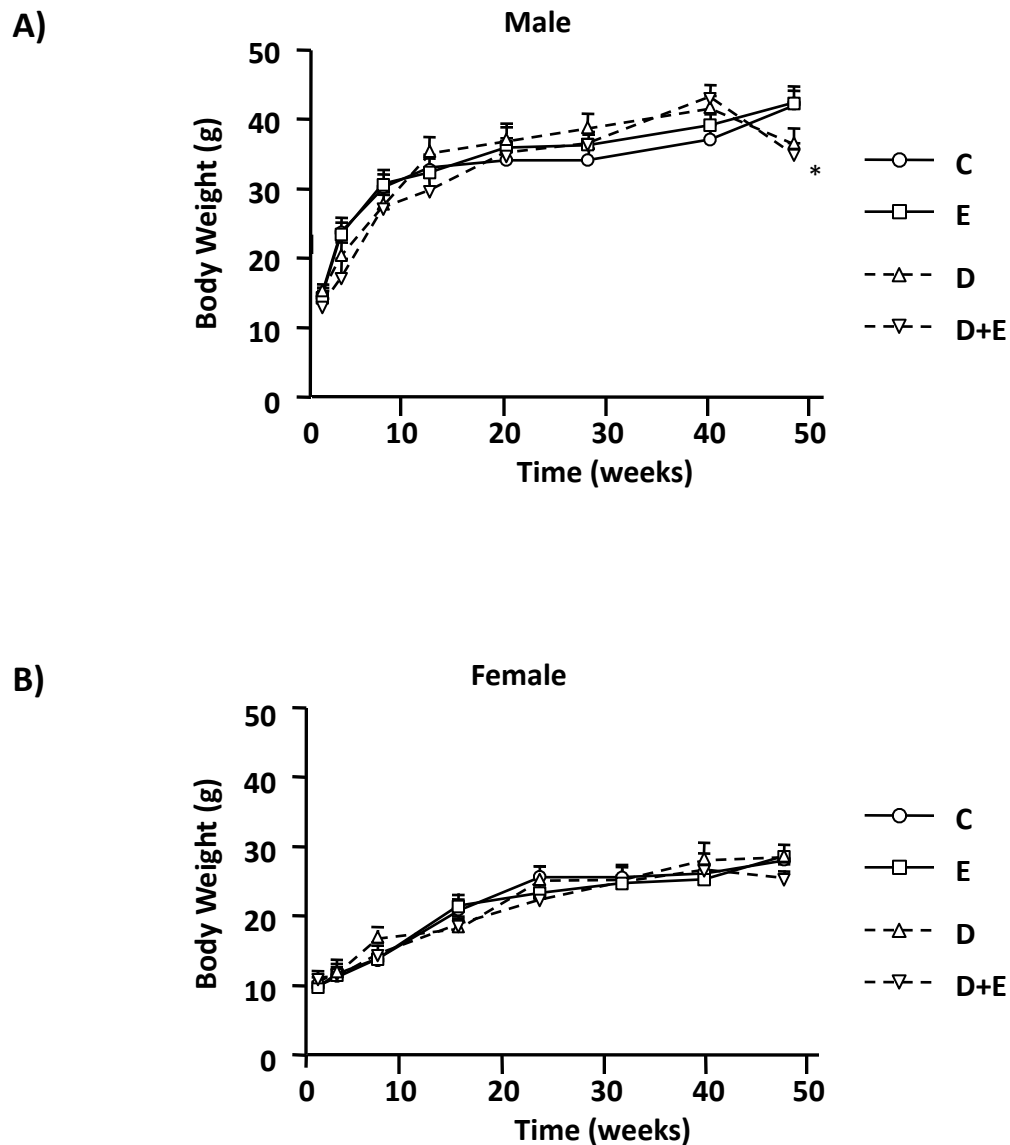


Pathological parameter	Score				
	0	1	2	3	4
<i>Steatosis</i>	Normal liver	Micro-vesicular fat vesicles in hepatocytes (<10%)	Micro/macro-vesicular fat vesicles present in hepatocytes (10-30%)	Micro & macro-vesicular fat vesicles present in hepatocytes (> 30%)	Macro-vesicular fat vesicles present in multiple zones, bridging between affected areas
<i>Necrosis</i>	Normal liver	Individual, scattered necrotic cells	Scattered necrotic cell clusters <10 cells	Scattered necrotic cell clusters >10 cells	Multiple scattered necrotic cell clusters
<i>Inflammation</i>	Normal liver	Scattered inflammatory cells	Scattered small inflammatory cells, hepatocyte damage in 1-3 zones	Scattered small inflammatory cell collections, hepatocyte damage in multiple zones	Large, multiple scattered small inflammatory cell, extensive damage
<i>Fibrosis</i>	Normal liver	0-4%	5-9%	10-14%	>15%

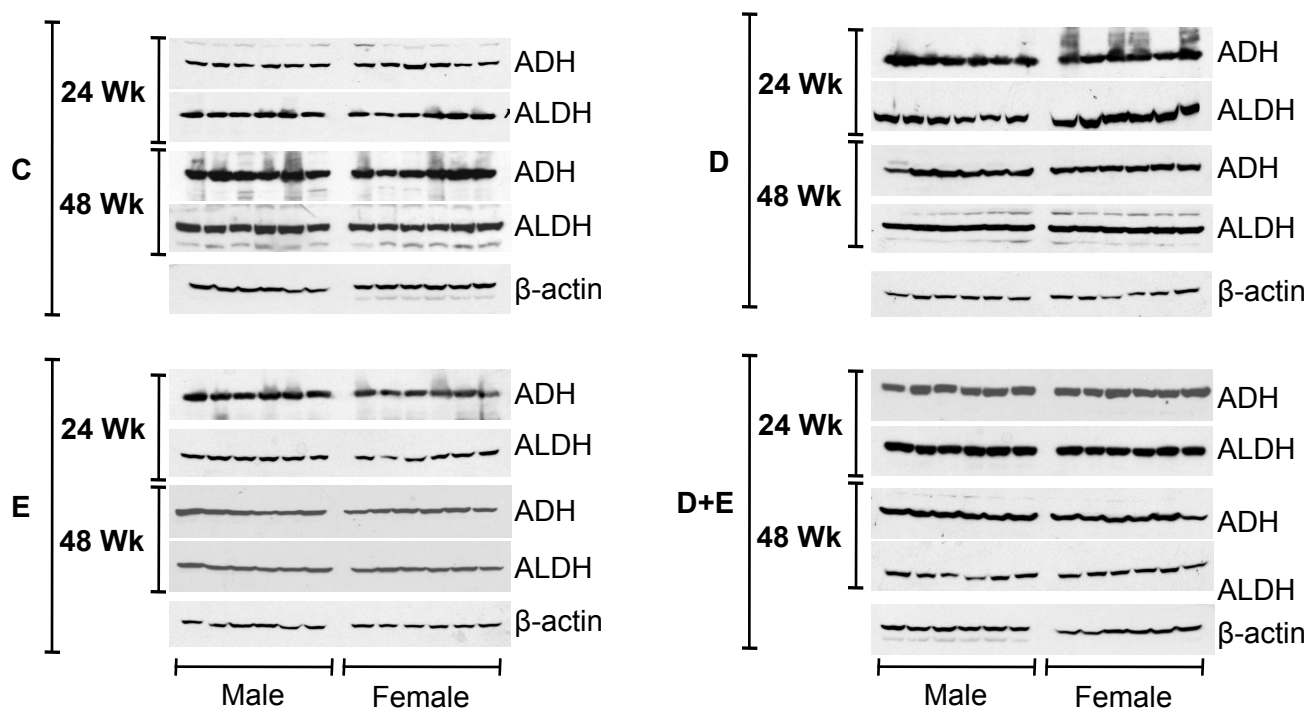
**Supplemental Table 1.** Pathological scoring criteria employed in blind scoring histology slides after H and E and Picrosirius red staining. Following complete scoring, individual scoring criteria were totaled and used to generate a total liver injury score (TLIS).

Pathological parameter	MALE (24 Wks) Group (n)				FEMALE (24 Wks) Group (n)			
	C (9)	E (9)	D (9)	D+E (14)	C (10)	E (10)	D (9)	D+E (14)
<i>Steatosis</i>	0±0	0.69±0.10	1.84±0.26	1.93±0.13	0±0	0.39±0.05	1.37±0.08	1.35±0.14
<i>Necrosis</i>	0±0	0.25±0.05	0.97±0.12	1.14±0.12	0±0	0.14±0.02	0.51±0.10	0.45±0.05
<i>Inflammation</i>	0.04±0.02	0.14±0.05	0.80±0.18	1.01±0.13	0.03±0.02	0.2±0.04	0.96±0.12	0.73±0.08
<i>Fibrosis</i> (% sirius red)	0.18±0.04	0.46±0.20	0.57±0.15	0.68±0.13	0.20±0.06	0.37±0.06	0.78±0.07	0.68±0.07
<b>TLIS</b>	<b>.22±0.04</b>	<b>1.54±0.15</b>	<b>4.18±0.51</b>	<b>4.75±0.32</b>	<b>0.23±0.07</b>	<b>1.10±0.11</b>	<b>3.61±0.18</b>	<b>3.21±0.23</b>
	MALE (48 Wks) Group (n)				FEMALE (48 Wks) Group (n)			
	C (9)	E (9)	D (8)	D+E (14)	C (10)	E (10)	D (9)	D+E (14)
<i>Steatosis</i>	0.01±0.01	0.93±0.17	1.76±0.27	3.00±0.13	0.01±0.01	0.40±0.13	1.10±0.21	1.24±0.30
<i>Necrosis</i>	0.03±0.03	0.31±0.08	0.93±0.06	2.19±0.16	0±0	0.14±0.05	0.60±0.08	0.84±0.10
<i>Inflammation</i>	0.10±0.04	0.16±0.05	0.64±0.13	1.61±0.31	0.13±0.04	0.40±0.14	0.89±0.10	1.63±0.31
<i>Fibrosis</i> (% sirius red)	0.20±0.01	0.35±0.03	1.83±0.08	2.31±0.11	0.16±0.08	0.44±0.12	1.37±0.07	1.51±0.13
<b>TLIS</b>	<b>0.34±0.05</b>	<b>1.75±0.25</b>	<b>5.16±0.29</b>	<b>9.11±0.54</b>	<b>0.30±0.12</b>	<b>1.39±0.19</b>	<b>3.96±0.44</b>	<b>5.13±0.53</b>

**Supplemental Table 2.** Mean pathological scores following blind scoring for steatosis, necrosis, inflammation and fibrosis in control male and female mice (C), and mice maintained on ethanol (E) DEN-initiated (D) or DEN-initiated followed by ethanol (D+E). Data were collected at 24 and 48 weeks and totaled to generate a total liver injury score (TLIS).



**Supplemental Figure 1. A)** Changes in body weight of control (C) male mice compared to those maintained on EtOH-DW (40-48-Wks; E), initiated with DEN (3-Wks; D) or initiated with DEN (3-Wks) followed by EtOH-DE (40-48-Wks; D+E). \* $p < 0.05$  48-Wks versus 40-Wks,  $n =$  minimum of 8/group). **B)** Changes in body weight of C female mice compared to E, D, or D+E).  $n =$  minimum of 8/group)



**Supplemental Figure 2.** Representative immunoblots of alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) expression in liver lysates from control (C) male and female mice compared to those maintained on EtOH-DW (E), initiated with DEN (D) or initiated with DEN followed by EtOH-DE (D+E). Each lane represents lysate from individual liver tissue sample resected at 24 or 48-wks. Equal sample loading was confirmed by stripping membranes and reprobing with an anti- $\beta$ -actin antibody.