

# Triple Antioxidant Therapy, an Alternative for Patients with Chronic Liver Disease – A Prospective Multicenter Interventional Study

Eugen DUMITRU<sup>a, b</sup>, Laura CONDUR<sup>a, c</sup>, Luana ALEXANDRESCU<sup>a, b</sup>, Sergiu CHIRILA<sup>a</sup>,  
Madalina GREERE<sup>d</sup>, Cristina RADU<sup>d</sup>, Daniela TABACELIA<sup>d</sup>, Cristian ROSIANU<sup>d</sup>,  
Ahmed MOHSSEN<sup>d</sup>, Agnes BALINT<sup>e, f</sup>, Elena TOADER<sup>g, h</sup>, Virgil POPESCU<sup>i</sup>, Brindusa PANAI

<sup>a</sup>Faculty of Medicine, “Ovidius” University of Constanta, Romania

<sup>b</sup>Gastroenterology Department, Clinical County Hospital Constanta, Romania

<sup>c</sup>Medsim Medical Center, Mangalia, Romania

<sup>d</sup>Gastroenterology Department, “St. Mary” Hospital, Bucuresti, Romania

<sup>e</sup>“George Emil Palade” University of Medicine and Pharmacy, Targu Mures, Romania

<sup>f</sup>“Harmomed” Medical Center, Targu Mures, Romania

<sup>g</sup>“Grigore T. Popa” University of Medicine and Pharmacy, Iasi, Romania

<sup>h</sup>Gastroenterology Department, “St. Spiridon” Emergency County Hospital, Iasi, Romania

<sup>i</sup>“Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

<sup>j</sup>“Prof. Dr. C. C. Iliescu” Emergency Institute for Cardiovascular Diseases, Bucharest, Romania

## ABSTRACT

**Background:** Non-alcoholic fatty liver disease (NAFLD) has increased exponentially in recent years in Western European countries, where the number of hepatitis of viral etiology has been declining, and it is thought to be the most common cause of chronic liver disease in the near future (1). Currently, NAFLD is both the second most common cause of hepatocellular carcinoma (HCC) and the second most common indication for liver transplantation (2-4). This problem is very serious, as cases of NAFLDs are increasingly in children, a population with a long life ahead, and in whom the disease has all the time to progress to cirrhosis and HCC (5, 6).

**Objectives:** The goal of this prospective study is to determine the effect of an original formula consisting in silymarin, organic selenium and alpha lipoic acid, in reducing liver damage in patients with chronic liver disease.

**Material and methods:** The study started in March 2018, initially with a group of patients from Bucharest, integrated in the study at St. Mary’s Hospital. In October 2018 it was expanded at the national level to

Address for correspondence:

Dr. Sergiu Chirila

Universitatii Aley nr.1, Campus B, Room E129, Constanta, Romania

Email: [sergiu.chirila@univ-ovidius.ro](mailto:sergiu.chirila@univ-ovidius.ro)

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1 718 patients, monitored by 145 investigating physicians from 134 centers, with an average of 11.8 patients per investigating physician.

**Outcomes:** Taking each stage of fatty liver disease (FLD) at T0 moment (the beginning of the study), we observed that 25% of patients with grade I FLD had no sign of disease at the end of the study, 74% of those with grade II FLD recovered or improved their health, and 83% of patients with grade III FLD recovered or improved their health. There were 149 patients with no FLD detected at the end of the study (recovered).

**Conclusions:** Based on triple antioxidant therapy, the original formula improved the evolution and prognosis of patients with chronic liver disease.

**Keywords:** fatty liver disease, silymarin, organic selenium, alpha lipoic acid, transaminases, triglycerides.

### INTRODUCTION

The frequency of FLD in the general population varies from 10% to 24%, reaching up to 75% in obese people. Incidence variation is due to socio-economic differences, level of education and lifestyle of the person or community to which he/she belongs. The incidence of this disease is increasing due to the modern diet based on sweets, fats, processed foods and alcohol consumption, neglecting fresh fruits and vegetables, but also due to sedentary lifestyle and lack of exercise (7).

The aim of the study was to evaluate the effect of the original formula consisting in silymarin, organic selenium and alpha lipoic acid, in reducing liver damage in patients with chronic liver disease, evaluated through the influence on:

- fatty liver disease grade reduction;
- normalization of alanine transaminase (ALT) and aspartate transaminase (AST) values;
- improvement of other lipid parameters (reduction of total cholesterol and LDL; increase of HDL), also in patients with hepatitis or cirrhosis. □

### MATERIAL AND METHODS

The study was conducted over a period of 27 months. It began in March 2018 and the latest data were collected in May 2020. Patients who completed the study took four capsules of an original formula consisting in silymarin, organic selenium and alpha lipoic acid on a daily basis for six months.

The population, aged between 20-90 years, was heterogeneous. Distribution by age groups is shown in Figure 1.

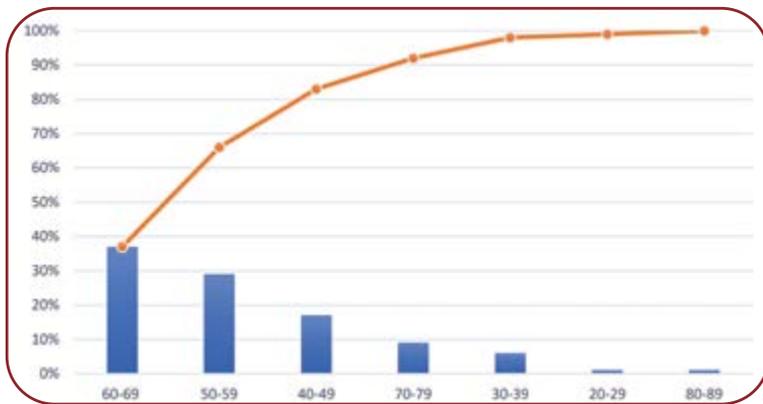


FIGURE 1. Distribution by age – Pareto chart

### Working hypothesis

A prospective multicenter interventional study, Triple Antioxidant Therapy, an Alternative for Patients with Chronic Liver Disease, was performed as an alternative therapy for patients with chronic liver diseases. This study provided information on decreasing FLD stages and transaminases levels, lipid parameters (reduction in total cholesterol, LDL and increased HDL) and blood glucose levels. It is important to mention that patients were not required to have a dedicated diet. Each patient was registered by a doctor (gastroenterologist, internal medicine physician or family doctor).

Laboratory tests that were part of the study were provided free of charge to participants and were performed at the start of treatment (T0), three months after the start of treatment (T3) and at the end of the follow-up period, at six months from the start of treatment (T6).

The following laboratory tests were performed in the three moments (T0, T3 and T6): transaminases (ALT, ALP), lipid profile (triglycerides, total cholesterol, LDL cholesterol,

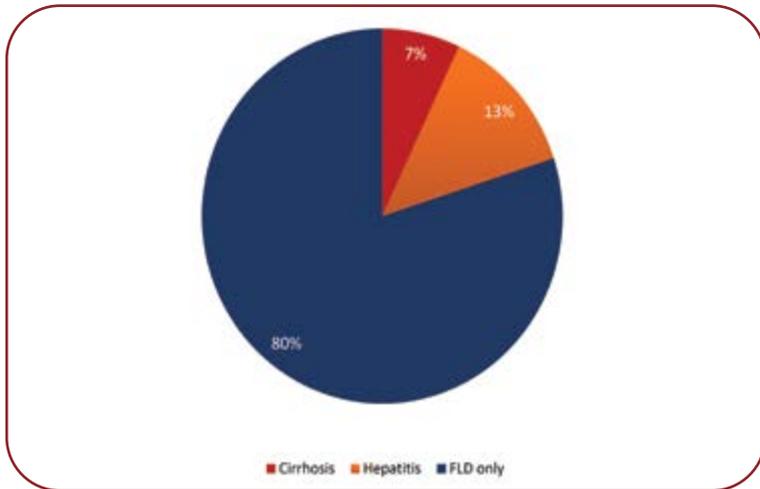


FIGURE 2. Associated liver conditions

HDL cholesterol), serum glucose, and abdominal ultrasound exam.

Patients were enrolled in the study based on inclusion/exclusion criteria:

- Inclusion criteria: patients with or without hepatic conditions (FLD, hepatitis, cirrhosis) associated with hyperlipidemia, hypertension or diabetes
  - Exclusion criteria: patients who participate in another clinical trial developed for a liver health product, or patients who are allergic to any of the ingredients of the original formula.
- There were patients of all FLD grades (I, II and III). There were also patients with several associated liver conditions: 13% had also hepatitis and 7% had also cirrhosis (Figure 2). □

OUTCOMES AND DISCUSSION

The results are based on data from the 1,718 participants. Out of these, 1 708 completed the study, with a drop-down rate of only 0.58%, which was caused by lack of treatment compliance (0.32%) and gastric events such as high acidity (0.26%).

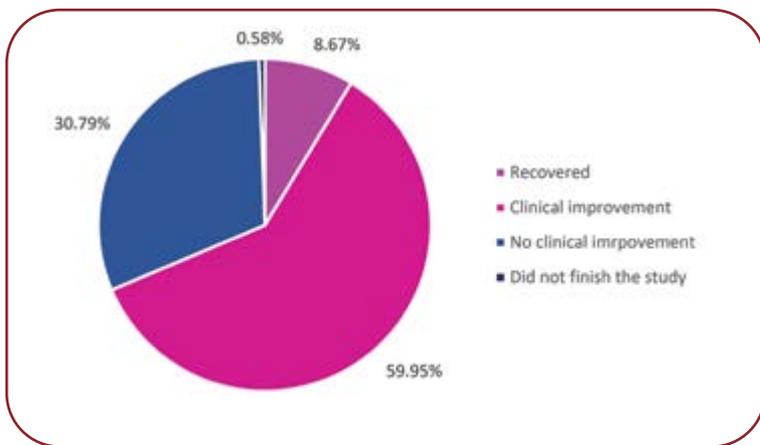


FIGURE 3. Evolution of fat liver disease

The evolution of the fatty liver disease stages

The main core of the treatment is regression of FLD. If at T0 most cases of fatty liver disease were grade II (60%), followed by grade III (24%) and grade I (16%), at T6 most cases were FLD grade I (61%), followed by grade II (26%) and grade III FLD decreasing to 4%.

The evolution of patients according to the study findings (recovered – patients who did not show any FLD sign at the final medical evaluation, regression of FLD etc.) is shown in Figure 3.

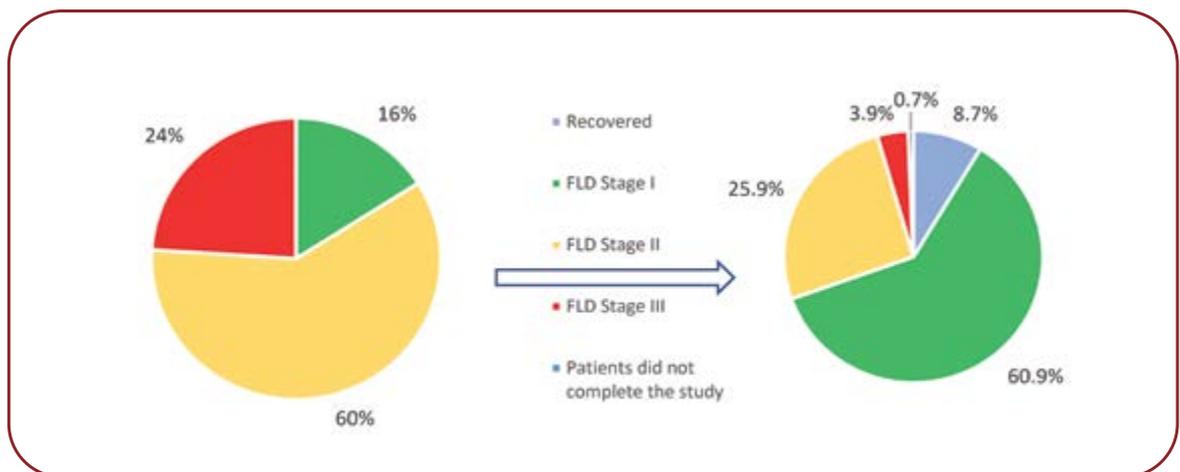


FIGURE 4. Evolution of FLD by grade T0 vs T6

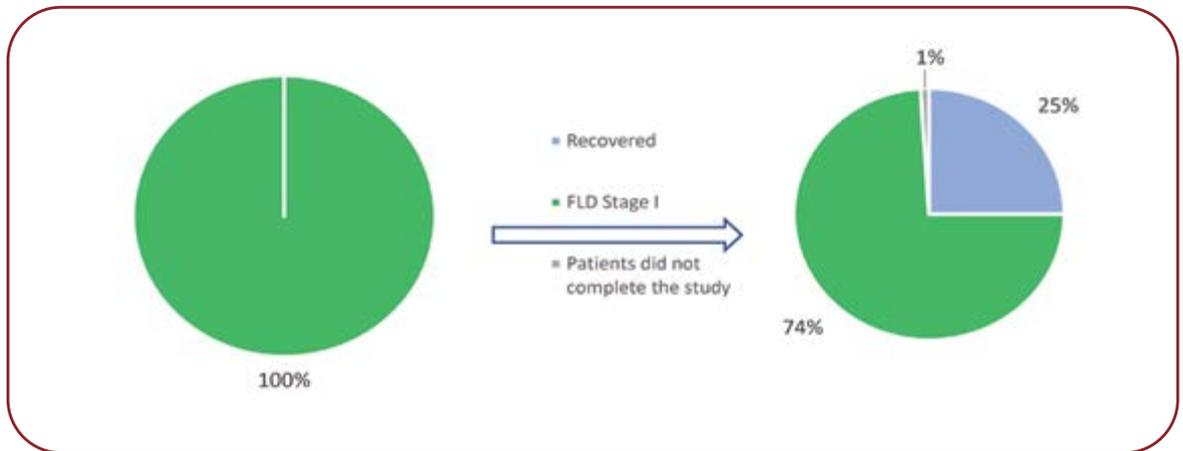


FIGURE 5. Evolution of FLD stage I at T0 vs T6

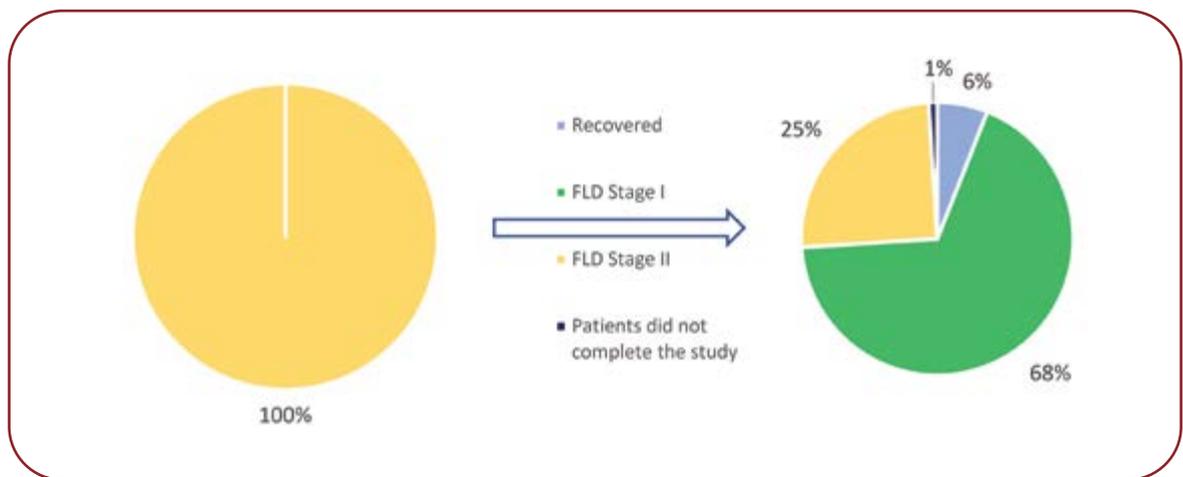


FIGURE 6. Evolution of FLD stage II at T0 vs T6

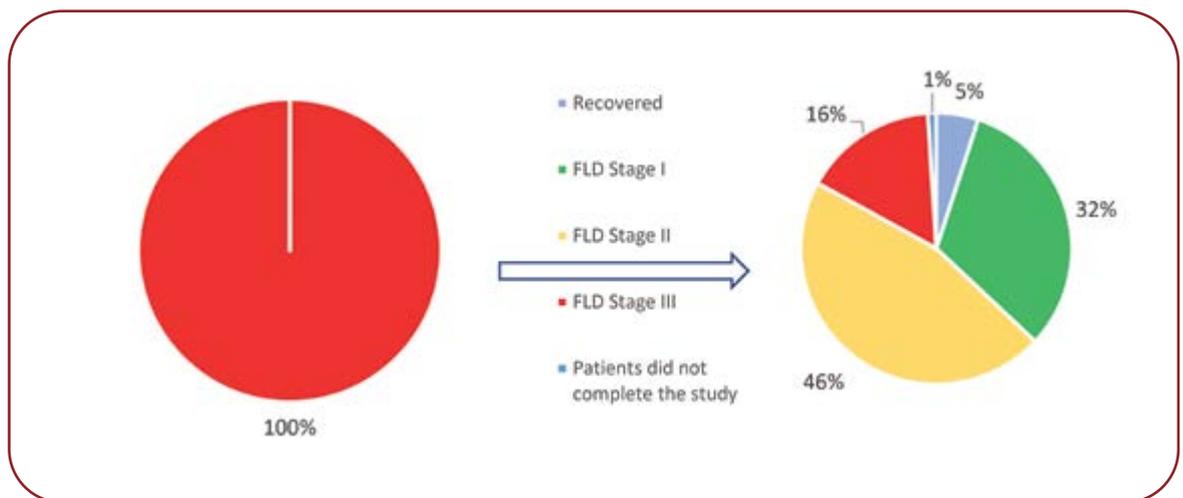


FIGURE 7. Evolution of FLD stage III at T0 vs T6

The evolution of the degree of hepatic steatosis was quantified with the help of abdominal ultrasound, which was performed at the beginning of the study and then at three and six months.

Taking each stage of FLD at T0, we can see that 25% of patients with FLD grade I were recovered, 74% of those with FLD grade II were recovered or had clinical improvement, and

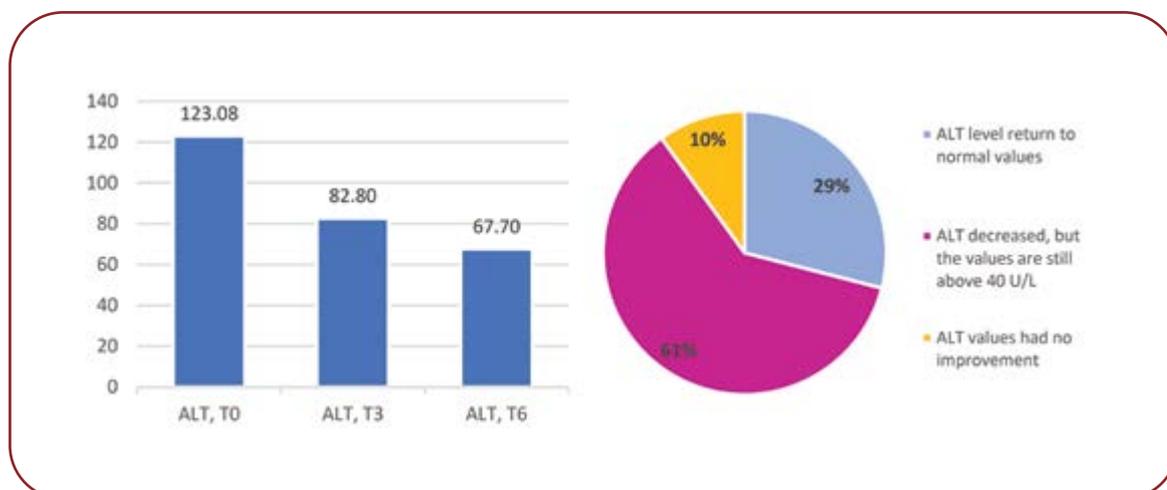


FIGURE 8. Patients with ALT above 80 U/L at T0, T3 and T6. ALT percentage evolution

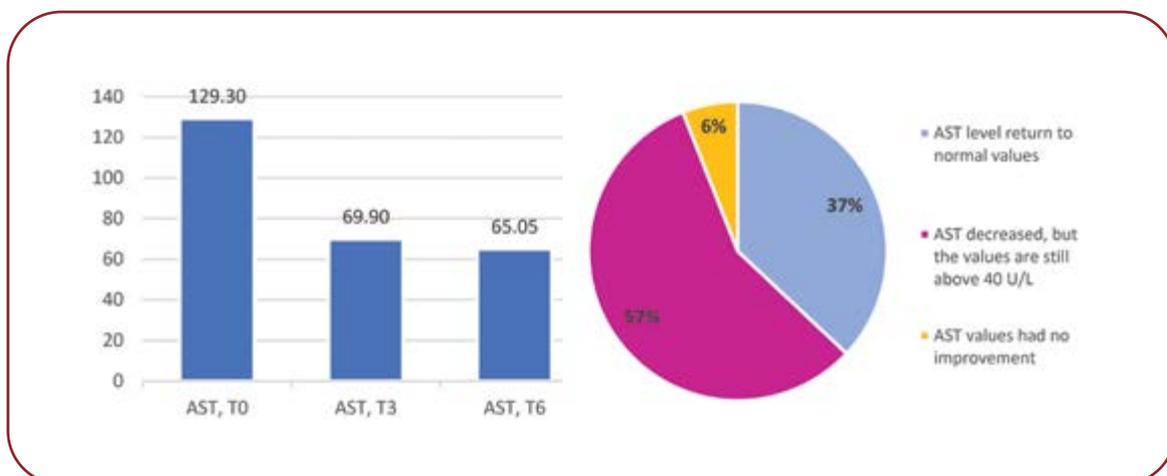


FIGURE 9. Patients with AST levels above 80 U/L at T0, T3 and T6. AST percentage evolution

83% of patients with FLD grade III recovered or had clinical improvement. There were 149 patients with no FLD detected at the end of the study.

### Evolution of ALT level

Two hundred and seventeen patients had high ALT levels (above 80 U/L), with an average ALT at T0 of 123.08 U/L.

At T6, ALT level returned to normal in 29% of these patients and decreased by up to 85% (but values remained above 40 U/L) in 61% of patients. Average ALT values at T6 decreased by 45%.

### AST level evolution

One hundred and forty three patients had high AST levels (above 80 U/L), with an average AST at T0 of 129.3 U/L.

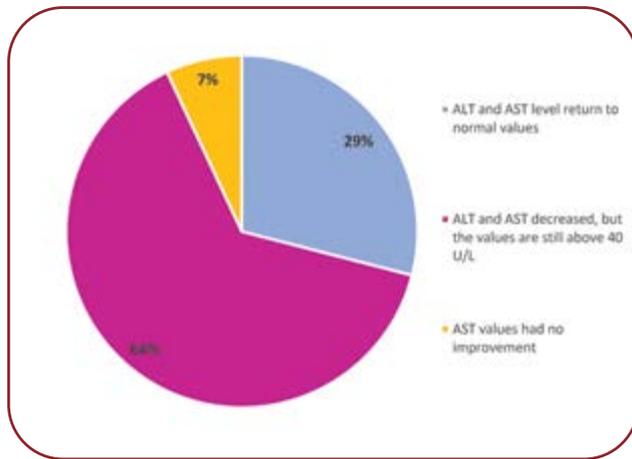
At T6, AST level returned to normal in 37% of these patients and decreased by up to 84% (but values remained above 40 U/L) in 57% of patients. Average ALT values at T6 decreased by 50%.

Analyzing the 100 patients who had both transaminases above 80 U/L, we observed that 29% returned to the normal level by the end of the study and 64% decreased their transaminase level (but values remained above 40 U/L).

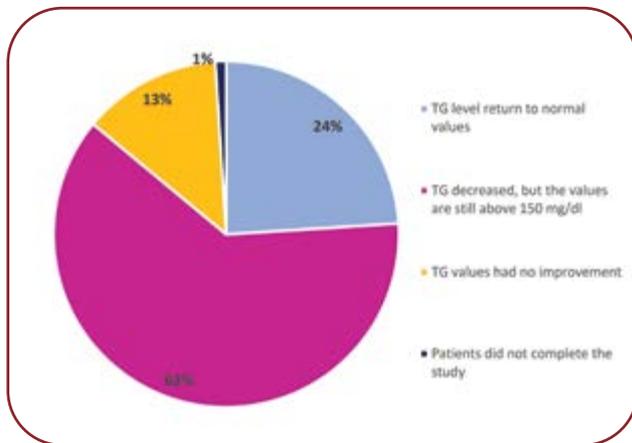
### Evolution of triglyceride values

Triglycerides (TG) evolution was another important marker of the study that had a total decrease between 6% and 20%, with an average of 14.7% during the six months study; the result had statistical significance ( $p < 0.001$ ).

Among the 474 patients with TG > 200 mg/dL, it was observed that at the end of the study, 24% had normal values (below 150 mg/dL), 61% had



**FIGURE 10.** Patients with ALT and AST levels above 80 U/L – percentage evolution



**FIGURE 11.** Patients with TG above 200 mg/dL – percentage evolution

a decrease up to 50% (but still above 150 mg/dL), 13% did not respond to treatment and 1% did not complete the study.

#### Evolution of total cholesterol level

Total cholesterol level decreased by 1-11%, with an average of 9.5%, during the six-month treatment based on the original formula consisting in silymarin, organic selenium and alpha lipoic acid. The result was statistically significant ( $p < 0.001$ ). This result was seen from the first three months of administration, when values were reduced by an average of 7.9%.

#### Evolution of LDL cholesterol level

LDL cholesterol decreased by 10.1% during the six months of study, and the result was statistically significant ( $p < 0.001$ ).

#### Evolution of blood sugar level

At the end of the study, a reduction in blood glucose by 4.7% was observed ( $p < 0.001$ ).

#### Evolution of HDL cholesterol level

HDL cholesterol level was constant throughout the six months of the study, with a slight increase of 1.6%; the result had statistical significance ( $p < 0.05$ ). □

### CONCLUSIONS

- 1) The original formula consisting in silymarin, organic selenium and alpha lipoic acid contributed to remission of FLD in one in 10 patients and it reduced the stage of FLD in six in 10 patients during the six months of administration.
- 2) Transaminase level normalized or had a significant decrease in nine in 10 patients with levels above 80 U/L.
- 3) One in four patients with a high level of triglycerides (above 200 mg/dL) at the beginning of the study returned to an optimal level (below 150 mg/dL) at the end of the study.
- 4) Total cholesterol level decreased by 1-11%.
- 5) LDL cholesterol level decreased by 10.1%.
- 6) Blood sugar level had a decrease of 4.7%.
- 7) HDL cholesterol level was constant throughout the six months of the study, with a slight increase of 1.6%.
- 8) The original formula consisting in silymarin, organic selenium and alpha lipoic acid can be administered from the early stages of liver disease (FLD regardless of grade) and up to chronic stages (represented by hepatitis or cirrhosis).
- 9) Study participants were not required to have a particularly diet, so the results accurately reflect the effectiveness of the formula.
- 10) The large number of patients participating in the study (1 718) confirms the efficacy and safety of using the product. □

*Conflicts of interest: none declared.*

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