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Cannabigerol (CBG) Inhibits Fibrosis Induced by Methionine/ CholineDeficient (MCD) Diet in C57BL/6 Mice

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Cannabigerol (CBG) Inhibits Fibrosis Induced by Methionine/Choline-Deficient (MCD) Diet in C57BL/6 Mice

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Background

NASH is characterized with hepatic inflammation and fibrosis caused by the buildup of fat and other stimuli in the liver (two-hit theory). The MCD diet is known to induce non-alcoholic steatohepatitis (NASH) in a short period of time. When MCD diet is used, more fat is trapped in the liver. Currently no medicine is approved for NASH treatment. Therefore, finding promising agents to alleviate the NASH symptoms in patients is critically needed. Cannabigerol (CBG) is a non-psychoactive cannabinoid component that has anti-inflammatory effects in other studies. However, the effect of CBG on NASH is unknown. We hypothesized that liver fibrosis decreases with low dose of CBG administration in MCD induced NASH mice models.

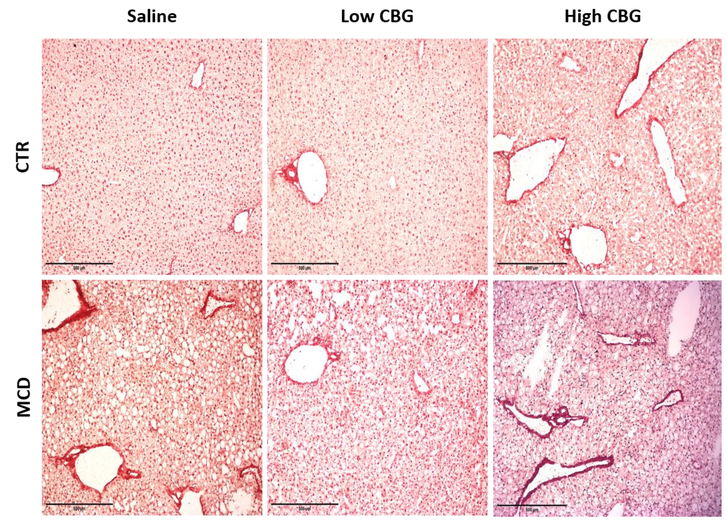
Aim

To assess how CBG affects liver Fibrosis in an MCD-induced NASH mice model.

Methods

- 7–8-week-old male and female C57BL/6 mice were fed with a MCD or matching control diet for a total of 5 weeks.
- Mice were I.P. injected with either vehicle, low dose (2.46 mg/kg/day), high dose (24.6 mg/kg/day) of CBG at the last two weeks.
- Liver fibrosis is evaluated with pico-Sirius red staining, the mRNA and protein levels of fibrosis biomarker, α-smooth muscle actin (SMA) by qRT-PCR, and immunofluorescence staining, respectively.

Sirius Red Staining



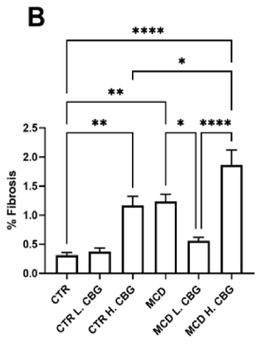
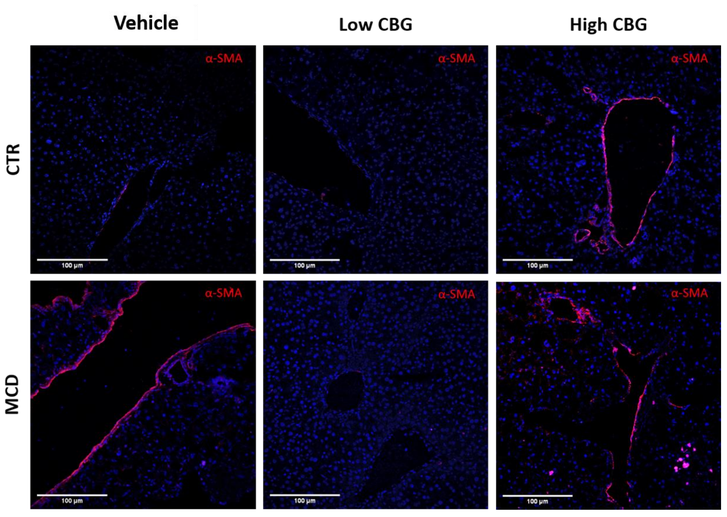


Figure 1. low CBG shows a decrease in Fibrosis in both control and MCD, high CBG does not show a decrease in Fibrosis in both control and MCD. **B.** Shows the % of fibrosis in each group.

α-SMA



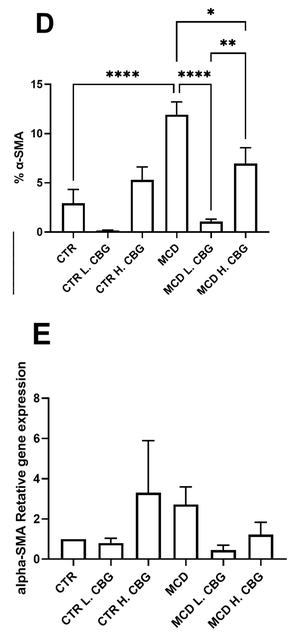


Figure Two. Gene expression is present in the control and MCD groups with high CBG, the gene expression decreased in the control and MCD groups with low CBG. **D.** Shows the % of Fibrosis in the α-SMA stain. **E.** Shows the gene expression in the α-SMA.

Results

- The gene expression of α-SMA increased in the control and MCD groups that received high CBG treatment and decreased in the mice that received low CBG treatment for both control and MCD groups.
- In the MCD group with vehicle, fibrosis is enhanced.
- Collagen deposition decreased with low dose of CBG, while high dose of CBG increased collagen when compared to MCD with vehicle.

Conclusion

Fibrosis was found to be decreased in the mice that received a low CBG dose demonstrated by the Sirius red and α-SMA staining in the control and MCD group, but not in the mice that received a high dose of CBG.

Future Direction

- Evaluate why a low dose of CBG decreases the expression of Fibrosis.
- Investigate what long term use of CBG has on the liver and on Fibrosis.

References Han, Yuyan,; Mu, Y., Ogawa, T., & Kawada, N. (2010). Reversibility of fibrosis, inflammation, and endoplasmic reticulum stress in the liver of rats fed a methionine-choline-deficient diet. Laboratory Investigation, 90(2), 245-56.; Oseini, A. M., & Sanyal, A. J. (2017). Therapies in non-alcoholic steatohepatitis (NASH). Liver international : official journal of the International Association for the Study of the Liver, 37 Suppl 1(Suppl 1), 97–103. https://doi.org/10.1111/liv.13302; Tam J, Liu J, Mukhopadhyay B, Cinar R, Godlewski G, Kunos G. Endocannabinoids in liver disease. Hepatology. 2011 Jan;53(1):346-55. doi: 10.1002/hep.24077. PMID: 21254182; PMCID: PMC3073545.; Zhou, J. H., Cai, J. J., She, Z. G., & Li, H. L. (2019). Noninvasive evaluation of nonalcoholic fatty liver disease: Current evidence and practice. World journal of gastroenterology, 25(11), 1307–1326. https://doi.org/10.3748/wjg.v25.i11.1307

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