D-Phenylglycine improves L-dopa binding to serum albumin,

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Abstract

D-phenylglycine-L-dopa, a dipeptide synthesized in this laboratory for improving the oral absorption of L-dopa, showed better absorption and distribution in rats. We assumed that the extensive distribution might explain its sustained release of brain dopamine. Since protein binding is a main factor of drug distribution, we investigated the effect of D-phenylglycine on the binding of L-dopa to human serum albumin. The degree of the binding of D-phenylglycine, L-dopa and D-phenylglycine-L-dopa to serum albumin was determined. Free and bound portion of test compounds were separated with ultrafiltration method and the assay of free drug portion was conducted with reversed phase HPLC. The LOQ for D-phenylglycine, L-dopa and D-phenylglycine-L-dopa was 0.5 μg/mL, 0.1 μg/mL and 0.5 μg/mL, respectively. Assay methods were validated by determining the precision and accuracy of interday and intraday variations. The coefficient of variation (CV) was within 12% and the relative error (RE) was within 10% (n = 3). The recovery rate was 95.4% - 98.1% for D-phenylglycine, 91.9 % - 98.8% for L-dopa and 96.8% - 97.9% for D-phenylglycine-L-dopa, respectively (n = 3). D-Phenylglycine showed higher serum albumin binding than L-dopa did at various concentrations. At a concentration of 600 μM, the degree of albumin binding of D-phenylglycine, L-dopa, D-phenylglycine-L-dopa was 27.98%, 8.20% and 19.18%, respectively. The albumin binding of L-dopa at this concentration increased by 2.4 folds when chemically bound to D-phenylglycine. The number of the binding sites of L-dopa increased by 5.8 folds and the binding constant Ka1 increased by 3.8 folds when L-dopa was chemically bound to D-phenylglycine. With the affinity to serum albumin, D-phenylglycine showed its possibility as a delivery moiety for drugs with limited distribution to use the body protein as a reservoir.

Key words: D-phenylglycine, L-dopa, D-phenylglycine-L-dopa, albumin, protein binding