GlucCell Glucose Meter

Materials and Methods

Preparation of test samples in various commercial culture media

A series of samples with different glucose concentrations were prepared by dissolving glucose (Sigma, cell culture grade) in PBS and various kind of commercial basal culture media, including αMEM, M199, DMEM, DMEM/F12 and RPMI 1640 with or without FBS (5 to 20 %). For preparing samples with different glucose concentration in commercial complete serum-free culture media, i.e. SF-900 II (GIBCO) and Excell 301 (JRH) and protein-free medium, HyQ PF-CHO MPS, the glucose concentration in culture media was increased by adding glucose and was decreased by cultivating with cells for several days.

Detection of glucose concentration

Samples prepared with different glucose concentration were detected by biochemical analyzers (YSI and NOVA Bioprofile 100), blood glucose meters (Accu-Chek Advantage (Roche), Accu-Chek Active (Roche), GlucoLeader Enhance (HMD) and GlucoSure II (Apex Biotec.)), cell culture media glucose meter (GlucCell (CescoBio)) and glucose detection kit (Unison Biotech. Taiwan).

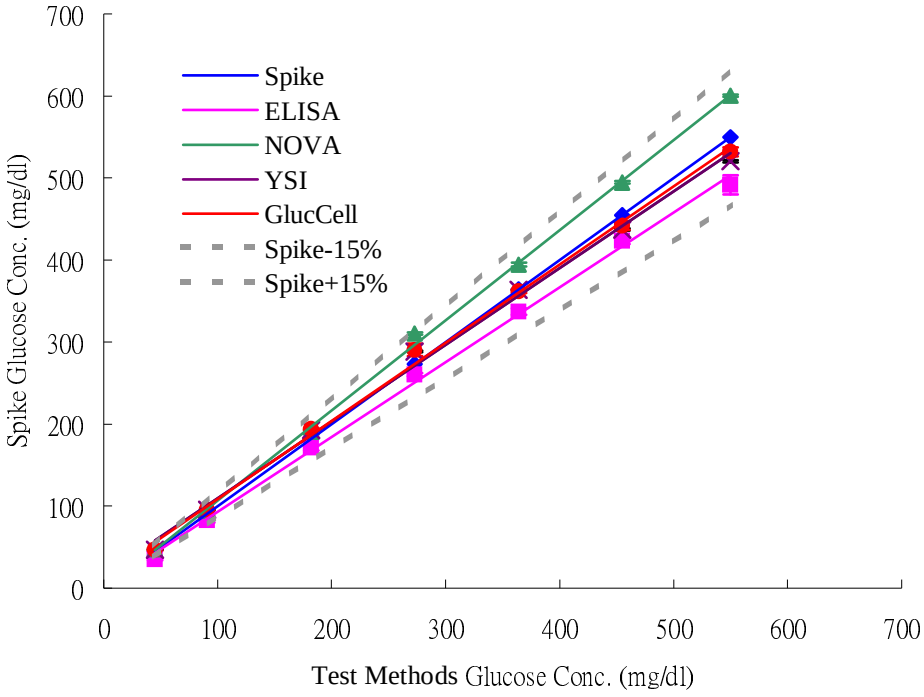
For glucose detection in biochemical analyzers, blood glucose meters, and cell culture glucose meter, the measurement was done according to their specific instructions. For glucose detection with glucose detection kit, briefly, 2 μl of glucose samples were loaded to ELISA plates, and then added glucose oxidease reaction solution 198 μl for 20 mins at 37 ℃. The absorption was measured at 500 nm.

Results

Comparsion between GlucCell glucose meter and biochemical analyzers

Various glucose concentrations prepared in αMEM basal medium were detected by various chemical analytic systems, including YSI, NOVA, enzymatic method and GlucCell glucose meter. The data, as shown in figure 1, illustrated that the concentrations of glucose detected by YSI and GlucCell were more close to actual concentration (spike) than NOVA and enzymatic method. However, all analytical methods fall in ± 15 % deviation area, which is usually an acceptable range for glucose detection.

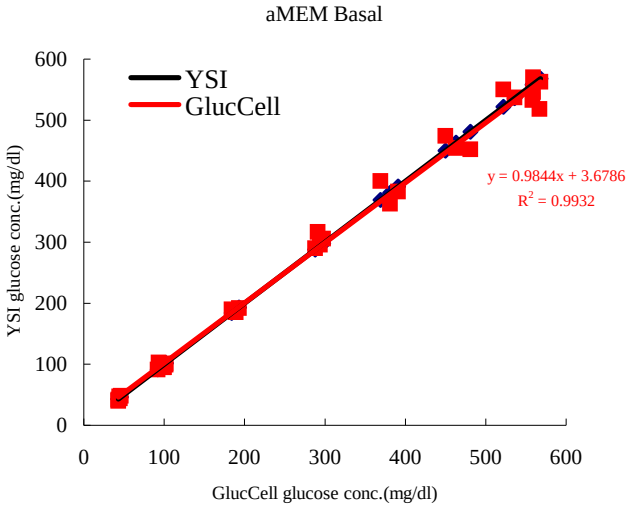
Figure 1

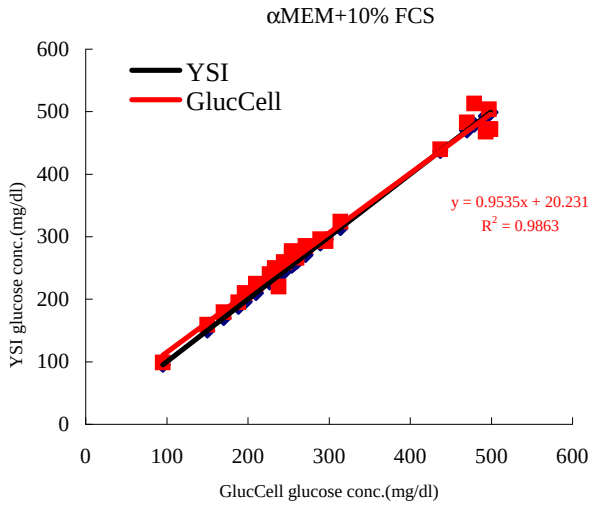


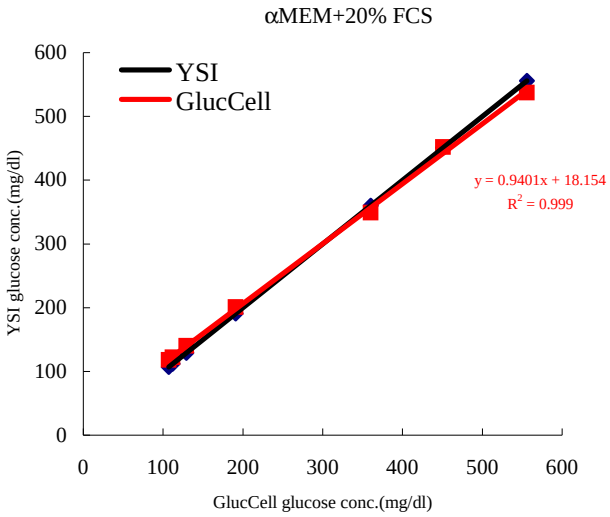
Detection of glucose concentration in various culture media with or without FBS

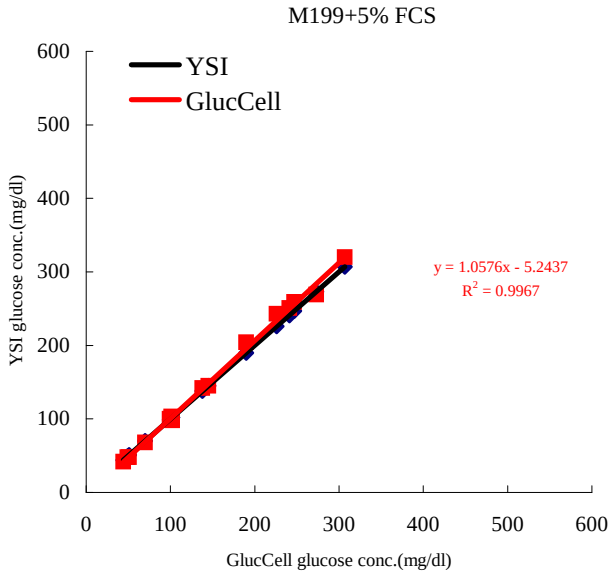
As demonstrated in fig. 1, the detection of glucose concentration by GlucCell glucose meter was very close to real spike concentration and YSI biochemical analyzer system in αMEM basal medium. The next experiment was designed to understand whether the glucose detection accuracy would be interfered with different kind of media and different concentrations of FBS. As shown in figure 2 and table 1, glucose concentration measurement between GlucCell and YSI biochemical analyzer system is very close, including PBS, and with different concentration of FBS. It indicates that the measurement of glucose concentration in GlucCell glucose meter does not affected by different basal media, and serum level, as it is usually seen in commercial blood glucose meter.

Figure 2.

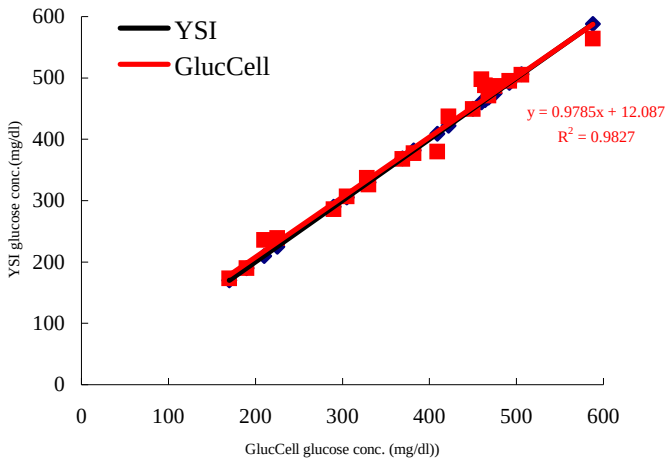




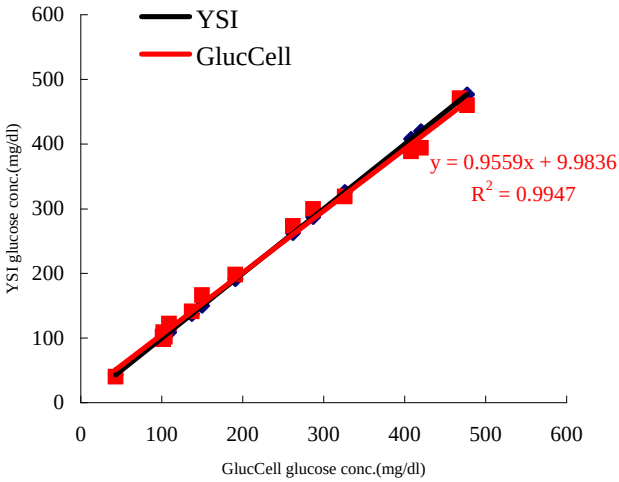

αMEM+20% FCS
YSI
GlucCell
y = 0.9401x + 18.154
R2 = 0.999
YSI glucose conc.(mg/dl)
GlucCell glucose conc.(mg/dl)
0
100
200
300
400
500
600


M199+5% FCS
YSI
GlucCell
y = 1.0576x - 5.2437
R2 = 0.9967
YSI glucose conc.(mg/dl)
GlucCell glucose conc.(mg/dl)
0
100
200
300
400
500
600

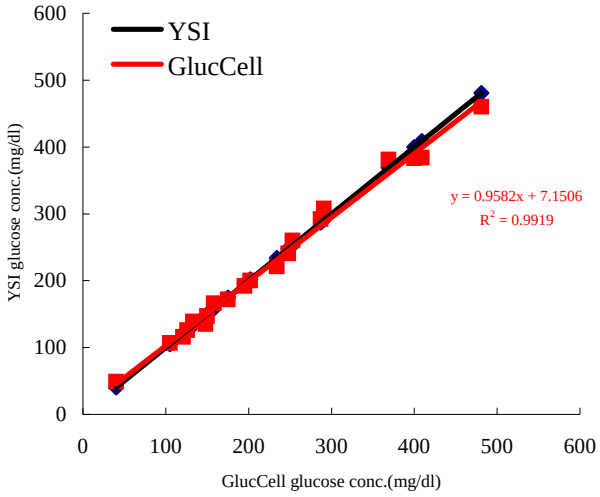
SF-900 II SFM



Excell 301 SFM



HyQ PF-CHO MPS PFM



PBS

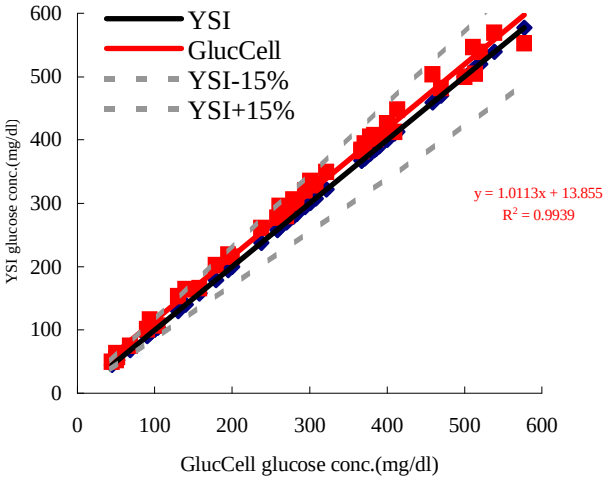


Table 1.

Medium	DMEM		DMEM/F12		RPMI 1640	
	YSI (mg/dl)	GlucCell (mg/dl)	YSI (mg/dl)	GlucCell (mg/dl)	YSI (mg/dl)	GlucCell (mg/dl)
with 10% FBS	410	397	321	317	194	206
	200	198	323	327		
without 10% FBS	434	441	314	320		
	451	461			184	198
	449	450			186	203

Culture media containing cells or without containing cells

Sometimes, it will require removing cells before doing analysis especially when we found it might cause variations in some blood glucose meters (data not shown). Therefore, we would like to know if cells would affect the measurement in GlucCell glucose meter. As shown in table 2, the glucose concentration in culture media with or without containing suspension cells had close results detected between GlucCell meter and YSI biochemical analyzer. These data suggest it is not necessary to remove suspend cells for detecting glucose before using GlucCell glucose meter.

Table 2. with or without suspension cells

Medium	HyQ PF CHO MPS	
	YSI (mg/dl)	GlucCell (mg/dl)
with $1.8x10^6$/ml Suspension CHO cells	370	378
	290	292
	164	162
without Suspension CHO cells	372	376
	283	289
	165	160

Precision, accuracy and linearity of GlucCell glucose meter

Precision was evaluated with triplicate in three independent tests by GlucCell meter (table 3). The value of precision (CV%) was counted with (SD/average)×100%. As indicated in Table 2, the values of CV% were all below 4% from lower to higher glucose concentrations.

Table 3. GlucCell Glucose Meter Precision Test

Test	1	2	3	Average	SD	**CV%**
GlucCell (mg/dl)	48	47	48	48	0.6	**1.2**
	95	91	93	93	2.0	**2.2**
	199	185	197	194	7.6	**3.9**
	297	306	289	297	8.5	**2.9**
	370	383	373	375	6.8	**1.8**
	444	452	454	450	5.3	**1.2**
	550	564	562	559	7.6	**1.4**

Accuracy was evaluated with triplicate in three independent tests by GlucCell meter. The value of accuracy (recovery%) was counted with (average/target)×100%. The table 4 shows that the values of CV% were all greater than 90% from lower to higher glucose concentrations.

Table 4. GlucCell Glucose Meter Accuracy Test

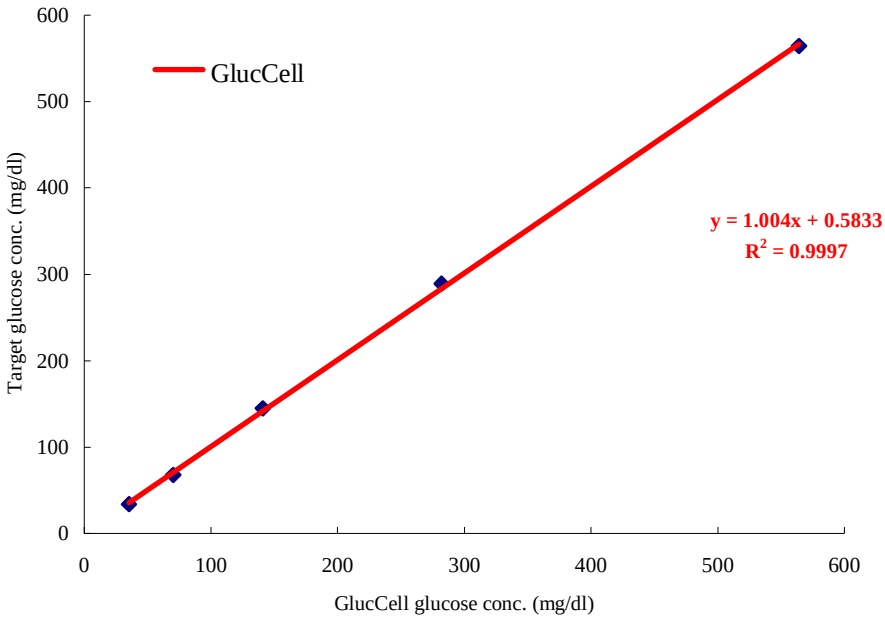
Test	Target (True conc.)	1	2	3	Average	Recovery% (Target)
GlucCell(mg/dl)	50	48	47	48	48	**95.3**
	100	95	91	93	93	**93.0**
	200	199	185	197	194	**96.8**
	300	297	306	289	297	**99.1**
	400	370	383	373	375	**93.8**
	500	444	452	454	450	**90.0**
	600	550	564	562	559	**93.1**

Linearity was evaluated with one test by GlucCell meter. The glucose concentration of first sample was detected (564 mg/dl) by GlucCell meter and then diluted by 0.5 fold series dilution (The true (target) values were 282 (564x0.5), 141 (282x0.5), 70.5 (141x0.5) and 35.25 (70.5x0.5).). These series 0.5 fold-diluted samples were detected by GlucCell meter (table 5), the detected values were name “test”. The values of “Target” is Y-axis and the values of “Test” is X-axis (fig. 3). The figure 3 obtained a R^2=0.9997 was linearity.

Table 5. GlucCell Glucose Meter Linearity Test

GlucCell (mg/dl)	Target	564	282	141	70.5	35.25
	Test	564	289	145	68	34

Figure 3



GlucCell glucose meter compared with various commercial blood glucose meters

Figure 4

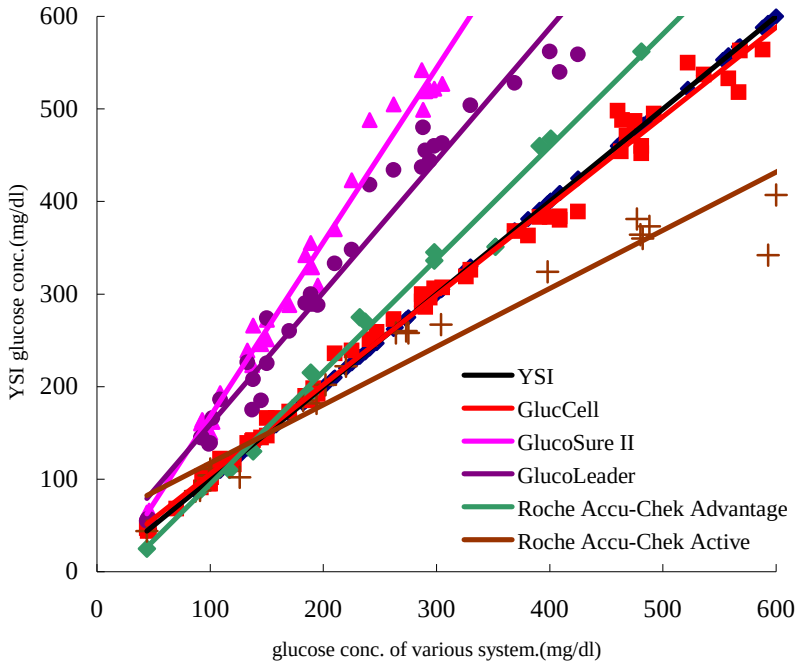
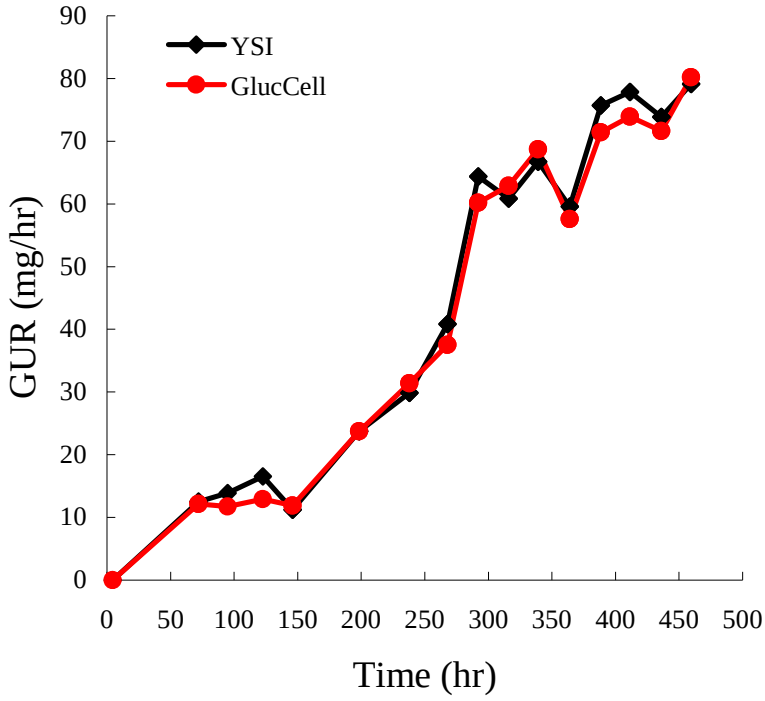


Figure 4 indicates that most commercial blood glucose meter originally designated for diabetes patients are not suitable for the purpose of glucose monitoring in cell culture. It is probably because of the background of blood and culture medium is different.

Glucose uptake rate measurement by GlucCell and YSI glucose meter during cell culture in bioreactor

CHO cells were cultivated in a BelloCell 500 bioreactor (CESCO Bioeng., Taiwan) in HyQ PF CHO MPS serum-free culture medium. The glucose concentration was detected both by GlucCell and YSI and glucose uptake rate (GUR, mg/hr) was calculated. Figure 5 shows that the data obtained from GlucCell and YSI is very close. It shows that the non-expensive, palm size and portable glucose meter is a very attractive and alternative tool to replace the complex and expensive biochemical analyzers such as YSI and NOVE Bioprofile.

Figure 5.


YSI
GlucCell
GUR (mg/hr)
Time (hr)
0
10
20
30
40
50
60
70
80
90
0
50
100
150
200
250
300
350
400
450
500