# The effects of TOTUM•448, a novel plant-based active principle, on liver, serum and cecal lipid contents among golden Syrian hamsters

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## Background

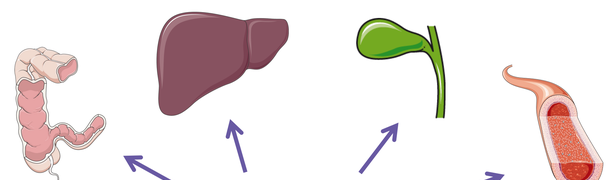
Many biological pathways are involved in the metabolic alterations related to non-alcoholic fatty liver disease (NAFLD) and its potential progression to a severe disease.

TOTUM•448, a polyphenol-rich combination of 5 plant extracts and choline, has shown beneficial impacts on certain features of NAFLD, including steatosis and inflammation in two different animal models of diet-induced NAFLD.

In a mouse model, supplementation with TOTUM•448 reduced NAFLD activity score with reductions observed in steatosis, ballooning and lobular inflammation. Interestingly, improvements in insulin sensitivity and glucose tolerance were also observed.

## Objectives

To assess the effects of TOTUM•448 on cecal, liver, bile and serum lipid contents, in a diet-induced animal model of NASH.



**TOTUM•448**
Plant-Based Active Principle

## Methods

Male Golden Syrian hamsters were fed a Western diet (WD, high-fat, mostly saturated, high-cholesterol) supplemented or not (n=12) with 2 doses of TOTUM•448 directly incorporated into the diet (WD+TOTUM•448 3.5%, n=12 and WD+TOTUM•448 5%, n=12) for 12 weeks. A group of hamsters fed a normal diet (ND, n=6) was used as control. Food intake, body weight and body composition (Echo-MRI) were monitored continuously. Following a 6-hour fast, hamster were euthanized. Then, serum was collected by intracardiac puncture and organs (cecum, liver and gallbladder) were removed and frozen immediately. Statistical post-hoc comparisons were run between WD, WD+TOTUM•448 3.5% and WD+TOTUM•448 5% only.

## Results

### Body weight gain and average energy intakes were similar across WD fed groups.

Fig1a. Body weight gain

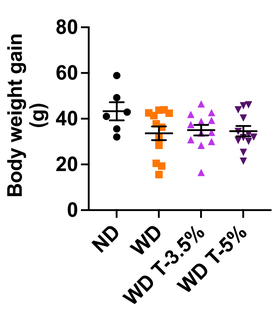
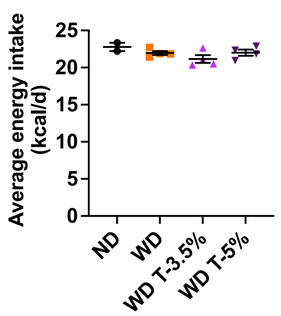



Fig1b. Average energy intake




### TOTUM•448 supplementation led to significant decreases in liver triglyceride, cholesterol and non-esterified fatty acid (NEFA) contents.

Fig2a. Liver triglyceride content

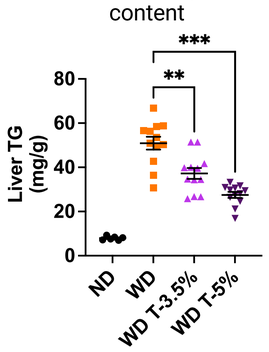



Fig2b. Liver cholesterol content

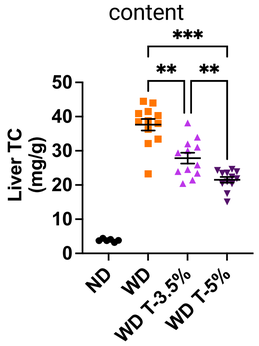



Fig2c. Liver NEFA content

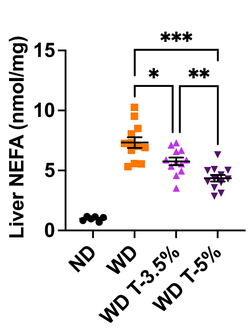



Fig2d. Liver total bile acid content

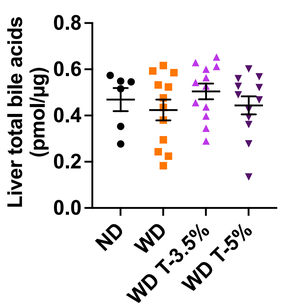
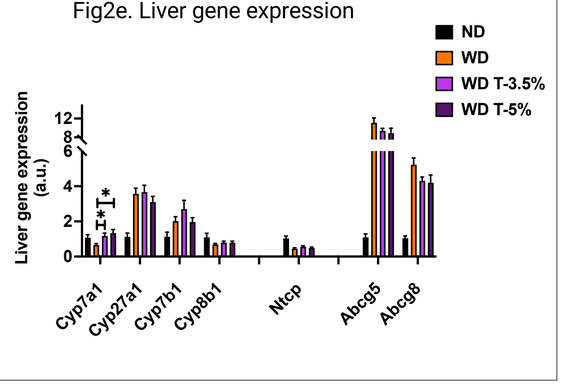



Fig2e. Liver gene expression




### Decreased cecal triglyceride and NEFA cecal contents as well as increased cholesterol and phospholipid contents were observed following TOTUM•448 supplementation.

Fig 3a. Caecal triglyceride content

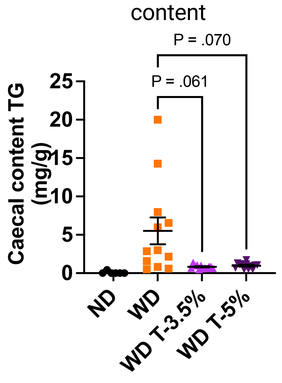



Fig 3b. Caecal NEFA content

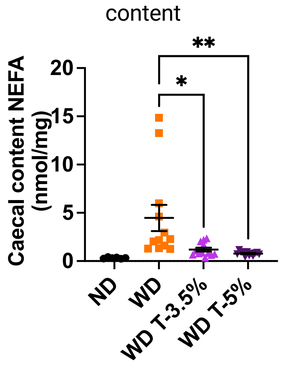



Fig 3c. Caecal cholesterol content

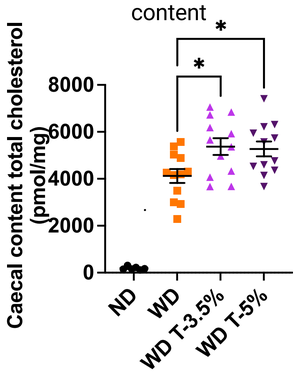



Fig 3d. Caecal phospholipid content

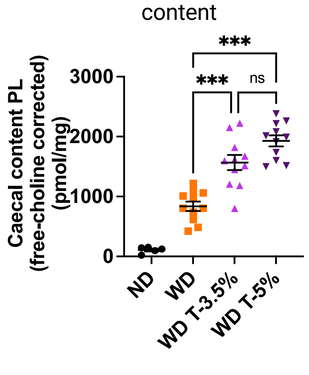



Fig 3e. Caecal total bile acid content

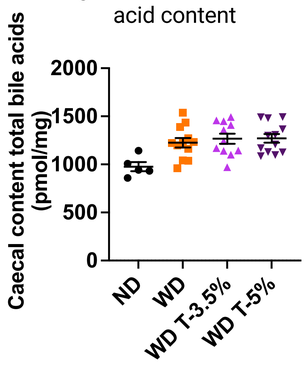



Fig 3f. Ileum Asbt protein abundance

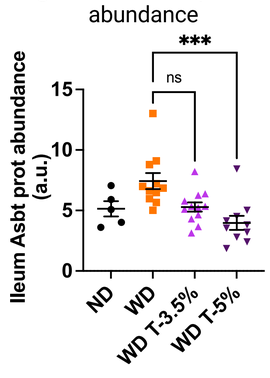
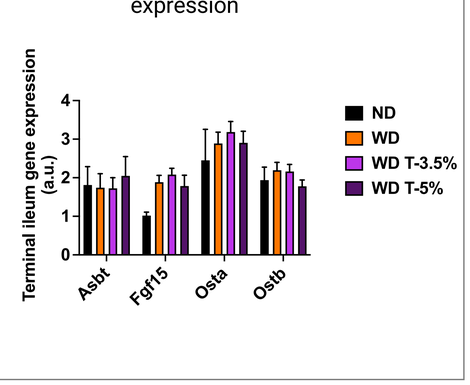
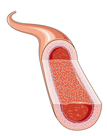
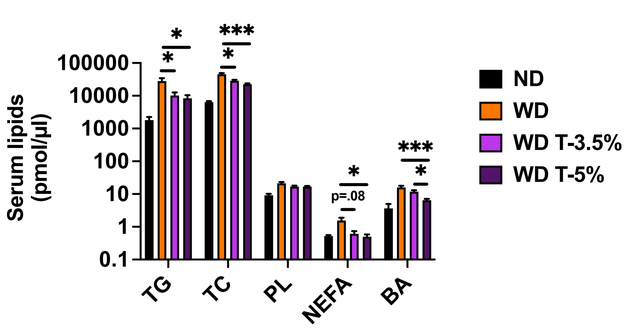



Fig 3g. Terminal ileum gene expression

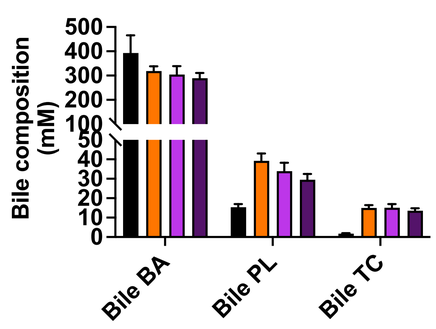



### Decreased serum triglyceride, total cholesterol, NEFA and total bile acid concentrations were observed following TOTUM•448 supplementation.






### The intake of TOTUM•448 did not modify bile composition in the gallblader.




| | |
|---|---|
| * | p<0.05 |
| ** | p<0.01 |
| *** | p<0.001 |
| ns | p≤0.1 |

## Conclusion

In summary, TOTUM•448 supplemention led to:

- ✓ Favorable modifications in lipid content of the liver and serum.
- ✓ Increased CYP7A1 gene expression in the liver.
- ✓ Modulation of lipid caecal content with a reduction in Asbt protein ileum abundance.
- ✓ No modification of bile composition in the gallbladder.

These results enhance our understanding of the potential effects of a polyphenol-rich combination of 5 plant extracts and choline, on certain lipids in the liver, serum and cecal contents. Further research is needed to elucidate the mechanisms of action of TOTUM•448 on gut and liver metabolisms and their interactions with lipid homeostasis.

**Disclosures**
BOUCHARD-MERCIER, A., CHAVANELLE, V., OTERO, F.Y., RIPOCHE, D., VALLIER, M., LANGHI, C., LE JOUBIOUX, F., PELTIER, S. AND SIRVENT, P.
are employees of Valbiotis.

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