Nonalcoholic Fatty Liver Disease (NAFLD) is the most common cause of chronic liver disease in North America. It has two clinical-histological phenotypes: nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH). NASH is associated with increased insulin resistance (IR), increased lipogenesis and a pro-apoptotic/inflammatory/fibrogenic state.

Omega-3 fatty acids can reduce plasma lipids, de novo lipogenesis, IR, and inflammation in the liver.

We have recently developed a Diet-Induced Animal Model Of NAFLD (DIAMOND model):

- C57Bl/6J cross mice
- 129S1/SvImJ and strain:
- Isogenic mouse

We evaluated the effect of omega-3 carboxylic acids (OM3-CA, Epanova®), a complex mixture including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in free fatty acid form, and dapagliflozin (DAPA, SGLT2 inhibitor) on steatohepatitis and fibrosis in the DIAMOND mouse model.

AIM

To characterize the effect of OM3-CA and dapagliflozin on steatohepatitis and fibrosis in the DIAMOND mouse model of NASH.

METHODS AND MATERIALS

- Animals and treatments: Male C57BL/6J/129S1/SvImJ mouse strain (B6/129) were fed a high-fat diet with 42 energy% from fat (Western Diet, WD, Harlan TD.88137) and with high fructose-glucose solution (HFS, 23.1g f-fructose + 18.9 g fructose-glucose) for a total of 20 weeks.

- 16 weeks of diet, mice were randomized into four groups (n=13-14) and gavaged daily with (1) vehicle (olive oil and water; Sham), (2) OM3-CA, 600 mg/kg, (3) DAPA, 1 mg/kg or (4) OM3-CA+DAPA (n=13/14 per groups).

- Protein levels: immunoblot analysis
- mRNA expression: real-time Q-PCR

**REFERENCES**


**CONCLUSION**

OM3-CA or OM3-CA+DAPA reduced liver injury in the DIAMOND model by significantly decreasing steatosis and fibrosis. Although this effect was not related to changes in glucose or lipid metabolism, or in the activation of apoptotic pathways, it was associated with a significant reduction in ERK (p42/44) signalling pathway and fibrogenesis markers expression and in a modest decrease, albeit not significant, in hepatocyte ballooning.