**Supplementary Table 3:** Inflammatory modulation by drugs in animal studies

Effects of drugs on inflammatory markers compared to induced cirrhosis in rodent models. \*=significant effect according to authors.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1. **Celecoxib** | | | | | | | | | | | | | |
| **Rat treatment/Marker** | **Cytokines** | **COX-2** | | | **VEGF** | | | **pErk** | | | **Collagen** | | | | | **α-SMA** | | | | | | **Other** | | |
| Celecoxib, TAA.induced cirrhosis  (Gao et al. 2016) | TNF-α↓\* and IL-6↓\* in liver tissue | mRNA and protein ↓\* | | |  | | |  | | | ↓\* | | | | | ↓\* | | | | | | LPS↓\*, effect on intestinal tissue, T-cellsubset sig. raised in portal vein, intestinal permeability↓\* | | |
| Celecoxib, TAA-induced cirrhosis  (Gao et al. 2013) | NA | ↓\* | | | ↓\* | | | ↓\* | | | ↓\* | | | | | mRNA of SMA↓\* | | | | | | Decrease in portal pressure,  CD31-expression ↓\*, Prostaglandin E2 ↓\*, HIF-1α and c-fos↓\* | | |
| Celecoxib,TAA-induced cirrhosis  (Wen et al. 2014) | TNF-α↓, IL-6↓, TGF-β1↓ | ↓\* | | | NA | | | NA | | | NA | | | | | ↓\* | | | | | | PGE2↓\*, MMP-2↓\*, MMP-9↓\*, Phospho-Smad2/3↓\*, Snail1↓\*, FSP-1↓\*, vimentin↓\*, restoring the levels of E-cadherin\* | | |
| Celecoxib and octreotide, TAA-induced cirrhosis  (Gao et al. 2016) | NA | ↓\* | | | ↓\* | | | ↓\* | | | ↓\* | | | | | mRNA of SMA↓\* | | | | | | Decrease in portal pressure, CD31-expression↓\*, Prostaglandin E2↓\*, HIF-1α and c-fos↓\* | | |
| Celecoxib, TAA-induced cirrhosis  (Su et al. 2020) | NA | ↓\* | | | NA | | | ↓\* | | | NA | | | | | NA | | | | | | Caspase3↓\*, Caspase 12↓\*, GRP78↓\*, CHOP↓\*, Hyp↓\*. UPR related pathway proteins: XBP1↓\*, ATF4↓\*, IRE1↓\*, ATF6↓\* | | |
| Celecoxib, TAA-induced cirrhosis  (Tang et al. 2021) | TNF-α↓\*, IL-1β↓\*, IL-6↓\*, TGF-β1↓\* | ↓\* | | | NA | | | NA | | | NA | | | | | NA | | | | | | Sig. decrease of extracellular matrix, decrease of spleen weight/body weight. NOX-4↓, non-sign. decrease of IgM and IgG | | |
| 1. **Curcumin** | | |
| **Rodent treatment/Marker** | **Cytokines** | **Nrf-2 mRNA** | | **NF-kB-p65** | | | | | | **iNos** | | | **eNos** | | | | **COX-1** | | **COX-2** | **VEGF** | | | | | | **pErk** | | **Phospho-Akt** | | **Other** | |
| Curcumin to BDL rats (Hsu et al. 2018) | NA | NA | | NA | | | | | | ↓ | | | ↓\* | | | | ↓ | | ↓\* | ↓\* | | | | | | ↓\* | | ↑ | |  | |
| Curcumin to CCl4 rats, (Cai et al. 2017) | TNF-α↓\*, IL-1β↓\*, IL-6↓\*, CINC-1/IL-8↓\* (in serum + liver tissue) | NA | | NA | | | | | | NA | | | NA | | | | NA | | NA | NA | | | | | | NA | | NA | |  | |
| Curcumin, doxazosin and/or carvedilol to CCl4 cirrhotic hamsters  (Macías-Pérez et al. 2019) | NA | Pos. cells to Nrf-2↑\* (for Cu+Ca+D and Cu+D, and Cu alone) | | Pos. cells to NF-kB↓\* (for Cu+Ca) | | | | | | NA | | | NA | | | | NA | | NA | NA | | | | | | NA | | NA | |  | |
| Curcumin to CCl4 rats,  (Hernandez-Aquino et al. 2020) | IL-1β↓\*, IL-10↓\*, TGF-β↓\* | NA | | ↓\* | | | | | | NA | | | NA | | | | NA | | NA | NA | | | | | | NA | | NA | | CTGF ↓\*MMP-9↓\*, MMP-2↓\*, Col-1↓\*, MMP-13↓\*, Smad-7↓\*, α-SMA↓\* and Smad-3↓\*. | |
| 1. **Pentoxifylline and Diosmin** | | |
| **Rat treatment/Marker** | **Cytokines** | **MDA** | **SOD** | | | | **GSH** | | **NADPH-oxidase** | | | **Cytoglobin** | | | | **Nrf-2 mRNA** | | **Keap-1** | | | **P38-MAPK** | | **NF-kB-p65** | **iNos** | **eNos** | | **Other** | | | | | |
| Diosmin  (Ali et al. 2018) |  | ↓\* | ↑\* | | | | ↑\* | | ↓\* | | | ↑\* | | | | ↑\* | | ↓\* | | | ↓\* | | ↓\* | ↓\* | ↑\* | |  | | | | | |
| Pentoxifylline  (Ali et al. 2018) |  | ↓\* | ↑\* | | | | ↑\* | | ↓\* | | | ↑\* | | | | ↑\* | | ↓\* | | | ↓\* | | ↓\* | ↓\* | ↑\* | |  | | | | | |
| Pentoxifylline + Diosmin  (Ali et al. 2018) |  | ↓\* | ↑\* | | | | ↑\* | | ↓\* | | | ↑\* | | | | ↑\* | | ↓\* | | | ↓\* | | ↓\* | ↓\* | ↑\* | |  | | | | | |
| Diosmin (high and low dose)  (Tahir et al. 2012) | TNF-α↓\* (both doses) | ↓\* (both doses) | NA | | | | ↑\*  (both doses) | | NA | | | NA | | | | NA | | NA | | | NA | | ↓\* (both doses) | ↓\* (both doses) | NA | | Alcohol dehydrogenase↓\* (high dose), COX-2↓\* (both doses), CYP 450 2E1↓\* (both doses), Xanthine oxidase↓\* (both doses), GPx↑\*(both doses), GR↑\*  (both doses), Catalase↑\*  (both doses) | | | | | |
| Diosmin  (Ali et al. 2018) | TGF-β ↓\* | ↓\* | ↑\* | | | | ↑\* | | NA | | | ↑\* | | | | ↑\* | | ↓\* | | | ↓ | | ↓ | ↓ | ↑ | | HYP↓\* | | | | | |
| Sildenafil  (Ali et al. 2018) | TGF-β ↓\* | ↓\* | ↑\* | | | | ↑\* | | NA | | | ↑\* | | | | ↑ | | ↓\* | | | ↓ | | ↓ | ↓ | ↑ | | HYP↓\* | | | | | |
| Sildenafil + Diosmin  (Ali et al. 2018) | TGF-β ↓\* | ↓\* | ↑\* | | | | ↑\* | | NA | | | ↑\*\* | | | | ↑\* | | ↓\* | | | ↓\*\* | | ↓\*\* | ↓\*\* | ↑ | | HYP↓\*\* | | | | | |
| 1. **Glycyrrhizin arginine salt** | | |
| Zhang et al. 2018: | | |
| **Rat treatment/Marker** | **Cytokines** | **MDA** | **SOD** | | | | **GSH** | | **NADPH-oxidase** | | | **Cytoglobin** | | | | **Nrf-2 mRNA** | | **Keap-1** | | | **P38-MAPK** | | **NF-kB-p65** | **iNos** | **eNos** | | **COX-1** | | **α-SMA** | | **Other** | | |
| Low dose | TGF-β↓\* immunof | NA | NA | | | | NA | | NA | | | NA | | | | NA | | NA | | | NA | | NA | NA | NA | | NA | | ↓ immunof+western blot | |  | | |
| High dose | TGF-β↓\* immunof+western blot, TNF-α ↓\* western blot | NA | NA | | | | NA | | NA | | | NA | | | | NA | | NA | | | NA | | ↓\* | NA | NA | | NA | | ↓\* immunof + western blot | | ↓\* for MMP-2 and MMP-9 | | |
| 1. **Statins** | | |
| **Rat treatment/Marker** | **Cytokines** | **iNOS** | | | | **Collagen** | | | **α-SMA** | | | | | | **Other** | | | | | | | | |
| Tripathi et al. 2018 | |
| LPS (ACLF) | mRNA: IL-1β ↑\*, IL-6 ↑ ↑\*, TNF-α ↑\*, IL-10 ↓ | ↑\* (protein), ↑\* (mRNA) | | | | NA | | | NA | | | | | | TLR-4 ↔, ICAM protein↑\*,mRNA↑\*, protein CD-68:↑ | | | | | | | | |
| Simvastatin | mRNA: IL-1β ↑\*, IL-6 ↑\*,\*\*, TNF-α↔\*\*, IL-10 ↓ | ↑ (protein), ↑\*.\*\* (mRNA) | | | | NA | | | NA | | | | | | TLR-4↔, ICAM protein↑ mRNA: ↑\*,\*\*, protein CD-68↓\* | | | | | | | | |
| Meireles et al. 2017 | |
| BDL + hypovolemic shock and resuscitation | IL-1β ↑, IL-6 ↑ | NA | | | | NA | | | NA | | | | | |  | | | | | | | | |
| BDL + hypovolemic shock and resuscitation + Simvastatin | Normalized IL-1β and IL-6 | NA | | | | NA | | | NA | | | | | |  | | | | | | | | |
| Jang et al. 2018 | |
| TAA+Simvastatin | TGF-β ↓\* | NA | | | | ↓ | | | ↓ | | | | | |  | | | | | | | | |
| TAA+Simvastatin + MSCs | TGF-β ↓\* | NA | | | | ↓ | | | ↓ | | | | | |  | | | | | | | | |
| 1. **Lanifibranor** | |
| **Rat treatment/Marker** | **Cytokines** | **iNOS** | | | | **Collagen** | | | **α-SMA** | | | | | | **Other** | | | | | | | | |
| Boyer-Diaz et al. 2020 | |
| TAA + Lanifibranor | mRNA: IL-1β↓, IL-6↓\*, TNF-α↓, IL-10↑ | ↓ | | | | NA | | | ↓\* | | | | | | Arg↑, Mrc1↑ | | | | | | | | |
| 1. **WKYMVm** | |
| Jun et al. 2021 | |
| BDL+WKYMvm | IL-6↑\* | NA | | | | ↓\* | | | ↓\* | | | | | | Gp130↑, STAT3↑\*, VEGF↑, VEGFR1↑\*, VEGFR2↑\*, | | | | | | | | |

**Table Legends:**

**α-SMA:** α-smooth muscle actin, **ACLF**: acute on chronic liver failure; **Arg1**: arginase 1; **BDL:** bile duct ligation; **CCl4:** carbon tetrachloride; **c-fos:** *a proto oncogene;* **CHOP:**CCAAT/enhancer binding homologous protein; **CINC-1**: cytokine-induced neutrophil chemoattractant 1; **COX-2:** cyclooxygenase 2; **CTGF:** connective tissue growth factor; **eNOS:** endothelial nitric oxide synthase; **iNOS:** inducible nitric oxide synthase; **FSP-1**: fibroblast specific protein 1; **gp130:** glycoprotein 130; **GPx**: gluthathione peroxidase;**GR**: gluthatione reductase; **GSH:** glutathione reductase; **GRP78:** glucose-regulated protein 78; **HIF-1a:** hypoxia-inducible factor 1a; **HYP:** hydroxyproline; **Keap-1**: Kelch-like ECH-associated protein 1; **IL-1β:** interleukine 1β; **IL-6:** interleukine 6; **IL-8:** interleukine 8; **ICAM:** intercellular adhesion molecule; **LPS:** lipopolysaccharide; **MDA:** malondialdehyde; **MMP-2:** matrix metalloproteinase-2; **MMP-9:** matrix metalloproteinase-9; **Mrc1**: mannose receptor C-type 1, **MSCs**: mesenchymal stem cells; **NADPH-oxidase:** nicotinamide adenine dinucleotide phosphate oxidase; **NF-kB-p65:** nuclear factor-kB p65; **NOX-4**: nicotinamide adenine dinucleotide phosphate oxidase-4; **Nrf-2:** Nuclear factor erythroid 2-related factor 2; **P38-MAPK:** P38 mitogen activated protein kinases; **pErk:** endoplasmatic reticulum kinase; **PGE-2:** prostaglandine E-2; **Phospho-Akt:** *antibodies;* **Phospho-Smad2/3:** *antibodies;* **SMA:** smooth muscle actin; **Snail1:** *a gene;* **SOD:** superoxide dismutase; **TAA:** thioacetamide; **TGF-β:** transforming growth factor-β; **TLR4:** Toll-like receptor 4; **TNF-α:** tumor necrosis factor-α; **UPR:** unfolded protein response; **VEGF:** vascular endothelial growth factor; **WKYMVm**: *a hexapeptide*