PHARMACOKINETIC COMPARISON OF TWO VALPROIC ACID FORMULATION

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We investigated the single- and multiple-dose pharmacokinetics of a new controlled-release formulation (Orfil^{R} retard enteric coated tablet) of valproic acid in comparison with those of the plain tablet as a reference. Twelve healthy volunteers were given each formulation of 300 mg in the single-dose study. In the steady-state multiple-dose study, twelve epileptic patients received 1200mg/day of the reference drug (300mg 9AM, 300mg 3PM, 600mg 9PM) and the test formulation (600mg 9AM, 600mg 9PM) with at least one week interval in cross-over manner. The AUC values of the test controlled release formulation were 91.7% (95% confidence interval: 78.4-100.4%) of the reference durg in the single-dose study and 98.2% (95% confidence interval:86.2-109.9%) in the steady-state study. The AUC's of the two formulations were not significantly different by ANOVA test. The Cmax and Tmax values of the test formulation were significantly different from the values of the reference in single- (Tmax:158.4%, Cmax:52.5% of the reference) and multiple-dose study (Tmax:153.5% of the reference). The MRT values of the test formulation were also significantly greater (129.4%) in the single-dose study. Regarding the controlled-release characteristics of the test formulation, fluctuation index and percentage fluctuation of the twice a day dosage regimen of the test formulation were comparable with those of the thrice a day dosage regimen of the conventional tablet. Area deviation was even smaller in the test regimen of the controlled release formulation. From these results, we concluded that the twice a day dosage regimen of controlled-release valproic acid was preferable or comparable to the thrice a day dosage regimen of conventional valproic acid formulation.