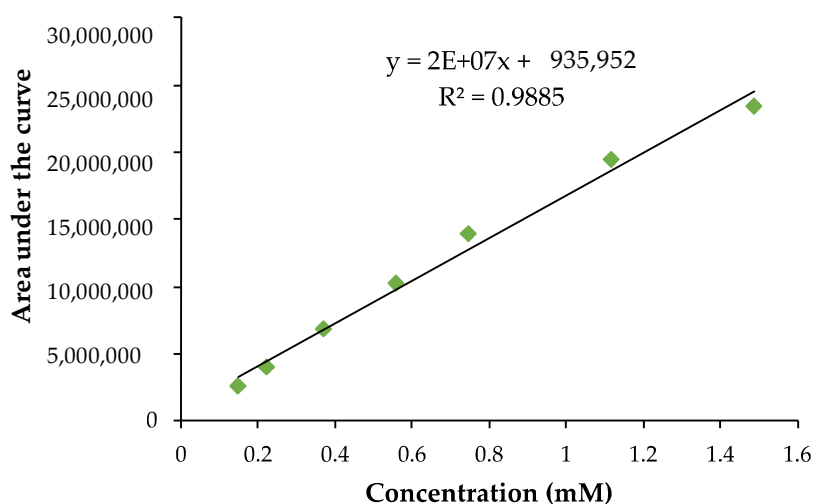


# Supplementary Materials: Increasing Brain Permeability of PHA-767491, a Cell Division Cycle 7 kinase Inhibitor, with Biodegradable Polymeric Nanoparticles

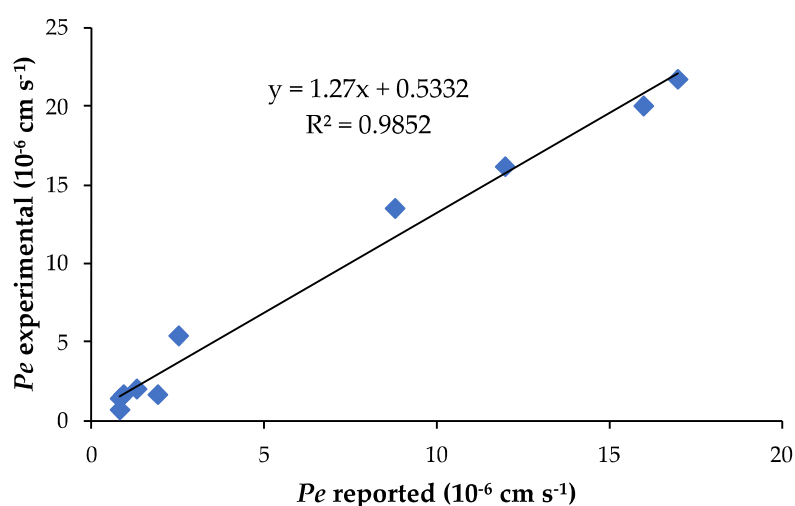
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**Table 1.** PAMPA-BBB assay permeability (reported and experimental) of ten commercial drugs used as controls and experimental permeability of PHA with its predictive penetration into the CNS. a) Reference [1]. b) Data represent the mean  $\pm$  SD of 2 independent experiments. c) Experimental prediction of BBB permeation by passive diffusion: CNS+: high BBB permeability, CNS-: low BBB permeability, CNS+/ CNS -: intermediate BBB permeability.

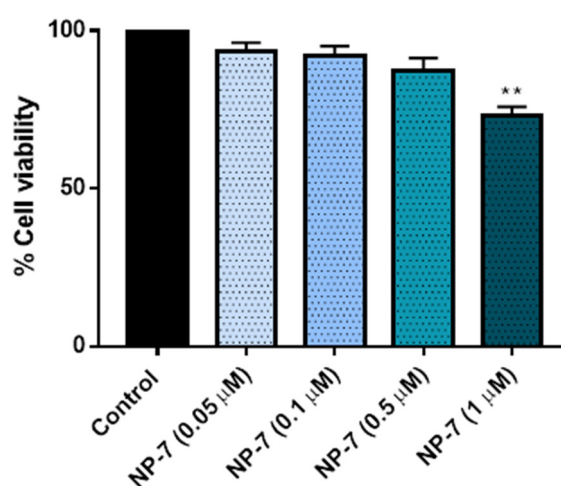
Compound	Bibl. <sup>a</sup>	$Pe$ ( $10^{-6}$ cm s <sup>-1</sup> ) <sup>b</sup>	Prediction <sup>c</sup>
Atenolol	0.8	$0.3 \pm 0.2$	CNS -
Caffeine	1.3	$0.7 \pm 0.0$	CNS -
Desipramine	12.0	$11.1 \pm 0.8$	CNS +
Enoxacin	0.9	$0.3 \pm 0.2$	CNS -
Hydrocortisone	1.9	$2.0 \pm 0.3$	CNS +/ CNS -
Ofloxacin	0.8	$0.2 \pm 0.1$	CNS -
Piroxicam	2.5	$0.8 \pm 0.1$	CNS +/ CNS -
Promazine	8.8	$10.0 \pm 1.4$	CNS +
Testosterone	17.0	$14.4 \pm 2.6$	CNS +
Verapamil	16.0	$13.2 \pm 2.4$	CNS +
PHA		$1.9 \pm 0.1$	CNS -



**Figure S1.** HPLC analysis. Linear correlation between the area under the curve and the concentration of free PHA.



**Figure S2.** PAMPA-BBB assay. Linear correlation between experimental and reported permeability of ten commercial drugs used for the experiment validation.



**Figure S3.** Cell viability of SH-SY5Y in the presence of NP-7 at 0.05, 0.1, 0.5 and 1  $\mu\text{M}$  of encapsulated PHA. Cell viability was measured 24 h after treatment by MTT assay. Data represent the mean  $\pm$  SEM of 3 different experiments. (\*\* $p < 0.01$  significantly different from control).

## References

1. Di, L.; Kerns, E. H.; Fan, K.; McConnell, O. J.; Carter, G. T., High throughput artificial membrane permeability assay for blood-brain barrier. *Eur. J. Med. Chem.* **2003**, *38* (3), 223–232.