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# **CCl<sub>4</sub> model**

**~Liver cirrhosis model~**

## ***Liver fibrosis***

Liver fibrosis is part of the wound-healing response to liver damage of various origins and represents a major health problem. Although intense research during the last 20 years has led to considerable improvements in the understanding of liver fibrosis pathogenesis, effective antifibrotic therapies are still lacking.

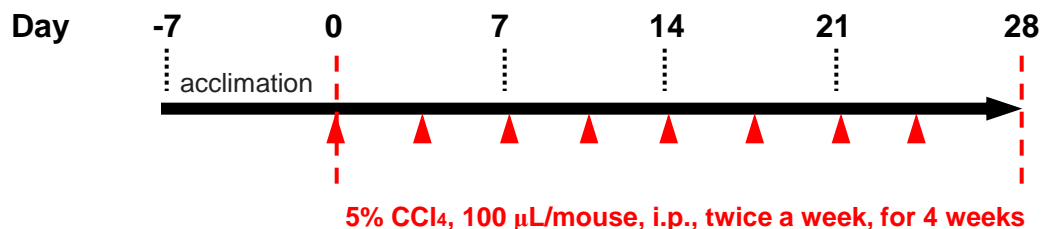
## ***Chronic CCl<sub>4</sub> model***

The carbon tetrachloride (CCl<sub>4</sub>)-induced model of liver fibrosis is a widely used and studies, reliable animal model of hepatic fibrosis. The long-term exposure to CCl<sub>4</sub> causes marked hepatotoxicity with resulting inflammation and fibrosis.

## Induction of the CCl<sub>4</sub> liver fibrosis model

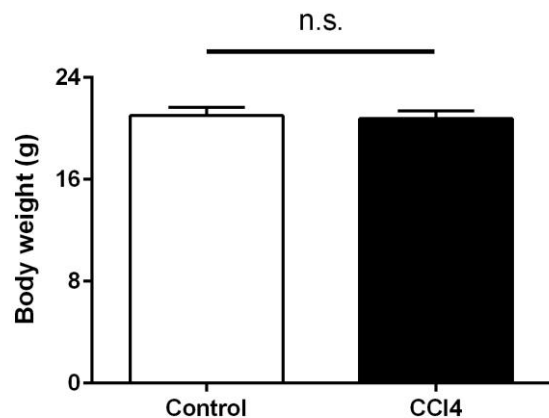
CCl<sub>4</sub> model  
(Mouse: C57BL/6J, ♀, 7 weeks of age)

*i.p.*: intraperitoneal administration

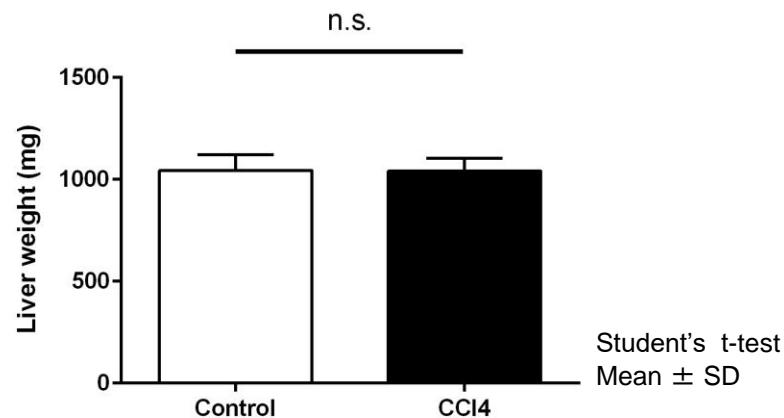


## Body weight and liver weight (General data)

### Body weight

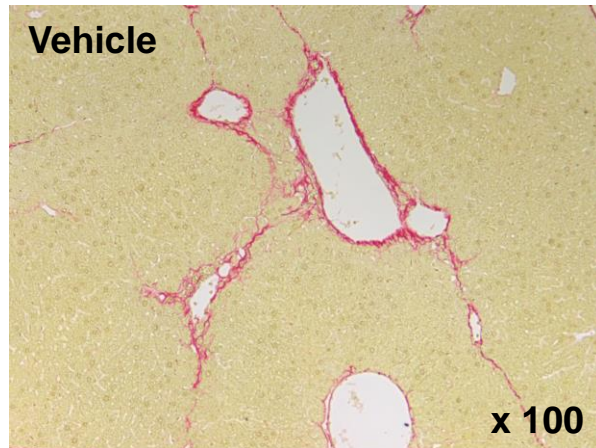
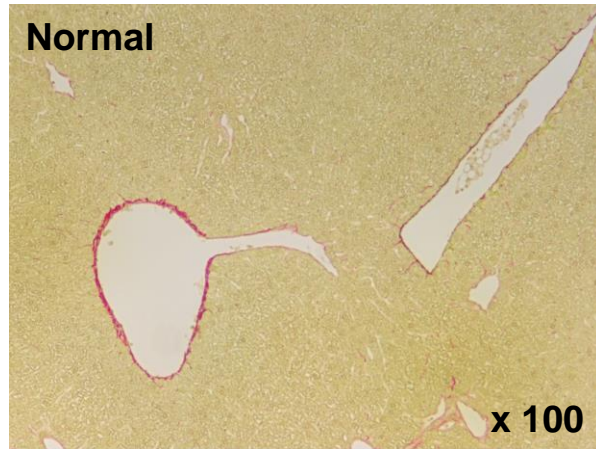


### Liver weight

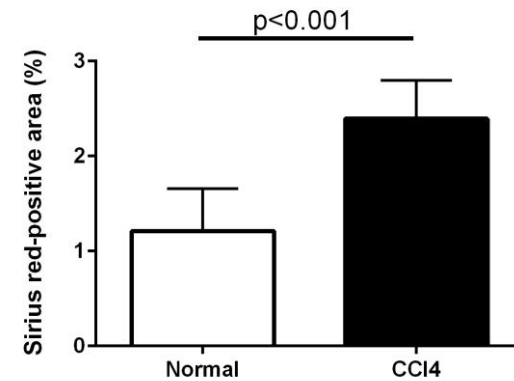


■ CCl<sub>4</sub> treatment does not affect general condition.

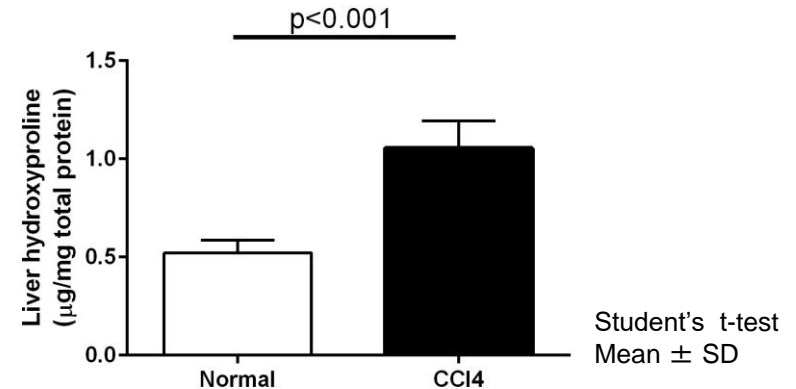
## Sirius red staining and Fibrosis area



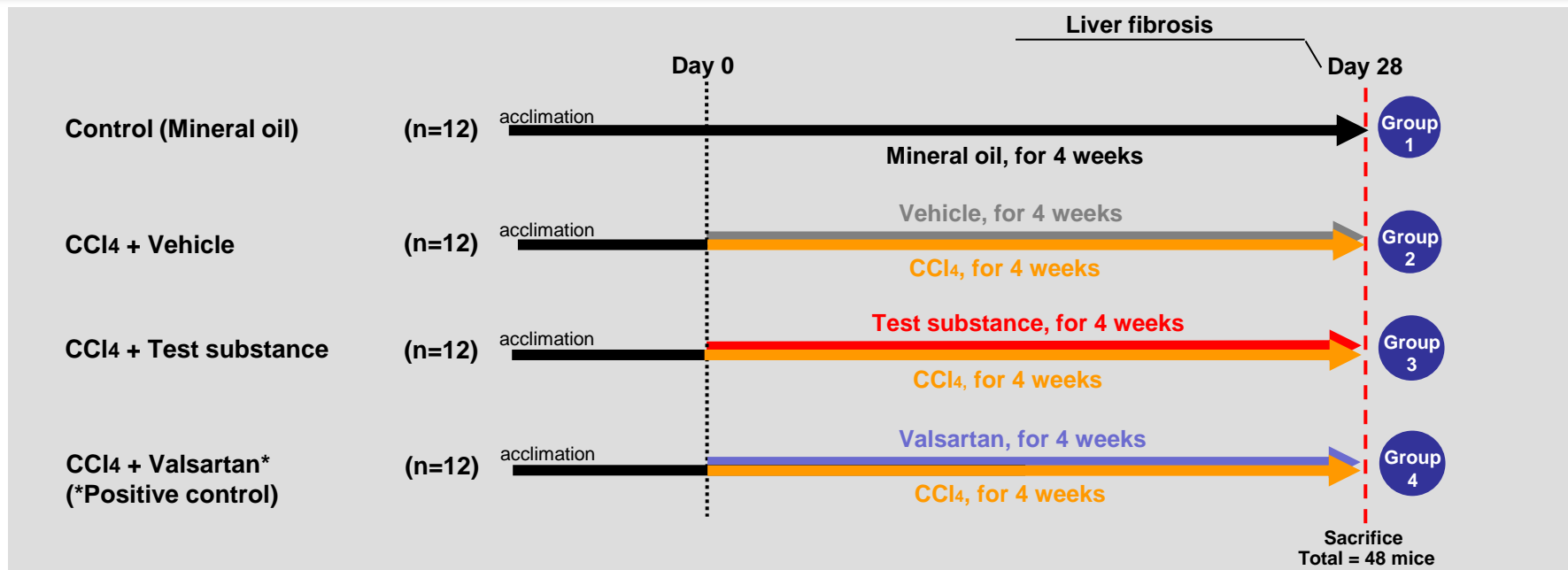
## Sirius red-positive area



## Liver hydroxyproline



■ Sirius red positive area and Liver hydroxyproline content are significantly increased compared with normal mice.



## Study design

- **Aim of the study:** To investigate the hepatoprotective efficacy of test substance on liver fibrosis

- **Route of administration:** oral/ i.p./ i.v./ s.c.

- **Arm:** 4

Control, vehicle, test substance, positive control

- **The number of mice/group** at initiation: n=12

- **Randomization:** Body weight before treatment

- **Treatment period:** CCl<sub>4</sub> for 4 weeks

- **Endpoints:**

Biochemistry: ALT, liver hydroxyproline

Histological improvement: Sirius red staining

<Optional analytical items>

Immunohistological staining (Collagen Type 1, Collagen Type 3,  $\alpha$ -SMA, ...)

Biochemistry (AST, ...)

Gene expression in the liver (Collagen Type 1, Collagen Type 3,  $\alpha$ -SMA, TNF- $\alpha$ , TIMP-1, ...)

General condition