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- ✓ Calibration-free
- ✓ Maintenance-free
- ✓ Easy-to-read Display

- ✓ High Accuracy
- ✓ Portable
- ✓ Disposable



Introduction

GlucCell® is a low-cost glucose monitoring system specially designed to facilitate the measurement of glucose. It is intended for use by laboratory researchers and bioprocessing professionals to obtain a quantitative measurement of glucose specifically in cell culture applications.

Many methods and devices have been developed for the measurement of glucose concentration. Multi-test biochemical analyzers and glucose detection kit with ELISA plating are some examples available on the market. Most biochemical analyzers are bulky and expensive. They require regular maintenance and calibration. ELISA is an expensive kit that requires a lot of work preparations for glucose measurement. It is also prone to contamination since the samples are exposed for a period of time.

Furthermore, most scientists who do not have the expensive biochemical analyzer are using blood glucose meter as an alternative for glucose measurement in cell culture media. The blood glucose meter is calibrated with respect to the wide array of molecules in blood. As a result, the error of glucose measurement in the culture medium, which contains different substances, is somewhat too large to be acceptable.

VacciXcell offers GlucCell® Glucose Monitoring System to meet your needs and lessen the work burden during glucose measurement in cell culture. The package includes a portable palm-size meter with pre-calibrated disposable test strips. GlucCell® is calibration-free and maintenance-free with easy-to-read display for viewing comfort. GlucCell® provides a simple, fast, accurate and economical alternative specifically for glucose monitoring in cell culture applications.

Importance of Monitoring Glucose Concentration during Cell Culture

During cell culture, it is important to properly mimic the chosen cell line's original in-vivo environment for it to grow and propagate. Glucose, being the main source of energy for heterotrophic cells, is one of the parameters that should be carefully monitored during the culturing process.

Wrong glucose concentration in the culture environment might have unwanted results on the cells being cultured. If there is a lack of glucose concentration in the culture medium, the cells will not have enough energy to properly grow and propagate. On the other hand, too much glucose within the culture media would subject the cells to a diabetic-like environment which could have detrimental effects such as glyoxidation and glycation.

Glucose concentration monitoring is also vital for determining cell growth and proliferation using metabolic analytical techniques. One of the most common technique is in the use of a glucose curve. By plotting glucose concentration versus the length of time of the culture (usually in days), cell density can be approximated by the rate of glucose consumption within the culture environment.



Without the use of such analytical techniques, sampling techniques are required in order to check cell growth and density during the culture process which is both labor intensive and time consuming. In addition, cell death due to lack of glucose cannot be immediately determined using sampling techniques.

The challenge of having the correct glucose concentration during cell culture is having the proper tools and equipment to measure it. As can be seen from Fig. 1, estimating glucose concentration relative to a timeline is a very poor measurement technique as glucose curves tend to be non-linear.

Glucose concentration in media is traditionally measured using wet chemistry which not only requires a lot of preparation but is also open to contamination. Automated chemical analyzers have also been developed for laboratory purposes but they are relatively expensive and bulky, making them impractical to most laboratories. Human blood glucose monitor has also been studied upon as a low-cost alternative to expensive chemical analyzers but due to the difference of chemical compositions of the human blood and culture media, the results from these devices are unreliable.

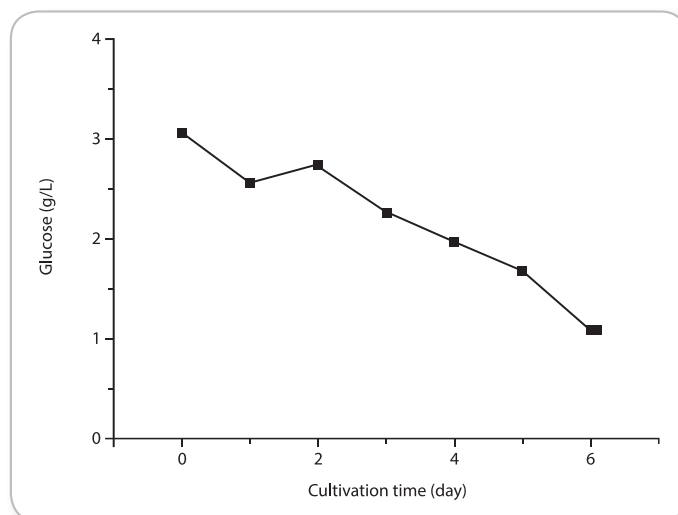


Fig. 1: Glucose Curve

Principle

GlucCell™ Glucose Monitoring System is a combination of glucose biosensor technology with microprocessor-based instrumentation. The glucose measurement is based on the oxidation of glucose by glucose oxidase enzyme.

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This is the perfect pocket size device for any researcher or bioprocessing personnel for periodic checking of glucose concentration of the culture media. It is fast, reliable, portable and easy to use with virtually no preparation needed, no contamination hazards and no waiting time.

This device is specifically developed and manufactured for the purpose of measuring glucose concentration in culture media and should not be used for diagnosis or monitoring of diabetes.

Features of GlucCell™

Portable Meter and Disposable Test Strips

GlucCell™ is a complete package with a portable meter and disposable test strips suitable for glucose measurement of both serum and serum-free culture media. It can be used for both mammalian and insect cell culture. The meter weighs only 70g and fits perfectly in a side pocket.

GlucCell's small and compact size allows measurements to be done right next to the culturing device (i.e. bioreactors, fermenters). It is also small enough to work comfortably under a biosafety cabinet.

The portable design and interface of the GlucCell™ meter is very intuitive, making it easy to use with minimal to no learning curve. The meter can store up to 180 test results with corresponding time and date, making recording of important data convenient and effective.

Small Sample Volume and Fast Analysis

The specially designed glucose test strip requires as little as 1.5 µl of sample volume of culture media in order to accurately analyze the glucose concentration. A minute glucose sample allow users to maintain the culture media cost to a minimum while being assured that the glucose concentration is being properly monitored. In addition, requiring only a small amount of culture media sample means that the disturbance of the culture environment would be minimal. Furthermore, it is not even necessary to separate the cells from the medium before testing, making the process even more user friendly.



Unlike the desktop biochemical analyzers that requires a few minutes to produce a numerical, actionable result, the GlucCell™ meter boast of being able to measure and display the result within just 15 seconds, ensuring minimal process and decision making delay for end users. In addition, it has a large LCD display for easy reading of results.

Safe and Secure Handling

Contamination is a problem for every step in bioprocessing and checking for glucose concentration of the culture media is no exemption. A contaminated sample may hinder the process in several ways. Firstly, a contaminated sample may produce the wrong analysis and results, resulting in wrong decisions and actions of the end user. This seemingly minor mistake may cause the whole experiment to yield undesirable results or at the very least waste unnecessary resources.

Secondly, contaminated samples may cause the analyzer to fail its analysis. This might seem like a minor setback at first but it would cause delay every time it happens, creating additional labor requirement which could have been allocated to other more important tasks.

Thirdly, when handling infectious samples, such as in virus production, the environment and end users must be protected from the biohazardous samples. Furthermore, biohazardous samples will contaminate biochemical analyzers and affect all succeeding samples.

One of the most common and cheapest way to ensure sample, personnel and environment protection would be is to do the process in a sterile environment such as under a class III biosafety cabinet. However, this is not possible with bulky desktop biochemical analyzers.

GlucCell™ glucose analyzer does not have this problem. Its size and portability allows end user to easily move it under a biosafety cabinet where the testing process can be done. The specially designed glucose test strip are also single use, ensuring that there would be no issues of cross contamination. The GlucCell™ gives end users much more flexibility on where and how to do their task.

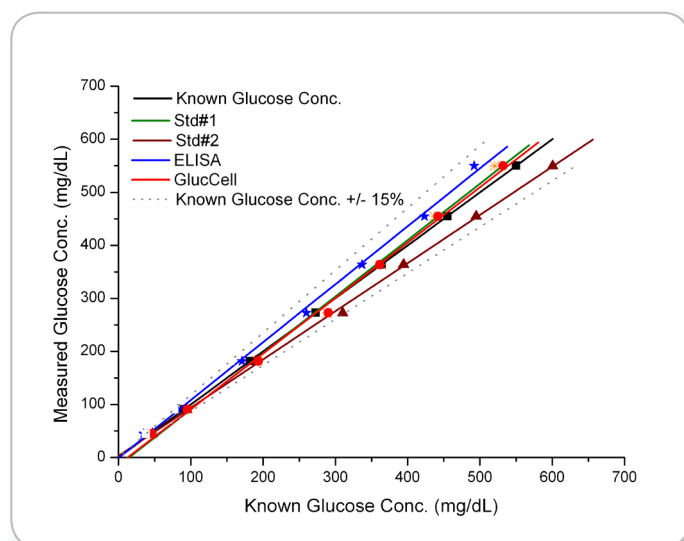
Accurate and Reliable Results

The accuracy is independent with the ingredients and components of either serum-containing or serum-free culture medium. GlucCell™ Glucose Monitoring System is capable of achieving results greater than 90% accuracy, 95% precision and 0.9997 linearity. Moreover, the result is 99.5% correlated with other expensive biochemical analyzers.

GlucCell™ Glucose Monitoring System is a innovative technology that combines the convenience of having a pocket sized glucose meter with the accuracy of the relatively bulkier desktop biochemical analyzers. GlucCell™ has a measurement deviation of 15%, which is generally acceptable in cell culture.



Fig. 2: Portable meter and disposable test strips enable the operation in a biosafety cabinet.



Studies and experiments have been made to test the accuracy of GlucCell™ glucose monitoring system. In a study published by Wang, Chang and Ho in 2006, GlucCell™ along with two biochemical analyzers (named as Std#1 and Std#2) and an ELISA testing kit was used to measure a known glucose concentration.

Fig. 3: Comparison of glucose concentration measurement by various devices and methods

As can be seen from the result that they gathered, GlucCell™ is well within the $\pm 15\%$ allowable tolerance (represented by broken lines). It has a very similar and even slightly better measurement accuracy compared to one of the two biochemical analyzer (green line) used in this study. It also produced a much more accurate result than the other two remaining methods used.

Blood glucose meters used for monitoring sugar levels of diabetic patients are also used as an alternative to the more expensive biochemical analyzers in measuring glucose concentration in culture media. In order to test the correlation of these blood glucose meters, an experiment was done in the same study. GlucCell™ along with other common blood glucose meters are compared to the measurement produced by a biochemical analyzer to determine correlation. Biochemical analyzers are currently accepted as the golden standard of glucose concentration measurement.

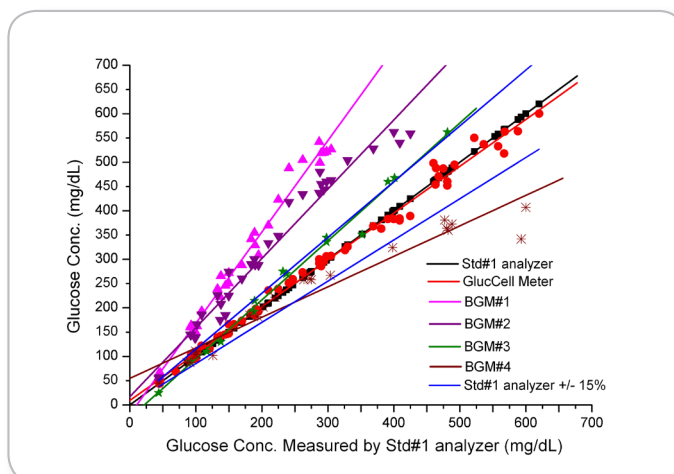


Fig. 4: Comparison of glucose concentration measurement by various blood glucose meters.

Among all the device tested, only GlucCell™ (red line) has a good correlation with the measurement of the biochemical analyzer (black line). The blood glucose meters all measured outside of the $\pm 15\%$ tolerance. This experiment shows that blood glucose meters are a poor alternative to biochemical analyzers.

The effects of various commercial media on the measurement accuracy of GlucCell™ has also been studied. The glucose concentration were measured using GlucCell™ and a biochemical analyzer and then compared.

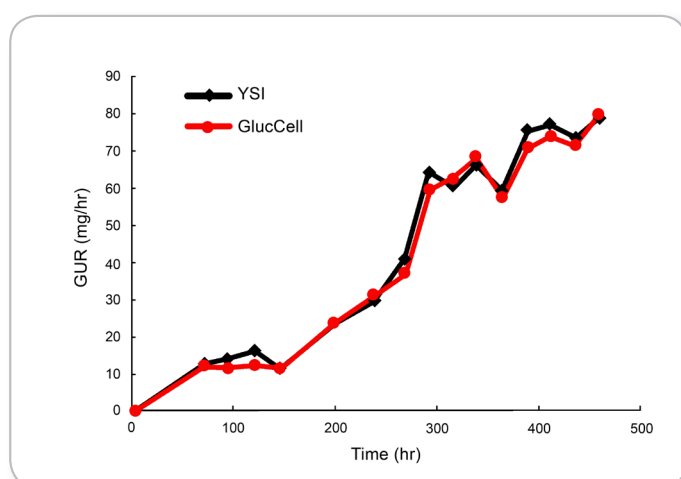


Fig. 5: Glucose measurement on actual application

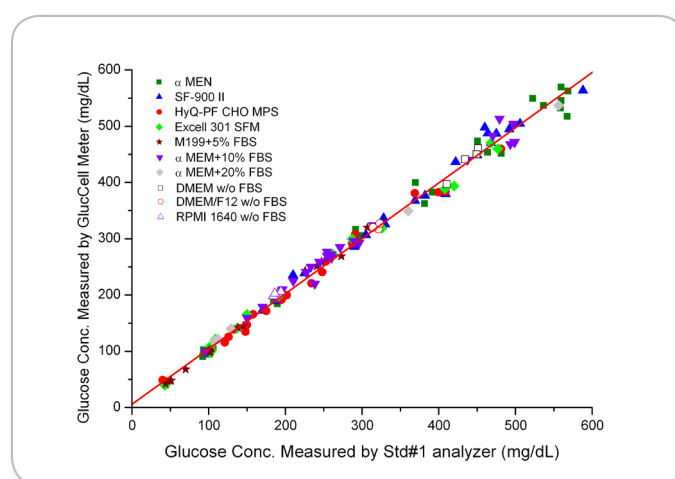
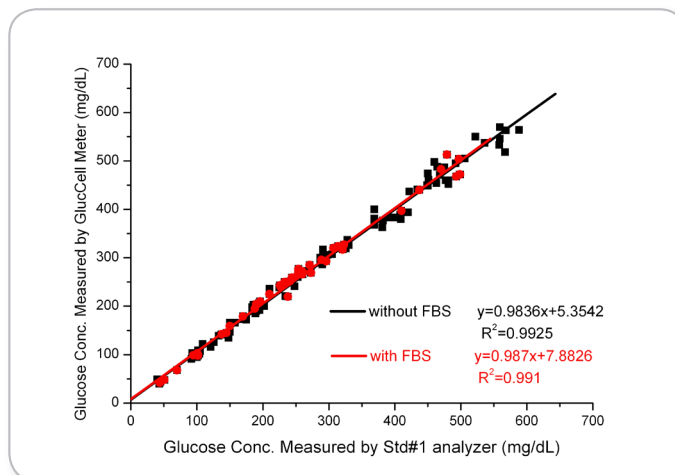


Fig. 6: Effect of medium on glucose measurement

GlucCell™ measurements and measurements from the biochemical analyzer are identical regardless of the FBS concentration. This experiment clearly shows that FBS concentration has negligible effect on the measurement accuracy of the GlucCell™.

Lastly, linearity of the GlucCell™ measurements were tested by using different known glucose concentrations.



Effect of FBS concentrations on the measurements were also studied. Again same as the previous experiment, GlucCell™ measurement were compared with measurements from a biochemical analyzer.

Fig. 7: Effect of FBS on glucose measurement.

Result showed that GlucCell™ measurements has 0.9997 linearity.

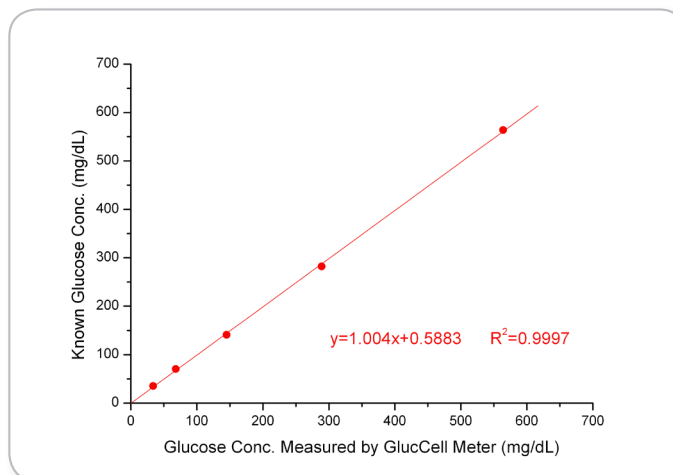


Fig. 8: Assays on five series dilution of a sample medium with known glucose concentration of 564 mg/dL was used to evaluate the linearity.



Specification

Assay Method	Electrochemical Biosensor
Test Sample	Mammalian cell culture medium or buffer solution
Test Result	glucose in mg/dL
Dimensions of the meter	96 mm x 60 mm x 18.5 mm
Weight of the meter	70 g including the battery
Battery Type	One R2032 3V-Lithium battery
Battery Life	Approximately 1,000 tests
Memory Capacity	Store up to 180 test results with date and time
Automation	Auto electrode inserting detection Auto sample loading detection Auto reaction time count-down Auto shut-off in 3 minutes
Operating Temperature Range	10°C~40°C(50°F~104°F)
Operating Relative Humidity	20%~80% RH
Strip Size	45 mm x 6 mm x 0.6 mm
Sample Volume	1.5 µL
Measurement Range	20~500 mg/dL Alarm HI when over 600 mg/dL, LO when over 20 mg/dL
Measuring Time	Less than 15 seconds
Regulatory compliance	CE0537

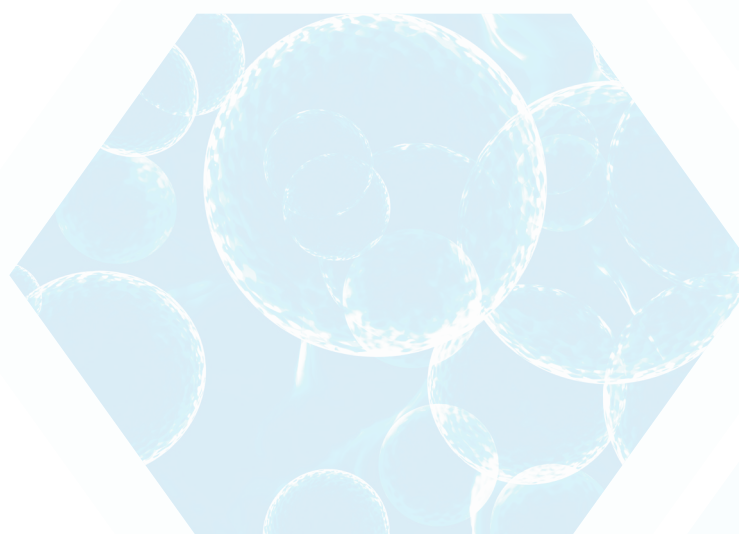
Ordering Information

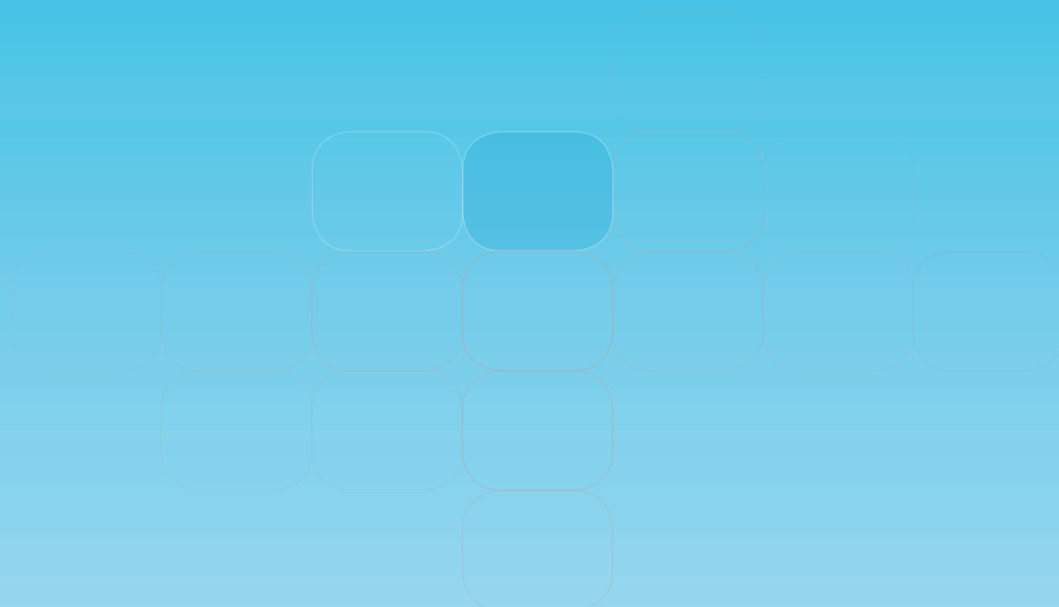
Product Name	Item Code	Package
GlucCell™ Glucose Monitoring System	1400009	1x GlucCell™ Glucose Meter 2 x bottles (25 strips/bottle)
GlucCell™ Glucose Test Strip (50 strips)	1400010	2 x bottles (25 strips/bottle)

Literature Support

The following are some of the literature support available online for the various application of GlucCell™.

1. Chang, K.J.L., C.M. Nichols, S.I. Blackburn, G.A. Dunstan, A. Koutoulis and P.D. Nichols (2014). Comparison of *thraustochytrids* *Aurantiochytrium* sp., *Schizochytrium* sp., *Thraustochytrium* sp., and *Ulkenia* sp. for production of biodiesel, long-chain omega-3 oils, and Exopolysaccharide. *Marine Biotechnolog.*, Volume 16 (4), 396-411.
2. Choy, V., N. Patel, and J. Thibault (2007). Blood glucose monitor: an alternative off-line method to measure glucose concentration during fermentations with *Trichoderma reesei*. *Biotechnol. Lett.*, Volume 29 (7), 1075-1080.
3. Pemberton, R.M., J. Xub, R. Pittsonc, N. Biddlec, G.A. Dragod, S.K. Jacksonb and J.P. Hart (2009). Application of screen-printed microband biosensors to end-point measurements of glucose and cell numbers in HepG2 cell culture. *Anal. Biochem.*, Volume 385 (2), 334-341.
4. TeSlaa, T. and M.A. Teitell (2014). Techniques to monitor glycolysis. *Methods Enzymol.*, Volume 542, 91-114.
5. Wang, I.K., K.M. Chang and L. Ho (2006). Glucose measurement for cell culture-GlucCell, a modified blood glucose meter. *MARY ANN LIEBERT INC*, 140.
6. Mulukutla, B. C., Khan, S., Lange, A., & Hu, W. S. (2010). Glucose metabolism in mammalian cell culture: new insights for tweaking vintage pathways. *Trends in biotechnology*, 28(9), 476-484.





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