**Supplementary Figure S1**



**Supplementary Figure S1**. Effects of ethanol consumption and SAMC co-treatment on mice diet intake, respiratory exchange ratio (RER), and energy expenditure in a chronic-binge alcoholic liver injury model (the NIAAA model). Data are expressed as means ± SEM (n = 4). Significant differences between the indicated groups: \*\**p* < 0.01.

**Supplementary Figure S2**



**Supplementary Figure S2.** Hepatic injury alleviation comparison between SAMC and other commonly used agents, including N-acetyl-L-cysteine (NAC, 100 mg/kg, gavage, every other day), resveratrol (0.0125% v/v of total diet), and silibinin (Legalon® SIL, 25 mg/kg, i.p. injection, every other day) in mice with chronic-binge alcoholic liver injury (the NIAAA model). Data are expressed as means ± SEM (n = 4). Significant differences against the pair-fed control group: \*\*\**p* < 0.001. Significant differences against the EtOH (the NIAAA model) group: #*p* < 0.05, ##*p* < 0.01.

**Supplementary Figure S3**



**Supplementary Figure S3.** Effects of ethanol consumption and SAMC co-treatment on mice hepatic insulin receptor (InsR) and insulin receptor substrate-1 (IRS1) expression, at both transcriptional and translational levels. Data are expressed as means ± SEM (n = 4).

**Supplementary Figure S4**



**Supplementary Figure S4.** Effects of ethanol consumption and SAMC co-treatment on mice white adipose tissue (WAT) lipolysis. Changes of (A) abdominal WAT tissue weight and (B) adipocyte size (diameter) in mice treated with a chronic-binge alcoholic liver injury model (the NIAAA model) in the absence or presence of SAMC co-treatment (n = 4). (C) Fatty acid release from epididymal WAT cut from mice and them cultured in Dulbecco’s modified Eagle’s medium for 2 hrs. (D) Key markers expression from epididymal adipose tissue extracted from mice at both transcriptional (n = 4) and translational levels (n = 3). The immunoblot bands were quantified by densitometry analysis. Data are expressed as means ± SEM. Significant differences between the indicated groups: \**p* < 0.05, \*\**p* < 0.01, \*\*\**p* < 0.001.

**Supplementary Figure S5**



**Supplementary Figure S5.** SAMC dose-selection and contribution of ethanol (EtOH) or palmitate acid (PA) to cell injury. (A) SAMC dosage optimization test in AML-12 cell with or without ethanol plus palmitate acid challenge, by the measurements of cell viability, apoptotic ratio, Oil Red O/MTT ratio, and the activity of caspase-3/7 (n = 4). (B) Contribution of EtOH or PA to AML-12 injury, in the absence or presence of SAMC (250 μM) co-incubation (n = 4).

**Supplementary Figure S6**



**Supplementary Figure S6.** Effects of ethanol+PA (palmitate acid) challenge and SAMC co-treatment on AML-12 cell insulin receptor (InsR) and insulin receptor substrate-1 (IRS1) expression, at both transcriptional and translational levels (n = 4).

**Supplementary Figure S7**



**Supplementary Figure S7.** Administration of IGF-1 partially alleviated alcoholic liver disease (ALD)-induced liver damage in mice, in coordination with SAMC. Changes of mice (A) serum chemistry, including ALT, AST, TC, and TG; (B) liver histology stained with H&E or Oil Red O; and (C) hepatic parameters including NAFLD activity score (NAS) score, TG, TNF-α and IL-6 contents after NIAAA induction with or without IGF/SAMC co-administration. (Scale bar = 20 μm; n = 4)

**Supplementary Figure S8**



**Supplementary Figure S8.** Long-term (90-d) safety check of SAMC administration in healthy mice (300 mg/kg, in normal saline; every other day gavage). (A) Histology of the liver, kidneys, spleen, and heart; and (B) key health parameters including serum ALT, AST, free fatty acid (FFA), and blood urea nitrogen (BUN) were tested (n = 6). (Scale bar = 20 μm)

**Supplementary Figure-uncropped WB data**



**Supporting information Table S1.** Primer sequence information for quantitative real-time PCR assay

|  |  |  |  |
| --- | --- | --- | --- |
| Target gene | Direction | Primer sequence (5’-3’) | A. Temp. (oC) |
| *Adiponection* | Forward | TGTTCCTCTTAATCCTGCCCA | 56 |
|  | Reverse | CCAACCTGCACAAGTTCCCTT |  |
| *ACC* | Forward | ATGGGCGGAATGGTCTCTTTC | 56 |
|  | Reverse | TGGGGACCTTGTCTTCATCAT |  |
| *ATGL* | Forward | GAGCCCCGGGGTGGAACAAGAT | 56 |
|  | Reverse | AAAAGGTGGTGGGCAGGAGTAAGG |  |
| *CPT1* | Forward | CTCCGCCTGAGCCATGAAG | 56 |
|  | Reverse | CACCAGTGATGATGCCATTCT |  |
| *GAPDH* | Forward | CTGGGCTACACTGAGCACC | 58 |
|  | Reverse | AAGTGGTCGTTGAGGGCAATG |  |
| *HSL* | Forward | GCCGGTGACGCTGAAAGTGGT | 57 |
|  | Reverse | CGCGCAGATGGGAGCAAGAGGT |  |
| *InsR* | Forward | ATGGGCTTCGGGAGAGGAT | 57 |
|  | Reverse | GGATGTCCATACCAGGGCAC |  |
| *IRS1* | Forward | CGATGGCTTCTCAGACGTG | 56 |
|  | Reverse | CAGCCCGCTTGTTGATGTTG |  |
| *PPARg* | Forward | TCGCTGATGCACTGCCTATG | 56 |
|  | Reverse | GAGAGGTCCACAGAGCTGATT |  |
| *SREBP-1c* | Forward | GATGTGCGAACTGGACACAG | 57 |
|  | Reverse | CATAGGGGGCGTCAAACAG |  |

A. Temp.: Annealing temperature