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# Pluronic P85 Enhances the Delivery of Phenytoin to the Brain *Versus* Verapamil *In Vivo*

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***SUMMARY*. In order to find out that whether Pluronic P85 could deliver phenytoin (PHT) to brain targeted or not, a bolus dose of PHT (35 mg/kg, i.v.) in PBS as blank control or in different concentrations of Pluronic P85 solution (0.1, 1, and 10%, m/v) was administered intravenously in rats. And another group of rats as positive control was administered of verapamil (VPM, 10 mg/kg, i.p.) 30 min prior to PHT injection. Samples of plasma and dialysate in brain were collected at 30, 60, 120, 180, 240 and 300 min after PHT administration in each rat. After termination of the experiment, liver and kidney were removed for study on drug distribution in tissues. Compared with VPM, Pluronic P85 produced a dose-dependent effect on PHT distribution in hippocampus, and it significantly increased PHT concentration in ECF of hippocampus after systemic administration. And there were no increase of PHT distribution in liver and kidney in Pluronic P85 groups, while the accumulation of PHT in liver had a significantly increase in VPM group, compared with PHT blank control group. These data indicated that Pluronic P85 could enhance the distribution of PHT in brain, and the usage of Pluronic P85 as an antiepileptic drugs delivery system to brain targeted might constitute an interesting novel approach for treatment of pharmacoresistant epilepsy.**

RESUMEN. Con el fin de determinar si Pluronic P85 podría entregar fenitoína (PHT) dirigida o no al cerebro, una dosis en bolo de PHT (35 mg/kg, iv) en PBS como blanco control o en diferentes concentraciones de solución de Pluronic P85 (0,1, 1 y 10%, m/v) se administró por vía intravenosa a ratas. A otro grupo de ratas como control positivo se les administró verapamilo (VPM, 10 mg/kg, ip) 30 min antes de la inyección de PHT. Las muestras de plasma y dializado de cerebro se recogieron a las 30, 60, 120, 180, 240 y 300 min después de la administración de PHT a las ratas. Al finalizar el experimento, hígado y riñones fueron retirados para estudiar la distribución del fármaco en los tejidos. En comparación con el VPM, P85 Pluronic produjo un efecto dosis-dependiente sobre la distribución de la HTP en el hipocampo y aumentó significativamente la concentración de HTP en ECF del hipocampo después de la administración sistémica. No hubo aumento de la distribución de la HTP en hígado y riñón en grupos Pluronic P85, mientras que la acumulación de HTP en hígado tuvo un aumento significativamente en el grupo VPM, en comparación con el grupo control blanco PHT. Estos datos indicaron que Pluronic P85 podría mejorar la distribución de la HTP en el cerebro y que el uso de Pluronic P85 como sistema de entrega específico de drogas antiepilépticas al cerebro puede constituir un enfoque interesante para el tratamiento de la epilepsia fármaco-resistente.

*KEY WORDS:* Microdialysis, P-glycoprotein, Pharmacoresistant epilepsy, Phenytoin, Pluronic P85.

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