

Effect of Shilajit on Obesity in Hyperlipidemic Albino Rats

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ABSTRACT

Background: Shilajit contains a large variety of several components with different anti-obesity effects on body metabolism and fat oxidation.

Aim: To find out the effect of shilajit on obesity in hyperlipidemic albino rats.

Study design: It is a case control interventional study of eight weeks.

Methods: 40 male albino rats of 8 week size, weighing 220-250 grams were included in this study. To all groups, hyperlipidemic diet containing 20% fat and 1% cholesterol was given for 8 weeks. Group A of 10 rats was taken as control which was on hyperlipidemic diet throughout the experiment. Based on dosage (50, 100 and 200mg) of shilajit, rats were subdivided into three groups B,C and D of 10 rats in each group. In the next step, all rats were given hyperlipidemic diet. Freshly prepared aqueous suspension (in distilled water) of shilajit was used for each experiment. In the last step, the herbal (Shilajit) was administered by flexible gastric intubation to group B, C and D. All rats were weighed at 0,4 and 8 weeks

Results: It is observed that with increase in dose of shilajit there is decrease in weight. It was observed that when high fat diet containing 20% fat and 1% cholesterol was given, there was a significant increase in weight of albino rats as compared to level of this parameter at zero week. However, it is observed that with a dose of 50 mg of shilajit, there was still increase in weight with a significant difference. We observed that with a dose of 100mg of shilajit, there was insignificant effect on weight reduction. It was observed that with a dose of 200mg of shilajit for 4-8 weeks, the weight was significantly decreased.

Conclusion: It is concluded that shilajit with a dose of 200 mg may be effective for reduction of body weight . However further research is needed to give attention on both safety and efficacy of herb.

Keywords: Shilajit, obesity, hyperlipidemia

INTRODUCTION

Obesity is the most prevalent public health problem associated with nutritional and clinical condition. The disease is widespread and may reach 2.3 billion of overweight and 700 million obese individuals by 2015¹. In recent years the children of both developed and developing countries are mostly affected^{2,3}.

The increase prevalence of overweight in children is 25% and in adults is >50% resulting into a substantial increase in mortality and morbidity related to diabetes, coronary heart diseases, metabolic syndrome and cancers^{4,5}.

Dyslipidemia related to obesity is associated with increased triglycerides (TG), cholesterol and LDL-c and decreased HDL levels. Association of dyslipidemia with obesity plays a key role in the development of cardiovascular disease and atherosclerosis in obese population⁶.

The pathophysiology of the dyslipidemia in obese people is multifactorial and include decreased circulating TG lipolysis, overproduction of VLDL,

formation of small dense LDL, altered peripheral free fatty acid (FFA) uptake, increased FFA fluxes from adipocytes to other tissue and liver. Impairment of the Acylation-stimulating protein pathway in adipose tissue is also associated with dyslipidemia⁷. Hypertriglyceridemia may be the main cause of the lipid abnormalities due to delayed clearance of the TG-rich lipoproteins and production of small dense LDL^{8,9}.

There are different pharmacological treatments for controlling obesity including Orlistat and Sibutramine¹⁰, appetite suppressants drugs, and pancreatic lipase inhibitors. However, their side effects make the use of these drugs limited^{11,12}. Herbal therapies for weight loss are most common alternative medicine and prevent diet-induced obesity^{13,14}. These herbal medicines containing the compounds with anti-obesity and anti-oxidant effects on fat oxidation and body metabolism¹⁵. Medicinal plants including shilajit used for obesity and their metabolic disorders treatments, exerting a positive effect on lipid and glucose metabolism, and anti-inflammatory activity through reduction of adipocytes differentiation and proliferation³.

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Shilajit is an ayurvedic herbomineral medicine. Its active constituents are dibenzo-alpha-pyrones and related metabolites, humic acid and fulvic acid. Historically it is used for general physical strengthening, anti-aging, blood sugar stabilization, libido, injury healing, immune system, arthritis and obesity etc^{16,17}. Shilajit has the property to decrease serum cholesterol levels. Its major constituent fulvic acid contains supercharged antioxidants, superoxide dismutases and free-radical scavengers, which may help in fat metabolism. It also maintains the energy metabolism via the prevention of conversion of excess calories into fat^{18,19}.

Prevention and treatment of obesity is a big problem for health systems. The main purpose of health system is to decrease the prevalence of obesity and its related complications throughout the world. The multifaceted pathogenesis of obesity shows a need of multiple intervention strategies to challenge this problem with suitable drugs. Herbal medicines have gained an attention for reducing body weight and body fat. Since obesity is related to increase cholesterol, triglyceride and decrease the level of HDL-C, these herbal drugs can affect treatment target by having effect on weight as well as on lipid profile.

An experimental study was designed to find out the effect of shilajit on obesity in hyperlipidemic albino rats.

MATERIAL AND METHODS

Forty male albino rats of 8 week size, weighing 220-250 grams were included in this study. These rats were collected from National Institute of Health (NIH), Islamabad. They were kept in separate cages in the animal house of Postgraduate Medical Institute, Lahore at ambient temperature of 25±2°C with 12 hours light dark cycle.

Shilajit was obtained by an authentic source which is the pharmacologically effective form of shilajit²⁰. Freshly prepared aqueous suspension (in distilled water) of shilajit was used for each experiment and doses were expressed as dry weight of the solid constituents.

The normal diet (containing per 100gms of wheat starch 62.10gms, casein 20gms, glucose 10gms and small amount of fat 2.9gms) and hyperlipidemic diet (containing per 100gms of wheat starch 43.7gms, casein 20gms, glucose 10gms, cholesterol 1gms, bile salt 0.30gms and fat 20gms) for albino rats was prepared fresh at 2 week interval and stored at 2-8°C in a close container²¹.

Rats were subdivided into four groups of 10 rats in each group. Rats of group A (Control) were on hyperlipidemic diet throughout experiment. Group B:

50mg/kg shilajit dissolved in distilled water given orally for 4 weeks. Group C: 100mg/kg shilajit dissolved in distilled water given orally for 4 weeks. Group D: 200mg/kg shilajit dissolved in distilled water given orally for 4 weeks.

Initially all groups were fed on normal diet for a period of two weeks for acclimatization before starting the experiment and water ad libitum. Animals were given food at 8.00 and 14.00 and 20.00 hours. Diet was prepared on weekly basis at the rate of 30gm of diet/day/animal²².

In next step, all rats were given hyperlipidemic diet for next 8 weeks²⁴. The herbal shilajit was prepared with different doses i.e. 50mg (480mg shilajit was dissolved in 3.0 ml of water and diluted to 30 ml of water), 100 mg (960 mg shilajit was dissolved in 3.0 ml of water and diluted to 30 ml of water) and 200 mg (1900 mg shilajit was dissolved in 3.0 ml of water and diluted to 30 ml of water). The herbal (Shilajit) was administered by flexible gastric intubation at 4 weeks to the three groups. The rats were weighed at 0, 4 and 8 weeks.

Statistical analysis: All numerical variables were represented as mean±SD. Pretreatment values of weight of all groups were compared to their post treatment values by using the paired t-test. A p-value of ≤0.05 is considered significant for all analysis while p value ≤0.001 is considered highly significant.

RESULTS

Table 1 shows the body weight of group of rats from A to D. It is observed that the body weight of group A (control) showed an increase of body weight from 240.6±4.81gms to 275.6±9.6gms at 4th week of introducing high fat diet. There was a highly significant increase in body weight to 302.6±7.89 at 8th weeks of high fat diet.

In Group B after 50mg/kg shilajit, an increase in body weight of (289.8±15.8) from 272.6±11.2 was observed. On the other, in Group C, the increased body weight (271.4±8.2) remain constant (272±11.85) after introducing 100mg shilajit. However, in Group D, the increased body weight (282.0±12.2) was significantly decreased (p≤0.001) after using 200mg shilajit.

Table 2 shows pair-wise comparison of weights of all groups (A versus B, C and D, B vs C and D, C vs D) at 4 and 8 weeks. At the 4th week of inducing high fat diet, it is observed that the body weight of groups B, C, and D was 272.6±11.2, 271.4±8.2 and 282.0±12.22gms. There was a slight change as compared to the weight of group A (275.6±9.6 gm). On the other, at 8th week of experimental period, as compared to group A (302.6±7.89gm), the weight in

all groups was decreased (289.9 ± 15.8 , 272.2 ± 11.85 and 242.40 ± 7.87 gm) significantly ($P \leq 0.001$). The change in weights of rats of Group B (289.8 ± 15.8) to Group C (272 ± 11.85) was non-significant ($P > 0.05$) while with Group D, there was significant ($P \leq 0.001$) decrease in weight (242.40 ± 7.87) as compared to

group B (289.8 ± 15.8). On the other, there was significant decrease in body weight of rats of Group D (242 ± 7.87) as compared to Group C (272.40 ± 11.85). This data suggest that is effective in decreasing the body weight at a dose of 200mg.

Table 1: Comparison of animal weight (in grams) of different groups at sampling times of 0, 4th and 8th week of experiment. Values are given as mean \pm SD.

Groups	Weight of animals		
	0 week	4 week	8 week
A (control)	240.6 \pm 4.81	275.6 \pm 9.6	302.6 \pm 7.89**
B (50 mg SJ)	238.0 \pm 9.04	272.6 \pm 11.2	289.8 \pm 15.8**
C (100 mg SJ)	240.2 \pm 8.2	271.4 \pm 8.2	272 \pm 11.85
D (200 mg SJ)	246.4 \pm 7.35	282.0 \pm 12.22	242.40 \pm 7.87**

Key: SJ (shilajit)

** $P \leq 0.001$ = Highly significant difference as compared to 4 weeks.

* $P \leq 0.05$ = Significant

$P > 0.05$ = non significant

Table 2: Pair- wise Comparison of the body weight (grams) of different groups of animals using hypelipidemic diet at 4th and 8th week. Values are given as mean \pm SD

Groups in comparison	4 weeks	8 weeks
A (control) versus B (50 mg SJ)	275.6 \pm 9.6 272.6 \pm 11.2	302.6 \pm 7.89* 289.8 \pm 15.8
A (control) versus C (100mg SJ)	275.6 \pm 9.6 271.4 \pm 8.2	302.6 \pm 7.89** 272 \pm 11.85
A (control) versus D (200 mg SJ)	275.6 \pm 9.6 282.0 \pm 12.22	302.6 \pm 7.89 242.40 \pm 7.87**
B (50 mg SJ) versus C (100mg SJ)	272.6 \pm 11.2 271.4 \pm 8.2	289.9 \pm 15.8 272 \pm 11.85
B (50 mg SJ) versus D (200 mg SJ)	272.6 \pm 11.2 282.0 \pm 12.22	289.9 \pm 15.8** 242.40 \pm 7.87
C (100 mg SJ) versus D (200 mg SJ)	271.4 \pm 8.2 282.0 \pm 12.22	272 \pm 11.85 242.40 \pm 7.87**

Key: SJ (shilajit), ST (simvastatin).

* $P \leq 0.05$ = Significant

** $P \leq 0.001$ = Highly significant

$P > 0.05$ = non significant

DISCUSSION

Herbal supplements and diet-based therapies for weight loss are alternative treatment of obesity and its complications²⁵. Anti-obesity mechanisms were included decrease lipid absorption, decreased energy intake, enhanced energy expenditure, reduction of pre-adipocyte differentiation and proliferation, as well as increased lipolysis and decreased lipogenesis²⁶.

Different plants contain a large variety of several components with different anti-obesity effects on body metabolism and fat oxidation, and for this reason have been investigated and reported to be useful in treatment of obesity, diabetes and other chronic diseases¹⁴.

Present study is observed that with increase in dose of shilajit, there is decrease in weight. Our study is in according to a study²⁷ that observed a decrease

in body weight after using shilajit. However, a study found that there was no gain in the body weight of female mouse after taking shilajit²⁷.

Another study found that shilajit is very potent excess fat dissolver in the body. The study proposed that the main cause of obesity is an improper energy metabolism resulting in storing up of the fat in the body. The role of shilajit is to balance the energy metabolism and burn excess fat of the body²⁸. A study reported that Visceral obesity is associated with high increased levels of serum triglycerides and serum high density lipoprotein-cholesterol (HDL-C)²⁹.

Present study is also tried to find the level of different fraction of lipid including cholesterol and triglyceride and their lipoproteins HDL-cholesterol and LDL- cholesterol in group A (a control group) taking no shilajit. It was observed that when high fat

diet containing 20% fat and 1% cholesterol was given, there was a significant increase in the level of cholesterol, triglyceride and the carrier proteins HDL-cholesterol and LDL-cholesterol as compared to level of these lipid parameters without hyperlipidemic diet. This shows that high fat diet significantly increased the level of cholesterol and triglyceride along with the carrier lipoproteins of cholesterol³⁰.

It is reported that high caloric diet causes hypertrophy and hyperplasia of adipocytes, which may lead to hypoxia³¹ (Poulain-Godefroy et al., 2008). Due to hypoxia, adipocytes direct the factor hypoxia-inducible which may modulates the genes involved with the expression of leptin which is responsible for development of obesity³².

According to our study that after inducing high fat diet (after 4 and 8 weeks) there was a significant increase in the level of cholesterol, triglyceride and the carrier proteins HDL-c and LDL-c as compared to level of these lipid parameters at zero week. However after inducing a dose of 50 mg of shilajit, the lipid parameters were still increased with a significant difference. This study is in contrast with a study who found shilajit is effective at 50mg/kg dose³³.

We observed that after inducing a dose of 100 mg of shilajit, the lipid parameters were increased after 4 weeks but these are significantly decreased after taking 100 mg shilajit for 8 weeks. Our study is inline with a study who found that the maximum effect of shilajit was observed with its dose of 100mg/kg/day³³. According to a study, shilajit has proven to decrease cholesterol and triglyceride levels. It helps in decreasing the accumulation of cholesterol and fatty substance in the arteries and inhibit the reaction of LDL cholesterol with free radicals¹⁹.

Present study was observed that after inducing a dose of 200 mg of shilajit for 4-8 weeks, the lipid parameter was significantly decreased. This study is in-accord with a number of studies who reported the anti-obesity effects of herbal plants including shilajit. These anti-obesity effects may include a reduction in BMI, body weight as well as total body fat content^{34,35,36}. Shilajit increase the oxygenation to tissue by increasing energy carrying capacity and facilitate blood transportation to tissue. It also counters free radicals and inhibit degenerative disorders and keeps the equilibrium of body energy metabolism¹⁷.

CONCLUSION

It is concluded that shilajit with a dose of 200 mg may be effective for reduction of body weight. However further research is needed to give attention on both safety and efficacy of herb.

REFERENCES

1. Malik VS, Willett WC, Hu FB. Global obesity: trends, risk factors and policy implications. *Nat Rev Endocrinol.* 2013;9:13–27.
2. Knight J.A. Diseases and disorders associated with excess body weight. *Ann. Clin. Lab Sci.* 2011;41:107–121
3. Claudia I. Gamboa-Gómez, Nuria E. Rocha-Guzmán, J. Alberto Gallegos-Infante, Martha R. Moreno-Jiménez, Blanca D. Vázquez-Cabral, and Rubén F. González-Laredo. Plants with potential use on obesity and its complications. *EXCLI J.* 2015; 14: 809–831.
4. Barquera S, Campos I, Rivera J. Mexico attempts to tackle obesity: the process, results, pushbacks and future challenges. *Obes Rev.* 2013;14(Suppl 2):69–78.
5. Eckel RH, York DA, Rössner S, Hubbard V, Caterson I, St Jeor ST, Hayman LL, Mullis RM, Blair SN. American Heart Association. Prevention conference VII obesity, a Worldwide epidemic related to heart disease and stroke: executive summary. *Circulation.* 2004;110:2968–2975.
6. Howard BV, Ruotolo G, Robbins DC. Obesity and dyslipidemia. *Endocrinol Metab Clin North Am.* 2003 Dec;32(4):855-67
7. Klop B, Proctor SD, Mamo JC, Botham KM, Cabezas C. Understanding Postprandial Inflammation and Its Relationship to Lifestyle Behaviour and Metabolic Diseases. *International Journal of Vascular Medicine* 2012 (2012):11 pages
8. Hassing HC, Surendran RP, Mooij HL, Stroes ES, Nieuwdorp M, Dallinga-Thie GM. Pathophysiology of hypertriglyceridemia. *Biochim Biophys Acta.* 2012 May. 1821(5):826-32.
9. Kolovou GD, Anagnostopoulou KK, Kostakou PM, Bilianou H, Mikhailidis DP. Primary and secondary hypertriglyceridaemia. *Curr Drug Targets.* 2009 Apr. 10(4):336-43.
10. Tziomalos K, Krassas GE, Tzotzas T. The use of sibutramine in the management of obesity and related disorders:an update. *Vasc Health Risk Manag.* 2009;5:441
11. Karamadoukis L, Shivashankar GH, Ludeman L, Williams AJ. An unusual complication of treatment with orlistat. *Clin Nephrol.* 2009;71:430–432
12. Slovacek L, Pavlik V, Slovackova B. The effect of sibutramine therapy on occurrence of depression symptoms among obese patients. *Nutr Metab Cardiovasc Dis.* 2008;18:e43–e44.
13. Barnes PM, Powell-Griner E, McFann K, Nahin RL. Complementary and alternative medicine use among adults: United States, 2002. *Adv Data.* 2002;343:1–19.
14. Hasani-Ranjbar S, Nayebi N, Moradi L, Mehri A, Larijani B, Abdollahi M. The efficacy and safety of herbal medicines used in the treatment of hyperlipidemia; a systematic review. *Curr Pharm Design.* 2010;16:2935–2947.
15. Hasani-Ranjbar S, Larijani B, Abdollahi M. A systematic review of the potential herbal sources of future drugs effective in oxidant-related diseases. *Inflamm Allergy Drug Targ.* 2009;8:2–10

16. Ghosal S. Shilajit Part 7- chemistry of shilajit, an immunomodulatory ayurvedic rasayana. *Pure App Chem (IUPAC)* 1990; 62: 1285-8.
17. Deo YK, Chaudary Arnand K. Shilajit for obesity. A Probable pharmacological postulates. *Inj J Res Ayuverda Pharm* 2015; 6(1):69-72
18. Murray K, Linder PW. Fulvic acids: Structure and metal binding. A random molecular model. *J of Soil Sci* 1983; 34:511-23
19. Pattonder RK, Chandola HM, Vyas SN. Clinical efficacy of Shilajatu (Asphaltum) processed with Agnimanth (Clerodendrum phlomidis Linn.) in Sthaulya (obesity). *Ayu.* 2011 Oct-Dec; 32(4): 526–531.
20. Nandkarni KM. Aspheltum. *Indian Materia Medica* 2002; 2: 23-32.
21. Sahito MM, Chang F, Zardari MK et al. An experimental study in albino rats fed on different fatty diets. *Med Forum* 1999; 10: 4-6.
22. Welhe WH. *The laboratory rat*. London: CV Mosby 1983: 309-329.
23. Lasser LN, Roheins Ps, Edelstin D, Eder HA. Serum lipoprotein of normal and cholesterol fed rats. *J Lipid Res* 1973; 14: 1-8.
24. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the conc. Of low density lipoprotein cholesterol in plasma – without use of the preparative ultracentrifuge. *Clin Chem* 1972; 18: 499-502.
25. Hasani-Ranjbar S, Jouyandeh Z, Abdollahi M. A systematic review of anti-obesity medicinal plants - an update. *J Diabetes Metab Disord.* 2013;12(1):28-32
26. Yun JW. Possible anti-obesity therapeutics from nature: a review. *Phytochemistry* 2010; 71:1625-1641
27. Hamaidi AR, and Mohammad U. Safe use of shilajeet during pregnancy of female mice. *Saudi J Biol Soc* 1999; 6: 82.
28. Bucci LR. Selected herbals and human exercise performance. *Am J Clin Nutr.* 2000 Aug;72(2 Suppl):624S-36S.
29. Chan DC, Barrett HP, Watts GF. Dyslipidemia in visceral obesity: mechanisms, implications, and therapy. *Am J Cardiovasc Drugs.* 2004;4(4):227-46.
30. Vanlenten Brian and Paul S Roheim. Changes in the concentrations and distributions of apolipoproteins of the aging rat. *J Lipid Res* 1982; 23: 1187-95.
31. Poulain-Godefroy O, Lecoecur C, Pattou F, Frühbeck G, Froguel P. Inflammation is associated with a decrease of lipogenic factors in omental fat in women. *Am J Physiol.*2008; 295:R1–7
32. Goossens GH. The role of adipose tissue dysfunction in the pathogenesis of obesity-related insulin resistance. *Physiol Behav.* 2008; 94:206–18.
33. Trividi NA, Mazmudar B, Bhatt. Effects of shilajiton blood glucose and lipid profile in allocation induced diabetic rats. *Indian Journal of Pharmacology* 2004; 36(6): 373-76.
34. Abidov M, Ramazanov Z, Seifulla R, Grachev S. The effects of Xanthigen™ in the weight management of obese premenopausal women with non-alcoholic fatty liver disease and normal liver fat. *Diabetes Obes Metab.* 2010; 12:72–81.
35. Razquin C, Martinez J, Martinez-Gonzalez M, Mitjavila M, Estruch R, Marti A. A 3 years follow-up of a Mediterranean diet rich in virgin olive oil is associated with high plasma antioxidant capacity and reduced body weight gain. *Eur J Clin Nutr.*2009;63:1387–1393.
36. Das A, Datta S, Rhea B, Sinha M, Veeraragavan M, Gordillo G, Roy S. The Human Skeletal Muscle Transcriptome in Response to Oral Shilajit Supplementation. *J Med Food.* 2016 Jul;19(7):701-9.