# Cannabidiol inhibits the mesothelial to mesenchymal transition in experimental pericarditis

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## INTRODUCTION

Pericarditis results from pericardial sac inflammation, leading to pericardial effusion and thickening that could evolve to fibrosis. Fibrosis results from deposition of extracellular matrix (ECM), mediated by the activation of fibroblasts.

The fibroblast source is unclear, but may originate from mesothelial cells, suggesting a mesothelial-to-mesenchymal transition (MMT). MMT is a process whereby epithelial cells are transcriptionally reprogrammed, resulting in decreased adhesion and enhanced migration, and acquire a mesenchymal phenotype.

Specific anti-fibrotic therapies are not currently available. Cannabidiol (CBD) is a non-psychoactive compound of Cannabis sativa that prevents effusion and thickening in this model of pericarditis and inhibits fibrosis in animal models of cardiac injury.

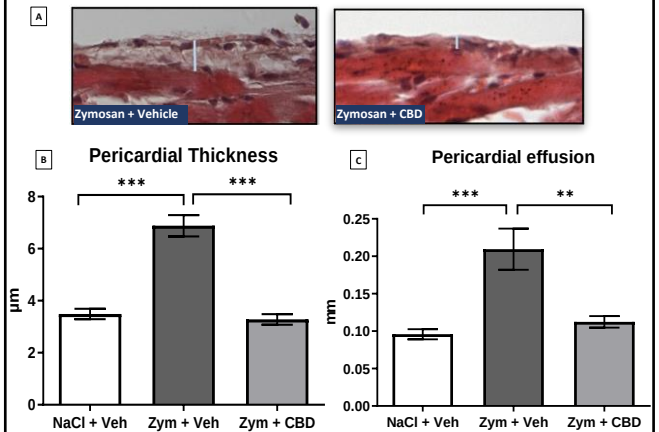


**Figure 1. A.** Representative images of the pericardial thickness of mice heart sections stained with hematoxylin and eosin. **B.** Average measurements of the pericardial thickness in pericarditis animal model. **C.** Average measurement of the pericardial space in the pericarditis animal model. * p<0.05, ** p<0.01, *** p<0.001,**** p<0.0001.

## HYPOTHESIS

CBD reduces MMT in a mouse model of acute pericarditis.

## METHODS

Pericarditis was induced in 10-week-old male mice by injecting 50 µl of ZymosanA (Zym, 1 mg), a component of the yeast wall known to induce pericarditis, into the pericardial sac. Control mice received equal volume of NaCl 0.9%.

Mice were randomized to daily intraperitoneal injections of pharmaceutically manufactured CBD (10 mg/kg, 0.1 ml; no detectable THC) or vehicle (Veh, 1:1:18 EtOH:Cremophor:H2O) 30 min post Zym/NaCl.

Pericarditis severity was assessed by the presence of effusion at echocardiography, pericardial thickening by Hematoxylin-eosin staining and MMT by the scoring of immunofluorescence staining of mesothelial cells (anti HEG-1 antibody) and fibroblasts (anti-Vimentin antibody).

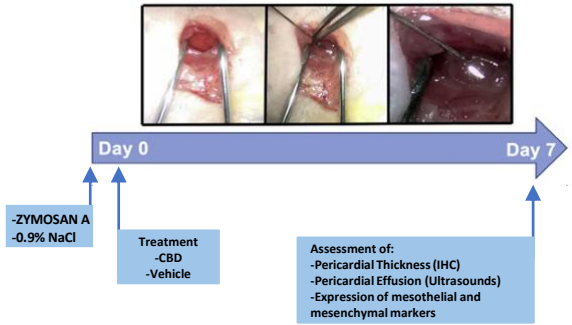


**Figure 2.** Study design and animal protocol

## RESULTS

Seven days after surgery, when compared to Zym+Veh mice, CBD treatment reduced MMT presence in the pericardium (0.89±0.36 vs 2.33±0.18, p<0.01), pericardial effusion (0.12±0.01 mm vs 0.26±0.05, p<0.01) and pericardial thickness (3.6±0.6 µm vs 6.5±1.1, p<0.05)

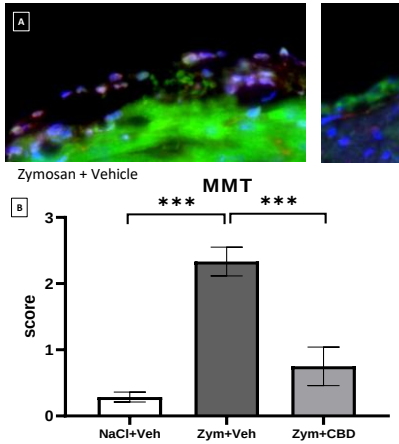


**Figure 3.**
**A.** Representative images of pericardial MMT of mice heart sections stained with immunofluorescence. (Green: HEG-1, Red: Vimentin, blue: DAPI).
**B.** Average score of MMT in pericarditis animal model.

* p<0.05
** p<0.01
*** p<0.001

## CONCLUSIONS

Here we show the emergence of fibroblast markers originating from mesothelial cells, suggesting MMT. CBD's inhibition of MMT, ECM release and local fibrosis may explain the beneficial effects observed in the mouse model of acute pericarditis. CBD may represent a novel strategy for the treatment and prevention of pericarditis.

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