TOTUM•448 improves diet-induced non-alcoholic steatohepatitis in golden Syrian hamsters fed a western-diet

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1 – Background and aim

Non-alcoholic fatty liver disease (NAFLD) encompasses manifold liver impairments that progress from simple steatosis to development of non-alcoholic steatohepatitis (NASH), characterised by increased inflammation and fibrosis. To date, no therapeutical solution has been approved for treatment of early stages of NAFLD. TOTUM•448 is a novel patented combination of 5 plant extracts and choline, designed to prevent the development of NASH in steatotic liver. The aim of this study was to assess the effects of TOTUM•448 in a diet-induced animal model of NASH.

2 – Methods

Male Golden Syrian hamsters were fed a western-diet (WD (N=12), high-fat, mostly saturated, high-cholesterol) supplemented or not with 2 doses of TOTUM•448 directly incorporated into the diet (3.5%: WD+T-3.5% (N=12), and 5%: WD+T-5% (N=12)) for 12 weeks. A group of hamsters fed a normal diet (ND) was used as control (N=6). Food intake, body weight and body composition (Echo-MRI) were monitored continuously. NASH was evaluated in all animals using circulating and hepatic biochemical, histological, and gene expression markers of steatosis, inflammation, and fibrosis. Statistical post-hoc comparisons were run between WD, WD T-3.5%, and WD T-5% only.

3 – Results

Figure 1: TOTUM•448 does not alter food intake or body composition in WD-fed hamsters.

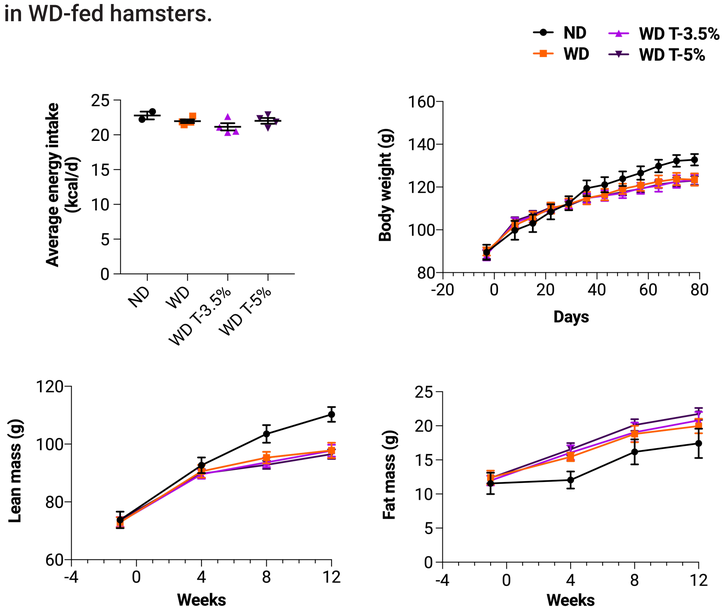


Figure 2: TOTUM•448 reduces hepatic and serum triglycerides (TG) and Total Cholesterol (TC) in WD-fed hamsters.

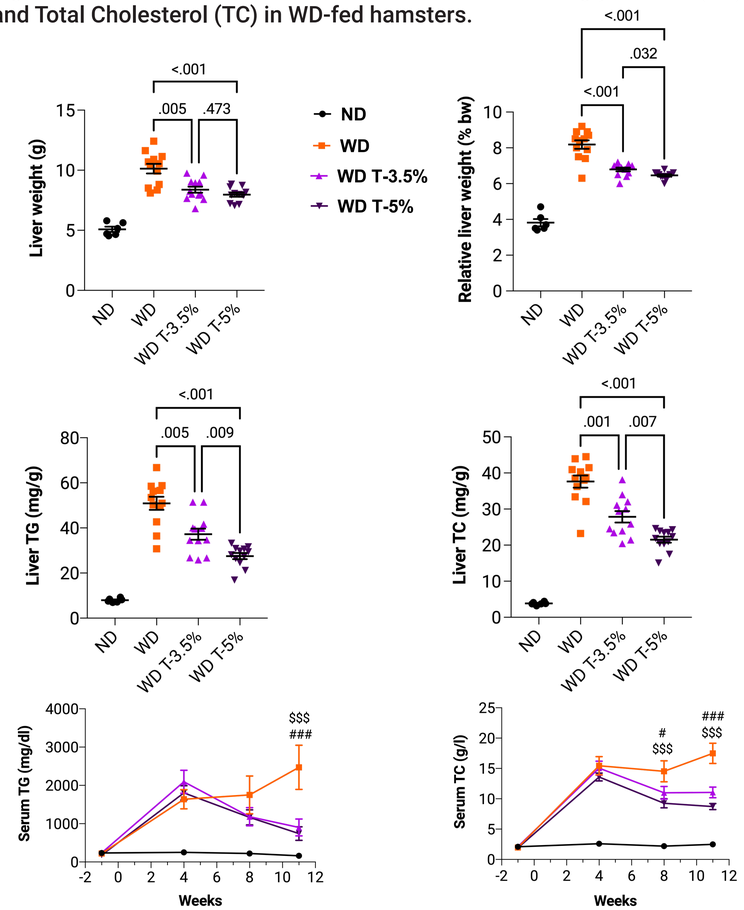


Figure 3: TOTUM•448 reduces the expression of genes related to liver inflammation and fibrosis in WD-fed hamsters.

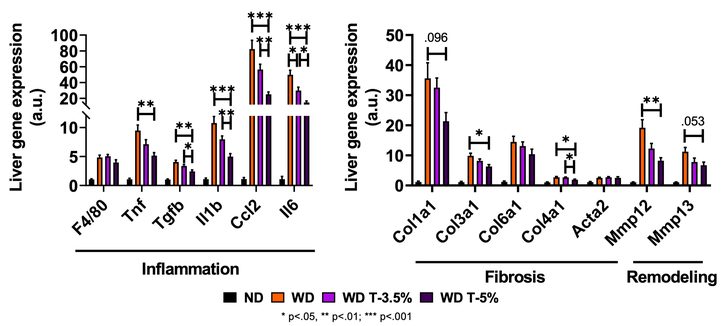
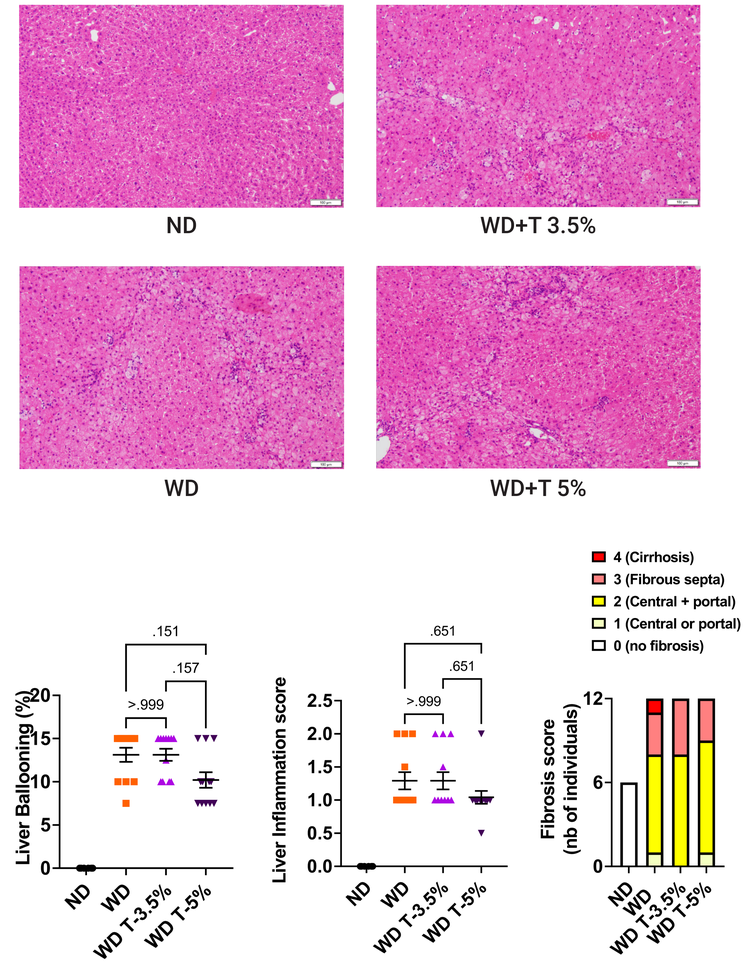


Figure 4: Histological scoring of ballooning, inflammation and fibrosis

Hematoxylin & Eosin staining



4 – Conclusion

This study demonstrates the dose-dependent efficacy of TOTUM•448 in improving circulating lipid profile and reducing liver steatosis, inflammation, and fibrosis in WD-fed hamsters, making it a promising candidate for NASH prevention.

Conflict of interest statement: VC, YFO, DR, MV, CL, FLJ are Valbiotis employees. SP is Valbiotis CEO, PS is Valbiotis CSO. TM is a member of Valbiotis' scientific and medical board.