Effects of Paeonia Radix, a traditional Chinese medicine, on the pharmacokinetics of phenytoin

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Abstract

BACKGROUND: Phenytoin (PHT), one of the most widely prescribed antiepileptic drugs, has been reported to be associated with numerous drug-drug interactions. However, there are far fewer reports about the pharmacokinetic interactions between PHT and traditional Chinese medicines (TCMs). Paeoniae Radix (PR), one of the well-known TCMs, is used as an adjunct in some epileptic patients. OBJECTIVE: In the present work, we studied the influences of PR on the pharmacokinetics of PHT in rats to identify the possible interactions between PR and PHT. METHOD: A single dose of PHT (100 mg/kg) alone or in combination with PR extract (300 mg/kg) was administered by gavage to male SD rats. Serial blood samples of PHT were obtained for up to 24 h post-administration and measured by high-performance liquid-chromatography. The free (unbound) plasma concentrations of PHT were determined by fluorescence polarization immunoassay. The plasma concentrations were used to construct pharmacokinetic profiles by plotting drug concentration-time curves. All data were subsequently processed by the computer program WINNONLIN. Statistical comparisons of pharmacokinetic parameters were performed with the unpaired Student t-test. RESULTS: The mean maximum plasma concentration of PHT was attained 2 h after oral administration of PHT alone and 4-6 h after oral administration of PHT in combination with PR. The plasma level of PHT declined with a half-life of 5.38 h after PHT alone and 4.03 h after PHT and PR given together. No statistically significant differences were obtained in most of the pharmacokinetic parameters (Cmax, AUC, t1/2, MRT and CL/F) and protein binding rates of PHT between the two treatments. However, significant differences in Tmax and Vd/F between groups were noted. CONCLUSION: The significant increase in Tmax indicated that simultaneous oral administration of PR delayed the absorption of PHT. The delayed absorption of PHT might lead to its slow onset of clinical effect. There were no significant differences in Cmax, AUC, t1/2, MRT and CL/F of PHT between the two groups, showing that PR could not significantly affect the extent of absorption, metabolism and elimination of PHT. No significant difference in protein binding rate was found, indicating that PR might not significantly alter the protein binding of PHT. While a significant decrease in Vd/F was noted, the mechanism

underlying the apparently decreased Vd/F of PHT influenced by PR needs further study.