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Liquid chromatographic determination of unbound flecainide in therapeutic drug monitoring

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An assay method was developed for determining unbound flecainide in serum by reversed phase-high performance liquid chromatography (HPLC). Serum water including unbound flecainide was separated by ultrafiltration of the serum sample and subjected to C(18)-cartridge extraction followed by HPLC analysis. The recovery of flecainide from serum water was greater than 93%. The coefficient variations for intra- and inter-day assay of flecainide were smaller than 2.4 and 3.7%, respectively. We applied the method to determining unbound flecainide in serum samples collected from 20 patients receiving oral flecainide (150-300 mg/day) for tachyarrhythmia. Total and unbound concentrations for serum flecainide were 403.5±200.8 ng/ml and 180.2±95.0 ng/ml, respectively. Linear relationship was observed between total and unbound concentrations ($r=0.978$, $p<0.0001$). Percent unbound (44.3±5.7%) determined in the present study agreed with the reported values. The percentage unbound tended to increase in the samples with lower alpha(1)-acid glycoprotein (<60 mg/dl). The assay method can be applied to routine determination of unbound flecainide in therapeutic drug monitoring.