

Variable Classifications of Glycemic Index Determined by Glucose Meters

Meng-Hsueh Amanda Lin, Ming-Chang Wu and Jenshinn Lin*

Department of Food Science, National Pingtung University of Science and Technology,
1, Shuefu Road, Neipu, Pingtung 91201, Taiwan

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Summary The study evaluated and compared the differences of glucose responses, incremental area under curve (IAUC), glycemic index (GI) and the classification of GI values between measured by biochemical analyzer (Fuji automatic biochemistry analyzer (FAA)) and three glucose meters: Accue Chek Advantage (AGM), BREEZE 2 (BGM), and Optimum Xceed (OGM). Ten healthy subjects were recruited for the study. The results showed OGM yield highest postprandial glucose responses of 119.6 ± 1.5 , followed by FAA, 118.4 ± 1.2 , BGM, 117.4 ± 1.4 and AGM, 112.6 ± 1.3 mg/dl respectively. FAA reached highest mean IAUC of 4156 ± 208 mg \times min/dl, followed by OGM (3835 ± 270 mg \times min/dl), BGM (3730 ± 241 mg \times min/dl) and AGM (3394 ± 253 mg \times min/dl). Among four methods, OGM produced highest mean GI value than FAA (87 ± 5) than FAA, followed by BGM and AGM (77 ± 1 , 68 ± 4 and 63 ± 5 , $p < 0.05$). The results suggested that the AGM, BGM and OGM are more variable methods to determine IAUC, GI and rank GI value of food than FAA. The present result does not necessarily apply to other glucose meters. The performance of glucose meter to determine GI value of food should be evaluated and calibrated before use.

Key Words: glycemic index, brown rice, yogurt drink, mango, glucose meter

Introduction

The recent findings showed that postprandial blood glucose may influence the development of diabetes, coronary heart disease, obesity, and some types of cancer [1–6], has attribute to the studies of glycemic index (GI) of food. Epidemiology studies have indicated that low glycemic index food is advisable to reduce the risk of diabetes (both type 1 and type 2 diabetes), such as the Nurses's Health Study [7–9] and the Health Professional Follow Up Study [10]. Numerous clinical trials also suggested that the low GI diets are conducive to help insulin sensitivity, blood lipids and blood glucose [11–14]. Although an international table of GI value has published [15], the needs of continuously

determining GI value of food are still increasing among health professionals and food manufactures.

In standard methodology, GI is determined by giving subjects test and reference foods (either white bread or glucose) containing 50 g of available carbohydrate portion of food and collecting their blood samples over 2 h [16]. Typically, the collected blood samples are analyzed by biochemical analyzer to obtain blood glucose concentrations and the incremental area under the glucose response curve (IAUC) is calculated for each test and reference food. Therefore, GI is defined as the ratio of IAUC of test food and reference food [16–18]. Numerous methodological issues such as collecting blood sample through venous or capillary [19], the duration and frequency of blood sampling can affect the accuracy of the glycemic response (expressed as IAUC) and thus the precision of GI value [17–19].

Recently, researchers have begun to use self-monitoring blood glucose meter (SMBG) to determine GI value of food [20–22], because they are convenient, inexpensive,

*To whom correspondence should be addressed.

Tel: 886 8 7740237 Fax: 886 8 7740378

E-mail: jlin@mail.npust.edu.tw

Table 1. Characteristics of self-monitoring glucose meters and biochemistry analyzer

	AGM	BGM	OGM	FAA
Technology	Electrochemical	Electrochemical	Electrochemical	Colorimetric
Sampling site	Strip	Strip	Strip	Slide
Testing time/	25 s	5 s	20 s	2–6 min
Sample size	4 μ l	1 μ l	2.5 μ l	10 μ l
Sample type	Whole blood	Whole blood	Whole blood	Plasma
Calibration	Code key	Automatic	Code key	QC card read in

AGM, advantage glucose meter; BGM, breeze 2 glucose meter; OGM, optimum xceed glucose meter; FAA, fuji automatic analyzer.

little blood sample (<5 μ l) and very short testing time (<30 s) required to give a result. Although studies have evaluated the accuracy and performance of SMBG for measuring blood glucose concentration in diabetic patients [21–24], it may not be applicable in the determination of glycemic responses (expressed as IAUC), GI values and thus rank GI value of food in healthy subjects. Therefore, the purpose of this study is to evaluate the performance of three different SMBGs to measure IAUC, and GI value of food in healthy subjects and compared the classifications of GI values obtained from SMBG and laboratory biochemical analyzer. The study used previous describe method [25] to classify food as high (GI>69), medium (GI = 56–69) and low (GI<56) GI. To observe the classification of GI value of food is crucial, it often provide an important information in clinical for patients to plan their meal. To our knowledge, no study evaluated the classifications of GI values between determined by biochemical analyzer and glucose meters.

Materials and Methods

Test foods

Three test foods and one reference food were tested in 50 g available carbohydrate portion. The test food includes brown rice, mango and yogurt drink. Brown rice was manufactured by Union Rice Company (Taipei, Taiwan), the mango (Chiin-Hwang Mango) was purchased from local supermarket, and yogurt drink (Yakult fermented milk drink) was produced by Yakult Company (Taipei, Taiwan). In food preparation, brown rice was prepared by soaking in 1:1.5 ratio of rice and water overnight and cooked by rice cooker (Tatung Co., Ltd. Taiwan) right before consumption. The skin of mango was removed and cut into 5 cm cubes. Yogurt drink was placed in a plastic cup. White bread (reference food) was made by the laboratory prior to the test. Each subject was asked to consume white bread 3 times at the beginning, the middle and the end of study to reduce the effect of day to day variation in glucose tolerance [17].

Self-monitoring glucose meters

Three different glucose meters were selected because they require little blood sample and very short testing time to give a result. The glucose meters include 1). Accue Chek Advantage glucose meter (AGM) (Roche Diagnostics, Indianapolis, IN), 2). BREEZE 2 glucose meter (BGM) (Bayer HealthCare LLC Diabetes Care, Mishawaka, IN), 3). Optimum Xceed glucose meter (OGM) (Abotte Diabetes Care Alameda, CA). Detail of glucose meters is listed in Table 1. The reproducibility of three glucose meters is not assessed in the study.

Subjects

Ten healthy university students were recruited for the study. The subjects were six females and four males. The age of the subjects was ranged between 20–30 y (mean = 23.6) and their mean body mass index (BMI: in kg/m^2) \pm SEM was 20.6 ± 0.5 . Subjects were excluded if they were smokers, taking prescription medication, on dieting, or had family history of diabetes. All ten subjects were asked to avoid consuming alcohol, legumes and fried food the day before the each test, and to refrain from unusual eating habit and activity [25]. Subjects were also need to complete a food questionnaire before test to ensure whether they have had irregular eating habits. Informed consent was obtained from each subject before enrolment. The study was approved by Institutional Review Board of the Kaohsiung Medical University.

Study protocol

All subjects were blinded to the name of the food being tested. White bread was used as reference food (GI = 100%) against which all test food were compared. On each test day, subjects were fed 50 g available carbohydrate portion of test food or reference food ($\times 3$) in random order after 10–12 h overnight fast. All test and reference food were served with 220 ml of water. Blood samples were taken from subjects' finger immediately before subjects start test/reference food (0 min) and 15, 30, 45, 60, 90, and 120 min after the start of the eating. An automatic lancet device (Safe-T-Pro, Roche

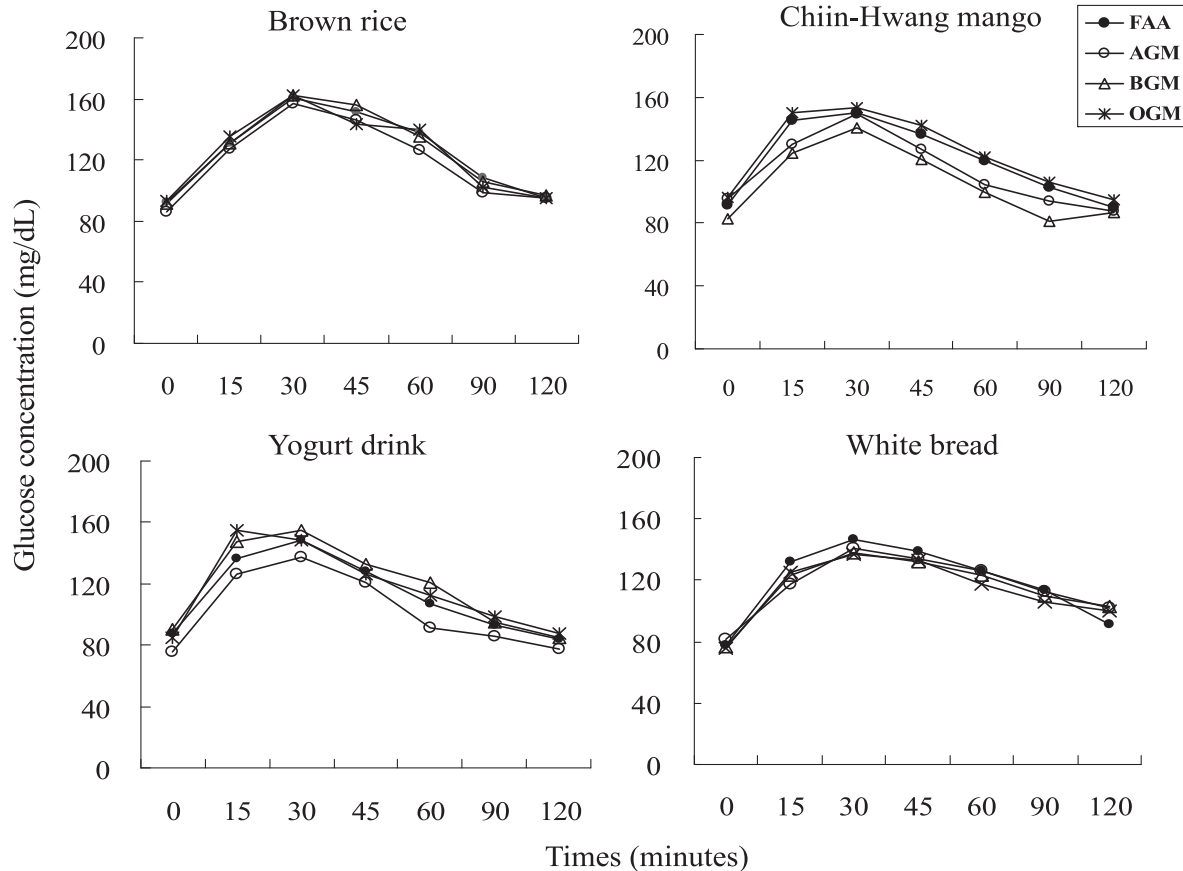


Fig. 1. Incremental changes in plasma glucose concentrations in brown rice, Chin-Hawn Mango, yogurt drink and white bread elicited by FAA, AGM, BGM and OGM. Closed circle, fuji automatic analyzer, (FAA); open circle, advantage glucose meter (AGM); open triangle, breeze 2 glucose meter (BGM); cross, optimum xceed glucose meter (OGM).

Diagnosics GmbH Mannheim, Germany) was used to collect finger capillary blood samples (6 drops). The first three drops of blood were separately placed onto the strip of each glucose meter and the rest 3 drops were collected in a heparin contained tube. The order of glucose meters being tested was varied and with minimal elapsed time between each glucose meter. The heparin contained tubes were then centrifuged ($10500 \times g$ for 3 min at 4°C) to obtain plasma. Plasma was spotted onto slide which contained a reagent layer (glucose oxidase and peroxidase) (Fuji Dri-Chem 3000, Fuji Film, Kanagawa, Japan) and analyzed with a Fuji Dri-Chem 3000s automatic biochemistry analyzer (FAA) (Fuji Film, Kanagawa, Japan) in each test day.

Statistics

The postprandial incremental area under curve (IAUC) was calculated by using trapezoidal method and consideration of the fasting pre-meal value [26]. The GI was calculated from the ratio of the IAUC of the blood glucose response curve of test food and reference food (mean IAUC of three reference white bread) expressed as percentage.

Because the GI value of white bread is 71, therefore, the resulting values need to be multiplied by 0.71 in order to convert them to GI values based on glucose [18, 27].

The results from each method (FAA, OGM, BGM and AGM) were analyzed by analysis of variance (ANOVA) with use of SPSS for Windows Release 13.00. The results are presented as mean \pm SEM. A value of $p < 0.05$ was considered significant.

Results

Postprandial glucose responses

The study protocol was well tolerated. All 10 subjects completed the study. The glucose responses elicited by three test foods and reference white bread, measured by four different methods (FAA, OGM, BGM and AGM) are shown in Fig. 1. Mean glucose concentration measured by AGM tends to have a lowest responses curve in every time point in all test foods whereas OGM showed highest response curve among four methods.

Scatter plot of all 420 results of each meter and bio-

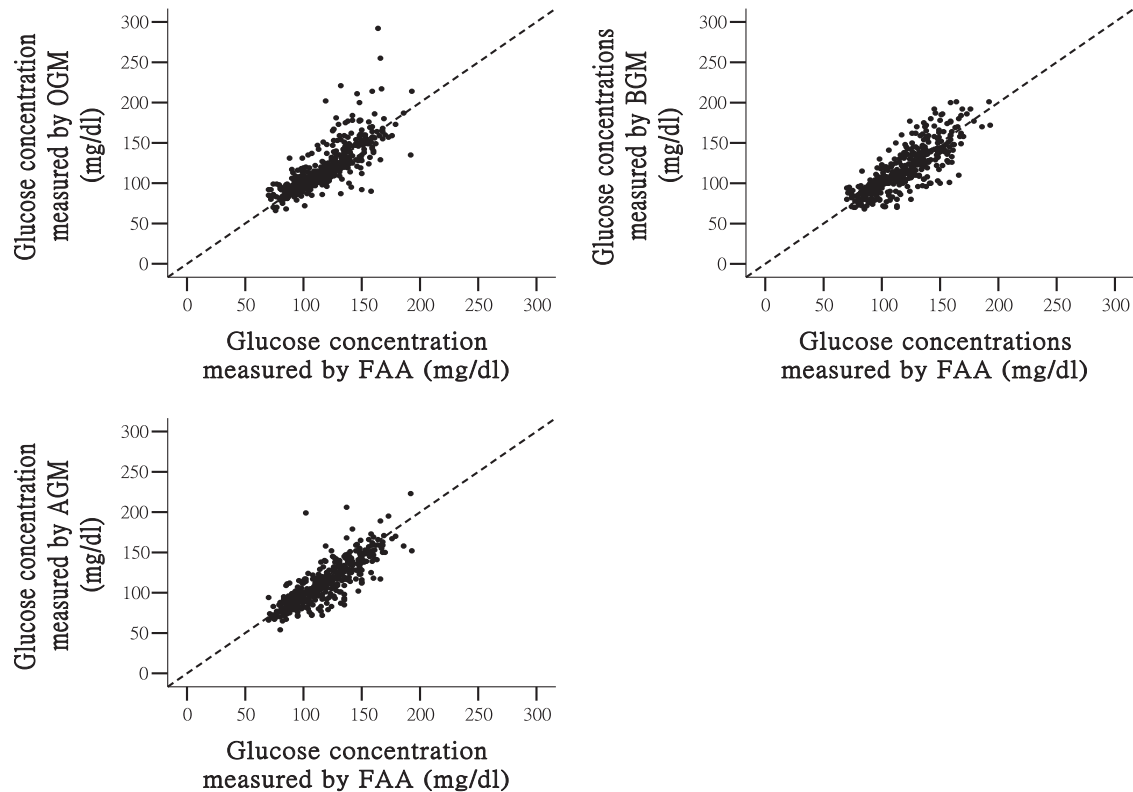


Fig. 2. Comparison of glucose concentrations between measured by FAA and OGM ($n = 420$, $r = 0.79$, $p > 0.05$), BGM ($n = 420$, $r = 0.82$, $p = 0.06$) and AGM ($n = 420$, $r = 0.84$, $p < 0.05$). Fuji automatic analyzer (FAA); advantage glucose meter (AGM); breeze 2 glucose meter (BGM); optimum xceed glucose meter (OGM).

Table 2. Glucose concentrations of the test foods and white bread as determined by FAA, OGM, BGM and AGM*

	Glucose concentration (mg/dl)							
	Brown rice	CV (%)	Chiin-Hwang Mango	CV (%)	Yogurt drink	CV (%)	White bread	CV (%)
FAA	125 ± 3.5	23.5	118 ± 3.0 ^a	21.3	113 ± 3.3 ^a	24.4	118 ± 3.0	21.2
OGM	125 ± 4.2	27.9	123 ± 3.4 ^c	23.0	116 ± 4.5 ^b	32.6	116 ± 2.8	20.1
BGM	126 ± 3.9	25.9	105 ± 3.4 ^{bc}	27.3	118 ± 4.1 ^b	28.9	115 ± 2.7	19.9
AGM	120 ± 3.8	26.8	113 ± 3.2 ^{ab}	23.4	102 ± 3.5 ^b	28.7	113 ± 2.9	21.2

* Means ± SEM. Values in the same column with different superscript letters are significantly different, $p < 0.05$. AGM, advantage glucose meter; GM, breeze 2 glucose meter; OGM, optimum xceed glucose meter; FAA, fuji automatic analyzer.

chemistry analyzer are shown in Fig. 2. The mean ± SEM glucose concentrations (test food and reference white bread) measured by OGM reached highest glucose concentration, followed by FAA, BGM, and AGM gave lowest (Table 2). ANOVA analysis showed the differences of glucose concentrations obtained using FAA was significantly greater than AGM ($r = 0.84$, $p < 0.005$), but not significantly with BGM ($r = 0.82$, $p > 0.05$) and OGM ($r = 0.79$, $p > 0.05$). In reference white bread, the glucose concentrations measured by FAA was significantly higher than measured by AGM ($r = 0.83$,

$p < 0.005$). No significant were found in FAA vs OGM ($r = 0.80$, $p > 0.05$) and FAA vs BGM ($r = 0.85$, $p > 0.05$) in white bread. All four methods did not reach statistical difference in brown rice and reference white bread ($p > 0.05$). However, Chiin-Hwang mango and yogurt drink showed significant difference among four methods ($p < 0.05$). The mean coefficient of variation (CV) of OGM was 25.9 % followed by BGM, 25.5 %, AGM, 25.0 % and FAA, 22.6 %, respectively.

Table 3. Incremental area under the curve of test foods and white bread as determined by FAA, OGM, BGM and AGM*

	Incremental area under the curve							
	Brown rice	CV (%)	Chiin-Hwang Mango	CV (%)	Yogurt drink	CV (%)	White bread	CV (%)
FAA	4133 ± 396 ^a	30	3351 ± 268 ^{ab}	25	4115 ± 385 ^a	30	5025 ± 467 ^a	29
OGM	3893 ± 610 ^a	39	3275 ± 443 ^a	27	3768 ± 467 ^a	35	4406 ± 643 ^a	36
BGM	3986 ± 526 ^a	42	2569 ± 307 ^{ab}	38	3442 ± 383 ^a	35	4926 ± 414 ^a	27
AGM	3540 ± 479 ^a	55	2173 ± 280 ^b	65	3098 ± 414 ^a	48	4766 ± 502 ^a	42

* Means ± SEM. Values in the same column with different superscript letters are significantly different, $p < 0.05$. AGM, advantage glucose meter; BGM, breeze 2 glucose meter; OGM, optimum xceed glucose meter; FAA, fuji automatic analyzer.

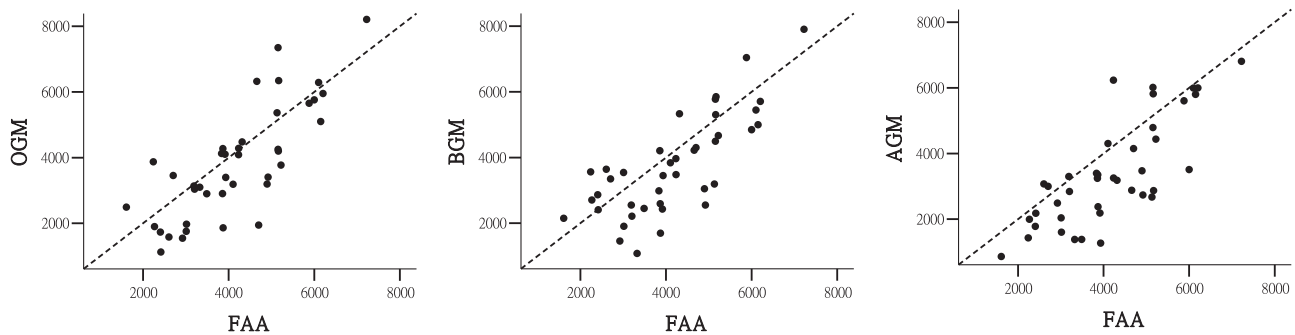


Fig. 3. Comparison of incremental area under the curve between measured by FAA and OGM ($n = 40$, $r = 0.79$, $p < 0.05$), BGM ($n = 40$, $r = 0.76$, $p < 0.05$) and AGM ($n = 40$, $r = 0.78$, $p < 0.05$). Fuji automatic analyzer (FAA); advantage glucose meter (AGM); breeze 2 glucose meter (BGM); optimum xceed glucose meter (OGM).

Incremental area under the curve

Table 3 shows the IAUC of all test food as measured by FAA, OGM, BGM and AGM. By paired sample ANOVA, mean IAUC of brown rice measured by FAA was significantly greater than three glucose meters (OGM: $p < 0.05$, BGM: $p < 0.05$ and AGM: $p < 0.05$). In mango, the mean IAUC measured by FAA was significantly higher than measured by BGM ($p < 0.05$) and AGM ($p = 0.005$), but not OGM ($p > 0.05$). In yogurt drink, the mean IAUC measured by FAA was not significantly higher than measured by OGM ($p < 0.05$), and BGM ($p < 0.05$). However, there was a significant effect between FAA and AGM ($p < 0.05$) on mean IAUC of yogurt drink. The mean IAUC of white bread did not reach statistic significance among FAA and three glucose meters (OGM and AGM, $p > 0.05$, BGM, $p > 0.5$). Scatter plot of all 40 results of IAUC are shown in Fig. 3. Overall, FAA reached highest mean IAUC, followed by OGM, BGM and AGM. The coefficient correlation of mean IAUC of FAA vs BGM ($r = 0.76$, $p < 0.05$), FAA vs AGM ($r = 0.78$, $p < 0.05$), and FAA vs OGM ($r = 0.79$, $p < 0.05$) were statistically significant respectively. When compare the CV of IAUC between FAA and each glucose meter, AGM gave highest CV greater than OGM, BGM and FAA.

Glycemic index

Mean GI was calculated for each test food and each method. Fig. 4 shows the mean GI value of three test food that determined by four methods. On average, the mean GI of brown rice measured by OGM produced highest of 93.1 ± 14.6 , followed by FAA, 82.2 ± 0.7 , BGM, 79.3 ± 6.2 and AGM, 75.4 ± 6.7 , respectively (Fig. 4). Mean GI value determined using OGM gave highest GI, 77.1 ± 4.0 , than determined by FAA (68.0 ± 0.4), BGM (53.6 ± 6.8) and AGM (45.2 ± 6.4) produced the lowest in mango. The mean GI of yogurt dink measured by OGM was 90.8 ± 6.5 greater than measured by FAA (81.8 ± 0.4), BGM (71.2 ± 7.0) and AGM (68.5 ± 8.9). Overall, OGM gave highest mean GI (87 ± 5), followed by FAA (77 ± 1), BGM (68 ± 4) and AGM produced the lowest (63 ± 5) in four test foods. Among four methods, FAA, AGM and BGM gave significantly different mean GI values ($p < 0.005$), but not OGM ($p > 0.05$). Fig. 5 shows the error variation of mean GI values of three test foods determined by FAA, OGM, BGM and AGM. Among four methods, FAA gave lowest error variation than three glucose meters. It is likely that error variation increased as GI value of food is increased in three glucose meters. We further use recommended method to classify the results of GI value as high, medium and low GI [23]. All

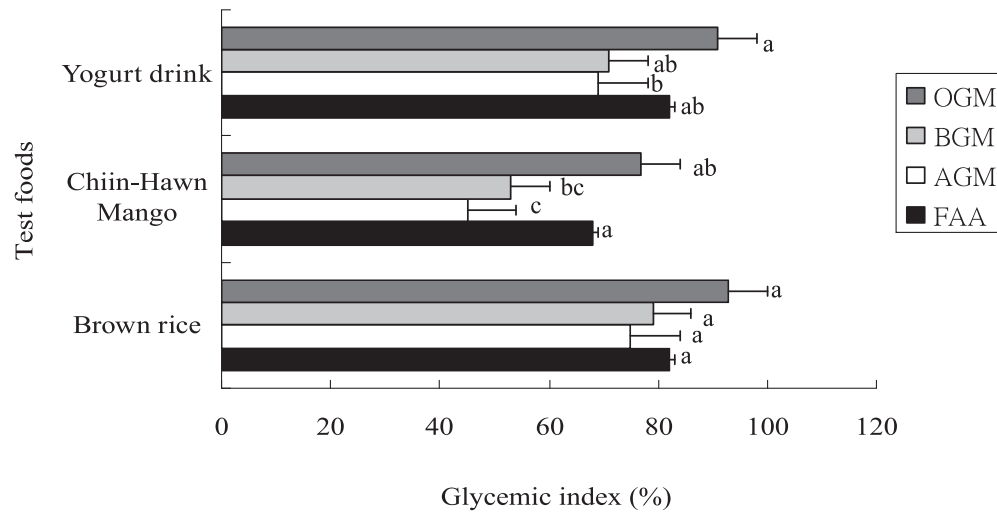


Fig. 4. Glycemic index of three test foods as determined by FAA, OGM, BGM and AGM. The values in the same group with different superscript letters are significantly different, $p < 0.05$. Closed square, fuji automatic analyzer, (FAA); open square, advantage glucose meter (AGM); light gray square, breeze 2 glucose meter (BGM); gray square, optimum glucose meter (OGM).

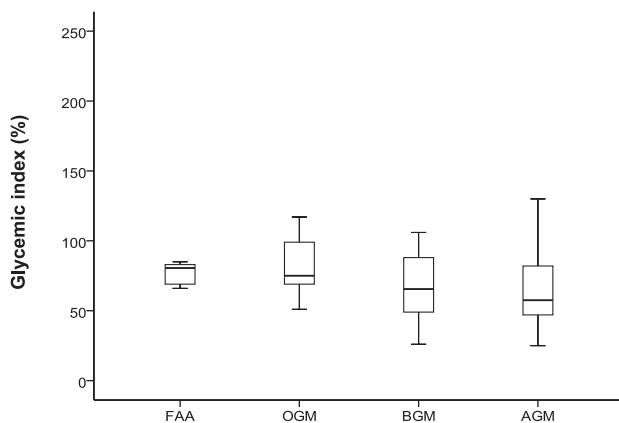


Fig. 5. Box and whisker error bar of three test foods. Dark line represents mean of GI value as determined by FAA, AGM, BGM and OGM. Whisker bars are the 95% of confidence interval. Fuji automatic analyzer (FAA); advantage glucose meter (AGM); breeze 2 glucose meter (BGM); optimum glucose meter (OGM).

four different methods indicated that the brown rice we tested is considered as high GI value. In mango, OGM showed high GI whereas FAA gave medium GI ranking. Both BGM and AGM indicated the mango we tested is low GI. In yogurt drink, FAA, OGM and BGM gave high GI ranking, whereas AGM yield medium GI value.

Discussion

Self-monitoring blood glucose meters is an important

device for diabetic patient to monitor their blood glucose at home. It is recommended that SMBG should be used as part of standard medical care for diabetes [28]. The features of SMBG are simple to use, inexpensive and produce rapid results, have attracted investigator to use SMBG to determine GI values of food [20, 22, 29]. In this study, we observed the differences on glucose concentrations, IAUC, GI values and GI classifications, between determined by biochemical analyzer (FAA) and three glucose meters. The GI values of three test food determined by FAA in our results were similar to previous research finding [15]. In our results, we found that the OGM yield highest glucose concentrations and GI values, whereas BGM and AGM produced the lowest. This explained that the GI value of food is related to the postprandial glucose responses of food [26, 30–31]. Moreover, this result appears to be similar to the reported information that OGM tends to has greater glucose reading than AGM [23, 32]. Among three glucose meters, AGM gave the largest variance than FAA and two glucose meters (BGM and AGM). Noticeable, all three glucose meters had greater variation than FAA in glucose concentrations and GI values. The difference in variance was mostly due to a difference in error variation among four methods.

Velangi and others (2005) [18] studied the performance of OTU glucose meter to determined GI value of 7 foods, and compared with biochemical analyzer. Their results showed higher between-subject variation in glucose meter and concluded that the OUT glucose meter is more variable method for determining AUC and GI than analyzer. The results of Velangi *et al.* can not be compared with present results because difference and numbers of glucose meters

and biochemical analyzer used in the two studies. Nevertheless, our results also indicated all three glucose meters had greater variation in between-subjects than biochemical analyzer.

The study used recommended method [25] to classify the results of GI values and found inconsistent classification among three glucose meters. We further evaluated the number of misclassified observed from using different methods between each subject were FAA (0%), OGM (40%), BGM (56%) and AGM (60%). In sum of all data (sum of glucose concentration, IAUC and GI), our results are consistent with this showing FAA had greater glucose concentrations and IAUC than BGM and AGM. Because IAUC was a result of all area below the glucose response curve and above the fasting concentration, a small increase in analytical variation for glucose may cause a large IAUC variation [33] and thus variable GI values.

The study did not evaluate the clinical acceptability and precision of glucose meters, because previous literatures [23, 34–37] have reviewed the acceptability and precision of three glucose meters we tested. However, our results showed all three glucose meters we tested were less precise and had greater error variation and SEM than FAA.

To be valid, the GI value of the same food in different subjects must be consistent. In our results, FAA showed consistent GI values in between-subject and within-subject. When classify GI value of each food, FAA also gave consistent ranking within each test food. The present results suggested that the AGM, BGM and OGM are more variable methods to determine IAUC, GI and rank GI value than FAA in healthy subjects. In addition, the present study indicated that different analytical methods can have a major effect on the accuracy of GI value of food. Although, there is no absolute way to measure glucose response, to produce consistent value, however, is important when determining GI value of food. As the accuracy and precision of glucose meter vary, the performance of SMBG to determine GI value of food should be evaluated and calibrated before use.

Abbreviations

GI, glycemic index; IAUC, incremental area under the curve; SMBG, self-monitoring blood glucose meter; AGM, advantage glucose meter; BGM, breeze 2 glucose meter; OGM, optimum xceed glucose meter; BMI, body mass index; FAA, fuji automatic analyzer.

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