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EFFECT OF BULGARIAN HERB EXTRACTS OF POLYPHENOLS ON METABOLIC DISORDERS - INDUCED BY HIGH-FRUCTOSE DIET

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ABSTRACT

Introduction Recently, fructose consumption has been suggested to be one of the environmental factors contributing to the development of insulin resistance, obesity, dislipidemia and other abnormalities of the metabolic syndrome. **Aim** Herbal extracts with established therapeutic efficiency in patients with obesity and diabetes have been traditionally used in Bulgarian ethnomedicine.This study investigated the protective effect of extract of selected Bulgarian herbs (high content of polyphenols- Herbal-Antiox 1) on high-fructose diet-induced metabolic disorders in rat liver. **Material and methods:** The animals were divided randomly into four groups (n=6); Control group rats- C; fructose-drinking rats- FRU (high-fructose corn syrup-12.5% fructose content); fructose- drinking rats treated with Herbal-Antiox-1 (HA-1**)-** FRU+HA1;control group rats treated with Herbal-Antiox-1 (HA-1**)-C+** HA1.Rats received 12.5% fructose solution in drinking water for 12 weeks, control rats were maintained on plain water. Phytochemical analysis and antioxidant capacity of the extract were determined. **Results:** We determine liver triglyceride (TG) concentration, body weight, liver weight, adipose tissue weight. In the FRU rat the levels of plasma glucose, liver TG as well liver and body weight were increased significantly. Herbal-Antiox-1 significantly reduced the hyperglicaemia, TG concentration and liver/body weight as well. In the control group Herbal-Antiox-1 had no effect on investigated parameters. **In conclusion** Herbal-Antiox -1 limits the accumulation of TG in liver, adipose tissue and contributes to reduction of body weight in rats .

Key words: Free-fructose diet, triglycerides, liver, body weight, Herbal-Antiox 1

INTRODUCTION

Recently, metabolic syndrome is occurring at epidemic rates with dramatic consequences for human health worldwide. This syndrome is a pathophysiological entity characterized by insulin resistance, hyperinsulinemia, hypertension, dyslipidemia and obesity (1). There is clinical and epidemiological evidence that suggests a progressive association between fructose consumption and metabolic syndrome (2, 3). A significant change in the western diet is he substantial increase in dietary fructose consumption, which due to a high fructose corn syrup, common sweetener used in the food industry (4).

Folk medical remedies in Bulgaria together with the traditional medicine are widely used in the traditional diet of the population in the form of teas, infusions and extracts (5). Herbal extracts with established therapeutic efficiency in patients with obesity and diabetes have been traditionally used in Bulgarian ethnomedicine.The herbal extracts a lot of Bulgarian plans are rich of polyphenols and exhibits antioxidant activity (6).

This study investigated the protective effect of extract of selected Bulgarian herbs (high content of polyphenols- Herbal-Antiox 1) on high-fructose diet-induced metabolic disorders in rat liver.

MATERIAL AND METHODS

The experimental procedures were approved by the Home Office for Care and Use of Laboratory Animals and performed with a strong consideration for ethics of animal experimentation according to the International Guiding Principles for Animal Research approved in Bulgaria. At the beginning of experiment the body weight of rat was 140-

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160g. Food intake was recorded daily and their weight was monitored weekly. Animals were housed in a 20±2 ^{o} C room with artificial light period. Experimental animals fed fructose-enriched diets are widely recognized as good models for metabolic syndrome (7). The animals were divided randomly into four groups (n=6); Control group rats-C; fructose-drinking rats-FRU (high-fructose corn syrup-12.5% fructose content); fructose-drinking rats treated with Herbal-Antiox 1 (HA1)-FRU+HA1;control group rats treated with Herbal-Antiox 1 (HA1)-C+ HA1. Phytochemical analysis and antioxidant capacity of the extract were determined. Rats received 12.5% fructose solution in drinking water for 12 weeks, control rats were maintained on plain water.At the end of the experiments, the rats were killing with lethal dose of thiopental. All manipulations were performed at 4-8^{o}C. Analysis was performed immediately after thawing of the samples.

Liver fat was extracted by method of *Folch et al*. and hepatic triglicerides were measured by commercial kits.

Statistical analysis

Data were analyzed statistically by one-way analysis of variance (ANOVA) and expressed as mean+SEM. A value of $p<0.05$ was considered statistically significant. Additionally the correlation analysis was used. The statistical procedure was performed with GraphPadInStat software.

RESULTS

Table 1 shows liver and body weight as well the levels of plasma glucose, liver TG in control and experimental groups. Significant elevation in plasma glucose levels is observed in fructose–fed rats as compared with control rats. In rats fed fructose and treated with HA-I, the levels were significantly lower as compared to untreated fructose-fed rats. The levels of TG in liver was higher in fructose-fed rats as compared to that in fructose–fed rats as compared to that in fructose-fed rat treated with HA-I than in rats treated with glucose only. In fructose–fed group the liver weight increased significantly as compared with control group **(Fig.1)**.

Table 1. *Effects of Herbal-Antiox 1 (HA1) fructose- induced metabolic disorders in rat.*

Groups	1.Control	2.Fructose (FRU)	3.Fructose+HA1 (FRU+HA1)	4.C+ HA1 (HA1)
Body weight (g)	226.3± 4.9	238.6± 7.8	240.1±8.6	214.6±14.7 [d]
Liver weight (g)	8.06±0.78	8.96±0.31 [a]	8.63±0.58	7.30±0.56
Liver triglyceride (mg/g)	11.8±1.2	15.7±0.98 [a]	11±1.83 [b]	10.4±1.01 [cc]
Adipose tissue weight (g)	1.67±0.27	2.92±0.80 [a]	1.87±0.25 [b]	1.7±0.56 [cc]
Plasma glucose (mmol/l)	5.75±0.85	8.13±0.33	7.61±0.46	6.75±0.52

Mean levels ± SEM; n= 6; C- control group rats *;* FRU-fructose-drinking rats; FRU+HA1- fructose- drinking rats treated with Herbal- Antiox 1 (HA1**) ;** C+HA1- control group rats treated with Herbal-Antiox 1 (HA1**).**

[a] P 1-2<0.05 ; [b] P 2-3<0,05 ; [cc] P 2-4<0.005 ; [d] P1-4<0.05

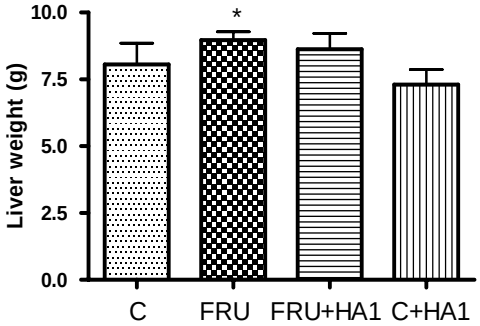

Figure 1. Effect of HFD and HA1 treatment on liver weight in rats.

Mean levels ± SEM; n= 6; C- control group rats *;* FRU-fructose-drinking rats; FRU+HA1- fructose- drinking rats treated with Herbal- Antiox 1 (HA1**) ;** C+HA1- control group rats treated with Herbal-Antiox 1 (HA1**).**

*P<0,05 significance between FRU and C+HA1.

A positive correlation between TG levels in liver and liver weight in the fructose fed rats (r =0,79, p<0.0005) **(Fig. 2)**, and TG levels and in treated with HAI fructose fed rats (r = 0,58, p<0.0005) **(Fig. 3)** was found. We failed to detect any significant correlation between these markers in the control animals **(Fig. 4)**.

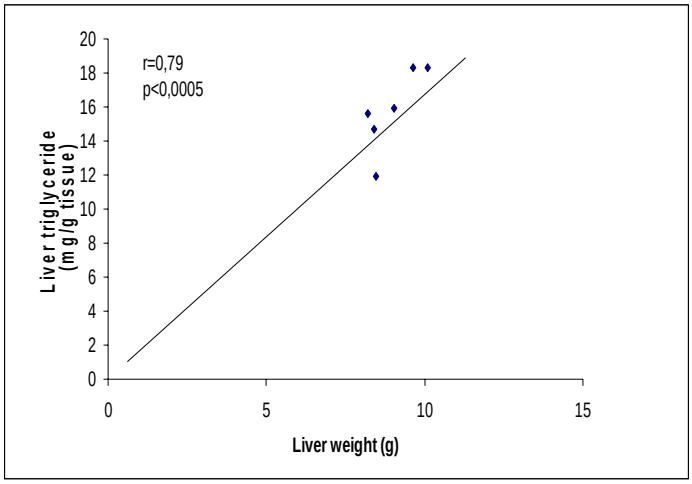

Figure 2.Correlation between liver triglyceride and liver weight in fructose-drinking rats (FRU) .

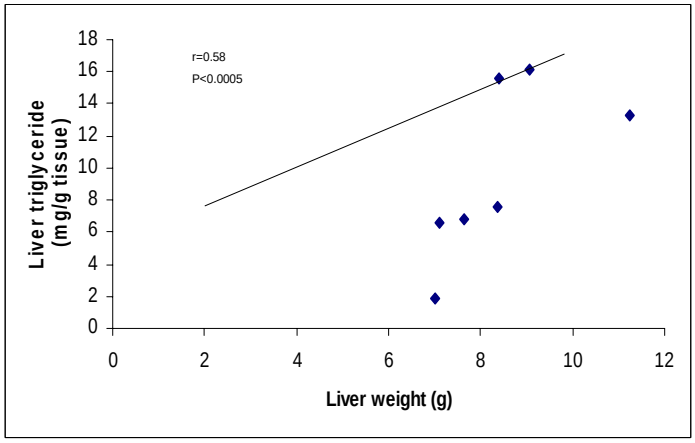

Figure 3. Correlation between liver triglyceride and liver weight in fructose- drinking rats treated with Herbal- Antiox 1 (FRU+HA1).

DISCUSSION

Increased consumption of fructose has been shown to induce obesity and contribute to metabolic abnormalities (1, 8) The results of the present study demonstrate that high-fructose diet causes an increase in body weight, fat mass, an accumulation of TG in liver and elevated levels of plasma glucose. Herbal-Antiox 1 restricts the accumulation of TG in the liver, and adipose tissue and reduces of body weight as well.

An overload of fructose to the liver perturbs the glucose metabolism and glucose uptake pathways leading to the enhanced rate of *de novo* lipogenesis and TG synthesis ultimately inducing insulin resistance (8). According to Lê and Tappy (2006) fructose is more lipogenetic than glucose and usually causes greater elevation of TAG content in the liver and insulin resistance. Increased plasma concentration of glucose in high-fructose feeding rats observed in this study may be attributed to elevated hepatic glucose production and decreased glucose disposal in

tissues. It has been shown that overproduction of free radicals and decreased antioxidant activity as a result of hyperglycaemia in fructose fed rats may suppress the activation of insulin receptors (7, 10).

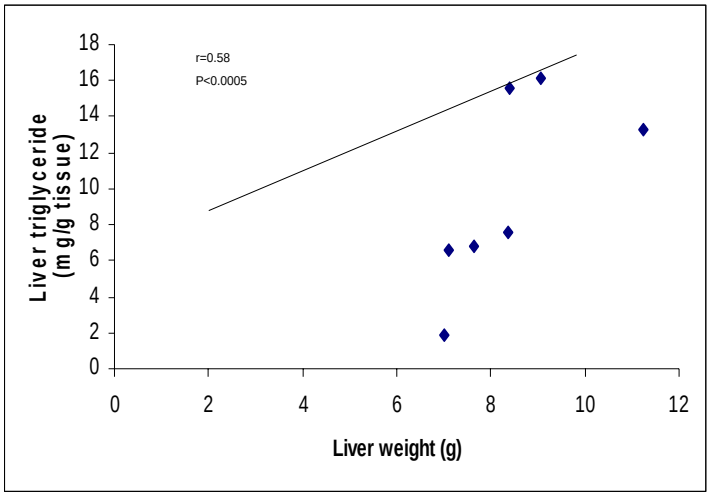

Figure 4. Correlation between liver triglyceride and liver weight in control group rats (C) .

Many plant polyphenols exert antioxidant effect and promote insulin action (11, 12). It has been reported that polyphenols from medical plants improve insulin action in fructose-enriched rats (13). Extracts of Bulgarian herbal are rich of polyphenols and exerts antioxidant effect also (6). It could be postulated that HA-I improves insulin action in the fructose-fed rats and may be this way contributes to decrease the levels of plasma glucose and TG in liver. A positive correlation ($r = 0,79$, $p<0,0005$) between TG accumulation in the liver/body weight ratio suggests that the increased liver weight in fructose fed rats is due to TG-accumulation and insulin resistance. There isn't any relationship between these parameters in the treated with HA-I control group.

It has been reported that TG-accumulation and lipid infiltration in the liver lead to development of steatosis, fibrosis in the liver and an increase of liver weight in fructose-fat rat (14). Further our studies would be directed to determine the relationship between fructose-induced lipogenesis, metabolic dislipidemia and insulin resistance.

In conclusion, our results show that high-fructose diet causes an increase in the body and fat weight as well as the accumulation of the triglycerides in liver and hyperglycaemia in rats. Herbal-Antiox 1 reduces the accumulation of TG in liver, adipose tissue and contributes to reduction of body weight in rats.

REFERENCES

1. Elliott SS, Keim NL, Stern, JS, Teff, K, Havel PJ. Fructose, weight gain, and the insulin resistance syndrome. *Am J Clin Nutr*, 76:911-22, 2002.
2. Basciano H, Federico L, Adeli K. Fructose, insulin resistance and metabolic dyslipidemia. *Nutr Metab* (Lond), 2: 1-14, 2005.
3. Stanhope KL, Havel PJ. Fructose consumption: potential mechanisms for its effects to increase visceral adiposity and induce dyslipidemia and insulin resistance. *Curr Opin Lipidol*, 19 :16-24, 2008
4. Tappy L, Lê KA. Metabolic effect of fructose and the worldwide increase in obesity. *Physiol Rev*, 90:23-46, 2010.
5. Ivanova D, Gerova D, Chervenkov T, Yankova T. Polyphenols and antioxidant capacity of Bulgarian medicinal plants. *J Ethnopharmacol*, 96: 145-150, 2005.
6. Kiselova Y, Ivanova D, Chervenkov T, Gerova D, Galunska B, Yankova T.Correlation between the in vitro antioxidant activity and polyphenol content of aqueous extracts from Bulgarian herbs. *Phytother Res*, 20:961-5, 2006.

7. Thirunavukkarasu V, Anitha Nandhini AT, Anuradha CV. Effect of alpha-lipoic acid on lipid profile in rats fed a high-fructose diet. *Exp Diabesity Res*, 5:195-200, 2004.
8. Rutledge AC, Adeli K. Fructose and the metabolic syndrome: pathophysiology and molecular mechanisms.*Nutr Rev*,65 : S13-23, 2007
9. Lê KA, Tappy L. Metabolic effects of fructose.*Curr Opin Clin Nutr Metab Care*, 9:469-75, 2006.
10. Busserolles J, Mazur A, Gueux E, Rock E, Rayssiguier Y. Metabolic syndrome in the rat: females are protected against the pro-oxidant effect of a high sucrose diet. *Exp Biol Med* (Maywood), 227 :837-842, 2002.
11. Yokozawa T, Kim HJ, Yamabe N, Okamoto T, Cho EJ. The protective role of Kangen-karyu against fructose-induced metabolic syndrome in a rat model. *J Pharm Pharmacol*, 59 :1271-8, 2007
12. Hininger-Favier I, Benaraba R, Coves S, Anderson RA, Roussel AM. Green tee extract decreases oxidative stress and improves insulin sensitivity in an animal model of insulin resistance, the fructose-fed rat. *J Am Coll Nutr*,28:355-61, 2009.
13. Kannappan C, Anuradha C.V. Insulin sensitizing actions of fenugreek seed polyphenols, quercetin & metformin in a rat model *Indian J Med Res*, 129: 401-40, 2009
14. Poudyal H, Campbell F, Brown L. Olive leaf extract attenuates cardiac, hepatic, and metabolic changes in high carbohydrate-, high fat-fed rats. *J Nur*, 140:946-53, 2010.