

Role of Crataegus (Hawthorn) Extract on Obesity in Hyperlipidemic Albino Rats

SAMINA KAUSAR¹, ZUJAJA ZAHEER², MUDASSARA SAQIB³, BUSHRA ZIA⁴

ABSTRACT

Background: obesity is on the rise globally and needs measures to maintain optimal body weight as to avoid complications such as diabetes mellitus, hypertension, dyslipidaemia, ischaemic heart disease infertility, sleep apnoea, cancer and osteoarthritis. *Crataegus monogyna* can help in losing weight by reversing metabolic alterations that cause increased synthesis and storage of fat.

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

Sample: 60 adult male albino rats weighing about 250-300g divided randomly into three groups A, B, and C.

Result: *Crataegus* is effective in lowering body weight.

Conclusion: *Crataegus* shows tremendous potential as natural weight lowering agent, devoid of side effects. There is scope of further study and use of this 'miracle herb' as anti obesity agent.

Key words: *Crataegus monogyna*, obesity, BMI

INTRODUCTION

Obesity is from the Latin *Obesitas*, which means stout, fat or plump¹. The Greeks were the first to recognize obesity as a medical disorder². According to A.D.A.M medical encyclopedia, obesity means having too much body fat. Excess weight of muscles, bone, fat and water in the body is overweight. These two can be differentiated by calculating body mass index; BMI (weight in kg/height in meter²). BMI=25-30 kg/m² is overweight and BMI \geq 30 kg/m² is obese³. Obesity is on the rise globally reason being consumption of unhealthy foods and lower levels of physical activity. According to the centre for disease control, as of 2009, 49 states have a prevalence of obesity of 20% or greater and nine states have a prevalence of over 30%. Obesity is associated with increased risk of type II diabetes, cardiovascular disease and several forms of cancer⁴. In Pakistan the overall prevalence of obesity and overweight in educated population is 8 and 29.6% respectively and together with overweight this prevalence is found to be sufficiently high⁵.

The WHO International Agency for Research on Cancer has estimated that overweight and poor physical activity accounts for quarter to one third of all cancers of breast, colon, endometrium, kidney and esophagus⁶. There is a marked increase in osteoarthritis in obese, in a study it was noted that each one kg increase in weight was associated with an increased risk of radiographic features of

osteoarthritis at the knee and carpometacarpal joint⁷. Obesity during pregnancy is associated with an increased risk of complications and is now estimated to be responsible for 6% primary infertility⁸.

Researchers from UCLA discovered that as many as two thirds of all dieters end up weighing more than they did before their diet within two years⁹. This indicates the need of other interventions as some forms of drugs or herbal medicines which supplement dieting and weight loss may be sustained. Different weight reducing and dieting agents were reviewed for potential toxicity, these included: syrup of ipecac, cathartics 2,4 Dinitrophenol, guar gum, phenylpropanolamine, mahuang/ ephedra, caffeine, clenbuterol, fenfluramine, sibutramine, thyroid hormone, orlistat and cannabinoid antagonists¹⁰. These weight reducing agents should be potentially non toxic. One of such weight reducing agent is found in *crataegus monogyna*. *Crataegus monogyna* has acquired a prominent status in modern herbal literature. The common name is Hawthorn, Extracts of both flowers and berries contain mixtures of chlorogenic acid and flavonoids such as quercetin hyperoside, vitexin and vitexin 4 rhamnoside. Other flavonoids identified are luteolin, apigenin-7-o-glucoside and rutin. It also contains other major constituents which have anti inflammatory and antihyperlipidemic properties¹¹. Hawthorn has also been shown to lower body weight significantly by reversing metabolic alterations that drive increased creation and storage of fat¹². The present study was conducted to find out effect of *crataegus monogyna* on body weight of albino rats fed high fat diet.

Department of Pharmacology Post Graduate Medical Institute/LGH¹, King Edward Medical university², Sheikh Zayed Federal Post Graduate Medical Institute³, Aga Khan University, Karachi⁴

Correspondence to Dr. Samina Kausar, Assistant Professor Email: samina.zia@hotmail.com

MATERIALS AND METHODS

It is a case controlled interventional experimental study that took 8 weeks for completion. 60 adult, male albino rats weighing about 250-300 grams were purchased and kept in PGMI animal house. Two hundred gram of good quality well dried berries of *crataegus monogyna* were purchased and ethanolic extract was prepared in PCSIR laboratories. Extract was administered in a dose of 0.5 ml /100 g of body weight per day by gavage. The dose was calculated on basis of flavonoid content which is 2.2%¹³. Normal rat chow contains wheat starch, casein, glucose, choline/methionine, mineral mixture, vitamin mixture and fat in quantities of 62.10, 20, 10, 0.50, 3.50,1 and 2.90 grams to make total 100 g of the diet as basic constituents¹⁴, High fat diet (HFD) contained 2g vegetable oil, 1g cholesterol and 0.3 g bile salt in 100g of normal diet¹⁵.

Sixty male albino rats were divided randomly into three groups (A,B,C). Initially all the groups were fed on normal rat chow for the first two weeks for acclimatization, then high fat diet was started to B and C groups. A group remained on normal diet for the whole study period of 8 weeks. Group B remained on high fat diet while group C received *crataegus* extract from 4th-8th week along with high fat diet. Rats were weighed at 0, 4 and 8 weeks by digital scale.

Parameter: Body weight of rats.

Data analysis: All numerical variables were represented as mean+standard deviation. The individual comparison between any two groups was

analyzed by t-test. ANOVA test was used for comparison of all groups simultaneously. P-value ≤0.05 were considered significant. All analysis was done through the statistical package SPSS Version 12.

RESULTS

Table 1 shows weight of different groups at zero week, 4th week and 8th week. Mean weight of all groups at the start of study ranged from 219.75 to 222.75. At 4th week mean weight of all groups increased. At 8th week, in group A and B there was an increase in mean weight. While in group C, treated with *crataegus*, there was decrease in mean weight.

Table 2 shows pair-wise comparison of weights of all groups at 0, 4 and 8 weeks. It shows that at zero week difference in weights of all groups is insignificant which means that at start of study the weight of rats of all groups was same. At 4th week, weight of animals in group B and C (HFD) increased significantly as compared to that of group A (normal diet). Results of B versus C are insignificant showing that the weight gain in group C is close to group B. At 8th week, weight of animals in group B is significantly high as compared to that of group A while weight of group C animals is significantly low as compared to group B and close to group A. In fact weight of group C animals is less than that of group A although not significant statistically. This data suggests that *crataegus* is effective in lowering body weight in presence of high fat diet.

Table 1: Comparison of body weight (grams) of different groups at 0, 4 and 8 weeks (Values are presented as mean, standard deviation (SD), minimum (Min.) and maximum (Max.) level of weight)

Groups	0 week				4 weeks				8 weeks			
	Mean	S.D	Min.	Max	Mean	S.D	Min.	Max	Mean	S.D	Min.	Max
"A" Normal diet	222.75	15.26	190	240	230.95	16.19	200	260	243.75	15.12	220	270
"B" High fat diet	222.25	14.00	200	240	252.75	19.70	220	285	287.50	22.45	245	320
"C" High fat diet + Crataegus	219.75	15.26	195	240	274.00	22.45	240	320	240.25	19.83	210	290

Table 2: Pair-wise comparison of body weight (Grams) of different groups at 0, 4 and 8 weeks

I) Groups	(J) Groups	0 week		4 Weeks		8 Weeks	
		Mean Difference (I-J)	P value	Mean Difference (I-J)	P - value	Mean Difference (I-J)	P - value
"A" Normal diet	"B" High fat diet	0.500	1.000	-21.800(*)	0.005	-43.750(*)	<0.001
	"C" High fat diet + Crataegus	3.000	1.000	-43.050(*)	<0.001	3.500	1.000
"B" High fat diet	"C" High fat diet + Crataegus	2.500	1.000	-21.250(*)	0.007	47.250(*)	<0.001

DISCUSSION

The prevalence of obesity and over weight is increasing world wide. Obesity and overweight have many causes including genetic, metabolic, behavioral and environmental. A comparison of data from 1960-1994¹⁶ with that from 1999-2000¹⁷ shows that the prevalence of overweight increased from 46% to 64.5% and the prevalence of obesity doubled to 30.5%. the rapid increase in prevalence suggests that behavioral and environmental influences predominate, rather than biological changes. Obesity is directly associated with many metabolic and cardiovascular diseases.¹⁸ Several weight lowering measures are being used including the use of herbs. *Crataegus monogyna* has acquired a prominent status in herbal medicine. Extract of both flowers and berries have been recommended to treat cardiac failure, atherosclerosis, hyperlipidemia, hypertension, angina and variety of geriatric conditions¹⁹. It is also found to have weight lowering effect in the present study. Previous studies have revealed that *crataegus* is a rich source of flavonoids which confer anti oxidant property to the plant. Antioxidants are substances that scavenge free radicals damaging compounds in the body that alter cell membranes, tamper with DNA and even cause cell death. Free radicals occur naturally in the body, but environmental toxins (including ultraviolet light radiation, cigarette smoking and air pollutants) can also increase the number of these damaging particles. While oxidation is part of a normal biological reaction, over loading the cells with free radicals could initiate the pathogenesis of many diseases.²⁰ Phenolic compounds of *crataegus* also have antioxidant activity.²¹ *Crataegus* causes significant decrease in blood levels of lipid.²² Part of mechanism for antihyperlipidemic effects of hawthorn fruit might involve the direct protection to LDL from oxidation. In the present study obesity was induced in albino rats by giving high fat diet. Then effect of extract of *crataegus* berries was observed on the weight of rats. It was found that *crataegus* has significant weight lowering effect. This study is in agreement with a previous study conducted in Department of Pharmacy Tajen University, Taiwan; in which overweight hamsters treated with *crataegus* extract for a period of seven days were found to have significant loss of total body weight. Size of white fat cells were markedly reduced in treated hamsters,²³ it also lowered total cholesterol, triglycerides, low density lipoprotein and elevated HDL levels. In a related study *crataegus* was shown to exert impressive metabolic and anti obesity benefits by acting on a family of receptors called Peroxisome Proliferators-Activated Receptors (PPARs). In that

study effects of *crataegus* were found to be inhibitory for triglycerides and glucose absorption *in vivo*. *In vitro* it suppressed the gene expressions of PPAR.²⁴

CONCLUSION

Obesity is linked with a large range of medical complications. Weight reduction has beneficial effects and an integral part of treating these morbidities. The current study shows that *crataegus* is an effective anti obesity agent, further work can unravel its underlying biological mechanism and unique properties that may prove useful to those seeking to manage weight gain.

REFERENCES

1. On line etymology dictionary: obesity Douglas Harper Retrieved December 31,2008.
2. Haslam D (March 2007) "obesity a medical history". *Obes Rev* 8 suppl 1:31-6.
3. Pi-Sunyer FX. The medical risks of obesity. *Obes Surg* 2002; 12 Suppl 1:6S - 11S.
4. Pi-Sunyer FX. The medical risks of obesity. *Postgrad Med* 2009; 121:21-33.
5. Khan A, Afridi AK and Safdar M . Prevalence of obesity in the Employees of Universities, Health and Research Institution of Peshawar. *Pak J Nutrition*(2003),2:¹ 182-188.
6. Vainio H, Bianchini F, editors. Weight control and physical activity. Vol. 6. Lyon : IARC; 2002. International Agency for Cancer hand book of cancer prevention. Available online at <http://www.iarc.fr/en/publications/pdfs-online/prev/handbook6/Handbook6-0.pdf>
7. Cicuttini FM, Baker JR, Spector TD. The association of obesity with osteoarthritis of the hand and knee in women:a twin study. *J Rheumatol* 1996; 23:1221-6
8. Green BB, Weiss NS, Darling JR. Risk of ovulatory infertility in relation to body weight. *Fertile sterile* 1988;50:721-6
9. Koh JH, Kim JM, Chang UJ, Suh HJ. Hypocholesterlemic effect of hot-water extract from mycelia of *Cordyceps sinensis*. *Biol Pharm Bull.*2003 ;26(1):84 - 7
10. Yen M, Ewald MB. Toxicology of weight loss agents. *J Med Toxicol*, 2012
11. Vibes J, Lasserre B, Gleye J. Inhibition of thromboxane A₂ biosynthesis in vitro by the main components of *crataegus oxyacantha* (Hawthorn) flower heads. *PLEFA* 1994; 50: 173-5.
12. Fan C, Yan J, Qian Y, Wo X, Gao L. Regulation of lipoprotein lipase expression by effect of hawthorn flavonoids on peroxisome proliferator response element pathway. *J Pharmacol Sci.*2006;100: 51-8.
13. Akila M, Devaraj H. Synergistic effect of tincture of *Crataegus* and *Mangifera indica* L. extract on hyperlipidemic and antioxidant status in atherogenic rats 2008;49:173-7
14. Weihe WH. The laboratory rat. London: CV Mosby 1983; 309-29.

15. Mahley RW, Holcombe KS. Alteration of plasma lipoproteins and apolipoproteins, following cholesterol feeding in the rat. *J Lipid Res* 1977; 18L: 313-24.
 16. Flegal KM, Carroll MD, Kuczmarski RJ, Johnson CL. Overweight and obesity in the United States: prevalence and trends, 1960-1994. *Int J Obes* 1998;22:39-47.
 17. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. *JAMA* 2002;288:1723-7
 18. Drenick EJ, Bale GS, Seltzer F, Johnson DG. Excessive mortality and causes of death in morbidly obese men. *JAMA* 1980;243:443-5
 19. Foster S. Hawthorn, *crataegus*. Steven Foster group. Boston: Houghton Wifflin Co, 2000.
 20. Dickinson TA. Hawthorn University of Maryland Medical Center. www.umm.edu/altmed/consherbs/hawthornch.html June 15, 2005.
 21. Rakotoarison DA, Greissier B. Antioxidant activities of phenolic extracts from flowers, *in vitro* callus and cell suspension cultures of *crataegus monogyna*. *Pharmazie* 1997; 52: 60-64.
 22. Kausar S, Zaheer Z, Saqib M, Zia B. The Effect of *Crataegus* (Hawthorn) extract alone and in combination with simvastatin on serum lipid profile in hyperlipidemic albino rats. *Biomedica*. 2011;27:140-7.
 23. Kuo DH, Yeh CH, Shieh PC, Cheng KC, Chen FA, Cheng JT. Effect of Shanza, a Chinese herbal product, on obesity and dislipidemia in hamsters receiving high fat diet. *J Ethnopharmacol*, 2009;124 (3):544-50.
 24. Tao W, Yating A, Chunfeng Z. Regulation effects of *crataegus pinnatifida* leaf on glucose and lipids metabolism. *J.Agric. Food Chem* 2011;59(9):4987-94.
-