

Liposome-embedded curcumin alleviates liver injury in *Atp7b*^{-/-} Wilson disease mouse model

Ho, Wai-In*; Yang, Jiayin*; Wei, Rui; Chang, Chi-Wah; Li, Na; Lai, Wing-Hon; Au, Ka-Wing; Hong, Xueyu; Wong, Lai-Yung; Tsang Wai-Ling; Esteban, Miguel A.; Tse, Hung-Fat

Background

- Wilson disease (WD) is a rare inherited genetic disorder caused by diverse mutations in the *ATP7B* gene located on chromosome 13.
- Impaired ATP7B protein causes accumulation of copper in a variety of tissues especially liver, which leads to severe physiological disorders such as hepatitis, progressive cirrhosis and acute liver failure.
- Curcumin, a natural polyphenolic compound extracted from *Curcuma longa* plants, has been studied extensively and proved to have anti-inflammatory, antioxidant and hepatoprotective activities.
- Previous studies have shown that liposome-embedded curcumin can successfully enhance bioavailability of curcumin in vitro and in vivo.
- Liposome-embedded curcumin may have the treatment potential to alleviate liver injury in Wilson disease patients

Methods

In this study, liposome-embedded curcumin was assessed in *Atp7b*^{-/-} transgenic WD mouse model to investigate the treatment effect of curcumin in Wilson disease.

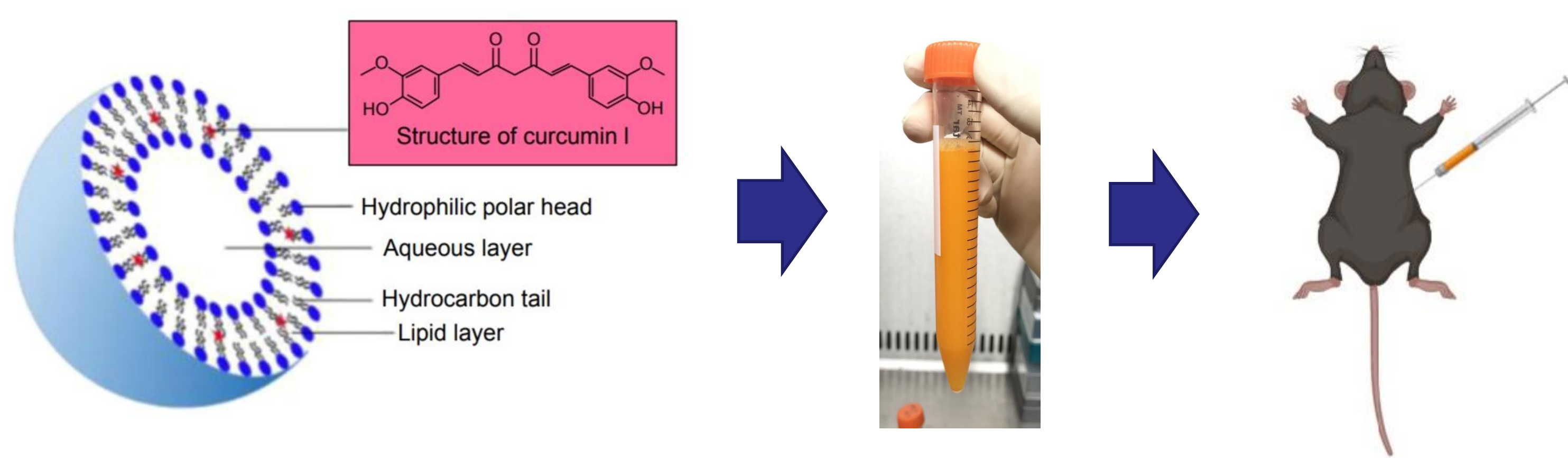


Figure 1. Intraperitoneal injection of 50 mg/kg liposome-embedded curcumin in 8 weeks old *Atp7b*^{-/-} WD mice, twice a week for 8 weeks.

Results

A. Macroscopic changes in the *Atp7b*^{-/-} spleens and livers compared to *Atp7b*^{+/-} (control)

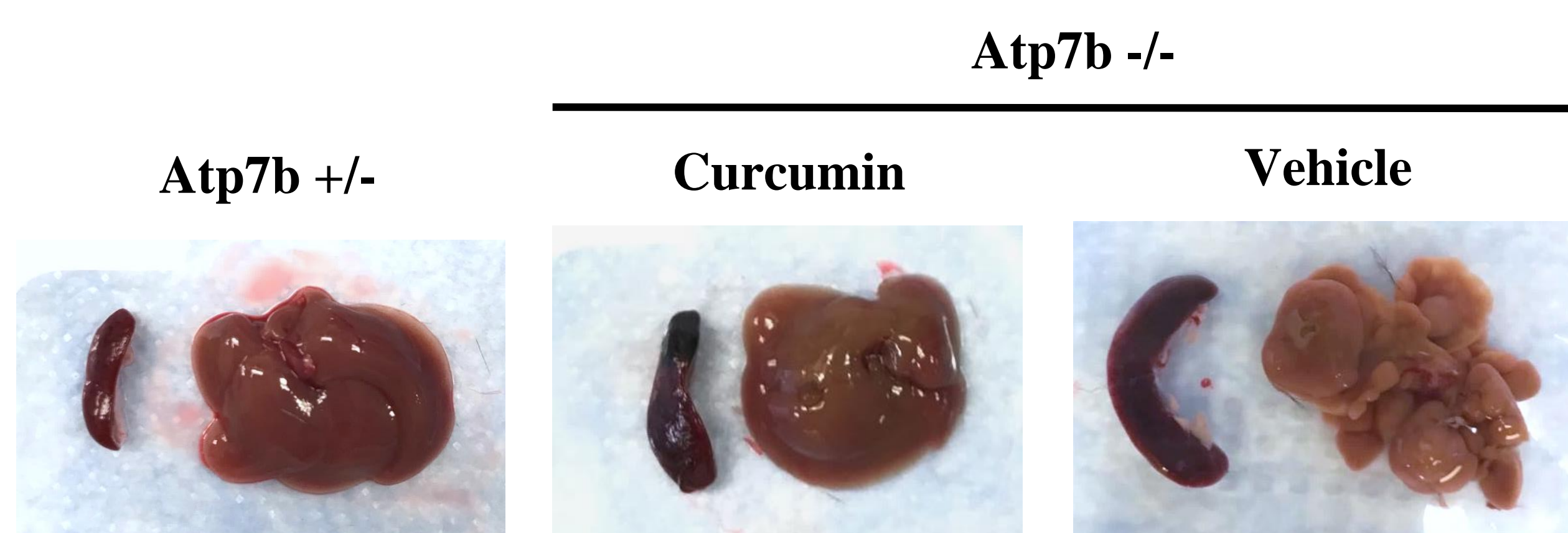


Figure 2. Liposome-embedded curcumin reduced splenomegaly and liver regenerative nodules caused by liver injury in *Atp7b*^{-/-} WD mice.

B. Examination of serum AST and ALT levels

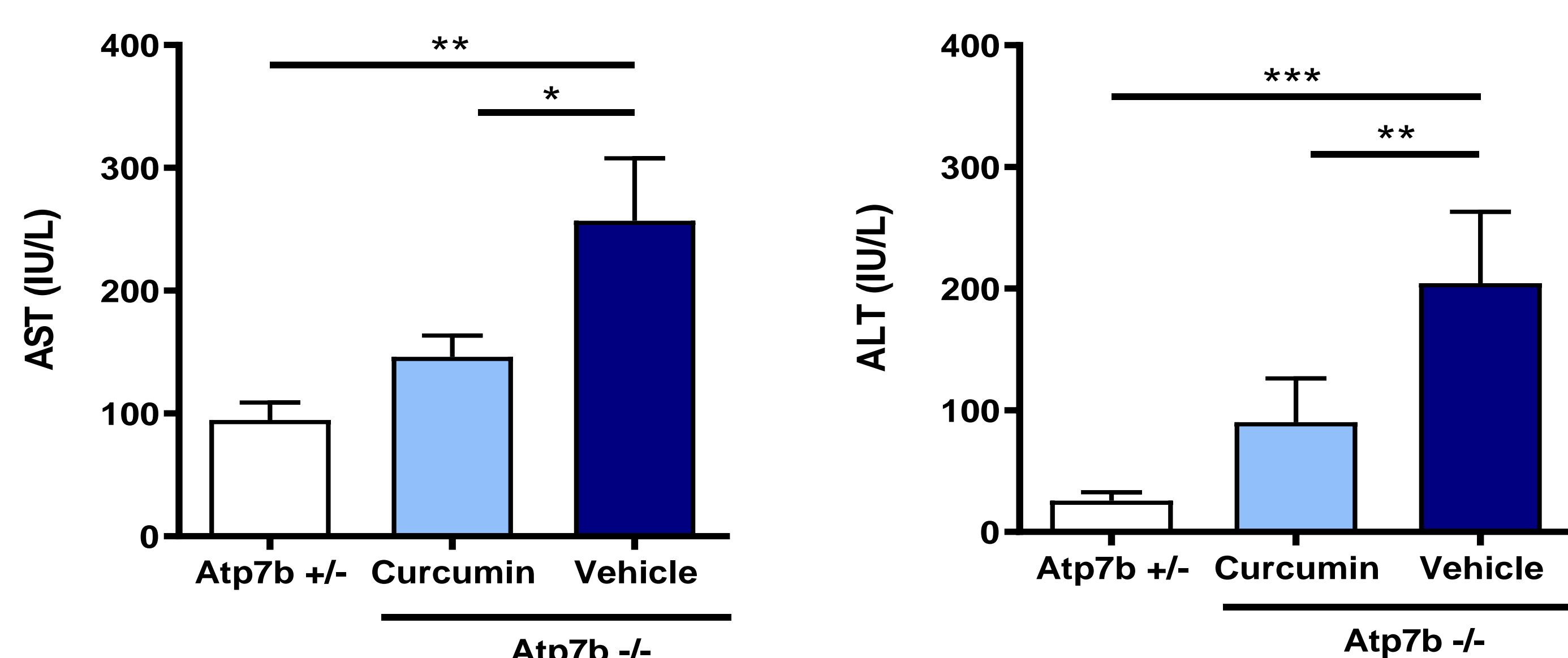


Figure 3. Serum AST, ALT levels are significantly reduced in liposome-embedded curcumin treated *Atp7b*^{-/-} WD mice.

Acknowledgement

This research is supported by the National Science Foundation of China (NSFC) Grant Hong Kong

Results (Continued)

C. Examination of serum lipid levels

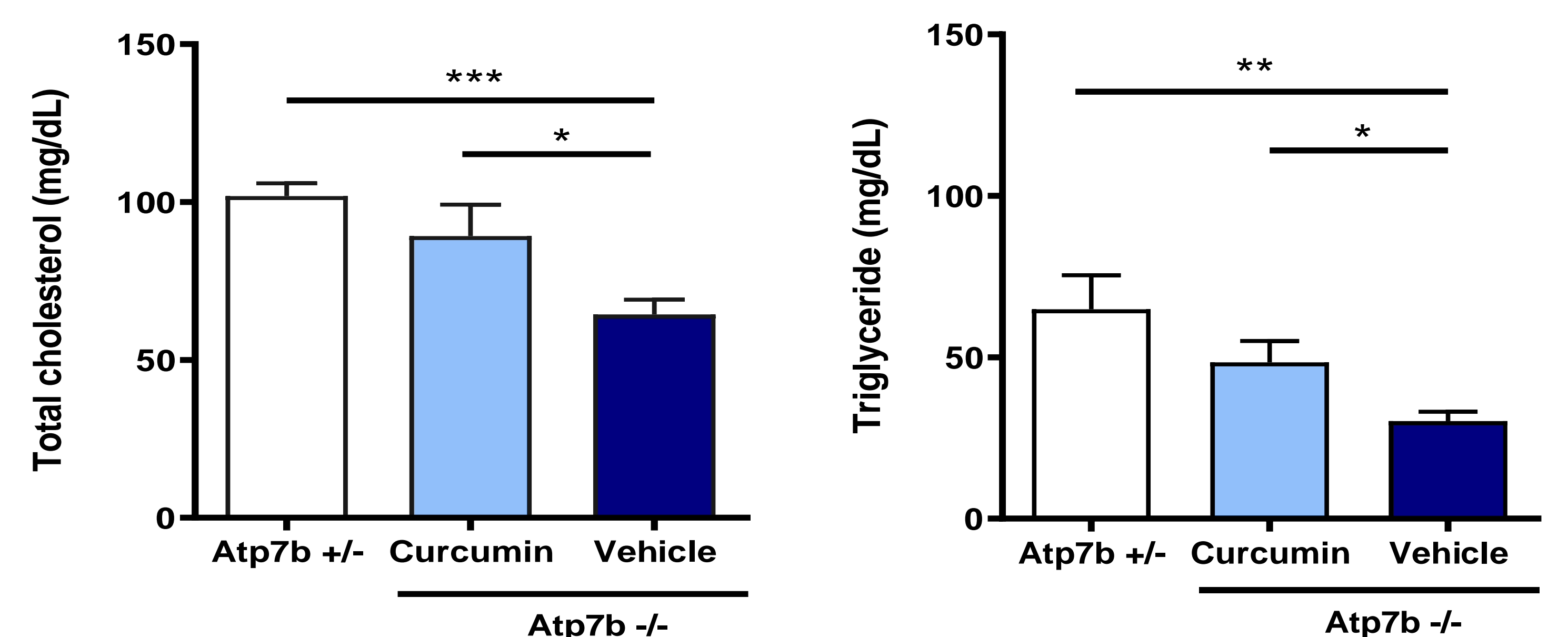


Figure 4. Serum lipid levels are significantly improved in liposome-embedded curcumin treated *Atp7b*^{-/-} WD mice.

D. Liver histology and pathological analysis

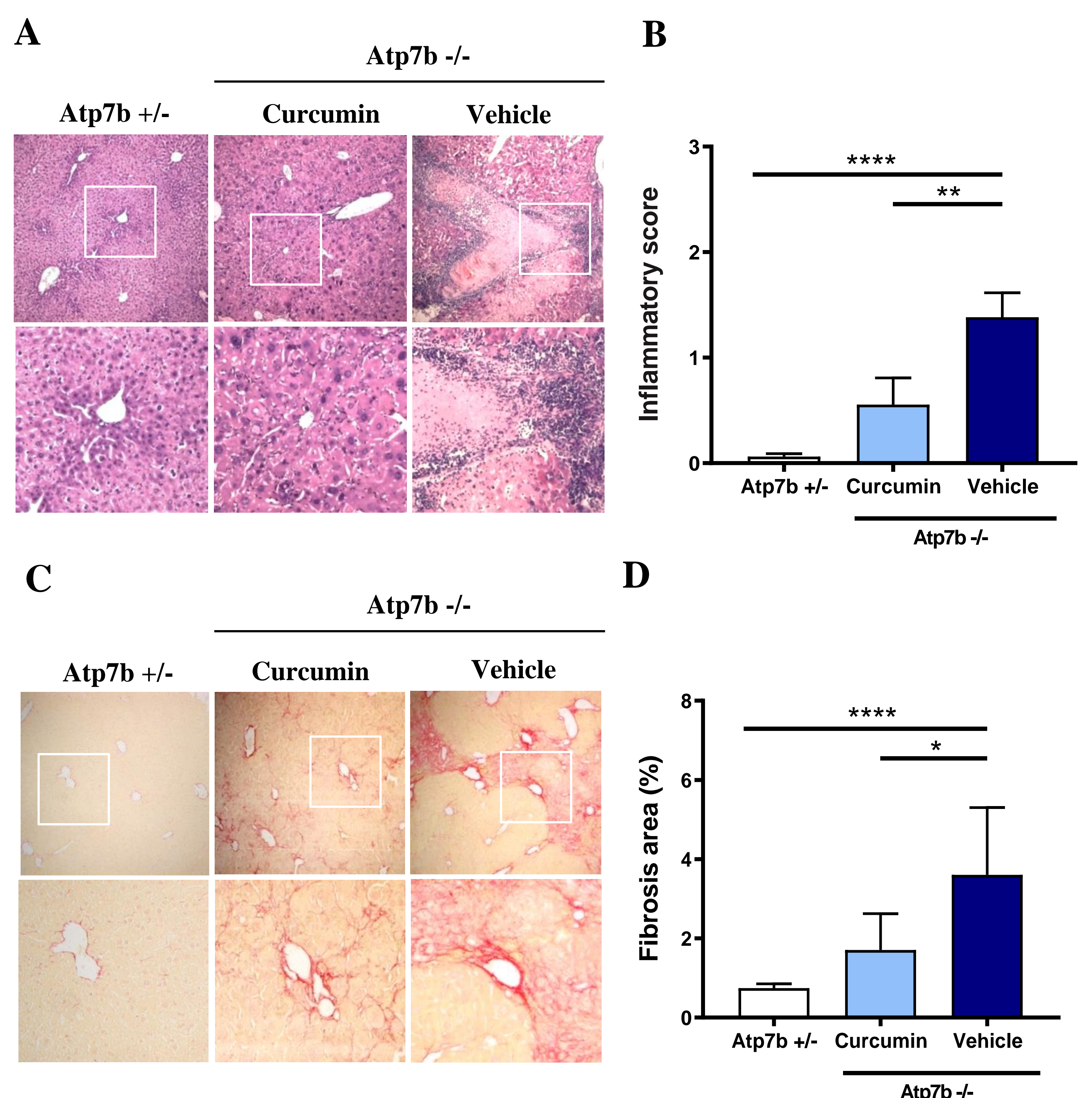


Figure 5. Liposome-embedded curcumin improved liver inflammation and fibrosis in *Atp7b*^{-/-} WD mice. A. Representative hematoxylin and eosin stained liver sections. (Upper 20X, lower 40X). B. Inflammation was scored as 0 = none, 1 = mild, 2 = moderate, and 3 = severe. C. Representative sirius red stained liver sections. D. Sirius red stained area of the liver sections were measured by computer software.

Conclusions

- Liposome-embedded curcumin successfully alleviates liver injury in *Atp7b*^{-/-} WD mice from improving liver morphology, reducing the splenomegaly caused by hepatocytes necrosis and fibrosis.
- Reduced AST, ALT levels and liver pathohistological analysis indicate reduction of liver injury, inflammation and fibrosis.
- Increased lipid levels indicate improvement of liver functions after liposome-embedded curcumin treatment.

References

- Dominik Huster, et al. *Am J Pathol.* 2006 Feb;168(2):423-34
James P. Hamilton, et al. *Hepatology.* 2016 Jun;63(6):1828-41
Ting Feng, et al. *Int J Nanomedicine.* 2017 Aug 21;12:6027-6044