

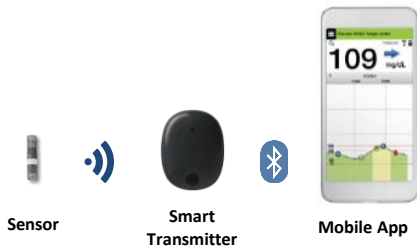
Freedom from Acetaminophen Interference with a Long Term Implantable CGM System

Carrie Lorenz PhD, Wendolyn Sandoval MS, Mark Mortellaro PhD, Lynne Kelley MD
Senseonics Incorporated, Germantown, MD, USA

Introduction

Accuracy of blood glucose meters (BGM) and continuous glucose monitoring (CGM) systems can be affected by exogenous and endogenous compounds in blood and interstitial fluid, resulting in the system reporting falsely high or falsely low glucose values. This is of special concern for over the counter medications which can be taken without medical supervision. Interference with acetaminophen (paracetamol), one of the most commonly used over the counter medications, has been shown to falsely elevate glucose readings in electrochemical CGM sensors.^{1,2} The new Eversense CGM Sensor was subjected to standard test methods to determine the effect of acetaminophen on sensor performance.

Eversense CGM System



The Eversense CGM System utilizes a long-term implantable glucose sensor powered by an external, wearable smart transmitter through a wireless inductive link. The sensor is fluorescence-based and developed for subcutaneous insertion in the upper arm. The smart transmitter wirelessly communicates with the mobile app to display real-time glucose readings, trends, and alerts.

Sensor

- Sensor lasts up to 90 days
- Five minute insertion procedure
- No weekly sensor insertion
- No open wound

Smart Transmitter

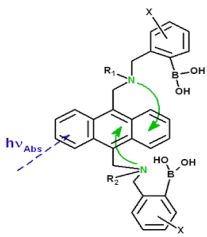
- Removable and rechargeable
- On-body vibration alerts
- Gentle-on-skin adhesive
- Wireless, secure, encrypted BLE communication with smartphone

Mobile App

- View real-time glucose readings
- Use your own smartphone - no extra device to carry
- iOS and Android compatible
- Customizable alert settings and reports

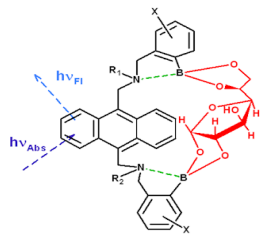
Fluorescent Glucose Indicating Technology

Low Signal



Amines quench anthracene fluorescence

High Signal



Glucose bound boron prevents quenching

- Fluorescence increases when glucose binds to indicator molecule.
- Potential interference modes:
 - ❖ A compound other than glucose binds to indicator.
 - ❖ A compound absorbs light at same wavelength range as the indicator.

Materials and Methods

- Paired-difference test^a used to screen potential interferents against ISO 15197 acceptance values.^b
- Dose-response testing for substances identified as interfering
- Test concentrations following EP7-A2^a and FDA Guidance^c
- 42 sensors (from 3 lots)
- Two glucose concentrations ("low" ~ 74, "high" ~ 320 mg/dL)

^a Clinical and Laboratory Standards Institute: Interference Testing in Clinical Chemistry, Approved Guideline, 2nd ed. Publication number CLSI EP7-A2. Wayne, PA: Clinical Laboratory Standards Institute, 2005.

^b ISO 15197:2013 Acceptance Values: Bias <10 mg/dL (0.55 mmol/L) for glucose concentrations <100 mg/dL (5.55 mmol/L) and <10% for glucose concentrations >100 mg/dL (5.55 mmol/L)

^c Guidance for Industry and Food and Drug Administration Staff: Blood Glucose Monitoring Test Systems for Prescription Point-of-Care Use. Rockville, MD: U.S. Food and Drug Administration, Guidance issued October 11, 2016.

Acetaminophen Results

Eversense CGM Sensor Bias to 20 mg/dL (1.3 mM) Acetaminophen:

In "low" glucose: **-9 mg/dL (-0.5 mmol/L)**

In "high" glucose: **-8%**

Bias does not exceed ISO 15197 acceptance values even at over 6 times the maximum therapeutic dose.

Maximum therapeutic concentration: 3 mg/dL (0.2 mmol/L) from EP7-A2 Guidance.

Conclusions

Eversense sensor glucose measurements in media containing a toxic concentration of acetaminophen were within ISO 15197:2013 specified acceptance values of measurement bias. Unlike short duration transcutaneous CGM systems, the Eversense sensor does not use electrochemical reactions to measure glucose and therefore is not affected by the same interferents. The Eversense CGM system retained the ability to accurately measure glucose concentrations in the presence of acetaminophen providing a potential safety advantage to patients.

References

- 1 Basu A et al, Direct Evidence of Acetaminophen Interference with Subcutaneous Glucose Sensing in Humans: A Pilot Study, Diabetes Technology & Therapeutics, Vol 18, Supp 2, 2016.
- 2 Maahs, D et al, Effect of Acetaminophen on CGM Glucose in an Outpatient Setting, Diabetes Care, 2015 Oct 38(10).