Cyclodextrin promotes liver inflammation and fibrosis in high fat/cholesterol/cholate diet fed mice

François Briand[1], Marjolaine Quinsat[1], Clément Costard[1], Julie Tessaire[1], Emmanuel Brousseau[1], Thierry Sulpice[1]

[1]PHYSIOGENEX, Labège, France

BACKGROUND

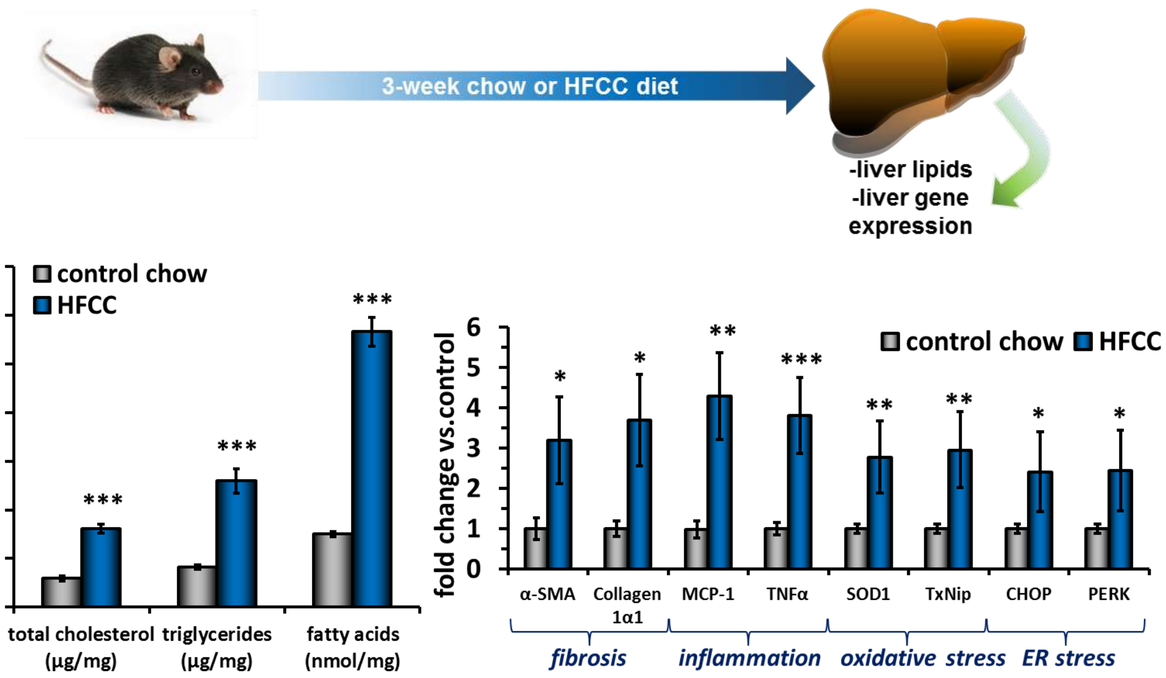
2-hydroxypropyl beta cyclodextrin (cyclodextrin) is often used as a vehicle for oral drug administration but also alters cholesterol absorption and metabolism. Here we investigated whether cyclodextrin administration affects liver complications in C57BL6/J mice fed a 60% high fat, 1.25% cholesterol, 0.5% cholic acid diet (HFCC) for 3 weeks.

METHODS

C57BL6/J mice were fed a 60% high fat, 1.25% cholesterol, 0.5% cholic acid diet for 3 weeks. This 3-week diet was initially found to increase lipids levels and expression of genes involved in inflammation and fibrosis in the liver, as compared with chow fed mice. After 1 week of diet, mice were treated for 2 weeks with drinking water (control) or 20% cyclodextrin by oral gavage once daily. Liver was collected at the end of treatment for biochemistry and histology analysis.

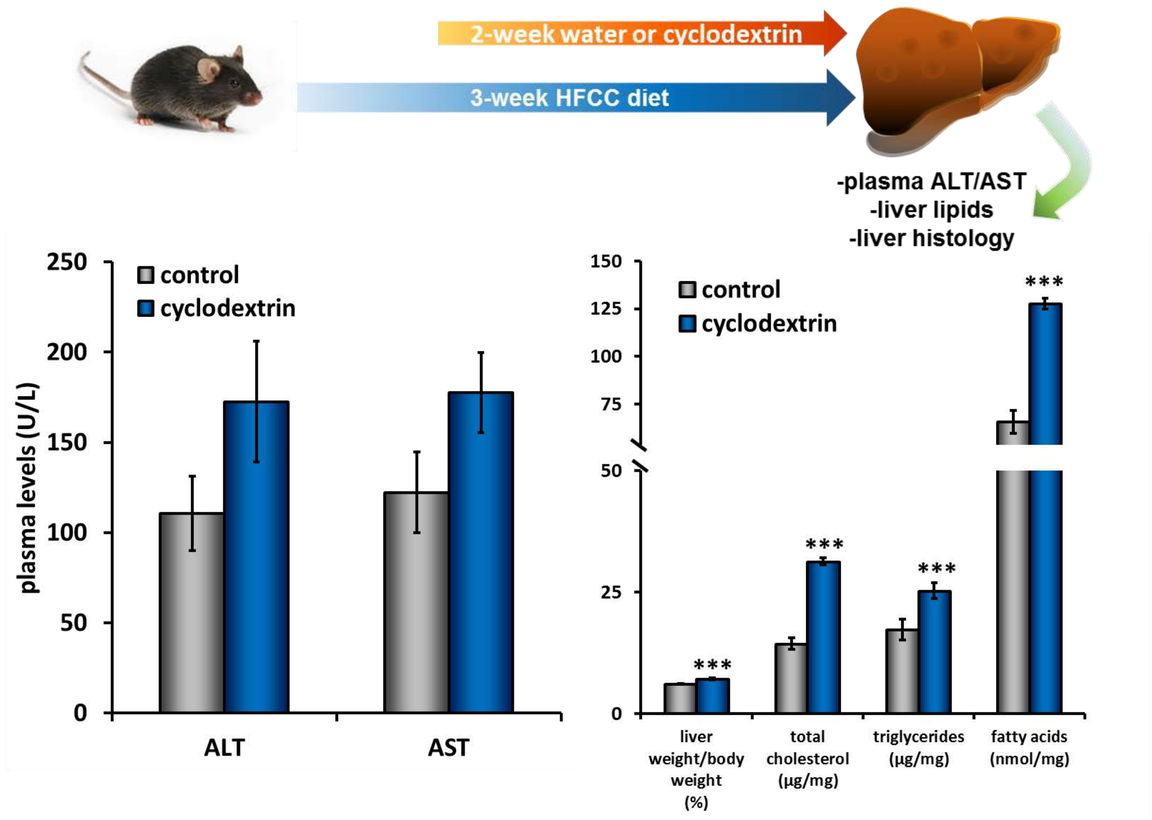
RESULTS

1. HFCC diet raises liver lipids and expression of genes involved in NASH.



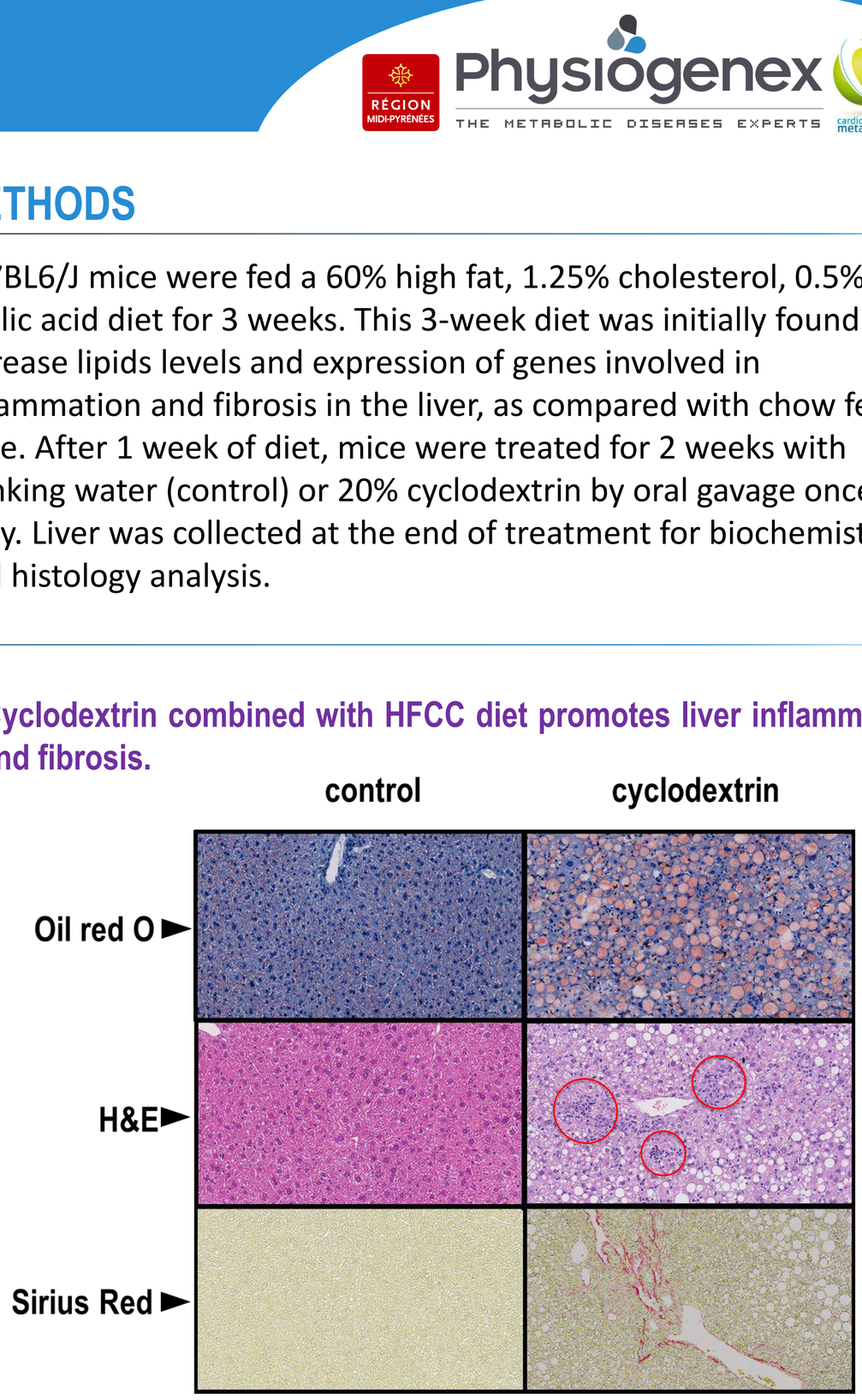
Liver was collected for hepatic lipids (left panel) and gene expression assays (right panel) after 3 weeks of chow or HFCC diet. Data are presented as mean ± SEM. *p<0.05, **p<0.01, ***p<0.001 vs. control chow diet (t-test).

2. Cyclodextrin combined with HFCC diet further raises liver lipids levels.



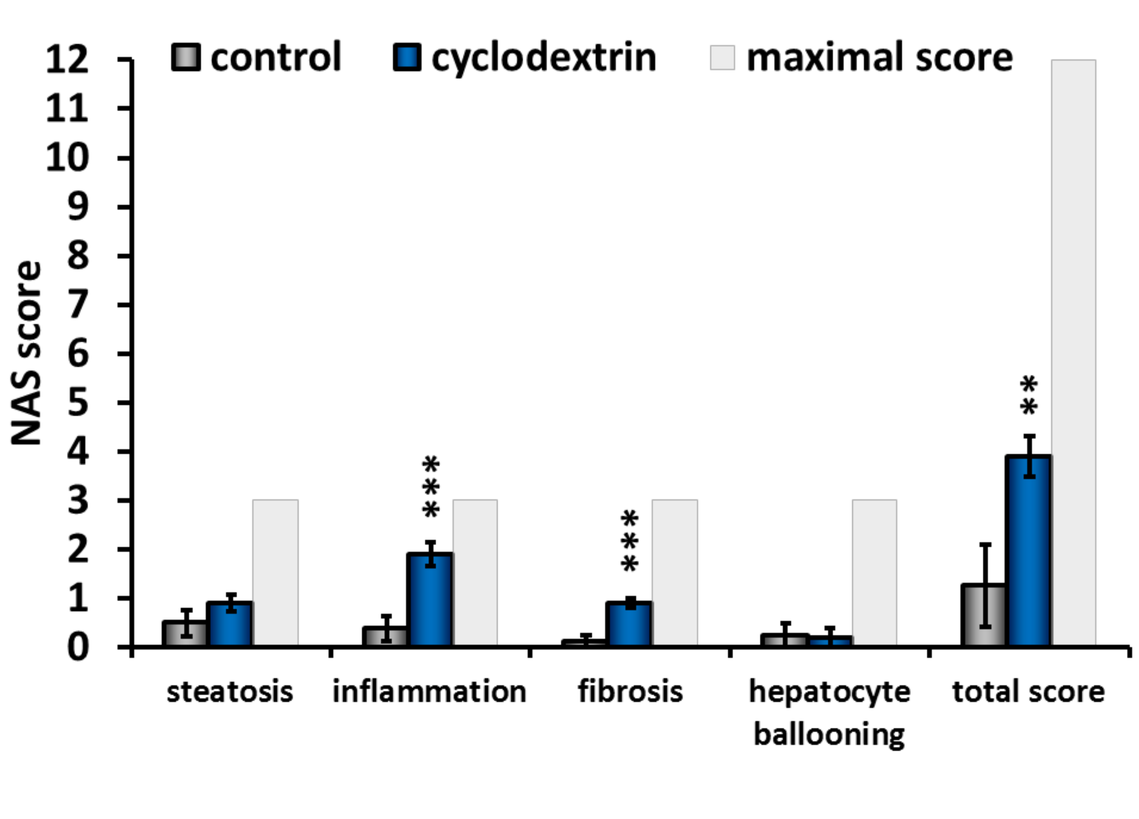
Plasma ALT/AST levels (left panel), liver weight and liver lipids (right panel) in mice treated for 2 weeks with water (control) or 20% 2-hydroxypropyl beta cyclodextrin (cyclodextrin). Data are expressed as the mean ± SEM. ***p<0.001 vs. control .

3. Cyclodextrin combined with HFCC diet promotes liver inflammation and fibrosis.



Liver was collected at the end of the 2-week treatment with water or 20% 2-hydroxypropyl beta cyclodextrin (cyclodextrin) for histology analysis with oil red O staining (steatosis), H&E staining (inflammation indicated by red circles) and Sirius Red (fibrosis) staining.

4. Cyclodextrin combined with HFCC diet aggravates NAS scoring.



Slides of hepatic lobe section stained with H&E and Sirius Red were digitized using a Nanozoomer from Hamamatsu for evaluation and NAFLD scoring. Data are expressed as the mean ± SEM. **p<0.01, ***p<0.001 vs. control .

CONCLUSION AND PERSPECTIVES

- Cyclodextrin oral administration induces inflammation and fibrosis in mice fed a 60% high fat, 1.25% cholesterol, 0.5% cholic acid diet in 3 weeks.
- This model seems relevant to rapidly induce liver complications and evaluate drugs targeting non-alcoholic steato-hepatitis.

PHYSIOGENEX SAS - Prologue Biotech – 516, rue Pierre et Marie Curie – 31670 Labège – France - Phone: +33 561 287 040 - Fax: +33 561 287 043 - business@physiogenex.com - www.physiogenex.com

APASL 2016. Tokyo, JAPAN