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Table 1. Nutritional and hepatic parameters.

	C	BD	CS	BDS
Increased body weight (g/day)	5.45 ± 0.24	5.10 ± 0.31	5.38 ± 0.35	5.30 ± 0.35
Kcal intake (Kcal/day)	53.7 ± 3.2	49.44 ± 2.96	55.67 ± 3.34	48.5 ± 2.9
Se from solid intake (µg/day)	3.1 ± 0.2	2.8 ± 0.2	3.13 ± 0.3	2.72 ± 0.2
Se from liquid intake (µg/day)	--	--	2.46 ± 0.21	2.18 ± 0.19
Total Se intake (µg/day)	3.1 ± 0.2	2.8 ± 0.2 aaa	5.6 ± 0.3 ccc	4.9 ± 0.3
HSI (g/g body weight (%))	3.6 ± 0.10	3.9 ± 0.08 *	3.67 ± 0.15	3.71 ± 0.11
AST (U/L)	127 ± 5.2	223 ± 17.1 ***, a	142 ± 4.5	175 ± 12.1
ATL (U/L)	41 ± 1.4	55 ± 2.9 **	42 ± 3.4	57 ± 3.0 ••
AST/ALT ratio	3.15 ± 0.15	4.1 ± 0.19 *, a	3.4 ± 0.20	3.1± 0.27
Total Bilirubin (mg/dL)	0.53 ± 0.034	0.71 ± 0.041 **	0.53 ± 0.036	0.61 ± 0.035
Serum Se levels (µg/L)	213.1 ± 8.3	180.28 ± 6.3 *, aaa	342.1 ± 8.5 ccc	245.1 ± 9.1 •••
Serum MDA levels (mmol/mg protein)	80.5 ± 4.8	139.4 ± 9.9 ***, a	96.4 ± 6.1	109.2 ± 7.5
Serum Se/MDA	100 ± 6.86	45 ± 5.70 ***, a	130± 7.91 c	72 ± 6.37 ••

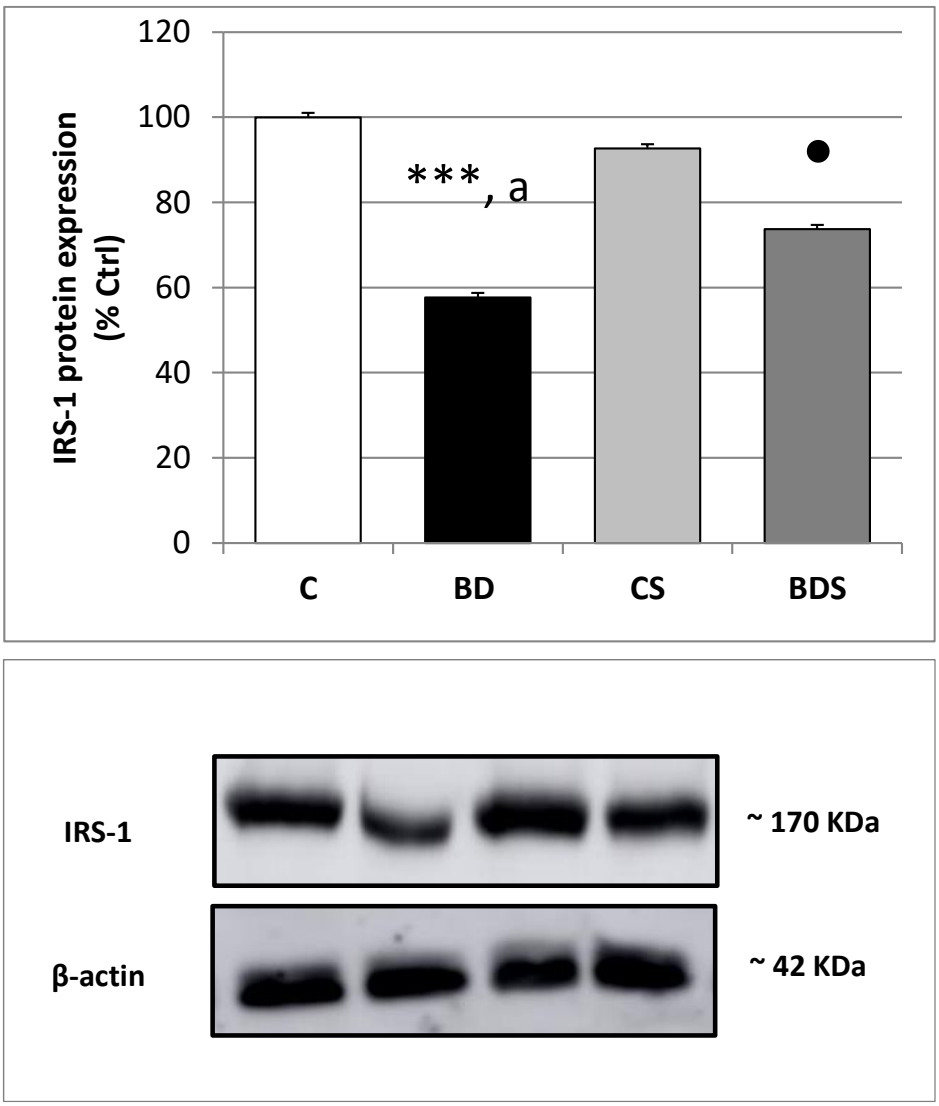
The results are expressed as mean ± SEM and analysed by a multifactorial analysis of variance (one-way ANOVA) followed by the Tukey´s test. The number of animals in each group is 8. HSI: Hepatic somatic index. Groups: C: control group, BD: binge drinking alcohol group, CS: control selenium group, and BDS: binge drinking alcohol selenium group. Signification: BD vs C: *p<0.05, **p<0.01, ***p<0.001; BD vs BDS: ^{a} p<0.05, ^{aaa} p<0.001; C vs CS: ^{c}p<0.05, ^{ccc}p<0.001; BDS vs CS: •p<0.05, ••p<0.01, •••p<0.001.

Table 2. Cardiometabolic risk factors.

	C	BD	CSe	BDSe
Weight (g)	97 ± 4.6	82.8 ± 5.8	92.2± 4.8	80.9± 6.2
Cranium–caudal length (cm)	16.78 ± 0.26	15.82 ± 0.32	16.7 ± 0.37	15.6 ± 0.18
Body Mass Index (BMI) (kg/m^2)	32.33± 2.1	32.34± 1.9	31.8± 2.3	32.9± 1.8
Thoracic Circumference (cm)	8.34 ± 0.23	8.5 ± 0.44	9 ± 0.35	8.7 ± 0.2
Abdominal circumference (cm)	8.5 ± 0.22	9.45 ± 0.32 *	9.43 ± 0.22 c	8.84 ± 0.26
Abdominal/ Thoracic ratio	1.02 ± 0.06	1.11 ± 0.06 *, a	1.04 ± 0.07	1.01 ± 0.04
Glucose (mg/dL)	169.2 ± 7.2	205.7 ± 6.3 *	175.8 ± 10.2	239.1 ± 12 •••
Triglycerides (mg/dL)	65.6 ± 1.2	95.6 ± 4.6 **,a	72.7 ± 3.6	80.3 ± 4.3
Cholesterol (mg/dL)	86.4 ± 2.1	96 ± 2.3 *	86.3 ± 2.3	101.2 ± 3.3 •
Urine albumin (g/dl)	12.73 ± 1.24	12.43 ± 0.96	11.38 ± 0.80	12.68 ± 1.04
MBP (mmHg)	81.9 ± 3.4	101.9 ± 3.6 **, a	82.6 ± 4.1	90.8 ± 2.9

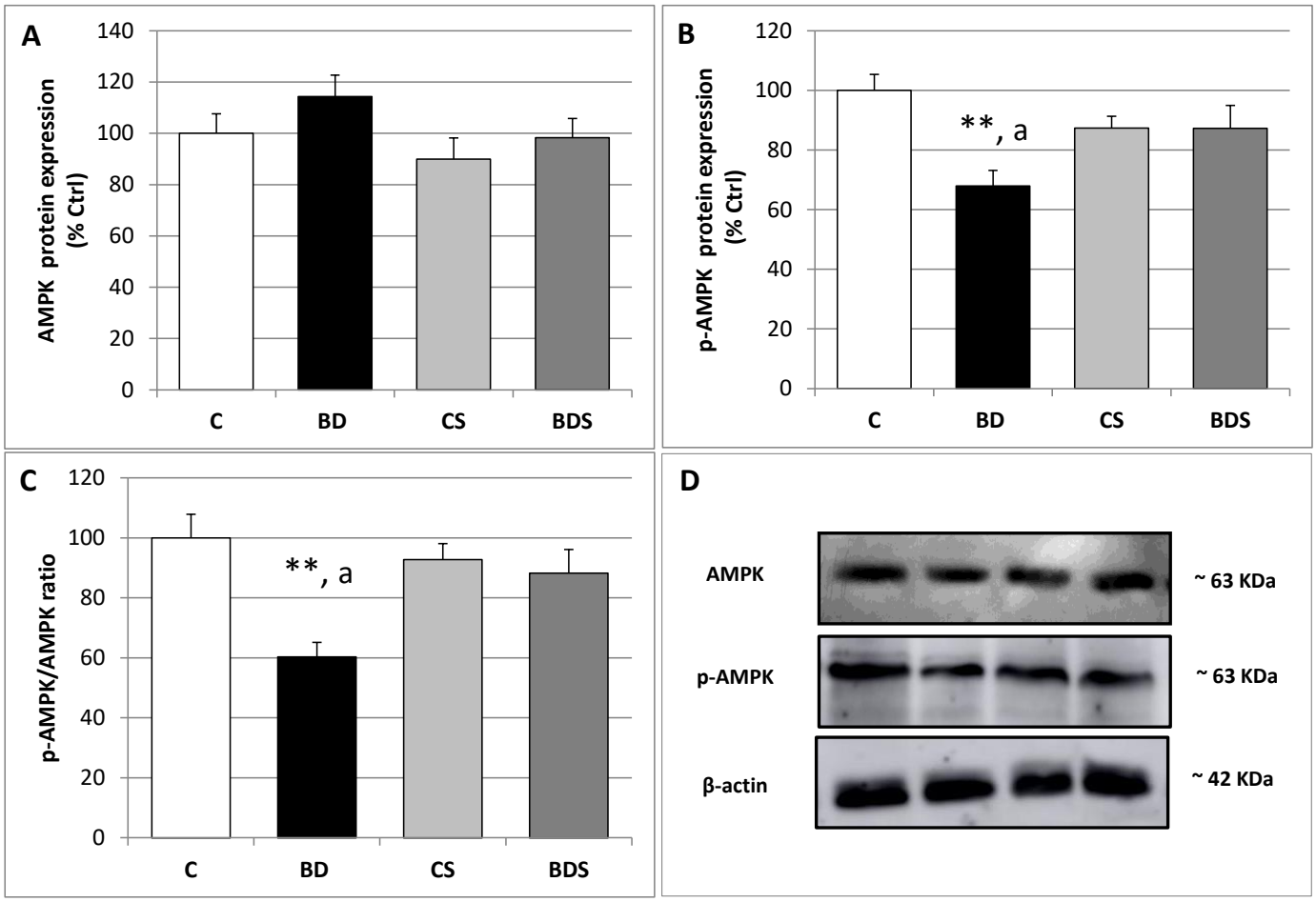
The results are expressed as mean ± SEM and analysed by a multifactorial analysis of variance (one-way ANOVA) followed by the Tukey´s test. The number of animals in each group is 8. Groups: C: control group, BD: binge drinking alcohol group, CS: control selenium group, and BDS: binge drinking alcohol selenium group. Signification: BD vs C: *p<0.05, **p<0.01; BD vs BDS: ^{a} p<0.05; C vs CS: ^{C}p<0.05; BDS vs CS: •p<0.05, •••p<0.001.

Figure 1. Expression of IRS-1 in the liver of adolescent rats. Representative western blot of protein (normalized to β-actin).



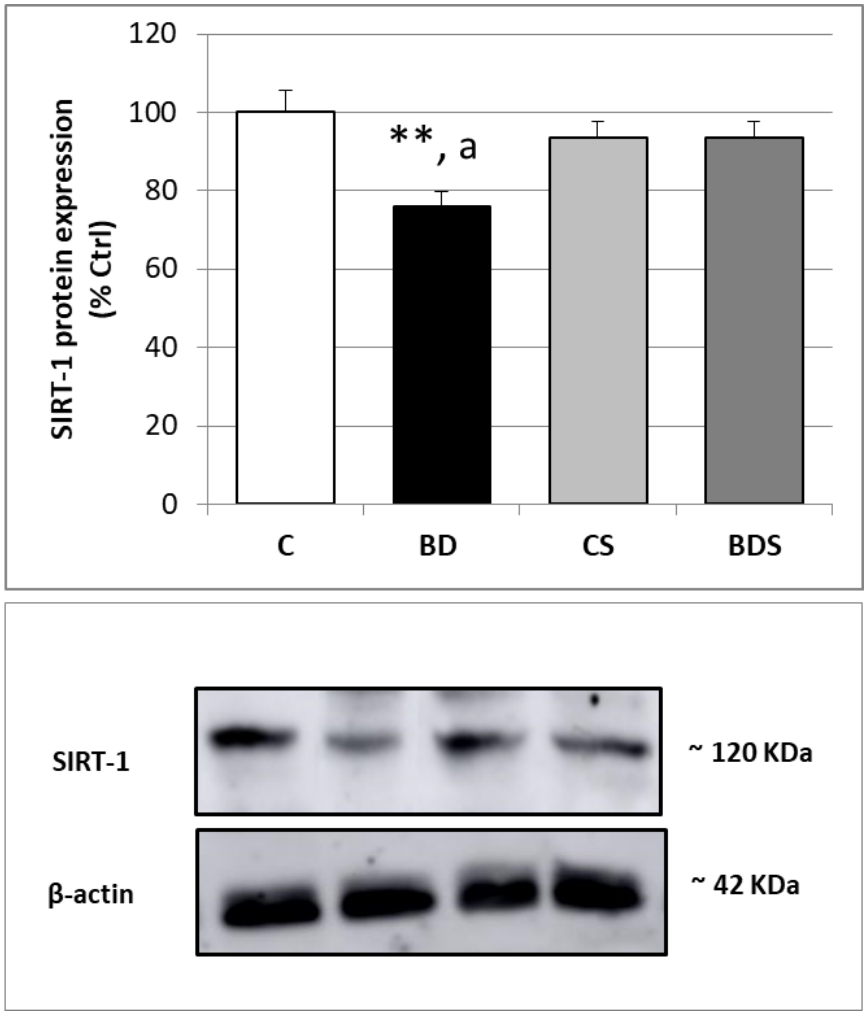
The results are expressed as mean ± SEM and analysed by a multifactorial analysis of variance (one-way ANOVA) followed by the Tukey´s test. The number of animals in each group is 8. Groups: C: control group, BD: binge drinking alcohol group, CS: control selenium group, and BDS: binge drinking alcohol selenium group. Signification: BD vs C: $^{***}p<0.001$; BD vs BDS: ^{a} $p<0.05$; BDS vs CS: $^{\bullet}p<0.05$.

Figure 2. Expression of AMPK (A), pAMPK (B) and its ratio (C) in liver of adolescent rats. Representative western blots of proteins (normalized to β-actin) (D).



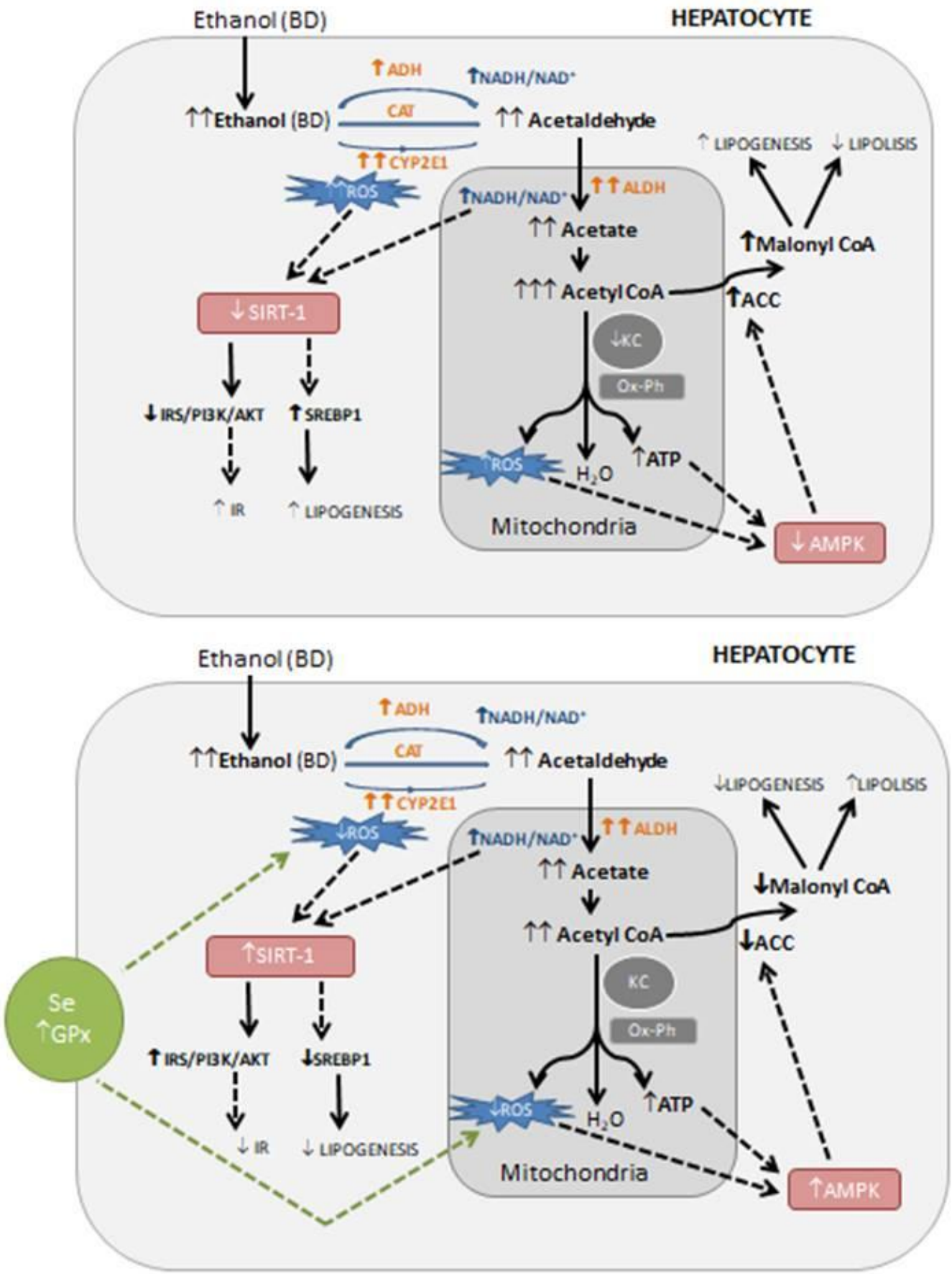
The results are expressed as mean ± SEM and analysed by a multifactorial analysis of variance (one-way ANOVA) followed by the Tukey´s test. The number of animals in each group is 8. Groups: C: control group, BD: binge drinking alcohol group, CS: control selenium group, and BDS: binge drinking alcohol selenium group. Signification: BD vs C: $^{**}p<0.01$; BD vs BDS: ^{a} $p<0.05$.

Figure 3. Expression of SIRT-1 in the liver of adolescent rats. Representative western blot of protein (normalized to β-actin).



The results are expressed as mean ± SEM and analysed by a multifactorial analysis of variance (one-way ANOVA) followed by the Tukey´s test. The number of animals in each group is 8. Groups: C: control group, BD: binge drinking alcohol group, CS: control selenium group, and BDS: binge drinking alcohol selenium group. Signification: BD vs C: $^{**}p<0.01$; BD vs BDS: ^{a} $p<0.05$.

Figure 4: Oxidative metabolism of ethanol after BD exposition in hepatocytes, and its relationship to SIRT1 and AMPK via EROS and NADH/NAD+. Effects of selenium



supplementation.

Ethanol is oxidized in hepatocytes, mostly through the enzyme alcohol dehydrogenase (ADH) which in turn produces an increase in cytoplasmic NADH/NAD+. In BD exposition, ADH is saturated (KM = 1.4 mM) and CYP2E1 increase its activity generating great amount of ROS. The great amount of acetaldehyde generated by these enzymes enters the mitochondria and is oxidized to acetate by acetaldehyde dehydrogenase (ALDH), increasing intramitochondrial NADH/NAD+ ratio. Acetate pass to Acetyl CoA which enters in Krebs cycle (KC) and via oxidative phosphorylation (Ox-Phos) produces ATP and ROS. The increase in ATP and ROS decreases the activity of AMP-dependent protein kinase (AMPK). This decrease leads to higher Acetyl-CoA carboxylase (ACC) activity and higher Malony CoA levels which increases lipogenesis and avoids lipolisis. At high ethanol levels, KC is decreased, increasing Malony CoA levels. High ROS and NADH/NAD+ levels also decrease SIRT-1 activity, which leads to an increase in sterol regulatory element-binding protein 1 (SREBP1) and increases lipogenesis. Decreased SIRT-1 leads to a decreasse in insulin signaling pathway (IRS/PI3K/AKT) increasing insulin resistance (IR). Selenite suplementation by increasing Glutathione Peroxidase (GPx) activity avoids ROS generation and lipid oxidation increasing AMPK and SIRT-1 activities, improving hepatic lipid and energetic profile. Solid lines and hatched lines indicate stimulatory and inhibitory actions, respectively.