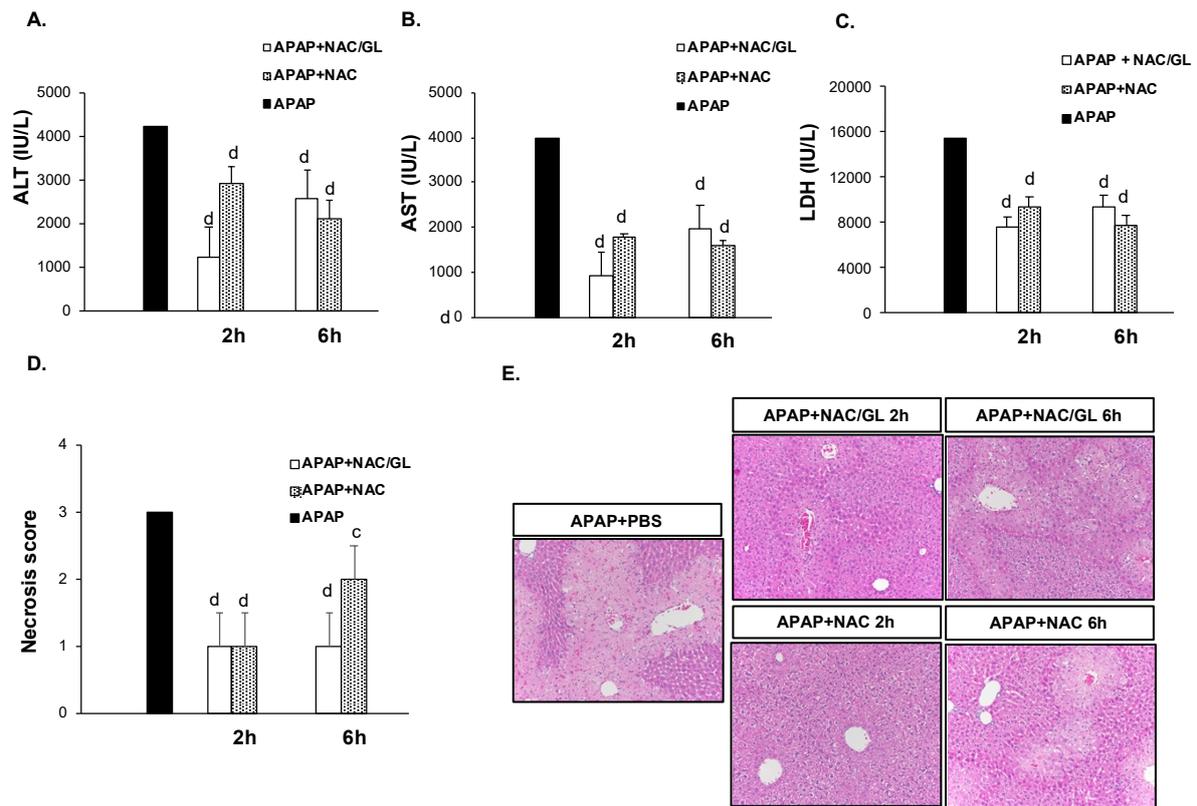


**Supplementary figure 1 Concomitant administration of N-acetyl-p-aminophenol and N-acetylcysteine/glycyrrhizin combination reduced the severity of liver injury in male mice.** A: Alanine aminotransferase levels were measured in vehicle-treated mice and in mice co-treated with N-acetylcysteine/glycyrrhizin (NAC/GL) and N-acetyl-p-aminophenol (APAP) at 12 h (7 mice in each group); B: Aspartate aminotransferase levels were measured in vehicle-treated mice and in mice co-treated with NAC/GL and APAP at 12 h (7 mice in each group); C: Lactate dehydrogenase levels were measured in vehicle-treated mice and in mice co-treated with NAC/GL and APAP at 12 h (7 mice in each group); D: Liver necrosis at 12 h after APAP challenge was scored in the same group of mice; E: Representative hematoxylin and eosin-stained images (magnification  $\times 200$ ) of murine liver 12 h after APAP challenge. Results are expressed as mean  $\pm$  SE. <sup>c</sup> $P < 0.05$ , <sup>d</sup> $P < 0.01$ , <sup>e</sup> $P < 0.001$  vs APAP. APAP: N-acetyl-p-aminophenol; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; NAC: N-acetylcysteine; GL: Glycyrrhizin; LDH: Lactate dehydrogenase.



**Supplementary figure 2 Delayed administration of N-acetylcysteine/glycyrrhizin combination in male mice reduced N-acetyl-p-aminophenol-induced hepatocytes necrosis compare to glycyrrhizin or N-acetylcysteine alone.** A: Plasma alanine aminotransferase levels were evaluated in vehicle-treated mice and in mice treated with N-acetylcysteine/glycyrrhizin (NAC/GL), 2 h or 6 h after N-acetyl-p-aminophenol (APAP) injection (7 mice in each group). Mice were scarified 12 h after APAP administration; B: Plasma aspartate aminotransferase levels were evaluated in vehicle-treated mice and in mice treated with N-acetylcysteine/glycyrrhizin, 2 h or 6 h after APAP injection (7 mice in each group). Mice were scarified 12 h after APAP administration; C: Plasma lactate dehydrogenase levels were evaluated in vehicle-treated mice and in mice treated with NAC/GL, 2 h or 6 hafter APAP injection (7 mice in each group). Mice were scarified 12 h after APAP administration; D: Liver necrosis at 12 h after APAP challenge was scored in the same group of mice; E: Representative hematoxylin and eosin–stained images (magnification  $\times 200$ ) of murine liver 12 h after vehicle or APAP challenge; Results are expressed as mean  $\pm$  SE. <sup>c</sup> $P < 0.05$ , <sup>d</sup> $P < 0.01$ , <sup>e</sup> $P < 0.001$  vs APAP. APAP: N-acetyl-p-aminophenol; AST:

Aspartate aminotransferase; ALT: Alanine aminotransferase; NAC: N-acetylcysteine;  
GL: Glycyrrhizin; LDH: Lactate dehydrogenase.