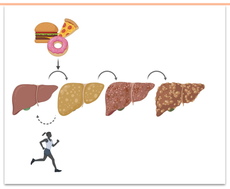
Cannabigerol Effects on Body and Liver Weights in Methionine- & Choline-Deficient Diet Induced NASH Mice Model

Ashley Snell, Taylor Tesch, Nouf Aljobaily, and Yuyan Han

School of Biological Sciences, University of Northern Colorado

Introduction



Background:

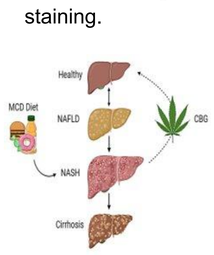
- NAFLD- Non-Alcoholic Fatty Liver Disease; Cause still unknown; Risk Factors- Obesity, High Cholesterol
- NASH - Non-Alcoholic Steatohepatitis; Type of NAFLD; Most severe form of NAFLD; potential treatments exercise (lose weight) or vitamin E
- MCD- Methionine/Choline Diet; Model used for NASH-like symptom; High sucrose and fat diet
- CBG- Cannabigerol (CBG); Cannabinoid;
- No research on this treatment in relation to NASH thus far.
- Therefore, the purpose of this study is to see if there is a correlation between food consumption, liver and body weights of mice after CBG treatment upon being subjected to an MCD diet.

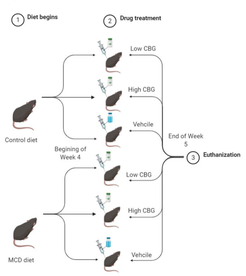
Hypothesis*:*

- This research aims to study the effects of CBG on MCD/Control diets on regulating the overall food consumption, body weight and liver weight. We predict that a low dosage of CBG will be most effective at reducing the symptoms of NASH.

Methods & Materials

- Age of 7-8 week old C56BL/6 male and female mice fed for five consecutive weeks with the corresponding diets (either MCD or control).
- The CBG doses were divided into a vehicle, low (2.46 mg/kg), and high doses (24.6 mg/kg)
- Body weights taken all weeks every Monday, Wednesday, and Friday; final body weights were recorded on the day of animal sacrifice.
- Afterwards, the livers were also dissected, examined, weighed, and put into frozen media for staining.





Results

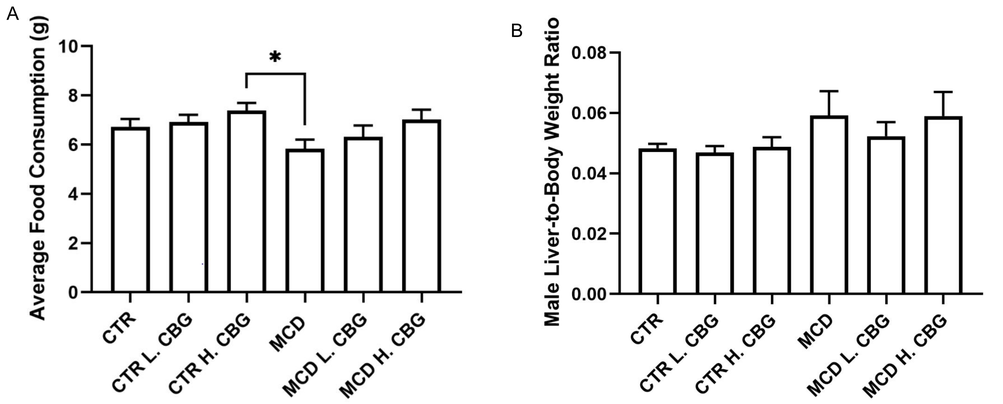


Figure 1. Average food consumption (A) and Liver to Body weight ratio (B) were obtained to evaluate the mices' response to the various treatments. It can be deciphered that for food consumption, there was an increase in the amount of food consumed as the CBG dose increased and there was a $p < 0.05$ significance when the CTR H. CBG was compared to the MCD. For the liver to body weight ratio, there was no significant correlation between any of the groups; however, the MCD diet and the MCD subjected to H. CBG did have a slight increase when compared to the other groups.

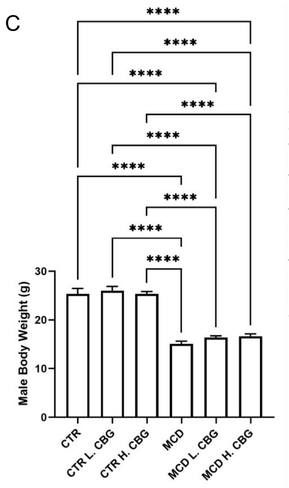
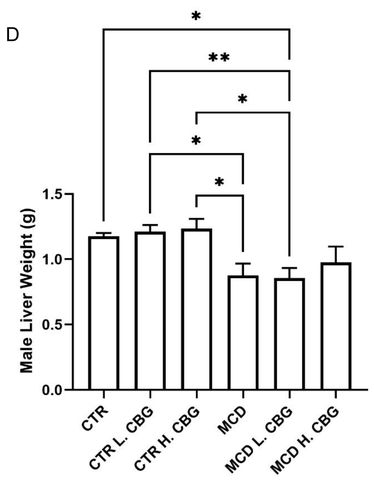


Figure 2. Shows the male body weight averages among the various treatment groups (C) and the average liver weights across the treatment groups (D). The body weights between CTR and MCD were highly significant as was the CBG treatments on both diets which is indicated at a p level of $p < 0.0001$. It can be seen that when treated with the MCD diet, there was a reduction in the liver weights. This reduction was minimized with the introduction of CBG treatment as seen in the H. CBG recovery of the liver loss. When comparing the CTR L. CBG to MCD L. CBG, there was a moderate significance at $p < 0.01$ and the other significances across CTR to MCD were just slightly significant at a $p < 0.05$.



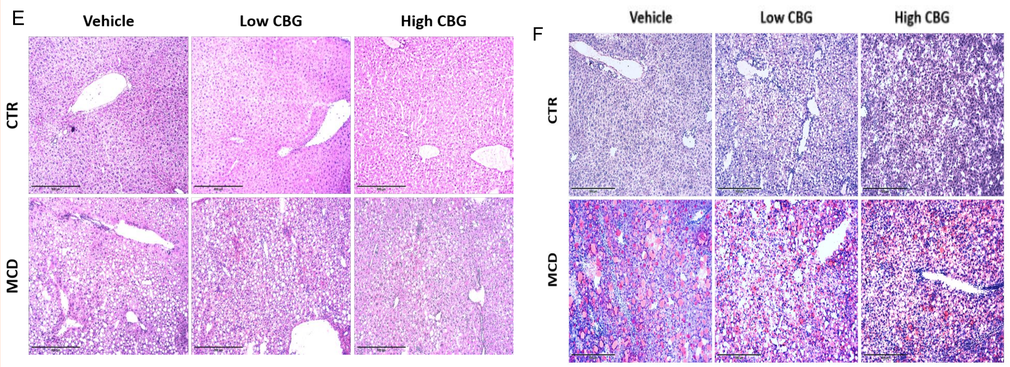


Figure 3. H&E staining (E) was performed for abnormal liver morphology and Oil-Red-O staining (F) was used for lipid droplets estimation within liver tissue. From the H & E staining, it can be determined that the liver tissue improved in the MCD groups with the use of L. CBG and not with H. CBG. For the Oil-Red staining, lipid accumulation can be described in the image by the white spaces. MCD has more lipid accumulation than the CTR groups and it can be noted that there is a slight decrease of lipid accumulation in the CBG treated groups.

Summary

- Average Food Consumption decreases significantly between Control High CBG groups and the MCD Control group
- Liver weights have significant difference between Control groups and MCD or MCD Low CBG groups
- Body weights are significantly different between all three Control groups with all three MCD groups
- When combining the liver weights to the body weights in a ratio, however, there is no statistically significant difference between overall Liver:Body Weight among any of the groups
- From the H&E staining, it is observed that L CBG treatment on either diet improves the overall liver tissue
- For Oil-Red-O staining, there is more lipid accumulation in the MCD diet indicating the symptoms of NASH, but this is reduced with CBG treatment

Discussion

Overall Conclusions: CBG could have implications in helping recover lost body and liver wight from the MCD induced diet. Low dosage of CBG was found to be beneficial in lessening tissue damage and fibrosis, while high dosage of CBG was found to negatively impact the liver by increasing tissue damage and fibrosis.

Future Directions:

- Further run the same tests to reaffirm conclusions and have replicates of the data
- Use a larger sample size (greater than the 6 sample size used here) to show the same effects across a large population
- Investigate a diet besides MCD that induces all of the symptoms of NASH instead of a majority of the symptoms
- Investigate the long term effects of CBG treatment on MCD diet by giving the treatment for a longer span of time

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