**Supplementary figures**

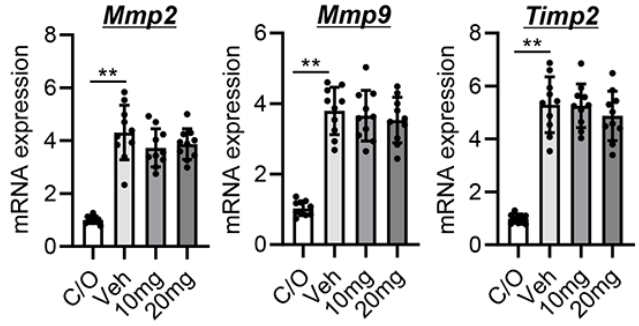


**Figure S1. Effect of tofogliflozin on MMPs and Timp2 expression.** Relative mRNA levels of *Mmp2*, *Mmp9*, and *Timp2* in the liver of experimental rats. *Gapdh* was used as an internal control for qRT-PCR. Quantitative values are indicated as fold changes to the values of C/O group. Data are the mean ± SD (n = 10). **P < 0.01, significant difference between groups by Student's t-test. N.S, not significant; C/O, corn oil-injected negative control group; Veh, $CCl_4$+vehicle-treated group; 10mg, $CCl_4$+tofogliflozin (10mg/kg/day)-treated group; 20mg, $CCl_4$+tofogliflozin (20mg/kg/day)-treated group.

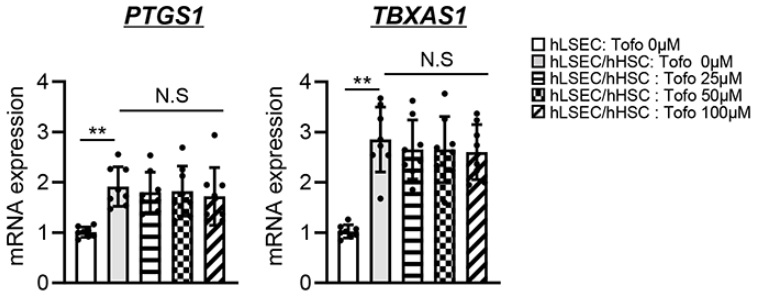


**Figure S2. Effect of tofogliflozin on COX-1 and TXA2 expression in LSEC co-cultured with activated HSC.** Effect of tofogliflozin (Tofo) on mRNA levels of *PTGS1* and *TBXAS1*, encoding cyclooxygenase (COX-1) and thromboxane A2 (TXA2) respectively, in activated human HSC (Ac-hHSC)-stimulated human liver sinusoidal endothelial cell (hLSEC). *GAPDH* was used as internal control for qRT-PCR. Quantitative values are indicated as fold changes to the values of mono-cultured LSEC without tofogliflozin treatment (hLSEC: Tofo 0μM) group. Data are the mean ± SD (n = 8). **P < 0.01, significant difference between groups by Student's t-test.

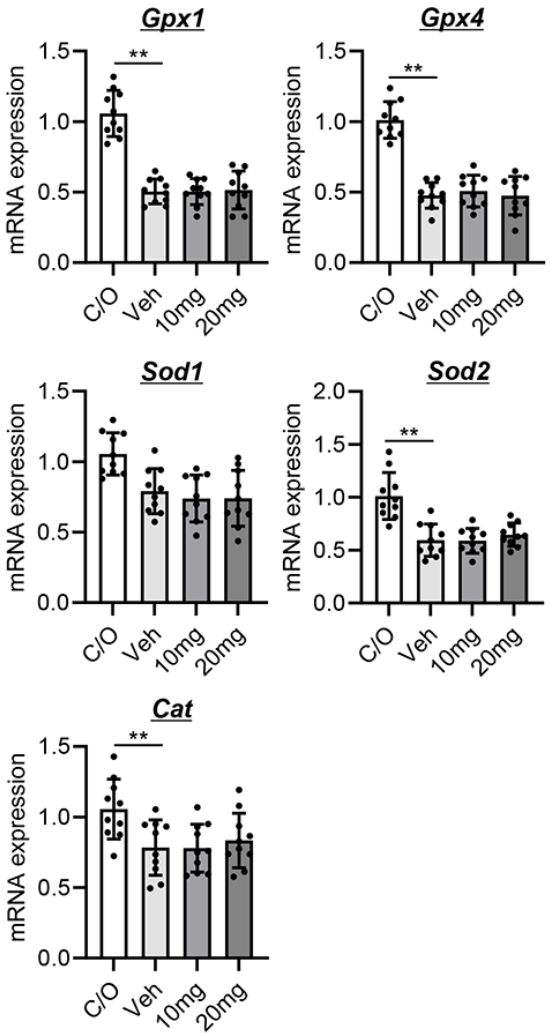


**Figure S3. Effect of tofogliflozin on the anti-oxidant gene expression in the liver of $CCl_4$-treated rats.** Relative mRNA levels of *Gpx1*, *Gpx4*, *Sod1*, *Sod2* and *Cat* in the liver of experimental rats. *Gapdh* was used as an internal control for qRT-PCR. Quantitative values are indicated as fold changes to the values of C/O group. Data are the mean ± SD (n = 10). **P < 0.01, significant difference between groups by Student's t-test. N.S, not significant; C/O, corn oil-injected negative control group; Veh, $CCl_4$+vehicle-treated group; 10mg, $CCl_4$+tofogliflozin (10mg/kg/day)-treated group; 20mg, $CCl_4$+tofogliflozin (20mg/kg/day)-treated group.

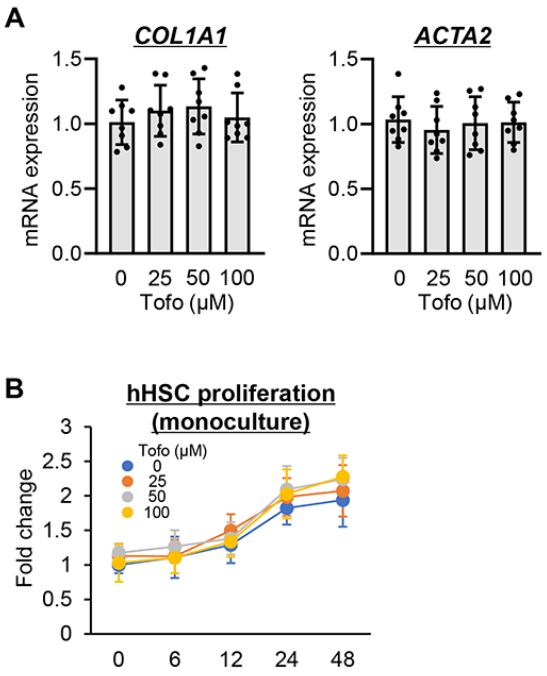


**Figure S4. Direct effect of tofogliflozin on the phenotypes of activated HSC.** (A) Effect of Tofo on the profibrogenic markers expression in activated human hepatic stellate cell (Ac-hHSC) under mono-culture condition. *GAPDH* was used as internal control for qRT-PCR. (B) Effect of Tofo on cell proliferation in in Ac-hHSC under mono-culture condition. Quantitative values are indicated as fold changes to the values of Tofo (0 μM) treatment group. Data are the mean ± SD (n = 8). Significant difference between groups was determined by Student's t-test.

**Supplementary Table S1. List of primers used in q−PCR.**

| Gene | Sense (5'-3') | Antisense (5'-3') |
|---|---|---|
| | Rat | |
| Cth | CCATCCACGTGGGACAAGAG | GGATTTCCAGAGCGGCTGTA |
| Ddah1 | CGTGGCCGATTCTTTGCATT | CATGCCCTTTGCTGGGGATA |
| Gch1 | TCACCTGGTCCCATTTGTGG | TGGCAAGTTTGCTGAGACCA |
| Vegfa | TATATCTTCAAGCCGTCCTGTG | TCTCCTATGTGCTGGCTTTG |
| Vwf | CCTTGTGAAGTGGCTCGTCT | GCAAGTTGCAGTTGACCAGG |
| Ang1 | CAGCTTCTCCAACAGACAAATG | ACGAGTAACCAAGCCTTGAAG |
| Ang2 | ATCTTGTCTTGGCCTCAGCC | AATGTGTAGCTGCAGGGTCC |
| Adgre1 | AATCGCTGCTGGCTGAATACGG | CCAGGCAAGGAGGGCAGAGTT |
| Tnfa | GGCTTTCGGAACTCACTGGA | CCCGTAGGGCGATTACAGTC |
| Il6 | CACTTCACAAGTCGGAGGCT | AGCACACTAGGTTTGCCGAG |
| Il1b | TTGAGTCTGCACAGTTCCCC | GTCCTGGGGAAGGCATTAGG |
| Col1a1 | GGAGAGAGCATGACCGATGG | GGTGGGAGGGAACCAGATTG |
| Acta2 | GGCATCCACGAAACCACCTA | AGGGCTAGAAGGGTAGCACA |
| Pdgfrb | CAGCAAAATAACAGGACAGCG | GCAATAGCACGAACAGCAAC |
| Tgfbr1 | ACTCCCAACTACAGAAAAGCA | CAACTTCTTCTCCCCGCCAT |
| Nrp1 | CACCCGGTCTTCCATAAGGG | AAATCCTCAGCCGGTCTTGG |
| Lgals1 | TCGCTTCAATCATGGCCTGT | GAAGCGGGGGTTGAAGTGTA |
| Mmp13 | TCCATCCCGAGACCTCATGT | CTCAAAGTGAACCGCAGCAC |
| Timp1 | TAAAGCCTGTAGCTGTGCCC | AGCGTCGAATCCTTTGAGCA |
| Mmp2 | GGTGGCAATGGAGATGGACA | CCCGGTCATAATCCTCGGTG |
| Mmp9 | GATCCCCAGAGCGTTACTCG | GTTGTGGAAACTCACACGCC |
| Timp2 | CCTCTTCGCCCCTTGACAAA | CCTCTTGATGGGGTTGCCAT |
| Gpx1 | CAGTCCACCGTGTATGCCTT | GTAAAGAGCGGGTGAGCCTT |
| Gpx4 | ATTCCCGAGCCTTTCAACCC | TATCGGGCATGCAGATCGAC |
| Sod1 | TAACTGAAGGCGAGCATGGG | TCCCAATCACACCACAAGCC |
| Sod2 | ACCGAGGAGAAGTACCACGA | CCTGAACCTTGGACTCCCAC |
| Cat | TTTTCACCGACGAGATGGCA | AAGGTGTGTGAGCCATAGCC |
| Gapdh | AGCTTGTCATCAACGGGAAG | TTTGATGTTAGTGGGGTCTCG |
| | Human | |
| SGLT2 | GGAGATGAATGAGCCCCAGG | GAGGCTGTGGCTTATGGTGT |
| CD34 | CTCCAGCTGTGCGGAGTTTA | TAATAAGGGTCTTCGCCCAGC |

| | | |
|---|---|---|
| VCAM1 | CGAATGAGGGGACCACATCTA | CGCTCAGAGGGCTGTCTATC |
| CD32b | AGCGGATTTCAGCCAATCCC | TGGATGTGGAACGGAAGAGC |
| ET1 | GCTGCCTTTTCTCCCCGTT | GGATGCTCCTGCTCTGATCC |
| GPX1 | TATCGAGAATGTGGCGTCCC | TCTTGGCGTTCTCCTGATGC |
| GPX4 | TCACCAAGTTTGGACACCGT | ATAGTGGGGCAGGTCCTTCT |
| SOD1 | AAAGATGGTGTGGCCGATGT | CAAGCCAAACGACTTCCAGC |
| SOD2 | GCACTAGCAGCATGTTGAGC | GCCTGTTGTTCCTTGCAGTG |
| CAT | AGTGATCGGGGGATTCCAGA | CCACCCTGATTGTCCTGCAT |
| COL1A1 | TGACGAGACCAAGAACTGCC | CCATTCTTTCCAGGGGGACC |
| ACTA2 | CACGATGTACCCTGGGATCG | GCCGATCCACACCGAGTATT |
| TGFB1 | ACCTGCCACAGATCCCCTAT | GAGCAACACGGGTTCAGGTA |
| PTGS1 | CGGAGTCTCTTGCTCTGGTT | GGGGGTAGTGCATCAACACA |
| TBXAS1 | TTTGCTTGGTTGCCTGTTCC | AAAAACAGAACGCTGTCGGC |
| GAPDH | AATGGGCAGCCGTTAGGAAA | GCGCCCAATACGACCAAATC |