

Supporting information

# Safety Evaluations of Oral Single Dose of The Olive Secoiridoid *S*-(-)-Oleocanthal in Swiss albino Mice

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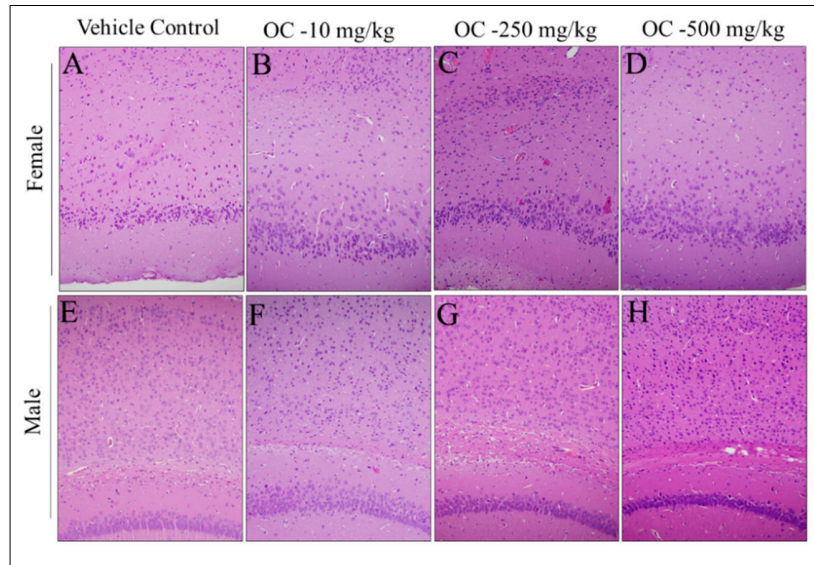


**Supplementary Table S1.** Summary of different organ histopathological evaluations and tentative toxicity scores of OC and vehicle control-treated Swiss albino mice.

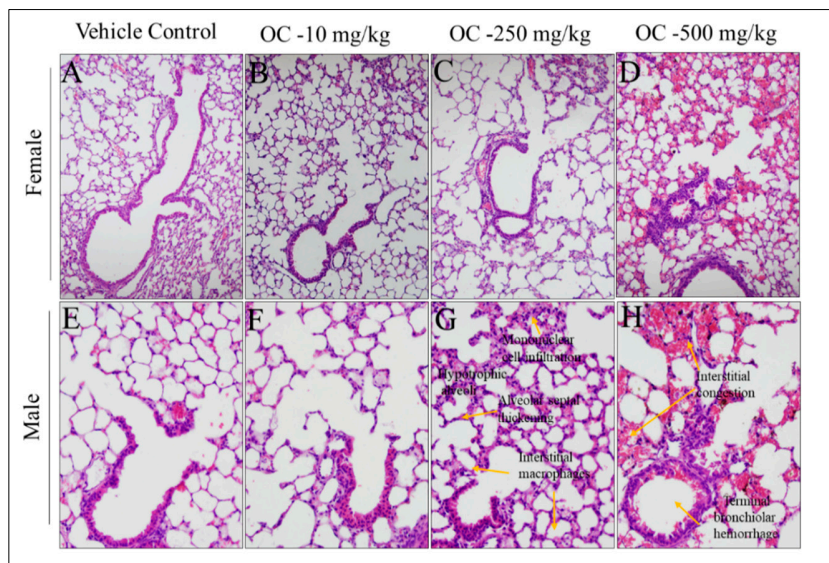
Tissue	Sex	OC Dose (mg/kg)	Toxicity scores (n=5)	Comments
Kidney	Female	Vehicle Control	1,1,1,1,2	1/5 with sporadic hypochromic distal tubules
		10 mg/kg	1,1,1,1,1	0/5 with finding
		250 mg/kg	1,1,1,2	1/4* with tubular dropout
		500 mg/kg	1,1,2,1,2	1/5 with tubular dropout
	Male	Vehicle Control	1,1,1,1,2	1/5 with sporadic exfoliation of proximal tubule cells
		10 mg/kg	1,1,1,2,1	1/5 with sporadic exfoliation of proximal tubule cells
		250 mg/kg	1,2,2,2,2	2/5 with dilated distal tubules 1/5 with sporadic exfoliation of proximal tubule cells 1/5 with tubular dropout 1/5 with mitotic cell
		500 mg/kg	2,3,3,2,2	4/5 with dilated tubules 3/5 with vacuolated tubular cells 2/5 with sporadic exfoliation of tubular cells 1/5 with intratubular cast
Heart	Female	Vehicle Control	1,1,1,1,1	0/5 with finding
		10 mg/kg	1,1,2,1,1	1/5 with hypochromatic foci
		250 mg/kg	2,2,3,2	3/4* with hypochromatic foci
		500 mg/kg	1,2,1,2,2	3/5 with hypochromatic foci
	Male	Vehicle Control	1,1,2,1,1	1/5 with hypochromatic foci
		10 mg/kg	1,1,1,2,1	1/5 with hypochromatic foci
		250 mg/kg	2,1,2,1,1	2/5 with hypochromatic foci
		500 mg/kg	1,1,1,2,3	3/5 with hypochromatic foci

**Toxicity result scores:** 1 = normal tissue, minimal pathological changes.

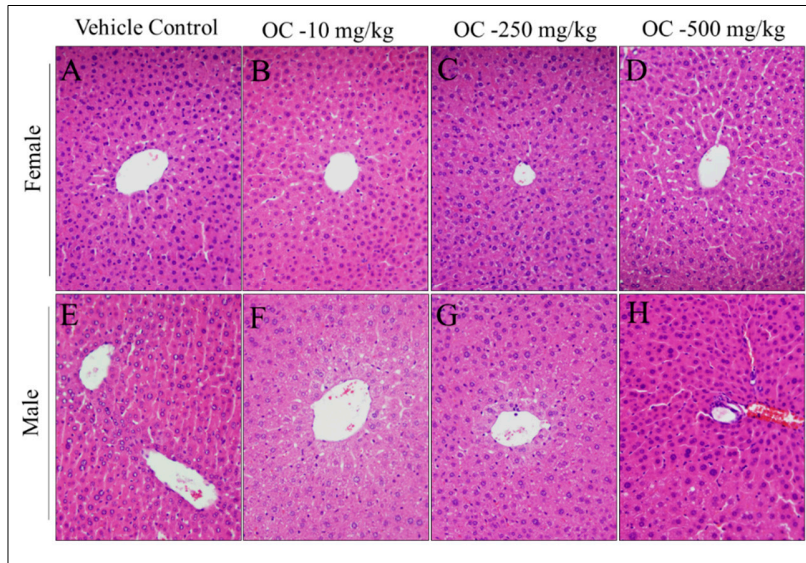
2 = modest pathological changes (limited alteration of specialized tissue structure and regularity, e.g., reduced white pulp, macrophage infiltration, apoptosis; red pulp hemosiderin, increased EMG; swelling; vacuolization). 3 = significant pathological changes (necrosis, hemorrhage, extensive inflammatory infiltrate, pyknosis, karyolysis, karyorrhexis).



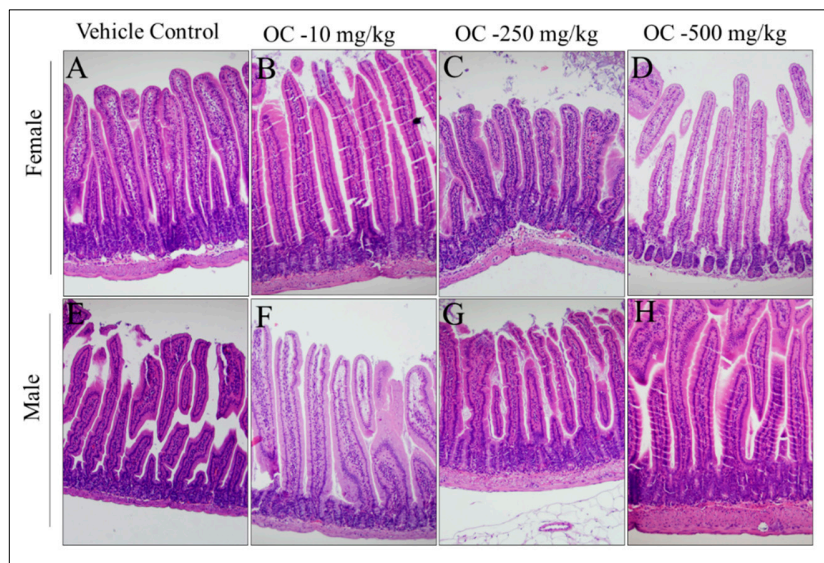
**Supplementary Figure S1-** Histopathological images of the Swiss albino mice brain sections 14 days after exposure to OC single dose treatments. (A) Female vehicle control, (B) Female OC-10 mg/kg, (C) Female OC-250 mg/kg, (D) Female OC-500 mg/kg, (E) Male vehicle control, (F) Male OC-10 mg/kg, (G) Male OC-250 mg/kg, (H) Male OC-500 mg/kg representative sections.



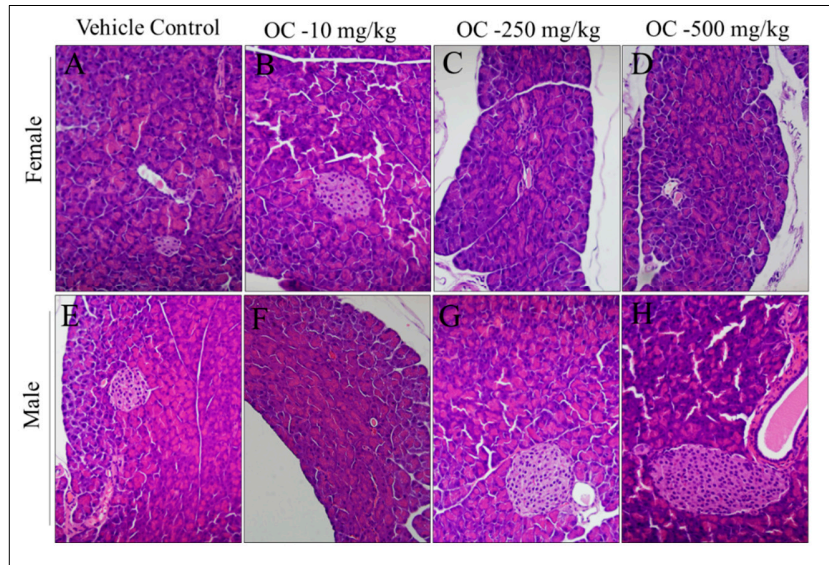
**Supplementary Figure S2-** Histopathological images of lung sections from Swiss albino mice 14 days after exposure to OC single dose treatments. (A) Female vehicle control, (B) Female OC-10 mg/kg, (C) Female OC-250 mg/kg, (D) Female OC-500 mg/kg, (E) Male vehicle control, (F) Male OC-10 mg/kg, (G) Male OC-250 mg/kg, (H) Male OC-500 mg/kg representative sections.



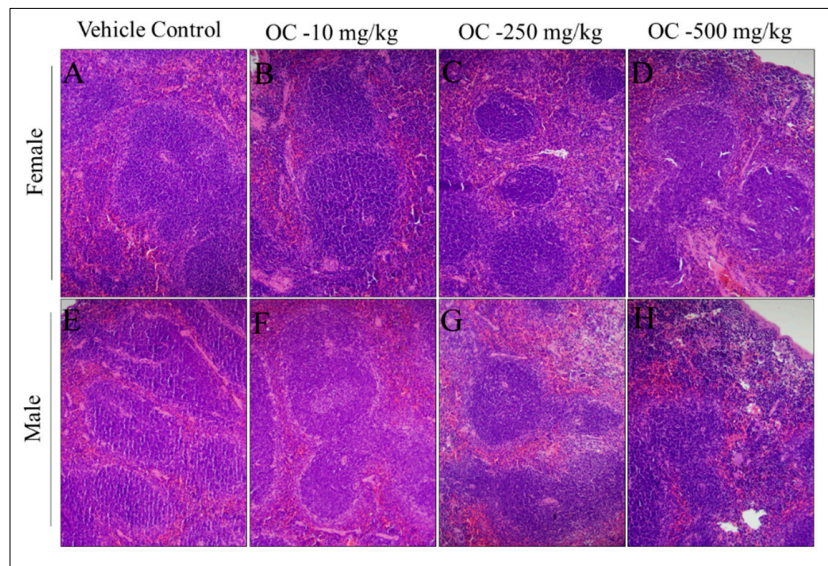
**Supplementary Figure S3-** Histopathological images of liver tissue from Swiss albino mice 14 days after exposure to OC single dose treatments. (A) Female vehicle control, (B) Female OC-10 mg/kg, (C) Female OC-250 mg/kg, (D) Female OC-500 mg/kg, (E) Male vehicle control, (F) Male OC-10 mg/kg, (G) Male OC-250 mg/kg, (H) Male OC-500 mg/kg representative sections.



**Supplementary Figure S4-** Histopathological images of intestine tissue from Swiss albino mice 14 days after exposure to OC single dose treatments. (A) Female vehicle control, (B) Female OC-10 mg/kg, (C) Female OC-250 mg/kg, (D) Female OC-500 mg/kg, (E) Male vehicle control, (F) Male OC-10 mg/kg, (G) Male OC-250 mg/kg, (H) Male OC-500 mg/kg representative sections.



**Supplementary Figure S5-** Histopathological images of pancreas tissue from Swiss albino mice 14 days after exposure to OC single dose treatments. (A) Female vehicle control, (B) Female OC-10 mg/kg, (C) Female OC-250 mg/kg, (D) Female OC-500 mg/kg, (E) Male vehicle control, (F) Male OC-10 mg/kg, (G) Male OC-250 mg/kg, (H) Male OC-500 mg/kg representative sections.



**Supplementary Figure S6-** Photomicrographs of H&E stained spleen from Swiss albino mice 14 days after exposure to OC single dose treatments. (A) Female vehicle control, (B) Female OC-10 mg/kg, (C) Female OC-250 mg/kg, (D) Female OC-500 mg/kg, (E) Male vehicle control, (F) Male OC-10 mg/kg, (G) Male OC-250 mg/kg, (H) Male OC-500 mg/kg representative sections.