

Design and In Vivo Evaluation of a Microparticulate Depot Formulation of Buprenorphine for Veterinary Use

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Supplement

Table S1: Number of mice used for different experimental set ups.

1. Mice used for hotplate assay and for PK study (Mice were only used once)	
Group	Number of Mice
BUP-Depot	24
Non-retard Formulation	18
NaCl	0
2. Mice used for PK only	
Group	Number of Mice
BUP-Depot	21
Non-retard Formulation	2
NaCl	2
3. Mice used only for hotplate assay once	
Group	Number of Mice
BUP-Depot	15
Non-retard Formulation	0
NaCl	1
4. Mice used for hotplate assay twice ^a	
Group	Number of Mice
First Round	
Non-retard Formulation	22
NaCl	9
Second Round	
BUP-Depot	9
Non-retard Formulation	9 ^b
NaCl	13 ^b
5. Surgical procedure ^b	
Group	Number of Mice
BUP-Depot	6
Non-retard Formulation	6

^a A total of 31 mice were used twice for the hotplate assay. After first round, mice were allocated randomly to new groups after a wash-out phase of 6 days to a second round. ^b Mice that were used twice for the hotplate assay and received only non-retard formulation or NaCl were used after a wash-out phase of 41 days for surgical procedures.

Table S2: Number of mice per group with average weight and average applied dose used for pharmacokinetic study. Data is presented as $\pm$ SD.

Group	Number of Mice	Time Points	Number of Mice per Time Point	Weight [g]	Dose [mg/kg]
BUP-Depot	45	0.5, 2, 5, 72 hours	6	17.7 $\pm$ 1.4	1.1 $\pm$ 0.04
		12, 24, 48 hours	7		
Non-retard Formulation	22	2 hours	6	17.2 $\pm$ 1.9	0.12 $\pm$ 0.01
		12, 24 hours	7		
NaCl	2	-	-	19.0	-

Table S3: Number of mice per group and time point with average weight and average applied dose used for hotplate assay. Data presented as $\pm$ SD.

Group	Number of Mice per Time Point	Time Points	Weight [g]	Dose [mg/kg]
BUP-Depot	12	2, 12, 48 hours	18.3 $\pm$ 1.3	1.1 $\pm$ 0.1
	11	24 hours		
Non-retard Formulation	12	2, 12, 24 hours	18.1 $\pm$ 1.8	0.11 $\pm$ 0.01
NaCl	12	2, 12, 24 hours	18.8 $\pm$ 1.8	-

Table S4: Number of mice per group with average weight and average administered dose used for surgical procedure (sham ovariectomy). Data presented as $\pm$ SD.

Group	Number of Mice	Weight [g]	Dose [mg/kg]
BUP-Depot	6	21.8 $\pm$ 1.3	1.1 $\pm$ 0.1
Non-retard Formulation	6	22.2 $\pm$ 1.2	0.11 $\pm$ 0.002

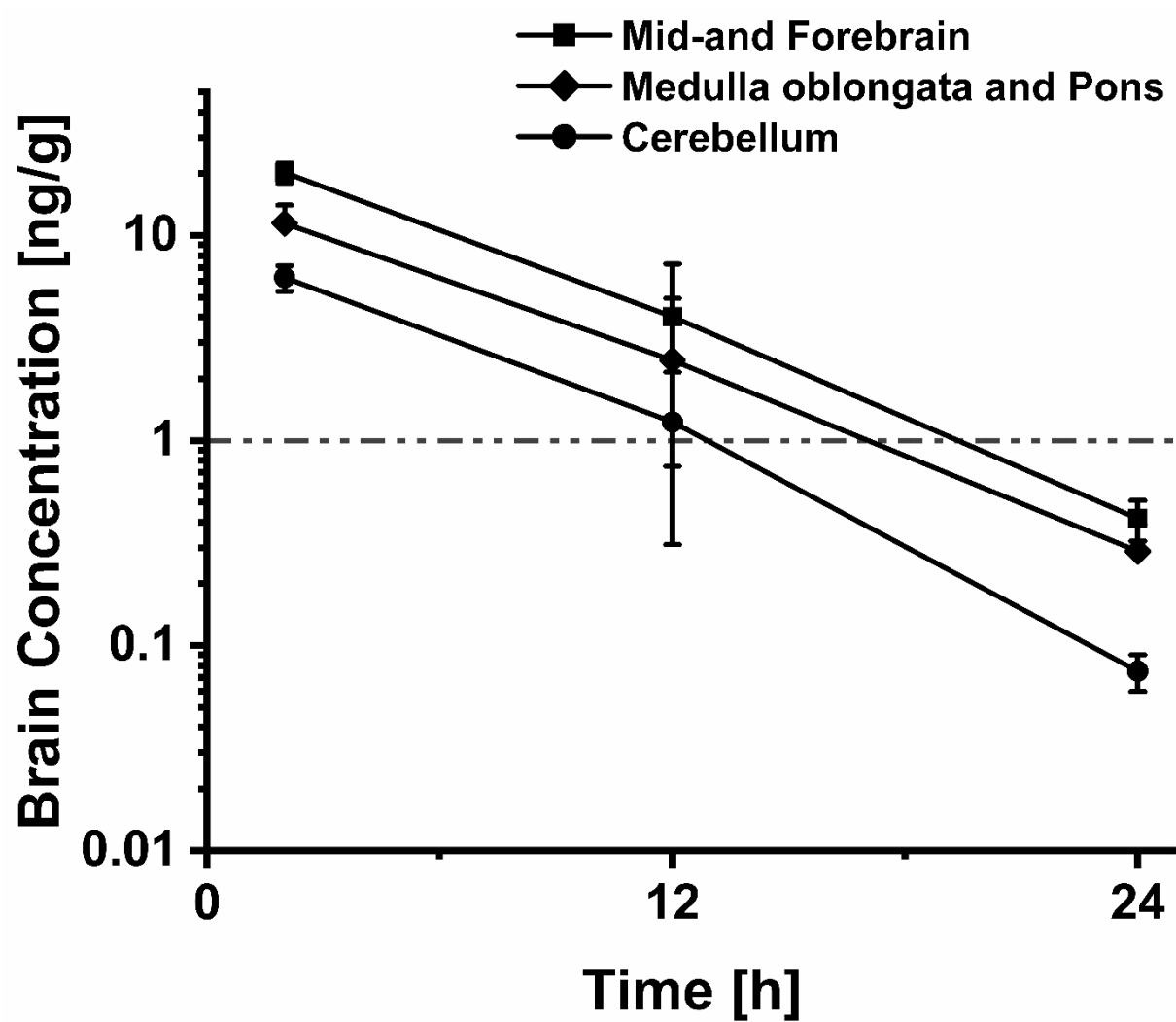


Figure S1: Regional brain concentration-time profile of non-retard formulation after single subcutaneous injection (0.1 mg/kg). Dashed line represents 1 ng/g and data is expressed as mean $\pm$ SD.