

Research Article

Antinociceptive properties of an oral formulation of Δ^9 -tetrahydrocannabinol in aqueous 2-hydroxypropyl- β -cyclodextrin in female rats

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Running title: Analgesic effect of orally administered THC/HP β CD complex

Supplementary material

Supplementary Table 1.

Distribution of the females used in the present study in the different phases of the estrous cycle the day of the behavioral experiments and the day of tissues' sampling for *ex vivo* analyses. The exact number of females belonging to the three treatment groups in each of the four estrous phases is reported (Chi square test, all not significant).

Cohort of female rats	Day of cycle evaluation	Treatment group	P	E	M	D
Acute THC (Tail flick + motor activity)	Day of behavioral tests	22% HP β CD	1	2	1	5
		0.3 mg/kg THC- HP β CD	2	1	2	5
		3 mg/kg THC- HP β CD	2	2	2	4
	Day of sacrifice for tissues sampling	22% HP β CD	2	1	1	5
		0.3 mg/kg THC- HP β CD	2	2	1	5
		3 mg/kg THC- HP β CD	1	2	1	6
Chronic THC (Tail flick + motor activity)	Day of behavioral tests	22% HP β CD	1	2	1	6
		0.3 mg/kg THC- HP β CD	1	3	1	5
		3 mg/kg THC- HP β CD	3	3	0	4
	Day of sacrifice for tissues sampling	22% HP β CD	2	2	1	5
		0.3 mg/kg THC- HP β CD	1	2	2	5
		3 mg/kg THC- HP β CD	2	3	2	3
Acute and chronic THC (Elevated plus maze)	Day of behavioral test after acute treatment	22% HP β CD	2	2	1	3
		0.3 mg/kg THC- HP β CD	1	1	2	4
		3 mg/kg THC- HP β CD	0	3	1	4
	Day of behavioral test after chronic treatment	22% HP β CD	1	3	0	4
		0.3 mg/kg THC- HP β CD	2	2	1	3
		3 mg/kg THC- HP β CD	1	3	1	3

Legend: P = proestrus; E = estrous; M = metestrus; D = dioestrus.

Supplementary Figure 1

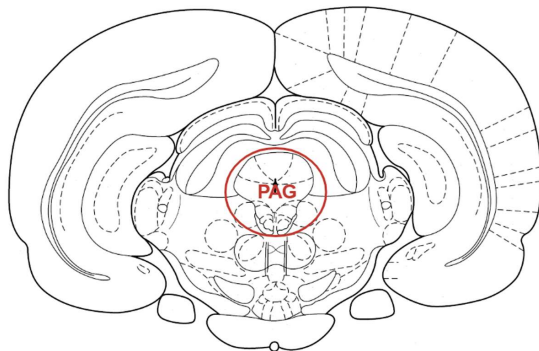


Figure S1. Schematic representation of the brain area interested by the micropunching for the collection of the PAG tissue (evidenced by the red circle) (Bregma = -6.3; Paxinos and Watson, 2007) [47].

Supplementary Figure 2

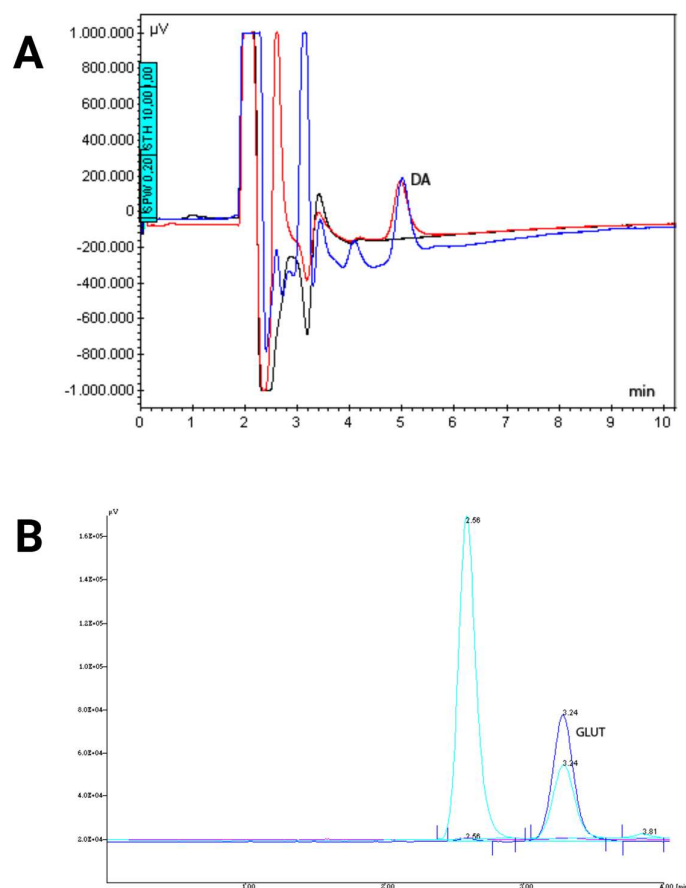


Figure S2. Representative HPLC chromatograms of (A) dopamine (DA) and (B) glutamate (GLUT) concentrations in the PAG tissues from female rats treated with the THC/HP β CD complex or HP β CD 22% (w/v) alone. The black and red lines in the DA chromatogram represent matched blank matrix and a standard sample (5 nM), respectively; the blue line represents a sample from an experimental animal. The purple and dark blue lines in the GLUT chromatogram represent matched blank matrix and a standard sample (10 μM), respectively; the light blue line represents a sample from an experimental animal.