andhra Pradesh, India. E-mail: drraju2020@gmail.com

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ABSTRACT

Background and Aim: The drug *Fucus vesiculosus* is used in alternative system of medicine and homoeopathy, for the treatment of obesity. But in homoeopathic literature survey, we found no substantial pharmacological evidence to prove its safety and efficacy. So, the study was taken up on this drug and evaluated it on different animal models (diet-induced and chemical-induced models) of obesity.

Material and Methods: Obesity was induced in adult female Wistar albino rats (100-120 g) by feeding the rats with cafeteria diet for 42 days in diet-induced model and by administration of single intraperitoneal injection of Triton X-100 in chemical-induced model. In the diet-induced model, weight of the animals was measured every week and parameters like total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), very low density lipoprotein (VLDL) and high density lipoprotein (HDL) were measured on 0, 21 and 43 days. Further, locomotor activity was assessed for all the animals on 43rd day. On the same day, the rats were sacrificed by cervical dislocation and their organ and fat pad weights were recorded. In the chemical-induced model, the above parameters were assessed on day 0 and day 8.

Results: Feeding cafeteria diet for 42 days resulted in significant increases in the body weight, TC, TG, LDL and VLDL levels and a reduction in the HDL level. Further, the locomotor activity was found to be reduced significantly. Treatment with *Fucus vesiculosus* significantly protected the cafeteria diet fed animals from all these changes and helped to maintain normal locomotor activity. Similar results were observed in chemical-induced obesity model also.

Conclusion: *Fucus vesiculosus* treatment prevented the rats from becoming obese and the biochemical and physical parameters were maintained to normal levels. So, the drug *Fucus vesiculosus* can be taken up for further research on human subjects.

Keywords: Antiobesity activity, Fucus vesiculosus, Diet induced obesity model, Chemical induced model

INTRODUCTION

Fucus vesiculosus is a seaweed commonly known as bladder wrack and is generally found on coasts of the North Sea, the western Baltic Sea, and Atlantic and Pacific oceans. *Fucus vesiculosus* is used in homoeopathic system of medicine for treatment of obesity. But in our literature survey, we found no substantial pharmacological evidence to prove its safety and efficacy. So, we have taken up this drug and evaluated it on diet and chemical models of obesity in rats.

Obesity is a chronic medical illness in which excess body fat accumulates in the body. The excess fat

may have adverse effects on health, in which it may reduce the life expectancy or increases the health problems.[1] The normal amount of body fat (expressed as percentage of body fat) is between 25 and 31% in women and 18 and 24% in men, and those who have more than the given limit can be called as obese. Generally, body fat is necessary for storing energy, heat insulation and shock absorption. The fundamental cause of obesity is an energy imbalance between calories consumed and calories expended. The regulation of energy balance requires a mechanism for sensing the level of energy stores in body fat and relaying the information to controlling sites in the hypothalamus. Integration of information in the hypothalamus and determination of energy balance through control of food intake and energy expenditure helps to maintain normal weight.[2] The most common method of measuring obesity is by calculating Body Mass Index (BMI). It is calculated by dividing body weight (kilograms) by height (meters) squared. If obesity is left untreated, it leads to complications such as Type 2 diabetes, gout, dyslipidaemia, osteoarthritis, hypertension, obstructive sleep apnoea etc.[3]

The drugs Phentermine and Orlistat are approved by the US Food and Drug Administration (FDA) specifically for obesity. The drugs Bupropion, Metformin, Topiramate and Zonisamide are approved for other indications but have been found to exhibit a significant weight loss effect.[4] Bariatric surgery is an option when diet, exercise and drug therapy have not produced satisfactory outcomes.[5] All the drugs and methods described above have serious adverse drug reactions and are not suitable old-age patients. So, there is a need for devolvement of drugs for the treatment of obesity, and alternative systems of medicine provide leads for the same.

MATERIAL AND METHODS

Animals

Forty-eight female Wistar albino rats[4] (100-120 g) were procured from Sanzyme Limited, (Hyderabad, India) and maintained in an air-conditioned room with a normal night and day cycle (temperature 21-25°C and humidity 45-65%). Rats were fed with normal pelleted diet and water *ad libitum*. The rats were allowed to acclimatise to the laboratory environment for a week before the start of the experiment. All experimental procedures were conducted in conformity with the guidelines of Institutional Animal Ethics Committee (approval number: 16/SPIPS/IAEC/12) for the care and use of animals and they were strictly followed throughout the study.

Chemicals and Reagents

Triglycerides (TG) kit, total cholesterol (TC) kit and high density lipoprotein (HDL) cholesterol kit were purchased from Coral Diagnostics Ltd, Mumbai, India and Triton X-100 was procured from Sigma-Aldrich Bangalore, India. *Fucus vesiculosus* mother tincture was procured from Dr. Willman Schwabe Pvt Ltd, Mumbai, India subsidiary of Schwabe International Ltd, Mumbai, India, Germany. Regular rat feed was supplied by Mahaveer Agencies, Hyderabad, India.

Experimental Procedures

The induction of obesity was carried out using two established methods[4] as follows.

Diet-induced model

In this method, rats were fed with cafeteria diet for 42 days. The cafeteria diet consists of three diets: (a) condensed milk (8 g) + bread (8 g); (b) chocolate (3 g) + biscuits (6 g) + dried coconut (6 g) and (c) cheese (8 g) + boiled potato (10 g).[6] The calorific value of the diet is given in Table 1.

Grouping of Animals (six rats in each group)

In the diet-induced model, cafeteria diet group was fed with cafeteria diet and the other group received the test drug (0.1 ml of the *Fucus vesiculosus* mother tincture) along with cafeteria diet after half an hour of feeding. Control group animals received normal saline. The treatment was continued for 42 days.

Grouping of animals (six rats in each group)

Treatment
Control
Cafeteria diet
Cafeteria diet+drug

Table 1: Calorie value of cafeteria diet

Ingredients	Calorie value (kcal/100 g)
Condensed milk	335
Bread	230
Chocolate	550
Biscuit	360
Dried coconut	660
Cheese	320
Boiled potato	80

Chemical-induced model

The rats were given single intraperitoneal (IP) injection of freshly prepared solution of Triton X-100 (100 mg/kg) in physiological saline solution after overnight fasting for 18 hours. After 72 hours of injection, one of the induced groups was treated with the test drug.[7]

Grouping of Animals (six in each group)

In the chemical-induced model, the drug treatment was given for 7 days after induction with Triton X-100 and the control group received normal saline solution for 7 days.

Grouping of animals (six in each group)	
Group I	Normal control
Group II	Cafeteria diet
Group III	Cafeteria diet+drug
Group IV	Triton X-100
Group V	Triton X-100+drug

Estimation of Physical Parameters

Estimation of body weight

The rats of different groups were weighed initially on day 1 and then after 7 days regularly for a period of 42 days.[8]

Evaluation of locomotor activity

It was recorded on day 43 for all the groups using photoactometer. The intact time in the instrument was 5 minutes.[8]

Estimation of biochemical parameters

The blood was collected on 43rd day in diet-induced model and on 8th day in chemical-induced model by retro-orbital puncture method and serum was separated using centrifugation. Then, the biochemical parameters such as TC, TG and lipoproteins were estimated. TC was assessed by cholesterol oxidase/phenol + aminophenazone method,[9] TG by glucoseoxidase/phenol + aminophenazone method[9,10] and HDL by polyethyleneglyco/cholesterol oxidase-phenol + aminophenazone method.[9,11] Low density lipoprotein (LDL)[12] was calculated by using the formula: TC − (TG/5) − HDL cholesterol, and very low density lipoprotein (VLDL)[12] by using the formula: TG/5.

Determination of organ and fat pad weights

The animals were sacrificed by cervical dislocation on 43rd day in diet-induced model and on 8th day in chemical-induced model, and then different organs (kidney, heart, liver and spleen) and fat pads mesenteric, uterine, ovarian and perirenal fat pads were removed and weighed. To collect the fat pads, the entire uterus and ovaries or testes were removed from their attachments to the pelvic floor. Entire intestinal loop was also removed from its attachment to the root of the mesentery and then straightened and unwound for the dissection of the mesenteric fat pad.

Statistical Analysis

The results are expressed as mean ± standard error of mean (SEM). Comparisons between the treatment groups and control were performed by analysis of variance (ANOVA) followed by Bonferroni's multiple comparison test. In all tests, the criterion for statistical significance was $P < 0.05$.

RESULTS

Effect of *Fucus Vesiculosus* on Body Weight in Cafeteria Diet Fed Rats

The diet-fed rats showed significant increase in body weight when compared to normal control group of rats [Figure 1]. But in *Fucus vesiculosus* (0.1 ml of the *Fucus vesiculosus* mother tincture) treated groups, the weight of the animals was not significantly changed when compared to normal control group animals.

Effect of *Fucus Vesiculosus* on Locomotor Activity in Cafeteria Diet Fed Rats

Cafeteria diet showed a significant decrease in locomotor activity due to the weight gain when compared to normal control rats [Table 2]. Drug treatment (0.1 ml of the *Fucus vesiculosus* mother tincture) to the test group did not significantly alter the locomotor activity and the values almost resembled those of normal control group rats.

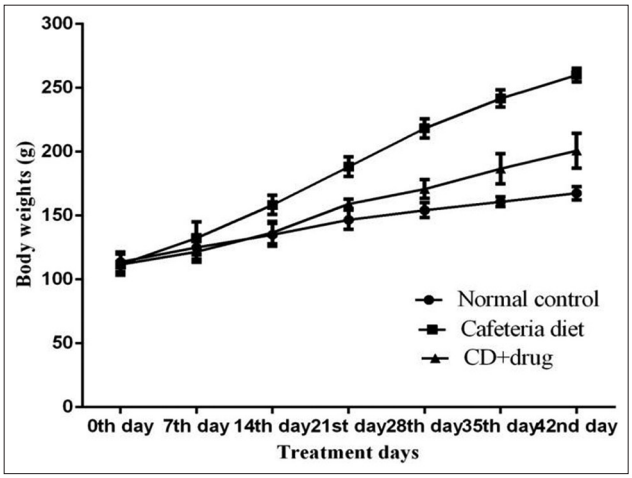

Figure 1: Effect of *Fucus vesiculosus* on body weight in Cafeteria diet fed rats

Effect of *Fucus Vesiculosus* on the Weights of Different Organs in Cafeteria Diet Fed Rats

Feeding the rats with cafeteria diet increased the weight of the organs significantly [Table 3]. Liver showed the maximum increase in weight when compared to other organs like spleen, heart and kidneys. The drug *Fucus vesiculosus* (0.1 ml of the *Fucus vesiculosus* mother tincture) significantly prevented the increase in weight of the liver.

Effect of *Fucus Vesiculosus* on The Weights of Different Fat Pads in Cafeteria Diet Fed Rats

The weight of the fat pads was significantly increased in diet-induced group of rats. But fat pads remained normal in *Fucus vesiculosus* treated groups [Table 4].

Effect of *Fucus Vesiculosus* on the Biochemical Parameters in Cafeteria Diet Fed Rats

Feeding of cafeteria diet caused a significant increase in the serum levels of TC, LDL, TG and VLDL and significant decrease in HDL levels, as compared to normal diet fed rats. In contrast, *Fucus vesiculosus* treatment significantly inhibited the increase in serum levels of TC, LDL, TG and VLDL and decrease in HDL levels [Tables 5-7].

Effect of *Fucus Vesiculosus* on the Biochemical Parameters in Triton X-100 Treated Rats

Treating the rats with Triton X-100 caused a significant increase in the serum levels of TC, LDL, TG and VLDL and significant decrease in HDL levels, when compared to control rats. In contrast, *Fucus vesiculosus* (0.1 ml of the *Fucus vesiculosus* mother tincture) treatment significantly inhibited the increase in serum levels of TC, LDL, TG and VLDL and decrease in HDL levels [Tables 8 and 9].

DISCUSSION

Two models of obesity, namely diet-induced model and Triton X-100–induced model, were employed to prove the effectiveness of the drug *Fucus vesiculosus* in the treatment of obesity. In the diet-induced model, cafeteria diet, which consists of high calorie value and high fat content, was administered to rats to induce obesity.[9] In general, it has been reported that rodents fed with high-fat diet are an excellent model of obesity where dietary environment is a major contributor[13] and it can be easily correlated with the obesity caused by diet in humans.[14] In the chemical-induced model, Triton X-100 was administered to rats at a dose of 100 mg/kg in IP route[10] and the lipid profile was significantly increased due to the action of Triton X-100 on serum lipoprotein lipase by some unknown mechanism. In the cafeteria diet model, the physical parameters such as body weight,[15] locomotor activity, and organ and fat pad weights and the biochemical parameters such as TC, TG, HDL, LDL and VLDL levels were measured.

Body weight is the predominant physical parameter in obesity in which the weight of an individual is increased to a great extent. After feeding the rats with cafeteria diet for 42 days, the body weight significantly increased due to the accumulation of fat in the body[9,15] and the drug *Fucus vesiculosus*

Table 2: Effect of *Fucus vesiculosus* on locomotor activity

Treatment	Locomotor activity
Control	152.5±3.59
Cafeteria diet	76.83±6.35#
Cafeteria diet+drug (0.1 ml)	128.17±4.82*

Values are mean ± SEM, *P<0.05 as compared to cafeteria diet control, #P<0.05 compared to normal control

Table 4: Effect of *Fucus vesiculosus* on the weights of different fat pads

Treatment	Weights of different fat pads (g)			
	Mesenteric	Uterine	Ovarian	Perirenal
Control	1.16±0.17	1.72±0.057	1.61±0.074	1.55±0.16
Cafeteria diet	1.88±0.21#	2.31±0.16#	2.29±0.25#	2.42±0.19#
Cafeteria diet+drug (0.1 ml)	1.21±0.13*	1.77±0.13*	1.65±0.096*	1.56±0.18*

Values are mean ± SEM, *P<0.05 as compared to cafeteria diet control, #P<0.05 compared to normal control

Table 3: Effect of *Fucus vesiculosus* on the weights of different organs

Treatment	Weights of different organs(g)				
	Kidney		Heart	Spleen	Liver
	Left	Right			
Control	0.58±0.030	0.55±0.035	0.59±0.13	0.58±0.038	3.92±0.22
Cafeteria diet	0.64±0.046	0.64±0.024	0.71±0.064	0.670.069	5.1±0.25#
Cafeteria diet+drug (0.1 ml)	0.54±0.035	0.55±0.030	0.65±0.025	0.48±0.046	4.51±0.23*

Values are mean±SEM; *P<0.05 as compared to cafeteria diet control, #P<0.05 compared to normal control

Table 5: Effect of *Fucus vesiculosus* on TG and TC

Treatment	TG			TC		
	Day 0	Day 21	Day 43	Day 0	Day 21	Day 43
Control	82.83±1.6	85±1.75	85.33±2.12	48.67±1.054	48.5±1.18	51.83±1.08
Cafeteria diet	71.5±1.8	116.33±2.37#	129.67±6.23#	46.83±1.014	74±1.065#	87±2.03#
Cafeteria diet+drug (0.1 ml)	67±1.86	97.83±1.72*	94.33±2.23*	48.17±1.941	58.83±1.08*	65.83±2.27*

Values are mean±SEM, *P<0.05 as compared to cafeteria diet control, #P<0.05 compared to normal control, TG: Triglycerides, TC: Total cholesterol

Table 6: Effect of *Fucus vesiculosus* on HDL and LDL levels

Treatment	HDL			LDL		
	Day 0	Day 21	Day 43	Day 0	Day 21	Day 43
Control	20.67±1.33	20.5±0.96	22.17±0.75	11.47±0.20	11±0.37	11.42±0.17
Cafeteria diet	20±1.15	10±0.86#	5.17±0.703#	12.5±0.22	39.67±0.42#	59.5±0.56#
Cafeteria diet+drug (0.1 ml)	20.16±1.49	14.33±0.67*	17.67±0.84*	14.67±0.33	25.33±0.42*	21.17±0.31*

Values are mean±SEM, *P<0.05 as compared to cafeteria diet control, #P<0.05 compared to normal control, HDL: High density lipoprotein, LDL: Low density lipoprotein

Table 7: Effect of *Fucus vesiculosus* of VLDL levels

Treatment	VLDL		
	Day 0	Day 21	Day 43
Control	16.67±0.33	15.83±0.94	16.25±0.25
Cafeteria diet	14.33±0.21	24.41±0.69#	34.67±0.33#
Cafeteria diet+ drug (0.1 ml)	12.17±0.31	19.33±0.67*	18±0.26*

Values are mean±SEM, *P<0.05 as compared to cafeteria diet control, #P<0.05 compared to normal control, VLDL: Very low density lipoprotein

Table 8: Effect of *Fucus vesiculosus* on TC and TG levels in Triton X-100 treated rats

Treatment	TC		TG	
	Day 0	Day 10	Day 0	Day 10
Control	47.67±1.52	58.83±1.08	74.17±2.39	79.67±0.56
Triton X-100	62.17±0.60	105.08±0.49#	78.33±1.94	122.17±3.79#
Triton X-100+ drug (0.1 ml)	54.83±1.30	64.33±0.56*	75.83±1.25	91.83±4.96*

Values are mean±SEM, *P<0.05 as compared to Triton X-100 control, #P<0.01 as compared to normal control, TG: Triglycerides, TC: Total cholesterol

Table 9: Effect of *Fucus vesiculosus* on the levels of lipoproteins in Triton X-100 treated rats

Treatment	HDL		LDL		VLDL	
	Day 0	Day 10	Day 0	Day 10	Day 0	Day 10
Control	20.67±1.33	20.67±1.02	10.75±0.17	22.33±0.56	16.33±0.42	15.91±0.33
Triton X-100	14.33±0.67	7.5±1.12#	33±0.73	67.75±1.06#	14.83±0.48	29.83±0.60#
Triton X-100+drug (0.1 ml)	19.5±0.56	17.67±0.84*	24.83±0.60	34.91±0.58*	12.33±0.49	11.75±0.31*

Values are mean±SEM, *P<0.05 as compared to Triton X-100 control, #P<0.01 as compared to normal control, HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very low density lipoprotein

exhibited its protective nature in rats by preventing their weight gain.

Locomotor activity[4] was decreased in obese rats due to the increased body weight. The activity was measured using photoactometer. The intact time in the instrument was 5 minutes and the number of crossings of the animals for 5 minutes in the instrument was measured. The activity was almost unaltered in the treated group when compared to obese rats. It was due to the protective nature of the drug *Fucus vesiculosus.*

Another physical parameter measured was organ and fat pad weights. Organs such as liver, kidney, heart and spleen were weighed. The weight of liver was significantly increased due to the accumulation of fat around the organ and the drug *Fucus vesiculosus* prevented the increase in weights of the organs in rats. Fat pad is a fatty tissue occurring in and around bony joints. It acts as a cushion helping to protect the joints from mechanical damage. On consuming high-fat diet, the extra fat accumulates around the mesenteric, ovarian, uterine and perirenal fat pats, which are easily prone for the accumulation of fat, and the weight increases. The drug *Fucus vesiculosus* protected the rats by preventing the weight gain of the fat pads.

Changes in biochemical parameters, especially in lipid profile, are the predominant changes caused in obese people. In obesity, the levels of TC, TG,

LDL and VLDL increases and the level of HDL, which is called as good cholesterol, decreases. Elevated serum levels of TG, cholesterol and LDL are the major risk factors for the premature development of cardiovascular diseases like atherosclerosis, hypertension, coronary heart disease, etc., Increase in plasma lipid levels, mainly TC, TG and LDL, along with decrease in HDL are known to cause hyperlipidaemia which is the reason for initiation and progression of atherosclerosis impasse.[16] Due to the intake of high-fat diet, TC and TG levels increase in the blood. The LDL and VLDL syntheses increase by the liver and it helps in the transportation of TC and TG into blood and to the tissues, whereas the HDL levels decrease due to its decreased synthesis by the liver in obesity. The rats receiving the drug *Fucus vesiculosus* did not have decreased levels of HDL and increased levels of TC, TG, LDL and VLDL.

In Triton X-100 model, the biochemical parameters such as TC, TG, HDL, LDL and VLDL levels were measured. The increased levels of TC, TG, LDL and VLDL and decreased levels of HDL can be addressed as hyperlipidaemic condition. The rats receiving the drug *Fucus vesiculosus* did not have increased TC, TG, LDL and VLDL levels and decreased HDL levels. The drug *Fucus vesiculosus* protected the rats by preventing changes in lipid profile.

CONCLUSION

Fucus vesiculosus was found to be beneficial when tested on two different animal models, i.e. diet-induced and chemical-induced models. Diet-induced animal model typically mimics the obesity gained through high-calorie diet in human beings. *Fucus vesiculosus* prevented the rats from becoming obese, when given along with high-calorie diet. Biochemical and physical parameters were also maintained at normal levels. Chemical-induced animal model typically represents hyperlipidaemia in the human beings without weight gain. When hyperlipidaemic animals were treated with *Fucus vesiculosus,* the levels of HDL, LDL and VLDL were brought back to normal. So, the drug *Fucus vesiculosus* can be taken up for further research on human subjects.

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फ्यूकस वेसीक्यूलोसस

पृष्ठभूमि और उद्देश्यः मोटापे के इलाज के लिए फ्यूकस वेसीक्यूलोसस दवा का होम्योपैथी में प्रयोग किया जाता है। परन्तु हमारे साहित्य सर्वेक्षण में, हमारे पास इसकी सुरक्षा और क्षमता को सिद्ध करने के लिए कोई पर्याप्त औषधीय प्रमाण नहीं मिला है। अतः हमने इस दवा को मोटापे के विभिन्न पशु मॉडलों (आहार प्रेरित और रासायनिक प्रेरित मॉडलों) पर मूल्यांकन के लिए प्रयोग किया है।

सामग्री एवं विधिः आहार–प्रेरित मॉडल को 42 दिनों के लिए कैफेटेरिया भोजन खिलाने से और रासायनिक प्रेरित मॉडल को ट्राइटन (एक्स–100) की एक इंट्रापेरीटोनियल इंजेक्शन लगाने से व्यस्क महिला विस्टर अल्बीनो चूहों में (100–120 ग्राम) मोटापा उत्पन्न किया गया। आहार प्रेरित मॉडल में, जानवरों का हर हफ्ते वजन किया गया और 0,21 और 43 दिन पर कुल कोलेस्ट्रॉल, ट्राइग्लिसराइड्स, कम घनत्व वाले लिपोप्रोटीन (एलडीएल), बहुत कम घनत्व वाले लिपोप्रोटीन (वीएलडीएल) और उच्च घनत्व वाले लिपोप्रोटीन (एचडीएल) जैसे मापदंडों का मूल्याकंन भी किया गया। इसके अलावा, 43 वें दिन पर, सभी जानवरों की गतिशील क्रियाओं का मूल्यांकन किया गया फिर उसी दिन चूहों को छोड दिया गया और अंग वसा पैड का वजन दर्ज किया गया। रासायनिक–प्ररित मॉडल में, ऊपर लिखित मानदंडो का 0 और 8 वें दिन पर मूल्यांकन किया गया।

परिणामः 42 दिनों के लिए कैफेटेरिया आहार खिलाने से शरीर के वजन, कुल कोलेस्ट्रोल, ट्राइग्लिसराइड्स, एलडीएल और वीएलडीएल स्तर में महत्त्वपूर्ण वृद्धि और एचडीएल स्तर में कमी देखी गई। इसके अलावा, गतिशील क्रिया में भी कमी देखी गई। इस प्रकार फ्यूकस वेसीक्यूलोसस दवा के साथ उपचार से कैफेटेरिया आहार खिलाये जाने वाले जानवरों को इन सभी परिवर्तनों से सुरक्षा मिली और गतिशील क्रिया को सामान्य बनाये रखने में मदद मिली इसी तरह के परिणाम रासायनिक प्रेरित मोटापे के मॉडल में भी देखे गये।

निष्कर्षः फ्यूकस वेसीक्यूलोसस उपचार ने चूहों को मोटा होने से बचाया और रासायनिक एवं शारीरिक मानदंडो को सामान्य स्तर पर बनाये रखा। अतः फ्यूक्स वेसीक्यूलोसस दवा को आगे के मानव विषयों पर अनुसंधान के लिए प्रयोग किया जा सकता है।

खोजशब्दः प्रतिस्थूलता गतिविधि, फ्यूकस वेसी–क्यूलोसस, आहार प्रेरित मोटापा मॉडल, रासायनिक प्रेरित मॉडल।