

P053 VALIDATED HPLC METHOD FOR DETERMINATION OF REPAGLINIDE IN HUMAN PLASMA USING LIQUID-LIQUID EXTRACTION

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Repaglinide is a novel prandial glucose regulator for the treatment of type 2 diabetes mellitus (Natrass, 2000; Hatorp *et al.*, 2003). The primary aim of the study was to develop and validate a rapid High Performance Liquid Chromatography (HPLC) method for determination of repaglinide in human plasma. The developed method was then applied to a pharmacokinetic study of 4 mg dose of repaglinide in 52 healthy volunteers. The study protocols were approved by Universiti Sains Malaysia Ethics Committee.

Following a liquid-liquid extraction using ethylacetate at pH 7.4, samples were separated by HPLC. The method was validated with respect to linearity, range, precision, accuracy, recovery, selectivity and stability (CDER, 2001).

The calibration curve was linear over the concentration range of 20-200 ng/ml. The limits of detection and quantification were 10 ng/ml and 20 ng/ml, respectively. Mean recovery for repaglinide was 89.73 ± 7.31. The inter-day (n=9) precision was from 9.47% to 11.96% and the intra-day (n=3) precision ranged from 1.95% to 5.01% (Table 1). The inter-day (n=9) accuracy ranged 89.58% to 101.85% and intra-day (n=3) accuracy ranged from 85.53% to 99.18% (Table 1) (see below).

Concentration (ng/ml)	Mean (ng/ml)	SD	Precision (CV)	Accuracy (%)
Repaglinide Interday (Between batch) (n=9)				
40	38.16	3.62	9.47	95.41
70	71.29	8.53	11.96	101.85
150	134.37	15.30	11.38	89.58
Repaglinide Intraday (Within batch) (n=3)				
40	38.17	1.91	5.01	95.44
70	69.43	1.36	1.95	99.18
150	128	3.98	3.11	85.53

A rapid, simple and reproducible HPLC method for the determination of repaglinide in human plasma has been developed and validated. This method has been successfully used to study repaglinide pharmacokinetics in healthy volunteers.

Guidance for Industry: Bioanalytical Method Validation, Food and Drug Administration (FDA), Centre for Drug Evaluation and Research (CDER), May, 2001.

Hatorp *et al.*, (2003). *Int. J. of Clin. Pharm. Ther.* 36(12), 636-641.

Natrass, M. (2000). *Hospital Medicine* 61(2), 112-115.