Antiobesity effect of Lipovedic formulation in rats fed on atherogenic diet

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Citation

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Abstract

Objective:
To study the antiobesity effect of Lipovedic, a polyherbal formulation in rats fed on atherogenic diet.
Methods:
Animals were fed atherogenic diet for 40 days. Lipovedic was administered in a dose of 900 mg/kg, p.o., twice a day to the drug treatment groups. The effect of Lipovedic on following parameters was recorded – body weight, body temperature (rectal temperature), locomotor activity, various biochemical parameters like serum glucose, total cholesterol and triglyceride levels, and organ and fat pad weight.
Results:
There was a significant reduction in body weight, organ and fat pad weight, increase in body temperature, locomotor activity and significant reduction in serum total cholesterol and serum triglyceride levels after treatment with Lipovedic in atherogenic diet fed rats.
Conclusion:
Lipovedic, a polyherbal formulation exhibited antiobesity effect in atherogenic fed rats.

INTRODUCTION

Obesity is a multifactorial, chronic disorder that has reached epidemic proportions in most industrialized countries and is threatening to become a global epidemic. Obese patients are at higher risk of coronary artery disease, hypertension, hyperlipidemia, diabetes mellitus, cancers, cerebrovascular accidents, osteoarthritis, restrictive pulmonary disease and sleep apnoea.[1]

Obesity is a challenging clinical condition to treat, because of their complex environmental components. Efforts to develop innovative antiobesity drugs with benefits for metabolic syndrome have been recently intensified. Moreover, due to absolute etiology of obesity, non-availability of drugs for its treatment, short-term efficacy and limiting contraindication and side effects of available drugs, the treatment is not satisfactory and thus there is a demand for search of new safer ones.

Ayurveda, alternative approach and the fractional medical practice of India, has been recognized to have convincing and credible healing power. So an extensive literature survey was carried out to find out the suitable drugs plant origin, which is claimed to have antiobese properties.

Lipovedic is a polyherbal formulation containing extracts of Commiphora mukul, Curcuma longa, Cyperus rotundus, Piper longum, Plumbago zeylanica and Juniperus communis plants. These plants have been reported to possess mainly thermogenic, hypocholesterolemic, body weight lowering, antidiabetic and digestive stimulant properties. Thus, the proposed study was carried out with an aim to investigate the antiobesity effect of polyherbal formulation, Lipovedic in rats fed on atherogenic diet.

MATERIALS AND METHODS

Drugs and chemicals: The polyherbal formulation Lipovedic was obtained from Vedic Biolabs, Bangalore, India. The constituents of Lipovedic include Commiphora mukul (gum resin), Curcuma longa (rhizome), Cyperus rotundus (rhizome), Piper longum (fruit), Plumbago zeylanica (root), and Juniperus communis (essential oil). The dried powder of the polyherbal formulation, Lipovedic was suspended in 3 % W/V gum acacia in distilled water and administered orally at

a dose of 900 mg/kg, p.o., twice a day for 40 days. Cholesterol, cholic acids were purchased from LOBA Chemie Pvt. Ltd., Mumbai; glucose from S.D.Fine chem. Ltd., Mumbai; glucose, cholesterol and triglyceride diagnostic kits were purchased from Diasys diagnostic systems, Germany. All the other reagents and chemicals were of analytical grade.

Animals: Wistar female rats (100-140g) procured from Central Animal Research Facilities, NIMHANS, Bangalore. They were housed, three per polypropylene cage under standard laboratory condition at room temperature (25 ± 2 C) with 12 h light/dark cycle. The animals were provided with pellet chow and water ad libitum. Ethical clearance was obtained from Institutional Animal Ethical Committee of VIPS, Bangalore.

Diet: The atherogenic diet consisted of cholesterol 1% W/W, cholic acid 0.5% W/W and lard oil 5 % W/W. These diets were provided in addition to normal pellet chow.[2]

Atherogenic diet induced obesity in rats: Thirty female Wistar rats 100-140 g were randomly divided into 5 groups of 6 each [Group 1: Normal control; Group 2: Control + Lipovedic (900 mg/kg); Group 3: Atherogenic diet control; Group 4: Atherogenic diet + Lipovedic (900mg/kg); Group 5: Atherogenic diet + Fluoxetine (reference standard 30 mg/kg)]. The drugs were given at a constant volume of 0.5 ml / 100 g body weights to rats. The control group animals received the vehicle in the same volume and through the oral route.

Parameter tested and procedures

Body weight: The body weight (g) was recorded on day 1 and then on alternate days for 40 days in each group using an electronic balance.

Body temperature: The body temperature was recorded on day 39 using rectal tele thermometer before and after drug administration at 30, 60, 90, 120, and 180 min with a contact time of 1 minute.[3]

Locomotor activity: On day 40, locomotor activity in different groups was recorded using open field behavior test apparatus, 30 min after Lipovedic administration to treatment groups. The apparatus consisted of circular wooden arena of 75 cm diameter and wall with a height of 25 cm. Open field test was performed by placing the rat in the center circle and visually monitoring its movements for 5 min. The ambulatory activity, in terms of the number of partitions crossed and the rearing activity, in terms of the number of times standing or rear paws during the 5 min test period were recorded.[4]

Biochemical parameters: On day 41 changes in glucose, total cholesterol and triglyceride levels were measured from serum samples using the biochemical kits.

Organ and fat pad weights: The animals were sacrificed by cervical dislocation and then different organs (liver, kidney, and heart) and fat pads (mesenteric, left and right perirenal and uterine fat pads) were removed and weighed immediately.

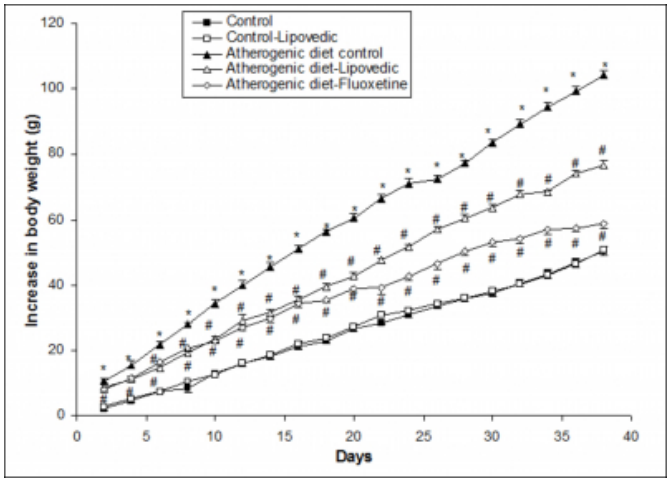
Statistical analysis: The results are expressed as mean ± SEM. Comparisons between the treatment groups and control were performed by analysis of variance (ANOVA) followed by Dunnett multiple comparison test.[3]

RESULTS

Effect on body weight: There was a significant increased in body weight of atherogenic diet group animals when compared to control group. Rats on atherogenic diet when treated with Lipovedic (900 mg / kg, p.o., and twice a day)/ fluoxetine (60 mg/kg, p.o., once daily) showed a significant decrease in body weight when compared to body weights of rats in atherogenic diet control group animals (Figure 1).

Figure 1

Fig 1: Effect of administration of Lipovedic (900 mg / kg, p.o., twice daily) / Fluoxetine (60 mg/kg, p.o., once daily) on body weight in rats fed normal pellet chow and atherogenic diet



Values expressed as mean ± SEM for six animals.

* $P < 0.01$ considered statistically significant as compared to control group.

# P < 0.01 considered statistically significant as compared to atherogenic diet control group.

Effect on body temperature: Treatment with Lipovedic produced significant increase in body temperature in atherogenic diet fed rats (Table 1) when compared to body temperature in atherogenic diet control group.

Administration of fluoxetine (60 mg/kg, p.o., once daily) in rats fed atherogenic diet did not shown a significant change in body temperature.

Figure 2

Table 1: Effect of administration of Lipovedic (900 mg / kg, p.o., twice daily)/ Fluoxetine (60 mg/kg, p.o., once daily) on body temperature in rats fed normal pellet chow and atherogenic diet

Sl. No	Treatment	Body temperature (°C) at time (min)					
		0	30	60	90	120	180
1.	Control	36.34 ± 0.07	36.37 ± 0.05	36.35 ± 0.05	36.33 ± 0.04	36.35 ± 0.04	36.43 ± 0.03
2.	Lipovedic	36.73 ± 0.06$	37.05 ± 0.06$	37.23 ± 0.03$	37.31 ± 0.04$	37.18 ± 0.04$	36.98 ± 0.05$
3.	Atherogenic diet control	36.42 ± 0.06	36.44 ± 0.05	36.42 ± 0.04	36.44 ± 0.03	36.45 ± 0.03	36.43 ± 0.05
4.	Atherogenic diet+Lipovedic	36.63 ± 0.06	36.84 ± 0.07*	37.08 ± 0.06*	37.34 ± 0.07*	37.18 ± 0.05*	36.88 ± 0.06*
5.	Atherogenic diet+Fluoxetine	36.57 ± 0.05	36.57 ± 0.06	36.51 ± 0.05	36.57 ± 0.04	36.55 ± 0.06	36.46 ±0.02

Values expressed as mean ± SEM for six animals.

$ P < 0.01 considered statistically significant as compared to control group

* P < 0.01 considered statistically significant as compared to atherogenic diet control group

Effect on locomotor activity: Treatment with Lipovedic/ fluoxetine produced significant increase in ambulatory and rearing activity in atherogenic fed rats (Table 2). Rats fed with atherogenic diet showed a significant decrease in rearing activity but not in ambulatory.

Figure 3

Table 2: Effect of administration of Lipovedic (900 mg/Kg, p.o., twice daily) / Fluoxetine (60 mg/kg, p.o., once daily) on locomotor activity in rats fed with normal pellet chow and atherogenic diet

Sl. No	Treatment	Ambulation	Rearing
1.	Control	58.33 ± 4.52	16.50 ± 2.87
2.	Lipovedic Control	81.33 ± 6.59$	25.00 ± 1.77$
3.	Atherogenic diet control	37.17 ± 3.57	07.83 ± 0.70$
4.	Atherogenic diet+Lipovedic	66.67 ± 8.32#	21.50 ± 1.93*
5.	Atherogenic diet+Fluoxetine	65.83 ± 9.28#	21.00 ± 2.63*

Values expressed as mean ± SEM for six animals.

$ P < 0.01 considered statistically significant as compared to control group

# P <0.05 and * P < 0.01 considered statistically significant as compared to atherogenic diet control group.

Effect on biochemical parameters: There was a significant increased in serum glucose level, total cholesterol and serum triglyceride level in atherogenic diet fed rats when compared to rats fed normal pellet chow, control group (Table 3).

Rats on atherogenic diet when administered Lipovedic showed a significant decrease in serum cholesterol and serum triglyceride level but not showed a significant change in serum glucose level when compared to rats in atherogenic diet control group.

Rats on atherogenic diet when administered fluoxetine showed a significant decrease in glucose, serum cholesterol and triglyceride level when compared to rats in atherogenic diet control group

Figure 4

Table 3: Effect of administration of Lipovedic (900 mg /kg, p.o., twice daily) / Fluoxetine (60 mg/kg, p.o., once daily) on biochemical parameters in rats fed normal pellet chow and atherogenic diet

Sl. No.	Treatment	Biochemical parameters (mg/dl)		
		Serum glucose	Serum total cholesterol	Serum triglyceride
1.	Control	72.422 ± 1.35	109.947 ± 4.42	92.432 ± 3.79
2.	Control Lipovedic	78.880 ± 2.69	102.123 ± 2.61	85.260 ± 2.45
3.	Atherogenic diet control	81.762 ± 2.48$	175.803 ± 2.06$$	168.982 ± 4.87$$
4.	Atherogenic diet +Lipovedic	88.208 ± 1.93	151.215 ± 7.02*	150.885 ± 7.76#
5.	Atherogenic diet +Fluoxetine	66.077 ± 1.52*	151.310 ± 6.40*	148.980 ± 3.83#

Values expressed as mean ± SEM for six animals.

$ P< 0.05 and $$ P< 0.01 considered statistically significant as compared to control group.

# P<0.05 and * P< 0.01 considered statistically significant as compared to atherogenic diet control group.

Effect on organ weight: Rats fed with atherogenic diet showed a significant increase in weight of heart, liver and left and right kidney when compared to

rats fed normal pellet chow, control group (Table 4). Rats on atherogenic diet when administered Lipovedic / fluoxetine showed a significant decrease in weight of heart, liver and left and right kidney when compared to rats in atherogenic diet control group.

Figure 5

Table 4: Effect of administration of Lipovedic (900 mg /kg, p.o., twice daily) / Fluoxetine (60 mg/kg, p.o., once daily) on organ weights in rats fed normal pellet chow and atherogenic diet

Sl.No	Treatment	Different organ weights (g)			
		Heart	Liver	Left kidney	Right kidney
1.	Control	0.620 ± 0.01	5.410 ± 0.18	0.658 ± 0.01	0.565 ± 0.01
2.	Control Lipovedic	0.607 ± 0.05	5.295 ± 0.07	0.522 ± 0.01	0.520 ± 0.01
3.	Atherogenic diet control	0.702 ± 0.02$	7.342 ± 0.19$	0.617 ± 0.03	0.637 ± 0.03
4.	Atherogenic diet+Lipovedic	0.627 ± 0.01*	6.625 ± 0.18#	0.518 ± 0.02*	0.547 ± 0.03#
5.	Atherogenic diet+Fluoxetine	0.585 ± 0.01*	6.547 ± 0.15*	0.502 ±0.02*	0.508 ±0.03*

Values expressed as mean ± SEM for six animals.

$ P < 0.01 considered statistically significant as compared to control group

# P < 0.05 and * P < 0.01 considered statistically significant as compared to atherogenic diet control group.

Effect on fat pad weights: Rats fed with atherogenic diet showed a significant increase in mesenteric, perirenal and uterine fad pad weight when compared to rats fed normal pellet chow, control group (Table 5). Rats on atherogenic diet when administered Lipovedic / fluoxetine showed a significant decrease in mesenteric, perirenal and uterine fat pad when compared to rats in atherogenic diet control group.

Figure 6

Table 5: Effect of administration of Lipovedic (900 mg /kg, p.o., twice daily) / Fluoxetine (60 mg/kg, p.o., once daily) on different fat pad weights in rats fed normal pellet chow and atherogenic diet

Sl.No	Treatment	Different fat pad weights (g)		
		Mesenteric	Perirenal	Uterine
1.	Control	0.767 ± 0.09	0.735 ± 0.02	0.803 ± 0.04
2.	Control Lipovedic	0.678 ± 0.09	0.675 ± 0.08	0.733 ± 0.06
3.	Atherogenic diet control	1.047 ± 0.04$	1.043 ± 0.03$$	0.992 ± 0.03$
4.	Atherogenic diet +Lipovedic	0.625 ± 0.04*	0.710 ± 0.05*	0.725 ± 0.04*
5.	Atherogenic diet + Fluoxetine	0.532 ± 0.02*	0.695 ± 0.04*	0.730 ± 0.03*

Values expressed as mean ± SEM for six animals.

$ P< 0.05 and $$ P< 0.01 considered statistically significant as compared to control group

* P< 0.01 considered statistically significant as compared to atherogenic diet control group.

DISCUSSION

In the present study, the antiobesity effect of Lipovedic was studied using the atherogenic diet induced obesity model. The atherogenic diet consists of cholesterol, cholic acid and lard oil. The results of our study showed that atherogenic diet fed rat showed significant increase in body weight, different fat pad weight, organ weight, significant increase in biochemical parameters including serum glucose, total cholesterol and triglyceride level, significant decrease in locomotor activity (rearing) when compared control group fed normal pellet chow. The significant increase in total cholesterol and triglyceride level in atherogenic diet fed animal can be attributed to increase in both de novo synthesis and intestinal absorption of cholesterol.[2]

Lipovedic is a polyherbal formulation containing extracts of Commiphora mukul, Cyperus rotundus, Piper longum, Curcuma longa, Juniper communis, and Plumbago zeylanica plants. Administration of Lipovedic to atherogenic diet fed rats showed significant increase in body temperature, locomotor activity, and significant decrease in serum total cholesterol, triglyceride levels and different organ weights and fat pad weights.

The increase in body temperature could be attributed to the thermogenic activity of Piper longum, [3] Curcuma longa has been reported to possess antidepressant activity[5] and this could explain the increase in locomotor activity in rats administered Lipovedic. Contribution of the antihyperlipidemic activity of Lipovedic and the resulting reduction in organ weight and fat pad weights could be due to Commiphora mukul [6, 7] and Cyperus rotundus. Commiphora mukul has been reported to contain guggulsterone that activates lipolytic enzymes in plasma and liver as well as stimulates receptor mediated catabolism of low density lipoprotein.[7] Guggulsterone is found to stimulate the thyroid gland and this could be considered as a possible mechanism for the lipid lowering activity of guggulsterone.[6] Cyperus rotundus containing a tertiary sesquiterpine alcohol, isocyperol exhibiting lipolytic action. It causes the activation of adenyl cyclase at the membrane with a subsequent increase in the intracellular levels of 3, 5- adenosine monophosphate, cAmp then activates a protein kinase which in turn activates triglyceride lipase.[8]

The observations above suggest that the Lipovedic, a polyherbal formulation possesses promising antiobesity activity. Further studies can be under taken to establish the possible mechanism of action of Lipovedic. This could include measuring serum leptin levels, serum lipoprotein lipase level, extra cellular availability of 5-hydroxy tryptamine in brain and other neurotransmitter involved in control of appetite, alteration in brown adipose tissue mass and activity. In vitro studies could include effect on -amylase and - glucosidase activities.

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