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Determination of Phenytoin in Human Plasma by a Validated Liquid Chromatography Method and its Application to a Bioequivalence Study

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***SUMMARY*. A sensitive and specific method based on liquid chromatography was developed and validated for the determination of phenytoin in human plasma using phenobarbital as internal standard. The drugs were extracted from plasma by liquid-liquid extraction and separated isocratically on a Phenomenex Synergi MAX-RP C_{12} column (150 x 4.6 mm i.d.), with water: acetonitrile: methanol (58.8:15.2:26, v/v/v) as mobile phase. Detection was carried out using photodiode array detector set at 205 nm. The chromatographic separation was obtained within 12 min and was linear in the concentration range of 50-2500 ng/mL (r^2 = 0.9999). The method was successfully applied for the bioequivalence study of two tablet formulations (test and reference) of phenytoin 100 mg after single oral dose administration to 28 healthy human volunteers. The 90% confidence intervals were calculated for the C_{max}, $AUC_{(0-t)}$ and $AUC_{(0-\infty)}$, giving values between 99.97–118.40% demonstrating the bioequivalence of the two formulations.**

KEY WORDS: Bioequivalence, Liquid chromatography, Liquid-liquid extraction, Pharmacokinetics, Phenytoin.

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