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

K. Bratoeva¹*, G. Bekyarova¹, Y. Kiselova², D. Ivanova²

¹Department of Pathophysiology, ²Department of Biochemistry, Molecular Medicine and Nutrigenomica, Varna University of Medicine, Varna, Bulgaria

ABSTRACT
Introduction
Recently, fructose consumption has been suggested to be one of the environmental factors contributing to the development of insulin resistance, obesity, dyslipidemia 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 hyperglycaemia, 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-
Food intake was recorded daily and their weight was monitored weekly. Animals were housed in a 20±2 °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°C. Analysis was performed immediately after thawing of the samples.

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

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

<table>
<thead>
<tr>
<th>Groups</th>
<th>1. Control</th>
<th>2. Fructose (FRU)</th>
<th>3. Fructose+HA1 (FRU+HA1)</th>
<th>4. C+ HA1 (HA1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (g)</td>
<td>226.3±4.9</td>
<td>238.6±7.8</td>
<td>240.1±8.6</td>
<td>214.6±14.7</td>
</tr>
<tr>
<td>Liver weight (g)</td>
<td>8.06±0.78</td>
<td>8.96±0.31</td>
<td>8.63±0.58</td>
<td>7.30±0.56</td>
</tr>
<tr>
<td>Liver triglyceride (mg/g)</td>
<td>11.8±1.2</td>
<td>15.7±0.98</td>
<td>11±1.85</td>
<td>10.4±1.01</td>
</tr>
<tr>
<td>Adipose tissue weight (g)</td>
<td>1.67±0.27</td>
<td>2.92±0.80</td>
<td>1.87±0.25</td>
<td>1.7±0.56</td>
</tr>
<tr>
<td>Plasma glucose (mmol/l)</td>
<td>5.75±0.85</td>
<td>8.13±0.33</td>
<td>7.61±0.46</td>
<td>6.75±0.52</td>
</tr>
</tbody>
</table>

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 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 HA1 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 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).

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


