



Supplementary Material

Escinosomes: Safe and Successful Nanovesicles to Deliver Andrographolide by a Subcutaneous Route in a Mice Model of Oxaliplatin-Induced Neuropathy

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Table S1. Effect of the acute administration of AG-loaded escinosomes on oxaliplatin-induced behavioral, autonomic, and neurological alterations by Irwin test. The Irwin test was performed 30 minutes following the acute administration of the treatments in oxaliplatin-treated rats. The signs were evaluated semi-quantitatively, according to the observer's personal scale (0 to +4, -4 to 0, or -4 to +4). Each value represents the mean ± SEM of 5 rats per group. **p* < 0.05 vs vehicle + vehicle group.

	Treatments					
	Vehicle + Vehicle	OX + Vehicle	OX + AG-Esc 10 mg/kg	OX + AG 10 mg/kg	OX + Esc	Limits
Behavior						
Spontaneous activity	4 ± 0	2.3 ± 0.2*	2.1 ± 0.1	2.4 ± 0.2	2.0 ± 0.2	4–0
Passivity	0 ± 0	2.0 ± 0.1*	1.9 ± 0.2	2.0 ± 0.2	2.2 ± 0.1	0–4
Cleaning	4 ± 0	4 ± 0	4 ± 0	4 ± 0	4 ± 0	4–0
Curiosity	4 ± 0	2.5 ± 0.2*	2.3 ± 0.1	2.3 ± 0.1	2.6 ± 0.2	4–0
Reactivity	4 ± 0	2.2 ± 0.1*	2.0 ± 0.2	2.3 ± 0.1	2.4 ± 0.1	4–0
Vocalization	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0–4
Central Nervous System Excitement						
Straub tail	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0–4
Tremors	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0–4
Convulsions	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	4–0
Movement						
Ataxia	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0–4
Stereotypies	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0–4
Straightening reflex	4 ± 0	4 ± 0	4 ± 0	4 ± 0	4 ± 0	4–0
Muscular Tone						
Physical strength	4 ± 0	4 ± 0	4 ± 0	4 ± 0	4 ± 0	4–0
Palpebral reflex	4 ± 0	4 ± 0	4 ± 0	4 ± 0	4 ± 0	4–0
Autonomic Signs						
Piloerection	0 ± 0	2.6 ± 0.1*	2.7 ± 0.1	2.5 ± 0.1	2.5 ± 0.2	0–4
Exophthalmos	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0–4
Cyanosis	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0–4
Flush	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0–4
Pallor	0 ± 0	2.8 ± 0.1*	2.7 ± 0.2	3 ± 0.1	2.7 ± 0.1	0–4
Palpebral opening	4 ± 0	4 ± 0	4 ± 0	4 ± 0	4 ± 0	4–0

Salivation	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0–4
Lacrimation	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0–4
Hypohyperthermia	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	- 4/+ 4
Toxicity						
Immediate death	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0–4
Delayed death (48 h)	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0–4

OX = oxaliplatin; **AG** = andrographolide; **Esc** = unloaded escinosomes; **AG-Esc** = AG-loaded escinosomes