

Evaluation of the Liver Function and its Histological Alterations in Rats Treated with Herbalife® Green Tea

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Abstract: A large number of drugs, especially the phytotherapeutical ones may cause hepatic lesions either by intrinsic toxicity or idiosyncratic reactions. In the scientific literature, very little information can be found regarding hepatopathy cases caused by natural supplements which are freely sold without any control. In many countries, they are considered dietary or herbal supplements and they are not submitted to safety or efficacy studies before they are marketed. Herbalife® products are mainly used on weight loss programs. Since, herbal-based products are sold as natural products, people in general consider their consumption safe. A study performed in Switzerland found 13 cases of toxic hepatitis caused by Herbalife® supplement intake between the years, 1998 and 2004. There were enough data in 10 out of those 13 cases that safely fit the World Health Organization criteria for hepatotoxicity. The objective of this study is to verify the hepatic histological and functional alterations in rats treated with Herbalife® supplements. The 14 male adult rats were kept with water and food *ad libitum*. The 7 animals (Control) received 0.5 mL day⁻¹ of saline solution and the other 7 were gavage fed with 100 mg/kg/day of Herbalife green tea for 2 months. After this period of time, a laboratorial analysis of a blood sample was performed as well as an anatomopathological analysis of the liver. The statistical analysis through the t-test was considered significant when p<0.05. Both groups gained considerable weight and there was no difference in relation to this gain. There were no significant alterations in the hepatic enzymes (AST, ALT, GammaGT, alkaline phosphatase, protein electrophoresis) in either group. Two animals in the control group and three animals in the Herbalife group presented subtle hepatic cell balonization in zone 3. There were no macroscopic alterations. Researchers did not observe any functional or pathological alterations in rats treated with Herbalife® green tea.

Key words: Herbalife, natural supplements, hepatic alteration, green tea, saline solution, Brazil

INTRODUCTION

In Brazil and all over the world, Herbalife® products are very much consumed by people who search for a kind of alternative medicine which offers prophylactic options and well-being to its consumers (Stickel, 2007; Schoepfer *et al.*, 2007). A great number of people see herbal products as a natural alternative and thus their intake is considered safe (Stickel, 2007; Schoepfer *et al.*, 2007; Elinav *et al.*, 2007). Most consumers do not seek medical advice before they start using these substances (Stickel, 2007). In many countries

such products are seen as dietary or herbal supplements and they are not submitted to safety or efficacy studies before they are marketed. Moreover, producers do not supply consumers with enough data on the substance efficacy and safety; these products are made from especially selected herbs and plants, enriched with nutrients, oligoelements, vitamins and minerals (Stickel, 2007; Schoepfer *et al.*, 2007).

The composition of most products is variable and ill-defined and their benefits are not completely elucidated for consumers (Stickel, 2007). Although, some hepatic lesion cases have been reported due to the intake of

Herbalife® products, the scientific literature on the hepatopathy occurrences due to the intake of freely-marketed, non-controlled natural supplements is small. Their effects on human health, especially on the liver, need to be better researched. This study aims to verify and discuss the effects of Herbalife® green tea on the hepatic histological and functional alterations in rats treated with this supplement.

MATERIALS AND METHODS

A 14 male adult rats, supplied by Faculdade de Medicina do ABC (ABC Medical School) lab animal facility were used. They were kept with water and food *ad libitum*. The animals were randomly divided into two groups:

Control group: Composed of seven animals, gavage fed with 0.5 mL of saline solution daily.

Experimental group: Composed of seven animals, gavage fed with 100 mg kg⁻¹ of Herbalife green tea daily.

The animals were under the treatment for 2 months. On the 60th day, the rats were anesthetized with ketamine (50 mg kg⁻¹) and xylazine (10 mg kg⁻¹) for blood sample collection, extracted from the aorta artery. The collected blood was used for hepatic enzyme (ALT, AST, GammaGT, alkaline phosphatase) determination for protein electrophoresis and for lipid profile evaluation (Triglycerides, total cholesterol and fractions). Next, the abdominal cavity of each rat was opened and the liver removed.

The livers were placed in a formol solution to 10% for the anatomopathological analysis. After the procedure was accomplished, the animals were euthanized in CO₂ chambers. The statistical analysis, performed through the t-test was considered significant when p<0.05. The research protocol was approved by the Committee of Ethics in Animal Experimentation of FMABC (Protocol number 14/2007).

RESULTS AND DISCUSSION

Laboratorial: In Table 1, researchers can observe that both control and Herbalife groups gained substantial weight and there was no difference in relation to this gain. When the hepatic enzymes, the lipid profiles and the protein electrophoresis were comparatively analyzed, no statistically significant differences between the groups could be observed.

Anatomopathological: In the microscopic analysis, two animals from the control group and three others from

Table 1: Comparison of lipid, hepatic profiles in control and Herbalife® groups

Variables	Control group	Herbalife group	p-values
Initial weight	322.6±5.10	320.3±12.7	0.6700
Final weight	418.0±22.2	404.0±23.8	p<0.0001 0.2700
AST	79.0±3.40	73.7±16.8	p<0.0001 0.6100
ALT	50.4±1.60	50.3±2.30	0.9600
GammaGT	3.3±1.50	2.8±1.10	0.5300
Alkaline phosphatase	207.1±51.5	187.7±44.4	0.4600
Total cholesterol	55.6±11.1	55.7±11.9	0.9800
HDL-C	20.9±4.80	20.3±3.90	0.8200
LDL-C	19.4±9.80	24.6±11.6	0.3900
Triglycerides	76.4±26.8	54.0±24.1	0.1300
Total proteins	6.9±0.40	6.5±0.40	0.0800
Albumin	3.1±0.30	3.1±0.20	0.8500
Alpha-1	1.5±0.20	1.3±0.20	0.0600
Alpha-2	0.5±0.10	0.5±0.10	0.9400
Beta	1.1±0.30	1.0±0.10	0.4400
Gamma	0.7±0.30	0.5±0.10	0.2500

the Herbalife group presented subtle hepatic cell balonization in zone 3. As for the macroscopic liver analysis neither group presented significant alterations. Being the liver responsible for the general metabolic modulation, it exerts uncountable functions in the body. A large number of industrial substances, xenobiotic agents and medicines, especially phytotherapeutical ones may cause hepatic lesions. Most hepatic lesions cause transitory increase in hepatic enzymes and these higher levels may go back to normal once the drug intake ceases. However, the liver reactions to the aggression are varied and they may practically simulate all sorts of hepatic diseases. Cases related to hepatic lesions caused by different Herbalife® products intake in Israel and Switzerland have been reported in two different researches. Among the 22 hepatic lesion cases, 2 patients developed fulminant hepatic failure (Stickel, 2007). A study performed in Switzerland found 13 cases of toxic hepatitis caused by the intake of Herbalife® supplements. Total 10 out of those 13 cases may safely fit the World Health Organization criteria for hepatotoxicity. All of the patients used such supplements for weight loss sake and consumed them in the dosages recommended by the manufacturer.

According to this study, the first symptoms (fatigue and loss of appetite) occurred at a median of 5 months. None of the patients had presented allergy symptoms or any other extra-hepatic disorders (Schoepfer *et al.*, 2007). Liver biopsies revealed hepatic necrosis, lymphocytic and eosinophilic infiltration in the liver, cholestasis, signs of hepatitis and sinusoidal obstruction. Laboratorial exams clearly showed the destruction of hepatocytes indicated by elevated hepatic enzymes (Schoepfer *et al.*, 2007; Shouval and Elinav, 2008). The 12 other similar cases were described in Israel (Schoepfer *et al.*, 2007). This research, however did not reveal any hepatotoxicity case. The occurrence of toxic hepatitis due to the intake of one or more Herbalife® products has been reported. The present

study focused on the use of one isolated product, the green tea but the intent is to proceed analyzing the effects of other products of the same line as well as the combination of such products, once hepatotoxicity may be caused by the concomitant use of those substances. One alternative explanation may be that most Herbalife® products are safe but some of them may lead to hepatotoxicity. Another explanation may be that the company manufactures its products with small variations in each country and thus the hepatotoxicity level also changes (Schoepfer *et al.*, 2007).

CONCLUSION

Finally in this study, researchers did not observe any relevant hepatic alteration in rats treated with Herbalife® green tea.

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