

# HbA1c platforms are variably affected by increasing lipemia

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## Background

- HbA1c testing is central in the screening, diagnosis and monitoring of diabetes mellitus<sup>1</sup>.
- Several analytical approaches for measuring HbA1c are available including those routinely used in clinical laboratories:
  - High performance liquid chromatography (HPLC)
  - Capillary electrophoresis (CE)
  - Immunoassay (IA)
  - Enzymatic
- Considerable attention has been paid to interference from hemoglobin variants in HbA1c methods, with less investigation of matrix-related interferences such as lipemia.
- Interference from clinical lipemia in HbA1c measurements is particularly relevant as non-fasting specimens are accepted and dyslipidemia is common in diabetic patients<sup>2</sup>.
- Manufacturer package inserts have variable claims for resistance to interference from lipemia.

Table 1. Manufacturer package insert lipemia interference claims for HbA1c assays included in this study.

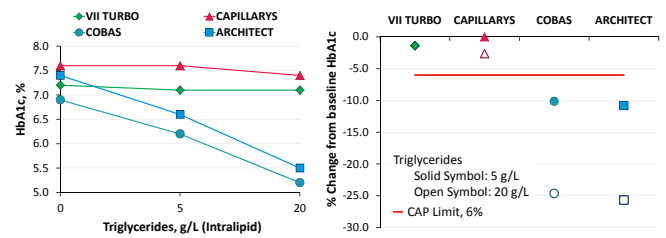
Method	Platform and assay	Package insert claim for lipemia interference	Source of lipemia
HPLC	Bio-Rad D-100™ HbA1c	None up to 60 g/L triglycerides	Intralipid
	Bio-Rad Variant™ II (VII) TURBO 2.0	None up to 60 g/L triglycerides	Clinical lipemic serum
	Bio-Rad VII HbA2/HbA1c Dual Program	None up to 60 g/L triglycerides	Clinical lipemic serum
CE	Sebia CAPILLARYS™ Hb A1c	None up to 11.2 g/L (12.8 mmol/L) triglycerides	Not stated
IA	Beckman Coulter AU® HbA1c	≤7% up to 5 g/L triglycerides	Intralipid
	Siemens Dimension Vista® HbA1c	<10% (5-10% HbA1c) up to 30 g/L (33.9 mmol/L) triglycerides	Intralipid
	Roche COBAS® c501 Tina-quant® HbA1c Gen. 3	≤±10% up to 6 g/L triglycerides	Intralipid
	Ortho VITROS® HbA1c	≤8% (6.5% HbA1c) or ≤7% (8.5% HbA1c) up to 5 g/L triglycerides	Intralipid
Enzymatic	Abbott ARCHITECT™ Hemoglobin A1c	≤±3% (5.7-7.0% HbA1c) or ≤±5% (>7.0% HbA1c) up to 30 g/L (33.9 mmol/L) triglycerides	Not stated

## Objectives

- To investigate the concentration of Intralipid®-sourced triglycerides that may cause significant interference on four platforms representing common Hemoglobin A1c (HbA1c) analytical methods.
- To assess the performance of nine routine HbA1c platforms using clinically lipemic specimens.

## Investigation of Intralipid interference in HbA1c assays

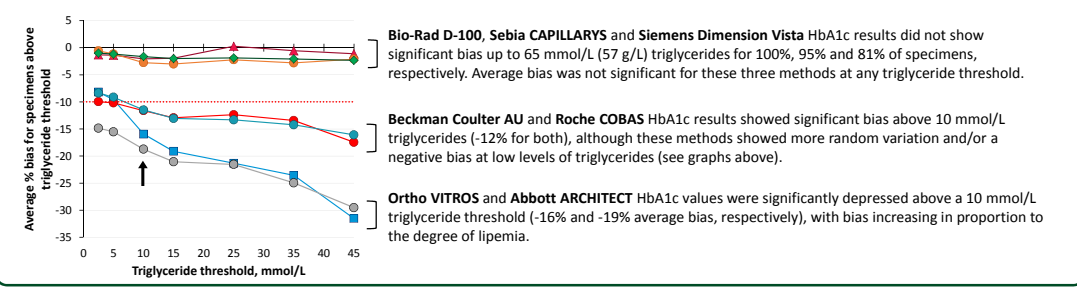
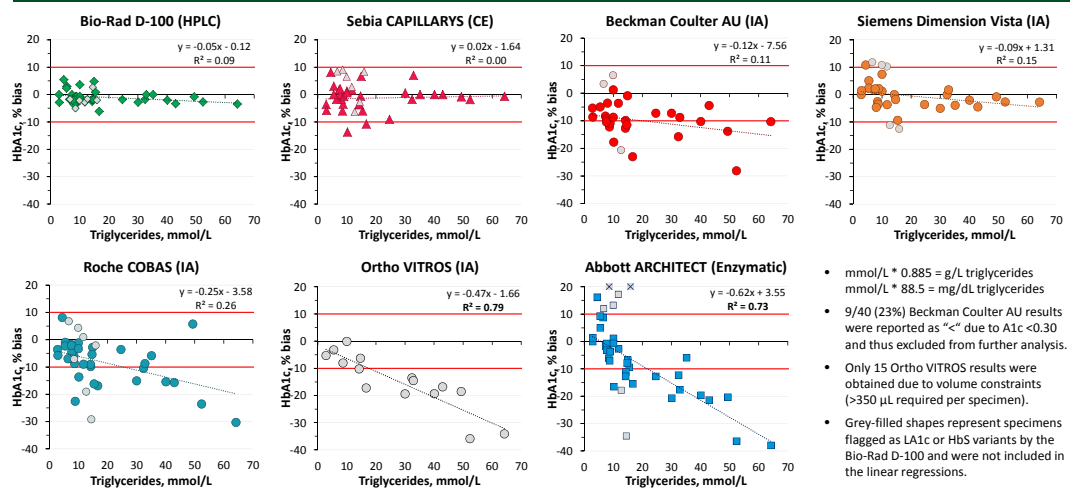
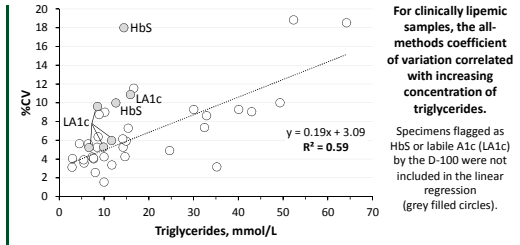
- Four specimens with 7.1 to 7.5% HbA1c were aliquoted and spiked with saline and/or Intralipid to generate triglyceride levels of 0, 5, and 20 g/L.
- Specimens were measured in singleton using the following four assays:
  - Bio-Rad VII TURBO (HPLC)
  - Sebia CAPILLARYS (CE)
  - Roche COBAS (IA)
  - Abbott ARCHITECT (Enzymatic)
- A significant difference was defined as >6% change from baseline (0 g/L Intralipid)<sup>3,4</sup>.



- The Bio-Rad VII TURBO and Sebia CAPILLARYS reported HbA1c values without significant change from baseline in the presence of up to 20 g/L Intralipid-sourced triglycerides.
- However, the Roche COBAS and Abbott ARCHITECT HbA1c values were negatively biased by approximately 10% and 25% at 5 g/L and 20 g/L triglycerides, respectively.

## Investigation of clinical lipemia interference in HbA1c assays

- Remnants of whole blood specimens (n = 40, minimum 1.5 mL each) that were identified as lipemic and ranged from 3.8 to 14.5% HbA1c were stored at -70°C within 48 hours of collection. Specimens were subject to a maximum of 2 freeze-thaw cycles. Shipment was done by same-day or overnight delivery on cold-packs and tested within 24 hours of receipt.
- Thawed, well-mixed specimens were analyzed on nine HbA1c platforms (Table 1) according to manufacturer instructions for each platform.
- Paired plasma specimens (n = 40) were obtained and stored at -70°C until testing on-site for triglycerides on the Abbott ARCHITECT chemistry analyzer.
- A significant difference was defined as >10% change from the average value reported by platforms with claimed resistance to clinical lipemia interference (Bio-Rad VII TURBO and Bio-Rad VII HbA2/HbA1c).



## Conclusions

- This study revealed that most immunoassays and the enzymatic method for HbA1c are susceptible to negative interference from elevated triglycerides, while HPLC and CE methods are resistant. These findings are consistent with a previous study assessing fewer assays and using triglyceride/cholesterol spiked specimens<sup>5</sup>.
- To avoid reporting falsely low HbA1c measurements, laboratories should consider evaluating their assay performance for interference from clinical lipemia.
- Although further investigations are needed, our data suggest that a serum triglyceride threshold of approximately 10 mmol/L may warrant a cautionary note when reporting HbA1c or reflexive testing to a lipemia-resistant platform.

## References

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