## Supplementary Data

***Supplementary Table 1. Synopsis of findings***

| Variable | ***nor*UDCA** | **T-*nor*UDCA** | **di*nor*UDCA** |
|---|---|---|---|
| **Histology** | improved | slightly improved | worsened |
| **Serum AST and AP** | improved | unchanged | worsened |
| **Biliary bicarbonate output** | increased | less increased | unchanged |
| **Detoxification pathways** | induced | unchanged | induced |
| **Cholangiocyte secretion** | stimulated | less stimulated | less stimulated |
| **Biliary bile acid concentration** | unchanged | unchanged | unchanged |
| **Hepatic bile acid levels** | increased | unchanged | unchanged |
| **Serum bile acid levels** | increased | unchanged | unchanged |

*Nor*UDCA-fed animals (*nor*UDCA), tauro-*nor*UDCA-fed animals (T-*nor*UDCA), di*nor*UDCA-fed animals (di*nor*UDCA).

***Supplementary Figure S1. Structures of* nor*UDCA*, *tauro*-nor*UDCA* and *di*nor*UDCA***. *Nor*-ursodeoxycholic acid (*nor*UDCA) results from side chain-shortening of ursodeoxycholic acid (UDCA) by one methyl group. Side chain shortening of *nor*UDCA by another methyl group results in di*nor*ursodeoxycholic acid (di*nor*UDCA). Tauro-*nor*ursodeoxycholic acid (T-*nor*UDCA) was obtained by taurine-conjugation of *nor*UDCA.

***Supplementary Figure S2*. Nor*UDCA is more effective than tauro-nor*UDCA and di*nor*UDCA in reducing sclerosing cholangitis and biliary fibrosis in Mdr2$^{-/-}$ mice*.** Liver histology (H&E staining) in standard chow-fed (Control), *nor*UDCA-fed, tauro-*nor*UDCA-fed (T-*nor*UDCA), and di*nor*UDCA-fed *Mdr2*$^{-/-}$ mouse (original magnification 20x). Compared to striking

reduction of bile duct injury in *nor*UDCA-treated *Mdr2*$^{-/-}$ mouse, the effects of tauro-*nor*UDCA are much weaker. Di*nor*UDCA had no influence on large bile duct injury. **bd**, bile duct; **pv**, portal vein.