# INHALED INSULIN DEMONSTRATES EARLIER COMPLETION OF TOTAL PHARMACODYNAMIC EFFECT COMPARED TO LISPRO

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## OBJECTIVE

To evaluate inhaled insulin vs subcutaneous insulin lispro as percent completion of total pharmacodynamic (PD) effect

## CONCLUSIONS

- Inhaled insulin completes a substantially larger fraction of its total PD effect early: inhaled insulin 12 U achieved 53% by 60 min vs 10% for lispro 8 U (5.3-fold).
- Cumulative PD effect makes timing differences visually explicit, supporting the interpretation that the action of inhaled insulin is largely completed much earlier than lispro, potentially enabling earlier correction dosing decisions with less concern for insulin stacking.

## INTRODUCTION

Inhaled insulin (Technosphere® insulin, TI) is a dry powder consisting of microscopic carrier particles onto which recombinant human insulin is adsorbed.

Standard clamp PD comparisons for prandial insulins commonly emphasize total glucose infusion rate (GIR) area under the curve (AUC). While GIR AUC captures overall glucose-lowering exposure, it provides limited resolution on when that effect occurs, especially when one product has a taller, narrower GIR profile (e.g., inhaled insulin) and another has a broader, lower profile (e.g., subcutaneous rapid-acting analogs).

To address this interpretability gap, we aimed to reframe the GIR-time response as a time-indexed completion curve: the cumulative percent of each treatment's own total PD effect achieved at each time point. This approach normalizes magnitude and highlights how quickly effect accumulates early and how much effect remains later.

## METHODS

Data from PDY14324, a randomized euglycemic clamp study conducted in adults with type 1 diabetes, were used for this analysis. Participants received inhaled insulin and subcutaneous insulin lispro across treatment periods under standardized clamp conditions, with GIR measured over time as the pharmacodynamic endpoint.

Inhaled insulin 12 U and insulin lispro 8 U were selected for primary comparison as doses with the closest overall PD exposure based on total GIR AUC, reflecting the higher unit relationship between inhaled insulin and rapid-acting analog insulin. Mean GIR–time profiles (mg/kg-min) were generated for each treatment.

GIR profiles were integrated using trapezoidal methods to calculate cumulative AUC over time, which was normalized to total AUC to express the fraction of total pharmacodynamic effect completed. Completion curves were constructed, and the proportion of total effect achieved by 30, 60, 90, and 120 minutes was summarized to compare early versus late insulin action.

## RESULTS

Mean GIR peaked earlier and declined more rapidly with inhaled insulin 12 U, whereas insulin lispro 8 U exhibited a slower rise to peak effect with more prolonged glucose-lowering activity over time, **Figure 1**.

The cumulative distribution function (CDF) curves show that inhaled insulin accumulated PD exposure more rapidly than insulin lispro, reaching higher fractions of total AUC earlier post-dose, **Figure 2.**

Cumulative percent of total PD effect over time was assessed for inhaled insulin and insulin lispro doses. At each time point, inhaled insulin delivered a substantially greater fraction of its overall glucose-lowering effect earlier than lispro, and left much less "late" effect remaining, **Figure 3**.

**Figure 1.** Mean Glucose Infusion Rate Over Time

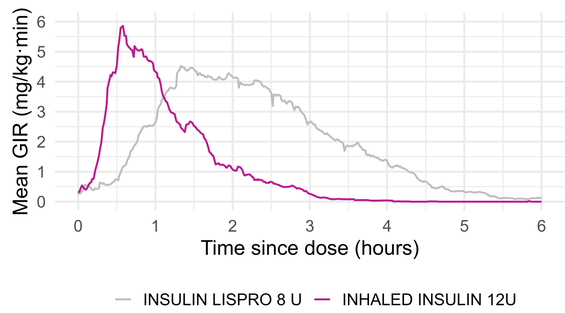



**Figure 2.** Time to Accumulated PD Effect

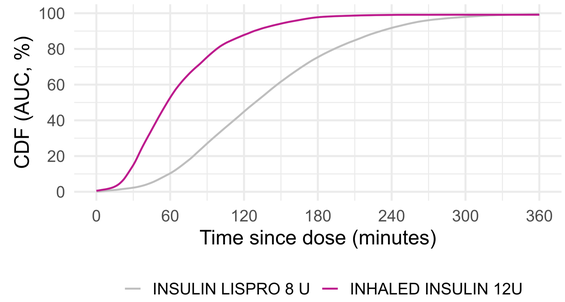
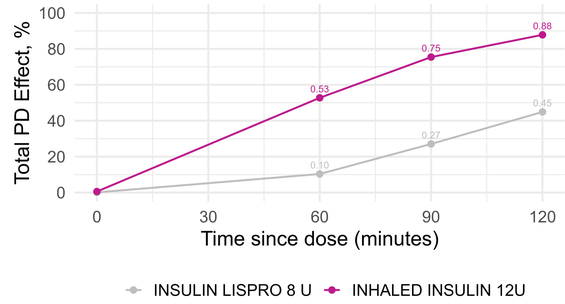



**Figure 3.** Percent of Total PD Effect Achieved Over Time

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