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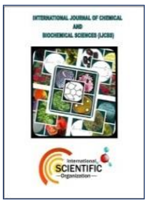

Thyme honey supplementation effects on weight status and biochemical blood parameters in High Fructose treated rats during prepuberty and adolescence

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Abstract

Thyme honey is known for its anti-inflammatory, analgesic and antibacterial capacity as well as its ability to promote wound healing. This study aims to evaluate the effect of honey supplementation weight status and biochemical blood parameters in High Fructose treated Wistar rats during prepuberty and adolescence. For this reason, we adopted experimental research carried out on 24 rats divided into 3 groups of 8 rats for each, control group (C): receiving normal diet, group 2: fructose (F), treated with fructose 23% /day for 6 weeks and group 3: Fructose + honey (FH), treating in 6 weeks fructose feeding combined to 2 weeks of thyme honey supplementation (5g/Kg/day). Administration by gavage of honey solutions significantly reduced the weight and biochemical parameters compared to the negative control, as well as the healing of ulcerative lesions. This may be due to a reduction in the production of factors of attacks and/or an increase in the synthesis of protective factors. Fructose diet alters body and organs weight, Honey supplementation decreased body weight. A fructose rich diet impairs biochemical parameters and increase the body weight leading to an obesity in rats. Honey administration regulated biochemical parameters mainly glucose and HDL.

Keywords: honey, fructose, blood sugar, cholesterol, prepuberty, adolescence.

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1. Introduction

Obesity is the consequence of a chronic imbalance between anabolism and catabolism of carbohydrates and lipids, due to a high intake of nutrients with high caloric content and a reduction in energy expenditure, it results by excessive storage of body fat in white adipose tissue [1-4]. Obesity becomes deleterious for metabolic health when this excessive storage leads to an expansion of visceral adipose tissue and the accumulation of lipids in non-adipose tissues such as the muscles, the liver, and the pancreas [5–7]. In addition, tissues affected by ectopic lipid accumulation potentially undergo major damage that defines insulin resistance, type 2 diabetes and impaired muscle function. Obesity is often associated with dyslipidemia combining an increase in triglycerides, sometimes LDL cholesterol, as well as a decrease in HDL cholesterol [6].

The management of dyslipidemia linked to obesity is close to the situation with normal weight; it mainly includes nutritional advice and physical activity, while medication is less often necessary.

Metabolic syndrome is a set of cardiometabolic risk factors associating abdominal obesity, glucose intolerance, even type 2 diabetes, hypertension, hypertriglyceridemia and reduction in HDL cholesterol. Patients with metabolic syndrome often have other lipid disturbances, namely an excess of very low density lipoprotein (VLDL), intermediate density lipoprotein (IDL) and low density lipoprotein (LDL), commonly grouped under the name of lipid-related dyslipidemia obesity.

This dyslipidemia is found in 30-60% of cases of overweight or obesity according to studies, partly explaining the increased risk of cardio-metabolic complications in obesity, combined with the low-level inflammatory state and insulin resistance [8,9].

However, other obese patients do not develop dyslipidemia: a situation nicknamed the “obesity paradox”.1 For some, this is consistent with the concept of metabolically healthy obesity. This subject remains debated, however, because certain studies show that this entity differs from normal weight by metabolic parameters bordering on the norm, which will later evolve into cardiometabolic complications.

Modern medicine is experiencing progress in the treatment of obesity with synthetic hypoglycemic drugs. However, these chemicals have several limitations and side effects, leading to the search for new drugs [10,11].

Traditional medicine based on herbal medicine to prevent or treat diabetes has been used for millennia by various populations and civilizations. Apitherapy is another approach which is widely practiced using bee products: honey, royal jelly, pollen, propolis to treat several pathologies such as diabetes and obesity.

Plant secondary metabolites, especially polyphenols like natural phenols, are believed to contribute significantly to the therapeutic effects of medicinal plants. They play a crucial role in safeguarding against various disorders such as urolithiasis, atherosclerosis, brain dysfunction, and obesity [12–19].

Honey therapy has a very long history, ancient Egyptian texts and even Chinese texts mentioned the medicinal properties of honey (treats wounds, digestive tract and kidney conditions, healing) [20].

Honey is defined as “A natural sweet substance produced by bees from plant nectar or secretions from living parts of plants or excretions left on them by sucking insects, which they forage, transform by combining them with specific clean materials, deposit, dehydrate, stored and left to ripen in the combs of the hive” [21].

Studies are aimed at researching the hypoglycemic activities of medicinal plants as well as bee products used traditionally. This work is established to discover new natural remedies that are more effective, less toxic and with fewer side effects. However, this area remains very little exploited in Morocco. In this context, our work consists of evaluating the effect of honey on a weight status and some biological parameters including glucose, lipids and liver enzymes in high fructose treated rats during prepuberty and adolescence.

2. Materials and methods

2.1 Honey

In current study, the used thyme honey was produced in Drâa Tafilalet area (near Assoul) province of Tinghir in Morocco, known for its therapeutic virtues and its physicochemical properties (figure1) [22].

2.2 Animals

The experiments carried out in this work were carried out on male Wistar strain laboratory rats, born and raised in the animal facility of the Department of Biology, Faculty of Sciences, Ibn Tofail University, Kenitra (Morocco). Three groups of male Wistar rats weighing between 350 and 375 grams (g) were used for this study. The animals were separated randomly into one of three pre-established groups and put on a diet upon their arrival. All animals had free access to water and food, subject to a photoperiod of12/12 (12 light/12 dark) and an ambient temperature of 22°C.They were regularly monitored by an increase in body weight during their breeding. The cages were regularly cleaned. The animals were distributed into 3 groups of eight rats each:

- Group 1: control group (C): consisting of 8 rats received normal diet.
- Group 2: fructose (F): made up of 8 rats treated with fructose 23% of fructose/day for 6 weeks during prepuberty and adolescence.
- Group 3: Fructose + honey (FH): includes 8 rats treating in 6 weeks fructose feeding combined to 2 weeks of thyme honey supplementation (5g/Kg/day).

2.3 Biochemical parameters

After completion of the experiment, the rats were kept fasting for 18 hours, then they are sacrificed. The blood taken from the portal vein of each rat was placed in heparin tubes, centrifugation was carried out to recover the plasma necessary for carry out the requested biochemical analyses. These analyzes allowed us to obtain the values of serum glucose, total cholesterol, triglycerides, low density lipids (LDL), high density lipids (HDL) and liver enzymes including alanine aminotransferase (ALAT) and aspartate aminotransferase (ASP).

2.4 Statistical analyses

Values were presented as mean ± standard error. As for the statistical tests, we first performed a one-way ANOVA analysis which made it possible to evaluate the effect of the diet and that of honey supplementation separately. When there was a significant interaction ($p<0.05$) we carried out an additional statistical test, Tukey Post-Hoc Test. This method allows you to observe significant differences between different pairs of data. Statistical analyzes were performed by using GraphPad Prism 7 software.

3. Results and Discussions

Compared to the controls, the liver weights of the test batches are lower, gradually increasing with the dose of the extract. Unlike the lungs, the weights of the test batches are higher and decrease with the dose of the extract (Figure 2).

Effects of the extract on the weight mass in rats during prepuberty and adolescence: The evolution of the mass of rats during prepuberty and adolescence shows that the weight of the animals generally increased over time and whatever the batch (Figure 3). Furthermore, this increase was significantly greater in animals to which the extract at dose 400 was administered as observed in males.

The effects of the extract on the biochemical parameters of the males showed no statistically significant value between the group taking distilled water and those treated with different doses of the extract for urea, ALT and AST (Table 1).

Figure 1: Thyme honey harvested on 2020.

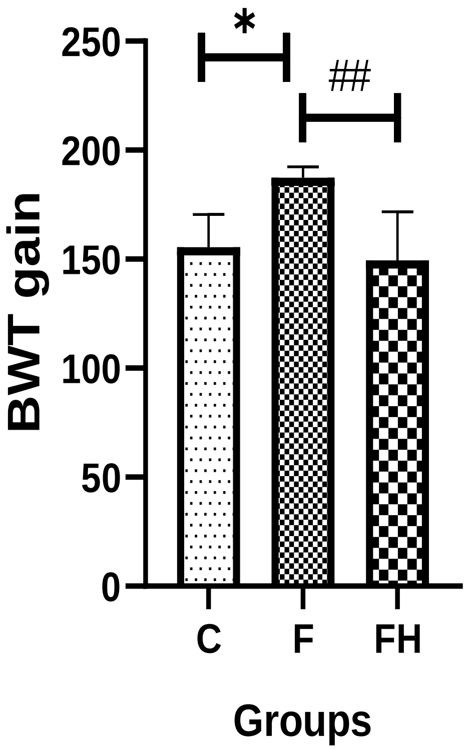

Figure 2. Effects of 6 weeks fructose feeding combined or not to 2 weeks orally administration of thyme honey on Body weight gain (BWT).
* p < .05, ** p < .01, *** p < .001. Values are mean ± SEM of seven rats per group (Control (C), Fructose (F) and fructose + honey (FH)). *P<0.05 vs C, # # P < 0.01 vs F.

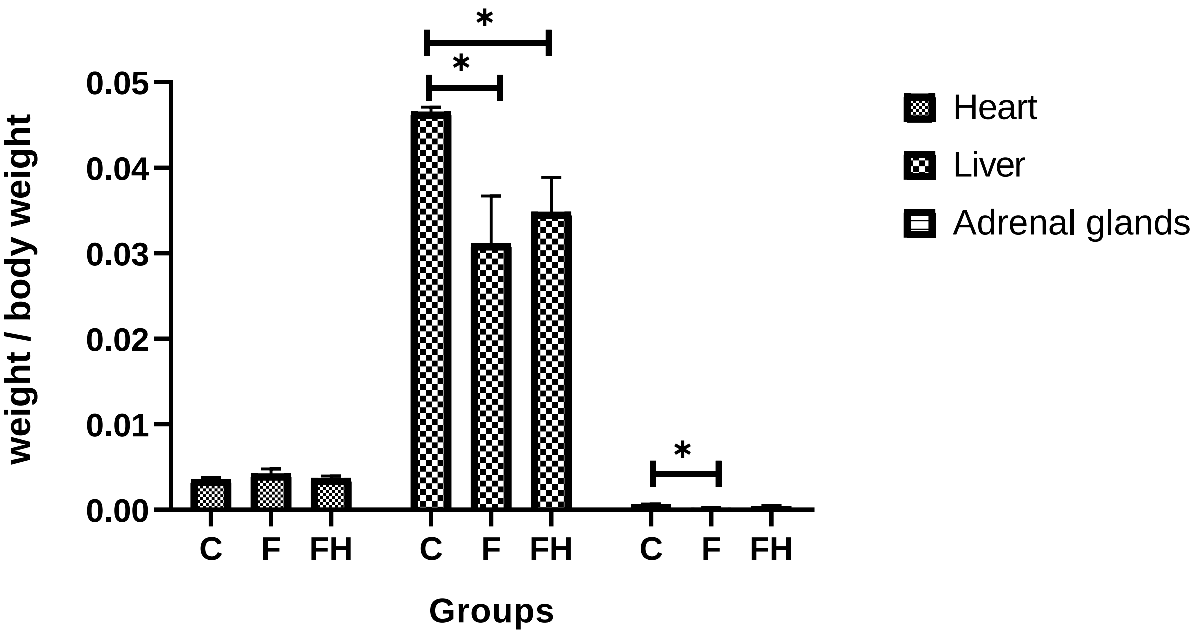

Figure 3. Effects of 6 weeks fructose feeding combined or not to 2 weeks orally administration of thyme honey on heart, liver and adrenal glands weight gain.
* p < .05, ** p < .01, *** p < .001. The results are expressed as Means ± SEM. * p <0 .05 vs C.

Table 1: Effects of 6 weeks fructose feeding combined or not to 2 weeks orally administration of thyme honey on Biochemical parameters.

Parameters mg/dl	Control	Fructose	Fructose + Honey
Glucose	65.43± 25.31	454.7± 19.63***	267± 38.12**##
Total cholesterol	785.5± 28.35	1044 ± 311.4	697.3 ± 59.38
Triglyceride	299.2± 77.52	242.4 ± 90.24	543.8 ± 17.51*##
LDL	549.8 ± 9.234	1232 ± 239.8*	546.5± 44.46#
HDL	182.6 ± 32.63	73.91 ± 8.976**	77.99 ± 8.075**
ALAT U/l	51.76 ± 25.78	18.04 ± 13.78	23.93 ± 7.275
ASP U/l	3.929 ± 0.4365	9.894 ± 5.532	5.529 ± 1.455

*P<0.05 vs C, **P<0.01 vs C, # P<0.05 vs F, ## P<0.01 vs F.

The objective of current study was to assess the effect of honey supplementation on weight status, blood sugar and biochemical parameters in high fructose treated rats during prepuberty and adolescence.

Fructose diet alters body and organs weight, the results represented in figure confirm the gain weight effect of fructose diet in rats.

According to ours results, fructose feeding impairs biochemical parameters, a significant increase in glucose and in LDL. However, honey supplementation decreased body weight and the biochemical parameters.

Honey is beneficial for diabetics for two reasons, one is that it is three times sweeter and contains fewer calories than sugar, and the other is that it provides vitamins: A, B, C, D, and mineral salts: calcium, potassium, phosphorus, iron, and magnesium. Honey contains at least 181 substances; hence the exact mechanism of its effect antidiabetic medication is complicated which requires in-depth studies.

Research has shown that the fructose included in honey can modulate the hypoglycemic or antidiabetic effect of this product.

Studies have shown that indigestible dietary oligosaccharides like fructo-oligosaccharides, galacto-oligosaccharides and lactulose have a preventive effect against obesity, insulin resistance, and diabetes mellitus by acting as prebiotics on the intestinal flora. The oligosaccharides contained in honey may contribute to its prebiotic effect, which may be linked to the antidiabetic, antihyperlipidemic, and hepatoprotective effect [23,24].

Minimal amounts of fructose reduced blood glucose by increasing hepatic glucose through the activation of glucokinase. The beneficial effect of this molecule on glycemic control has been proven in patients with type 2 diabetes [25].

Other studies have shown on the one hand that the antioxidant effect of honey and its free radical scavenging activity on the oxidation of LDL, and on the other hand the anti-lipid effect can delay or prevent the development of atherosclerosis. The beneficial effect of antioxidants included in honey to control blood sugar levels affects tissues or organs susceptible to oxidative stress caused by diabetes [26,27]. It results in a reduction in diabetic nephropathy, retinopathy, neuropathy, and cardiomyopathy [22,28].

This study allowed us to observe the effects of consuming a diet rich in fat on the weight status of rats as well as on lipids. We found also that honey administration helped decrease blood sugar, HDL, LDL and triglyceride levels. The same effect was demonstrated in other studies [29,30]. Thyme honey administration has a high significant effect in decreasing blood glucose ($p<0.01$)

We attempted to explain this increase in liver function by verifying the level of the main enzymes involved in several tissues (heart, liver, muscles), namely that ALAT and ASP. However, the results obtained were not sufficient to provide an explanation of the phenomenon. Furthermore, we did not observe no change in energy metabolism enzyme activity at this stage of the disease.

4. Conclusions

In summary, the findings of this study support the idea that a subchronic HFD is associated with body weight gain and increase in glucose, lipids and liver enzymes in adult Wistar rats. Moreover, our results suggest that thyme honey administration could serve as potential therapeutic agents for obesity induced by HFD. Further investigations are required to reveal the undergoing mechanisms in this therapeutic effect.

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