Laboratory Evaluation of the Glucocard™ Blood Glucose Test Meter

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The Glucocard (Kyoto Daiichi Kagaku) blood glucose meter is designed for self-monitoring of blood glucose concentrations in capillary blood through use of an electrochemical test strip. Evaluated in this laboratory, the Glucocard had CVs of 4.6%, 6.6%, and 3.5% at blood glucose concentrations of 2.4, 4.1, and 18.9 mmol/L, respectively. The meter's response varied linearly with blood glucose concentration between 2.2 and 27.8 mmol/L. Hemolysis, urate, ascorbate, and acetaminophen interfered by >5%. Different hematocrits, in the range 0.20–0.70, did not affect the measured glucose concentration. Comparison with glucose results measured in whole blood with a NOVA Stat Profile 5 instrument yielded the following: Glucocard = 0.898 NOVA − 0.184 ($r = 0.995$). The main advantages of the Glucocard are its small sample volume (5 μL), wide linear range, and fully automated sample-handling steps, which reduce user-related variability.

Additional Keyphrases: *amperometry · test strips · diabetes · monitoring therapy · glucose electrodes*

The self-monitoring of blood glucose in patients with diabetes mellitus is now widely established and supported by a variety of test strips and meters. The majority of test strips use "dry chemistry" based on glucose oxidase–peroxidase chromogenic reactions, with the color change being measured either by comparison with a color chart or by a reflectance photometer. Unfortunately, this approach has several common problems: sample volume, incubation time, removal of excess blood, and timing of color development all need to be controlled precisely (*1*); sample hematocrit influences the measured glucose concentration (*2, 3*); and competing substances such as urate, ascorbate, and bilirubin interfere in the chromogenic reaction (*4*). Moreover, reflectance photometry lacks accuracy and precision at the extremes of glucose concentration because of the shape of the reflectance–concentration curve (*5*).

The Glucocard blood glucose meter (Model GT-1610; Kyoto Daiichi Kagaku Co., Ltd., Kyoto, Japan) is a light-weight, card-sized instrument for self-monitoring blood glucose concentrations. Measurement is based on amperometric electrochemistry rather than reflectance photometry. The sample is aspirated by capillary action directly into a chamber within the test strip; measurement commences automatically, producing a blood glu-

cose result in 60 s. The user is not required to regulate the sample volume, remove excess blood from the strip, or monitor the measurement steps in any way. I evaluated a Glucocard meter under laboratory conditions before undertaking a clinical assessment in diabetic patients.

Materials and Methods

The Glucocard Meter

The battery-powered meter (Figure 1) has dimensions of 86 × 54 × 13 mm and weighs ~50 g. The meter is activated by inserting a disposable glucose-electrode test strip into the side of the meter. Measurement is initiated by aspirating 5 μL of whole blood into the test strip. Glucose oxidase (EC 1.1.3.4), deposited in dry form in the reagent layer, catalyzes the oxidation of glucose to gluconic acid, and electrons are transferred to an underlying electrode by an electron mediator (potassium ferricyanide). The current generated is proportional to the blood glucose concentration, which is displayed on a large digital screen in either mmol/L or mg/dL. The result is stored by the meter and redisplayed when the next test strip is inserted.

The measuring range of the meter is quoted as 2.2–27.8 mmol/L (40–500 mg/dL). Results above or below this are displayed as "Hi" or "Lo." The disposable electrode test strips are supplied in individually sealed aluminum foil packs, which are stored at room temperature. A calibration strip is enclosed with each package of test strips, and a check strip is provided with each meter to allow periodic checking of meter function.

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Fig. 1. Glucocard blood glucose test meter with a glucose-electrode control strip

Changes in room temperature are compensated for by a thermo-sensor within the meter.

I used fresh heparinized venous whole blood during each evaluation of the meter, completing all measurements in <20 min to minimize loss of glucose from the samples. All test strips used were from the same batch.

Analytical Performance

Imprecision. Ten replicates of each of three venous samples were measured. I evaluated two meters (A and B) at each of the three glucose concentrations and assessed differences between the meters by the *F*-test.

Linearity. Linearity was evaluated by assaying a series of dilutions made by mixing two venous samples, one with a high, and the other a low, glucose concentration.

Hematocrit. The influence of hematocrit was assessed by dividing a venous sample into eight 2-mL aliquots and centrifuging each aliquot at $3000 \times g$ for 10 min. Plasma was then either removed from or added to each aliquot to create samples having a range of hematocrits (0.20–0.75).

Molality. The effect of altered glucose molality was examined by varying the albumin concentration in solutions with constant glucose concentration. By diluting a stock human albumin solution (200 g/L), I prepared 11 solutions with albumin concentrations ranging from 0 to 200 g/L. To 9.5 mL of each solution, I added 0.5 mL of a stock glucose solution (200 mmol/L).

Interference. Interference from hemolysis, lipemia, bilirubin, uric acid, ascorbic acid, acetaminophen, and acetylsalicylic acid was assessed in pooled sera having a glucose concentration of ~5 mmol/L. I followed published guidelines (6, 7) for interference studies and evaluated interference at concentrations at least 10-fold the upper limit of the reference, or therapeutic, interval for each potential interferant tested. Interference was considered significant if the percentage change in measured glucose was greater than the coefficient of variation (CV) for the meter.

Method comparison. Venous samples from 36 adult patients were analyzed by both the Glucocard and a NOVA Stat Profile 5 (NOVA Biomedical, Waltham, MA). The NOVA uses a direct-reading glucose electrode to measure glucose activity in whole-blood samples and is calibrated against an aqueous glucose standard; its performance has been evaluated by others (8). The hematocrit of the comparison study samples, as determined by the NOVA, ranged from 0.35 to 0.52. Linear regression (Deming's model) was used to interpret the comparison data.

Analytical recovery. I assessed analytical recovery by adding glucose, 10 mmol/L, to venous samples from 15 adult patients with normal hematocrit and glucose content.

Results and Discussion

Analytical Performance

Imprecision. The results of the replicate measurements of the three samples with different glucose con-

Table 1. Glucocard Imprecision at Three Glucose Concentrations in Heparinized Venous Blood

	I	II	III
Meter A			
Mean, mmol/L	2.41	4.12	18.91
SD, mmol/L	0.11	0.27	0.65
CV, %	4.6	6.6	3.5
Meter B			
Mean, mmol/L	2.49	4.30	19.79
SD, mmol/L	0.16	0.19	0.79
CV, %	6.4	4.4	4.0
n = 10 each.			

centrations are shown in Table 1. Difference in the variances for each meter at each concentration was not significant. The mean glucose measurement reported by meter A was consistently lower at each concentration than the results by meter B; however, this difference was significant at only the highest concentration tested ($P < 0.05$, Student's *t*-test).

Inaccuracy. There was no difference in the glucose concentration measured in whole blood at 37 °C or at room temperature (~20 °C). The glucose concentration measured in samples stored at 4 °C was ~10% lower, in keeping with the temperature dependence of the glucose oxidase in the test strip. Lithium heparin and sodium fluoride/potassium oxalate anticoagulants did not interfere.

The meter's response varied linearly with glucose concentration between the imposed limits of 2.2 and 27.8 mmol/L, in contrast to the nonlinearity of reflectance photometers at glucose concentrations >13–15 mmol/L (5). The ability to accurately estimate glucose concentrations above this amount is important, particularly in sick diabetic patients requiring adjustment in insulin dosage.

The Glucocard was not influenced by alterations in glucose molality within the albumin concentration range 0 to 190 g/L. This is in contrast to other direct-reading glucose electrodes (8) and is possibly explained by dilution of the sample in the relatively large reagent layer of the test strip.

There was no significant interference (<5%), at the interferent concentrations indicated, from triglyceride (22.5 mmol/L), bilirubin (1000 μmol/L), or acetylsalicylic acid (20 mmol/L). Interference from hemolysis, urate, ascorbate, and acetaminophen was significant (>5%). A plasma hemoglobin concentration of 5 g/L reduced the measured glucose concentration by 20%. There was positive interference from uric acid (12%) and ascorbic acid (9%) concentrations at the upper limit of their reference intervals. This interference increased linearly to ≥4.4 mmol/L for urate and 1200 μmol/L for ascorbate and presumably reflects their ability to reduce the electron mediator in the reagent layer. The urate interference is of clinical importance for diabetics with renal failure (9). The positive interference from acetaminophen (8%) occurred at concentrations within the

therapeutic interval (66–199 μmol/L) and increased linearly at concentrations above this.

Venous samples from 36 adult patients were analyzed simultaneously by a NOVA Stat Profile 5 and the Glucocard. The comparison showed a linear relation, with a slope of 0.898, intercept of −0.184, correlation coefficient of 0.995, and standard error of the estimate of 0.578. Analytical recovery of glucose at 10 mmol/L ranged from 99% to 123%, with a median recovery of 108%.

Hematocrit in the range 0.20–0.70 did not affect the measured glucose concentration. When the hematocrit exceeded 0.70, the measured glucose concentration decreased. The glucose concentration measured in plasma was 5% greater than that of whole blood. Other blood glucose test strips—Glucostix (Ames, Slough, UK), ExacTech (MediSense, Abingdon, UK), and BM Glycemie 1-44 (Boehringer, Mannheim, FRG)—are known to overestimate glucose concentration when the hematocrit is <0.30–0.35 (2, 3, 9) and to underestimate glucose concentration when the hematocrit is high. The lack of effect of hematocrit that I observed with the Glucocard needs confirmation by assaying samples from patients with abnormal hematocrit and comparison with a Reference Method.

Comments

The use of electrochemistry, particularly amperometry, for the estimation of blood glucose is not new. These techniques are now well established in routine laboratories for measuring glucose concentrations in whole blood and plasma. The technology was applied commercially to the self-monitoring of blood glucose with the ExacTech meter and strips in the 1980s (10) and now with the Glucocard. Direct-reading glucose electrodes respond to glucose at a rate proportional to the glucose activity in the sample. Because this activity is related to the glucose molality (mmol of glucose/kg of water), results from glucose electrodes will differ from conventionally measured glucose concentrations unless allowance is made for the differences in water content of the samples (8).

The Glucocard is a small, portable instrument that I found easy to operate and maintain; the fully automated functions of the meter make learning to use the Gluco-

card simple. The imprecision and inaccuracy I observed with the Glucocard compare favorably with the results obtained by blood glucose meters based on reflectance photometry, when tested under laboratory conditions (11, 12).

The main advantages of the Glucocard lie in its small sample volume, wide linear range, and fully automated sample-handling steps, which limit user-induced variability. The major source of variability with blood glucose meters is attributed to the user, with as many as 50% of the results varying by >20% from the results of the comparison method in general use (1). The features of the Glucocard should improve blood glucose monitoring in diabetic patients.

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