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A Subcutaneous Insulin Pharmacokinetic Model for Computer Simulation in a Diabetes Decision Support Role: Model Structure and Parameter Identification

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Abstract

Objective:
The goal of this study was to develop a unified physiological subcutaneous (SC) insulin absorption model for computer simulation in a clinical diabetes decision support role. The model must model the plasma insulin appearance of a wide range of current insulins, especially monomer insulin and insulin glargine, utilizing common chemical states and transport rates, where appropriate.

Methods:
A compartmental model was developed with 13 patient-specific model parameters covering six diverse insulin types [rapid-acting, regular, neutral protamine Hagedorn (NPH), lente, ultralente, and glargine insulin]. Model parameters were identified using 37 sets of mean plasma insulin time-course data from an extensive literature review via nonlinear optimization methods.

Results:
All fitted parameters have a coefficient of variation <100% (median 51.3%, 95th percentile 3.6–60.6%) and can be considered a posteriori identifiable.

Conclusion:
A model is presented to describe SC injected insulin appearance in plasma in a diabetes decision support role. Clinically current insulin types (monomeric insulin, regular insulin, NPH, insulin, and glargine) and older insulin types (lente and ultralente) are included in a unified framework that accounts for nonlinear concentration and dose dependency. Future work requires clinical validation using published pharmacokinetic studies.

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Abbreviations: (CV) coefficient of variation, (MI) monomeric insulin, (NLS) nonlinear least squares, (NPH) neutral protamine Hagedorn, (PK) pharmacokinetic, (RI) regular insulin, (SC) subcutaneous, (SSE) sum squared error

Keywords: blood glucose, compartmental models, decision support, diabetes, hyperglycemia, insulin, simulation, subcutaneous injection

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