Glycemic Index and Glucose Utilization of Rice Vermicelli in Healthy Subjects

Shinji Sato,∗,a Keiji Fukumura,b Ayae Nishiyama,b Ikuo Kanamoto,c Yutaka Inoue,c and Tetsuya Konishi2

a Department of Functional and Analytical Food Sciences, Faculty of Applied Life Sciences, Niigata University of Pharmacy and Applied Life Sciences; 265–1 Higashijima, Akisha-ku, Niigata, Niigata 956–8603, Japan; b Kenmin Foods Co., Ltd.; 5–1–1 Kaigan-street, Chuo-ku, Kobe, Hyogo 650–0024, Japan; and c Laboratory of Drug Safety Management, Faculty of Pharmaceutical Sciences, Josai University; 1–1 Keyakidai, Sakado, Saitama 350–0295, Japan.

Received February 12, 2010; accepted May 10, 2010; published online May 19, 2010

Glycemic index (GI) is an indicator of glucose absorption into the systemic circulation after ingestion of foods. However, the plasma glucose level is determined by not only the absorption of glucose, but also the disappearance of glucose which is regulated by the insulin response. The aim of this study was to estimate the values of GI and glucose utilization including the absorption and the disappearance of glucose (UGLU) in the rice vermicelli (RV) using the resulting glucose clearance (CLGLU). Fifteen healthy subjects participated in this study. Alterations in plasma glucose and insulin levels were determined after ingestion of a reference food (12.5, 25, 50, 75 g glucose) and the test foods (white rice, long grain rice and six RV products; 50 g available carbohydrate). Time–course changes in plasma glucose levels were analyzed using a simple kinetic model. The values of CLGLU were calculated using the resulting kinetic parameters. A standard curve in which the incremental area under the curve of plasma insulin levels (AUCINS) was plotted against the resulting CLGLU, was generated using the reference food. The values of GI and UGLU in the RV products were calculated from the observed clearances (CLGLU), and the predicted clearances (CLGLU(predict)) respectively, which were estimated using the standard curve of AUCINS(ref) vs. CLGLU(ref). It was clarified that the values of UGLU in the RV products (20—57%) were lower than those of GI (35—62%).

Key words glycemic index; glucose absorption; glucose utilization; glucose clearance; insulin

Postprandial hyperglycemia increases oxidative stress and protein glycation. Western dietary patterns are associated with substantially increased risk of type 2 diabetes in men. Reduction of postprandial hyperglycemia is important in the prevention and treatment of type 2 diabetes and impaired glucose tolerance. Glycemic index (GI) is a classification of carbohydrate foods based on acute plasma glucose response. Low GI foods produce lower glycemic responses as a result of slower rate of digestion of carbohydrate in the intestinal lumen and subsequent suppression of absorption of glucose into the plasma circulation. Absorption of glucose from the small intestine into the plasma circulation is influenced by the intrinsic properties of the carbohydrate, fiber and fat content of the foods. Variability in the GI is dependent on numerous factors such as amount and type of ingested carbohydrates, composition of the preceding meal, and gastric emptying rate.

Glucose uptake from the plasma into the tissues is primarily influenced by the secretion and action of insulin on the tissues. Incretin hormones such as glucose dependent intrinsotropic polypeptide (GIP) and glucagon like peptide-1 (GLP-1) are released from endocrine cells in the intestinal mucosa after ingestion of carbohydrates, and enhance postprandial insulin release from the pancreatic beta cells. Released insulin stimulates glucose uptake into the skeletal muscles and adipocytes, and enhancement of the glucose clearance (CLGLU) from plasma into the tissues is promoted by facilitative sub-cellular redistribution of the glucose transporter isofrom (GLUT4) from an intracellular compartment to the plasma membrane. Intraluminal glucose is one of the triggering factors for the secretion of these hormones. The ability to stimulate incretin hormone secretion differs among the various types of carbohydrates. Increased amounts of fat and protein in the gut also induce secretion of the incretin hormones. Postprandial insulin responses are not always proportional to plasma glucose levels, and several insulinitropic factors such as protein and fat-containing foods induce substantial insulin secretion.

Schenk et al. indicated that lower GI of bran cereal was not caused by the suppression of glucose absorption into the plasma circulation, but was associated with earlier hyperinsulinemia and subsequent enhancement of glucose disappearance from the plasma. Low GI foods may have either a relatively lower amount of glucose for absorption, or a relatively higher glucose uptake from plasma into the tissues. Rice shows considerable variation in GI. Large differences in the GI value for rice are due to variations in species, process condition conditions and differences in amylose and amylopectin content. Rice with normal amylose content (17%) has been classified as a high GI food. On the other hand, high amylose rice (28% amylose content) has been shown to undergo a slower rate of digestion and to produce lower glycemic and insulin responses. Although the insulinemic index (II) of rice has been shown to be positively correlated with GI, the values of II were lower compared with those of GI. Rice vermicelli (RV) is produced using long grain high amylose rice. The purpose of the present study was to estimate the GI from the observed clearance value (CLGLU), and glucose utilization including the absorption and the disappearance of glucose (UGLU) from the predicted clearance value (CLGLU(predict)) which is altered by the insulin response.

∗ To whom correspondence should be addressed. e-mail: sato@nupals.ac.jp

© 2010 Pharmaceutical Society of Japan
MATERIALS AND METHODS

Subjects Fifteen healthy subjects (eight men and seven women) aged 34±9 year and with a normal body mass index (21.5±1.6 kg/m²) participated in this study. None of the subjects had impaired glucose tolerance, nor were they receiving medication. All subjects gave their informed consent to participate in this study. The study protocol was performed in accordance with the principles of the Helsinki Declaration and approved by the Human Ethics Committee of the Nigata University of Pharmacy and Applied Life Sciences (Nigata, Japan).

Experimental Design Subjects were instructed not to consume food, alcohol or beverages (except water) after 2100 h the night before the tests. On the morning of the test, subjects were asked to refrain from physical activity. Finger prick capillary blood samples were taken using a puncture appliance (Terumo Co., Ltd., Tokyo, Japan). Blood samples (0.1 ml) were collected into a polyethylene heparinized capillary tube (Hematlon-L, Minato Medical Co., Ltd., Tokyo, Japan) and immediately centrifuged (30 s, 10000 g) and the plasma was stored at −20 °C for glucose and insulin measurements. Plasma glucose concentration was determined by the glucose oxidase–peroxidase method (Wako Chemicals, Osaka, Japan). Plasma insulin concentration was measured by enzyme-linked immunosorbent assay (ELISA) (Yanaihara Institute Inc., Shizuoka, Japan). Subjects were given a reference or a test food in random order on separate days. Reference or test food was consumed at an even pace over a period of 10 min. Capillary blood samples were collected at 15, 30, 45, 60, 90, and 120 min after ingestion of the reference or the test food. Treland-G75 (glucose concentration: 333.3 mg/ml, Shimizu, Shizuoka, Japan) was used as the reference food (12.5, 25, 50, 75 g glucose dose). A standard curve was generated, in which the incremental area under the curve of plasma glucose levels from time zero AUC of the reference food containing 12.5, 25, 50, and 75 g glucose. Six RV(a−f) products (Kenmin Food Co., Ltd., Kobe, Japan) were studied in accordance with the principles of the Helsinki Declaration and approved by the Human Ethics Committee of the Nigata University of Pharmacy and Applied Life Sciences (Nigata, Japan).

Table 1. Macronutrient Composition of White Rice, Long Grain Rice and Rice Vermicelli Products

<table>
<thead>
<tr>
<th></th>
<th>Protein (%)</th>
<th>Fat (%)</th>
<th>Carbohydrate (%)</th>
<th>Energy (kcal/100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White rice</td>
<td>5.1</td>
<td>1.1</td>
<td>77.9</td>
<td>342</td>
</tr>
<tr>
<td>Long grain rice</td>
<td>7.6</td>
<td>0.9</td>
<td>78.9</td>
<td>346</td>
</tr>
<tr>
<td>Rice vermelli (a) [RV(a)]</td>
<td>6.3</td>
<td>1.0</td>
<td>78.5</td>
<td>363</td>
</tr>
<tr>
<td>Rice vermelli (b) [RV(b)]</td>
<td>6.5</td>
<td>0.9</td>
<td>78.8</td>
<td>349</td>
</tr>
<tr>
<td>Rice vermelli (c) [RV(c)]</td>
<td>2.9</td>
<td>0.7</td>
<td>81.3</td>
<td>343</td>
</tr>
<tr>
<td>Rice vermelli (d) [RV(d)]</td>
<td>4.9</td>
<td>1.1</td>
<td>79.6</td>
<td>363</td>
</tr>
<tr>
<td>Rice vermelli (e) [RV(e)]</td>
<td>6.1</td>
<td>0.6</td>
<td>79.3</td>
<td>347</td>
</tr>
<tr>
<td>Rice vermelli (f) [RV(f)]</td>
<td>4.0</td>
<td>0.7</td>
<td>80.3</td>
<td>344</td>
</tr>
</tbody>
</table>

Calculation Methods for the Incremental Area under the Curve of Plasma Glucose Levels (AUCGLU), Glucose Clearance (CLGLU), Glycemic Index (GI), Insulinemic Index (II) and Glucose Utilization (UGLU) Incremental area under the curve of plasma glucose levels from time zero to the time when increment of plasma glucose level returns to zero (T) after ingestion of glucose (AUCGLU(ref)) was calculated of the symbols used in all equations are listed in Table 2. In order to quantitatively describe the kinetics of changes in plasma glucose levels after ingestion of the test foods, a one-compartment model with first-order absorption and elimination kinetics was applied and is shown in Fig. 1. The time-course changes in plasma glucose levels after ingestion of the test foods were expressed by Eq. 2 as follows.

\[ C_{GLU} = \frac{F \cdot DOSE \cdot k_a}{V} \left( e^{-k_a t} - e^{-k \cdot T} \right) \]  

(2)

In order to estimate the kinetic parameters, the data for the plasma glucose levels were fitted using a nonlinear least squares regression program, WinNonlin. When a difficulty was encountered in least-squares fitting of a one-compartment model with first-order absorption such that estimated values of the rate constants of absorption and elimination (k_a and k) were almost identical, the following special Eq. 3 was used (k_a=k=k').

\[ C_{GLU} = \frac{F \cdot DOSE \cdot k \cdot T}{V} e^{-k \cdot T} \]  

(3)

Fig. 1. Schematic Representation of Kinetic Model for Glucose in Healthy Subject Plasma
Using the following equation (Eq. 6) as follows.

\[ AUC_{GLU(ref)} = \frac{DOSE}{V} \left[ T - \frac{1}{k_a} \left(1 - e^{-k_a T}\right) \right] - k_a \frac{T^2}{2V} \]  

Incremental area under the curve of plasma glucose levels from time zero to infinity after ingestion of the reference food (AUC_{GLU(ref)}) was calculated using Eq. 5 as follows.

\[ AUC_{GLU} = \frac{F \cdot DOSE}{k_a} \]  

Since the glucose clearance (CL_{GLU}) could be calculated using the volume of distribution and the elimination rate constant of glucose (CL_{GLU} = Fk_a). \(^{21}\) the value of CL_{GLU} after ingestion of test food was calculated using Eq. 6 as follows.

\[ CL_{GLU} = \frac{F \cdot DOSE}{AUC_{GLU}} \]  

Glycemic index (GI) of the test food was estimated by Eq. 7 as follows.

\[ GI = \frac{AUC_{GLU}}{AUC_{GLU(ref)}} \times 100 \]  

If the kinetics of changes in plasma glucose levels after ingestion of glucose could be described by a one-compartment model with first-order absorption and elimination kinetics and \( F_{ref} = 1 \), the value of AUC_{GLU(ref)} could be calculated using the following equation (AUC_{GLU(ref)} = DOSE/CL_{GLU(ref)}). Since the glycemic index (GI) is the percentage intestinal absorption of glucose after ingestion of test food (F), Eq. 7 is rearranged to Eq. 8 as follows.

\[ GI = \frac{CL_{GLU(ref)} \cdot AUC_{GLU}}{DOSE} \times 100 = F \]  

Postprandial insulin responses are not always proportional to plasma glucose levels. Released insulin stimulates the disappearance of glucose from plasma and subsequently decreases plasma glucose levels. Thus, the plasma glucose level is determined not only by the absorption of glucose, but also the disappearance of glucose, which is regulated by insulin. Incremental area under the curve of plasma insulin levels after ingestion of the reference and test foods (AUC_{INS(ref)} and AUC_{INS}) was calculated using the trapezoidal rule. Insulineemic index (II) of the test food was estimated by Eq. 9 as follows.

\[ II = \frac{AUC_{INS}}{AUC_{INS(ref)}} \times 100 \]  

A standard curve was generated in which AUC_{INS(ref)} was plotted against the resulting CL_{GLU(ref)} using the reference food containing 12.5, 25, 50 and 75 g glucose. The predicted glucose clearance value (CL_{GLU(predict)}) could be estimated using the value of AUC_{INS} after ingestion of the test food and the standard curve of AUC_{INS(ref)} vs. CL_{GLU(ref)}. Assuming that the effect of insulin on glucose uptake from plasma into the tissues did not change after ingestion of glucose and the test foods, the values for glucose utilization including the absorption and the disappearance of glucose (U_{GLU}) in the test foods were calculated using Eq. 10 as follows.

\[ U_{GLU} = \frac{CL_{GLU(predict)} \cdot AUC_{GLU}}{DOSE} \times 100 \]  

### Statistical Analysis

Statistical differences were determined to compare glucose 50 g with glucose 12.5 g, 25 g, 75 g and test foods. Values of plasma glucose and insulin levels, AUC_{GLU} and AUC_{INS} were compared for differences using Student’s t-test. \(^{22}\) Statistical significance was established at the p<0.05 level. \(^{23}\) Correlations between DOSE and CL_{GLU(ref)}, DOSE and AUC_{INS(ref)} GI and U_{GLU}. GI and II,
RESULTS

Plasma Glucose and Insulin Levels after Ingestion of the Reference Food  Time–course changes in plasma glucose levels after ingestion of the reference food are shown in Fig. 2. Peak plasma glucose levels were observed at 30—45 min after ingestion of the reference food. Peak plasma glucose levels at the highest glucose dose were almost the same as those at lower glucose doses. Plasma glucose levels in the terminal phase (90—120 min) after ingestion of lower glucose doses (12.5, 25, 50 g) were lower than those before ingestion of glucose (time zero). Plasma glucose levels at 15, 30, 45, 60 and 90 min in glucose 12.5 g, and at 60 and 90 min in glucose 25 g were significantly lower than those in glucose 50 g, and at 120 min in glucose 75 g, the level was significantly higher than that in glucose 50 g. Dotted lines in Fig. 2 represent the calculated values using Eq. 2. Although the time–course changes in plasma glucose level after ingestion of the highest glucose dose could not be described using Eq. 2. Solid lines in Fig. 2 represent the calculated values using the one-compartment model with first-order absorption and elimination kinetics (Eq. 2), plasma glucose levels in the terminal phase after ingestion of the lower glucose doses could not be described using Eq. 2. Solid lines in Fig. 2 represent the calculated values using the one-compartment model with first-order absorption and zero-order elimination kinetics (Eq. 1). Kinetic parameters were estimated using the nonlinear least squares method, and the resulting parameters are listed in Table 3.

Time–course changes in plasma insulin levels after ingestion of glucose are shown in Fig. 3. Peak plasma insulin levels were observed at 15—45 min after ingestion of glucose. Times to peak plasma insulin levels after ingestion of glucose were shorter than those of plasma glucose levels. Plasma insulin levels at 45, 60 and 90 min in glucose 12.5 g and at 60, 90 and 120 min in glucose 25 g were significantly lower than those in glucose 50 g, and at 15 and 30 min in glucose 75 g were significantly higher than those in glucose 50 g.

Correlation between DOSE and $AUC_{GLU(ref)}$ and $DOSE$ and $AUC_{GLU(ref)}$

<table>
<thead>
<tr>
<th>Glucose dose (g)</th>
<th>12.5</th>
<th>25</th>
<th>50</th>
<th>75</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOSE* (mg/kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$k_{b1}^b$ (h⁻¹)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$k_{b2}^b$ (mg/h/kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$k_{b3}^b$ (h)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$k_{a1}^b$ (mg/dl/h)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$k_{a2}^b$ (dl/kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$AUC_{GLU(ref)}^b$ (mg/dl/kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$CL_{GLU(ref)}^b$ (dl/h/kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$AUC_{DOSE}^b$ (mg/ml/h)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$AUC_{GLU25x}^b$ (mg/dl/h)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Values of Kinetic Parameters for Glucose in Healthy Subjects Obtained from Computer Fitting of Plasma Glucose Levels, $AUC_{GLU(ref)}$ and $DOSE$ after Ingestion of the Reference Food (12.5, 25, 50, 75 g Glucose)

a) Values of DOSE were calculated using the following equation; DOSE = glucose dose/body weight, body weight = 58.3 ± 8.8 kg, n = 15. b) Values of the kinetic parameters were estimated by fitting the data of the plasma glucose levels using Eqs. 1 or 2. All kinetic parameters were estimated by the computer program WinNonlin. All data express mean ± S.E.M. of the estimated parameter. c) Values of T were length of time from time zero to the time when increment of plasma glucose level returns to zero after ingestion of glucose. d) Values of $AUC_{GLU(ref)}^b$ were calculated using Eq. 4 (zero-order) or the following equation, $AUC_{GLU(ref)} = DOSE/T(1/T)$. e) Values of $CL_{GLU(ref)}^b$ were calculated using the following equation; $CL_{GLU(ref)} = DOSE/AUC_{GLU(ref)}$. f) Values of $AUC_{DOSE}^b$ and $AUC_{GLU25x}^b$ were calculated by the trapezoidal rule. g) Since plasma glucose levels in the terminal phase after ingestion of 12.5 and 25 g glucose doses were lower than those before ingestion of glucose, values of $AUC_{GLU25x}^b$ are the values for up to 1 and 1.5 h. Values of $AUC_{GLU25x}^b$ for up to 2 h after ingestion of 12.5 and 25 g glucose dose were 25.4 ± 5.6 and 47.8 ± 5.7 (mg/dl/h), respectively. Data are expressed as means ± S.E.M., n = 15. * Significantly different from the result of glucose 50 g ingestion group, p < 0.05, by Student t-test.
DOSE and orthogonal regression analysis. There were significantly positive correlations between AUC glucose dose (DOSE) was plotted against the resulting 50 g (Table 3). A standard curve was generated in which the intercept for the relationship between GLU(ref) was shown to be hyperbolic. Glucose clearances after ingestion of glucose (CL GLU(ref)) were calculated using Eq. 6 and $F_{ref}=1$ (Table 3). The $CL_{GLU(ref)}$ value increased as the dose increased and there was a significantly positive correlation between DOSE and $CL_{GLU(ref)}$ ($r^2=0.948, p<0.05$) (Fig. 4B). Values of $AUC_{INS(ref)}$ after ingestion of glucose were calculated using the trapezoidal rule and these values in glucose 12.5 and 75 g were significantly lower and higher than that in glucose 50 g, respectively (Table 3). The $AUC_{INS(ref)}$ value increased with dose and there was a significantly positive correlation between DOSE and $AUC_{INS(ref)}$ ($r^2=0.974, p<0.05$) (Fig. 4C). A standard curve in which $AUC_{INS(ref)}$ was plotted against the resulting $CL_{GLU(ref)}$ was generated (Fig. 4D). The values of slope ($a$) and intercept ($b$) for the relationship between $AUC_{INS(ref)}$ and $CL_{GLU(ref)}$ were estimated using orthogonal regression analysis ($a=2.481, b=4.085$). The intercept expresses the value of the glucose clearance that is not caused by the increase in insulin. Predicted glucose clearance values ($CL_{GLU(predict)}$) after ingestion of the test foods were estimated using the resulting values of $AUC_{INS after}$ ingestion of the test foods, and the values of slope and intercept for the standard curve of $AUC_{INS(ref)}$ vs. $CL_{GLU(ref)}$.

**Glycemic Index (GI) and Glucose Utilization ($U_{GLU}$) of the Test Foods**  Time–courses changes in plasma glucose levels after ingestion of the test foods (50 g available carbohydrate) are shown in Fig. 5. Peak plasma glucose levels were observed at 15—30 min after ingestion. Peak plasma glucose levels in the test foods were lower than that in glucose 50 g. Plasma glucose levels in the terminal phase (120 min) after ingestion of the test foods were higher than those before ingestion (time zero). Plasma glucose levels at 15 min in long grain rice and RV(c), and at 30, 45 min in the test foods except for white rice, and at 60 min in the test foods except for white rice and RV(a), and at 90 min in RV(b), were significantly lower than those in glucose 50 g. On the other hand, these levels at 120 min in all test foods were significantly higher than that in glucose 50 g. Solid lines...
Table 4. Values of Kinetic Parameters of Glucose in Healthy Subjects Obtained from Computer Fitting of Plasma Glucose Levels, $AUC_{GLU}$, $CL_{GLU}$ and $AUC_{GLU}$ after Ingestion of the Test Food (50 g Available Carbohydrate)

<table>
<thead>
<tr>
<th>Test food</th>
<th>White rice</th>
<th>Long grain rice</th>
<th>RV(a)</th>
<th>RV(b)</th>
<th>RV(c)</th>
<th>RV(d)</th>
<th>RV(e)</th>
<th>RV(f)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k^{a}$ (h$^{-1}$)</td>
<td>1.94±0.15$^a$</td>
<td>2.04±0.36.5</td>
<td>9.17±3.39</td>
<td>2.87±1.38$^a$</td>
<td>2.94±115.6</td>
<td>7.91±2.47</td>
<td>9.60±4.57</td>
<td>6.69±2.55</td>
</tr>
<tr>
<td>$V^{a}$ (h$^{-1}$)</td>
<td>1.94±0.15$^a$</td>
<td>2.09±0.37.5</td>
<td>1.46±0.23</td>
<td>2.87±1.38$^a$</td>
<td>2.96±116.6</td>
<td>1.19±0.19</td>
<td>0.99±0.19</td>
<td>1.13±0.26</td>
</tr>
<tr>
<td>$V^{b}$ (mg/kg)</td>
<td>5.35±0.31$^a$</td>
<td>7.39±0.323.5</td>
<td>11.4±1.14</td>
<td>8.43±0.25$^a$</td>
<td>8.77±464.6</td>
<td>13.1±1.29</td>
<td>15.4±1.63</td>
<td>13.2±1.88</td>
</tr>
<tr>
<td>$CL_{GLU}$ (ml/kg)</td>
<td>10.4±0.77$^a$</td>
<td>15.4±1.77</td>
<td>16.6±1.22</td>
<td>18.5±0.80$^a$</td>
<td>25.9±1.77</td>
<td>15.6±1.19</td>
<td>15.2±1.58</td>
<td>14.9±1.57</td>
</tr>
<tr>
<td>$AUC_{GLU}$ (mg/dl/h)</td>
<td>72.5±0.87$^a$</td>
<td>48.6±0.70*</td>
<td>45.5±7.1*</td>
<td>38.9±6.0*</td>
<td>46.8±7.2*</td>
<td>45.9±8.2*</td>
<td>48.2±7.2*</td>
<td></td>
</tr>
<tr>
<td>$AUC_{INS}$ (ng/ml/h)</td>
<td>1.41±0.25*</td>
<td>2.12±0.52</td>
<td>0.90±0.18*</td>
<td>0.96±0.14*</td>
<td>0.41±0.18*</td>
<td>0.94±0.28*</td>
<td>1.86±0.27</td>
<td>0.83±0.23*</td>
</tr>
<tr>
<td>GP (%)</td>
<td>89</td>
<td>60</td>
<td>55</td>
<td>50</td>
<td>59</td>
<td>60</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>GI (%)</td>
<td>45</td>
<td>60</td>
<td>55</td>
<td>50</td>
<td>35</td>
<td>59</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>$CL_{GLU,pre}$ (dl/kg)</td>
<td>7.57</td>
<td>9.33</td>
<td>6.32</td>
<td>5.97</td>
<td>5.11</td>
<td>4.20</td>
<td>5.63</td>
<td></td>
</tr>
<tr>
<td>$U_{GLU}$ (%)</td>
<td>73</td>
<td>61</td>
<td>38</td>
<td>32</td>
<td>20</td>
<td>41</td>
<td>57</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Kinetic parameters were estimated by fitting the data of the plasma glucose levels using Eq. 2. All kinetic parameters were estimated by the computer program WinNonlin. All data express mean±S.E.M. of the estimated parameter. $^b$ Values of $AUC_{GLU}$ were calculated using Eq. 5. $^c$ Values of $CL_{GLU}$ were calculated using Eq. 6. $^d$ Values of $AUC_{GLU}$ and $CL_{GLU}$ were calculated by the trapezoidal rule. Data are expressed as means±S.E.M., n=15. $^e$ Values of GI were calculated using Eq. 8. $^f$ Values of II were calculated using Eq. 9. $^g$ Values of $CL_{GLU,pre}$ were estimated using the value of $AUC_{GLU}$ after ingestion of the test food and the standard curve of $AUC_{GLU}$ vs. $CL_{GLU,pre}$ in Fig. 4D. $^h$ Values of $U_{GLU}$ were calculated using Eq. 10. $^i$ Since the value of $k$ was the same as the value of $k_{GLU}$, the kinetic parameters were estimated using Eq. 3. $^*$ Significantly different from the result of glucose 50 g ingestion group, p<0.05, by Student t-test.

Values of $AUC_{GLU}$, $CL_{GLU}$ and GI of the test foods were calculated using Eqs. 4—6, and the resulting values are listed in Table 4. Values of $AUC_{GLU}$ and $CL_{GLU}$ for the test foods were lower and higher respectively, than those of glucose 50 g. Values of $AUC_{GLU}$ after ingestion of the test foods were calculated using the trapezoidal rule and these values in the test foods, except for white rice, were significantly lower than that in glucose 50 g (Table 4). The GI value in white rice (89%) was found to be higher than that in long grain rice (60%), RV(a) (55%), RV(b) (50%) and RV(c) (35%) were foods with lower GI values. Values of $AUC_{INS}$ after ingestion of the test foods were calculated using the trapezoidal rule and these values in white rice, RV(a), RV(b), RV(c), RV(d) and RV(f) were significantly lower than that in glucose 50 g (Table 4). II values were calculated using the Eq. 9, and II in long grain rice (96%) was higher than that in white rice (64%). RV(a) (41%), RV(b) (44%), RV(c) (19%), RV(d) (43%) and RV(f) (38%) were foods with lower II values, but not RV(e) (84%). The relationship between $AUC_{INS}$ and $CL_{GLU}$ was a straight line with slope (a) and intercept (b) as shown in Fig. 4D ($y=2.481x+4.085$). Values of $CL_{GLU}$ were estimated using the values of $AUC_{INS}$ after ingestion of the test foods and the values of slope (a) and intercept (b). Values of $CL_{GLU}$ in all test foods were lower than that in glucose 50 g (9.17±0.33 (dl/h)/kg) (Table 4). Values of $U_{GLU}$ in the test foods were calculated using Eq. 10, and there was a significantly positive correlation between GI and $U_{GLU}$ ($r^2=0.797, p<0.05$) (Fig. 7A). Since the values of $AUC_{INS}$ in other test foods were significantly lower than that in glucose 50 g, the values of $U_{GLU}$ were lower than those of GI (Table 4). The values of $U_{GLU}$ in long grain rice (61%) and RV(e) (57%) were almost the same as the values of GI (60% and 60%) (Table 4). These test foods, except for long grain rice and RV(e), were located in the lower part in the correlation between GI and $U_{GLU}$ (Fig. 7A). The correlation between GI or $U_{GLU}$ and II is shown in Fig. 7B. The broken line represents the regression line between GI and II, and there was no significantly positive correlation between these ($r^2=0.230, p=0.230$). The arrows express changes from GI to $U_{GLU}$. The solid line represents the regression line between $U_{GLU}$ and II.
Ingestion of the Test Foods

**DOSE**

... glucose 50 g (Table 3), and the standard curve of was not significantly increased compared with that after ingestion of the highest glucose dose, 75 g. The value of \( \text{AUC}_{\text{GLU}(2h)} \) after ingestion of glucose was 100% (Fig. 4C). Incretin hormones such as GIP and GLP-1 are released from endocrine cells in the intestinal mucosa after ingestion of carbohydrates and enhance postprandial insulin release from the pancreatic beta cells. 19 Release of incretin hormones is not caused by elevated blood glucose concentrations, but rather by glucose binding to the sweet taste receptors of the tongue and gut. 20 Trafficking of GLUT4 containing storage vesicles from the intracellular storage pool and insertion into the plasma membrane is caused by the increase in plasma insulin levels. 10 In fact, the value of \( \text{CL}_{\text{GLU}(ref)} \) increased as the dose increased and there was a significantly positive correlation between DOSE and \( \text{CL}_{\text{GLU}(ref)} \) \((\gamma^2=0.948, p<0.05)\) (Fig. 4B). The hyperbolic nature of the curve of DOSE vs. \( \text{AUC}_{\text{GLU}(ref)} \) may not be due to suppression of glucose absorption from small intestine after ingestion of higher glucose dose, but may rather be caused by the acceleration of the glucose clearance from plasma into the tissues. Livesey et al. reported that when the percentage absorption of glucose after a 50 g oral glucose load (containing \( \delta^{[13]C_6} \) glucose) in healthy humans was calculated using a two-compartment model, the resulting absorption of glucose was 100%. 20 Therefore, it was assumed that the percentage intestinal absorption of glucose after ingestion of glucose was 100% (\( F_{\text{ref}}=1 \)) in this study.

**DISCUSSION**

Plasma glucose levels in the terminal phase (90—120 min) after ingestion of lower glucose doses (12.5, 25, 50 g) were lower than those before ingestion of glucose (time zero) and could not be described using Eq. 2 (Fig. 2). Arumugam et al. examined the effects of variations in postprandial glycemia with a large glucose beverage consumed with breakfast and lunch (Rapid), and with the same volume of glucose beverage consumed in eight portions at 20-min intervals (Slow). 23 It was observed that the glucose level fell below baseline in the subjects with “Rapid” consumption, which was markedly different from the relatively stable levels of glucose in the subjects with “Slow” consumption; in addition the ratings of hunger and appetite with “Rapid” consumption were higher than those with “Slow” consumption. These results indicated that the glucose level was more strongly correlated with appetite ratings in the “Rapid” consumption group than with those in the “Slow” consumption group. In this study, the kinetics of glucose changes in plasma after ingestion of glucose were analyzed using the one-compartment model with first-order absorption and zero-order elimination kinetics (Eq. 1) to explain decreases in plasma glucose level below baseline. This kinetic model of plasma glucose levels may be useful for future evaluation of foods using the glucostatic theory, which states that “hunger and the initiation of eating use useful for future evaluation of foods using the glucostatic baseline. This kinetic model of plasma glucose levels may be first-order absorption and zero-order elimination kinetics (Eq. 2). White rice is the normal grain rice (Japonica rice, Koshihikari) harvested in Japan. Rice has been assigned a wide range of the GI values. 14 Large differences in GI values for rice are caused by the variation in species, processing conditions and differences in amylose and amyllopectin content. 15—17 Rice with normal amylose content (17%) has been classified as a high GI food. 18 In fact, the GI value of white rice is 89%. However, the \( U_{\text{GLU}} \) value of white rice (73%) was lower compared with the GI value, because white rice has a lower II value (64%). The observed lower value of II compared to that of GI in white rice is in agreement with a previous report. 15 High amylose rice (28% amylose content) has been shown to undergo a slower rate of digestion and produce lower glycemic and insulin responses. 19 Long-term intake of a high amylopectin corn diet has been shown to improve fasting triglyceride and cholesterol levels in healthy subjects compared with a high amyllopectin diet. 22 Long grain rice is Indica rice harvested in Thailand. Plasma glucose levels at 15, 30, 45, 60 min and the value of \( \text{AUC}_{\text{GLU}(2h)} \) in long grain rice were significantly lower than those in glucose 50 g, and the GI value was 60%. Plasma insulin levels at all times and the value of \( \text{AUC}_{\text{INS}} \) in long grain rice were not significantly different from those in glucose 50 g, and the II value was 96%. Since the value of \( \text{AUC}_{\text{INS}} \) in long grain rice was almost the same as that in glucose 50 g, the \( U_{\text{GLU}} \) value (61%) was almost the same as the GI value (60%) and long grain rice was located in the upper part in the correlation between GI and \( U_{\text{GLU}} \) (Fig. 7A).

**RV(a)** is produced from 100% long grain rice, and RV(b) is produced from 99% long grain rice + 1% calcium. Although no significant difference was found in \( \text{AUC}_{\text{GLU}(2h)} \), the
values of GI, II and $U_{GLU}$ in RV(a) (55, 41, 38%, respectively) and RV(b) (50, 44, 33%, respectively) were lower than those in long grain rice (60, 96, 61%, respectively). Resistant starch is defined as starch fragments remaining undigested in the upper gastrointestinal tract of humans that can be fermented by human gut bacteria. High levels of resistant starch are formed after heating and cooling of amylose and amylopectin starches. $RV(a)$ and $RV(b)$ used in this study were produced by the pushing out process (pressurization and heating) and two cycles of the steaming process; the aging process was carried out in a cold location. The lower values of GI, II and $U_{GLU}$ observed in $RV(a)$ and $RV(b)$ compared with those in long grain rice may have been caused by the enhancement of resistant starch production. $RV(c)$ is made from long grain rice, tapioca and corn starch and is “side dish” rice vermicelli. Values of GI, II and $U_{GLU}$ in $RV(c)$ (35, 19, 20%, respectively) were lower than those in $RV(a)$ (55, 41, 38%, respectively). It has been reported that the GI values of tapioca (cassava) and sweet corn are 46—70% and 37—62%, respectively. The proportions in which rice, tapioca and corn starch are mixed is a trade secret. The glycemic response decreased when whole or cracked cereal grains were substituted for milled flour in bread, and the reduction in glycemic response was greater after ingestion of bread including higher proportions of whole grains. Lower values of GI, II and $U_{GLU}$ in $RV(c)$ compared with those in $RV(a)$ may be caused by the combination effect of tapioca and corn starch. $RV(d)$ is made from long grain rice, tapioca and potato starch and is “instant” rice vermicelli. $RV(d)$ and $RV(e)$ were almost the same as those in $RV(a)$ (55, 41, 38%, respectively). Although the GI value of boiled potato was 58%, the combination effect of tapioca and potato starch was not observed after ingestion of $RV(d)$. $RV(e)$ is made from long grain rice and potato starch and is the flat type noodle “kway teow.” Values of GI, II and $U_{GLU}$ in $RV(e)$ were 60, 84 and 57%, respectively. II value in $RV(e)$ was higher than that in $RV(a)$. Wachter-Hagedoorn et al. investigated the correlation between rate of intestinal glucose absorption and plasma GLP-1 and GIP levels after ingestion of glucose and starch foods with differing content of rapidly and slowly available glucose. It was found that plasma GLP-1 levels increased significantly after ingestion of uncooked cornstarch which has a high content of slowly available glucose. The higher II value in $RV(e)$ may be caused by the differences in kinetic behavior of GLP-1 in plasma. $RV(f)$ is made from long grain rice and tapioca starch and is the flat type noodle “pho.” Values of GI, II and $U_{GLU}$ in $RV(f)$ (62, 38, 41%, respectively) were almost the same as those in $RV(a)$ (55, 41, 38%, respectively). The combination effect of tapioca starch and higher value of II were not observed after ingestion of $RV(e)$.

Various attempts have been made to overcome problems in assessing insulin action. Homeostatic model assessment which is calculated from fasting insulin and glucose levels is also a useful method for the assessment of insulin action. Bergman et al. developed a physiological model (minimal model) to analyze the plasma glucose and insulin dynamics in the intravenous glucose tolerance test (IVGTT); this minimal model method is widely used to estimate glucose effectiveness and insulin sensitivity from the IVGTT data. The euglycemic clamp technique is the most useful method for providing an index of whole body insulin sensitivity; however this technique needs a fixed rate of intravenous insulin infusion and a variable glucose infusion rate to maintain euglycemia. In this study, the values of $AUC_{GLU(ref)}$ and $CL_{GLU(ref)}$ after ingestion of glucose were calculated using Eq. 4 and the following equation: $CL_{GLU(ref)} = \frac{DOSE}{AUC_{GLU(ref)}}$. Resulting values of $CL_{GLU(ref)}$ correlated well with $AUC_{INS(ref)}$ (Fig. 4D). This result indicated that $CL_{GLU(ref)}$ reflects the plasma insulin level and is altered in accordance with $AUC_{INS(ref)}$. Since the predicted glucose clearance values ($CL_{GLU(predict)}$) for the test foods were estimated using the standard curve of $AUC_{INS(ref)}$ vs. $CL_{GLU(ref)}$, the $CL_{GLU(predict)}$ included insulin actions after ingestion of the test foods. The glucose utilization value, including the absorption and disappearance of glucose ($U_{GLU}$) in the test food was calculated by Eq. 9. Equation 9 is rearranged to Eq. 11 as follows.

$$U_{GLU} = GI \times CL_{GLU(predict)}$$  \hspace{1cm} (11)

The standard curve of $AUC_{INS(ref)}$ vs. $CL_{GLU(ref)}$ was a straight line with slope (a) and intercept (b). The values of $CL_{GLU(predict)}$ and $CL_{GLU(ref)}$ could be calculated using the following equation: $CL_{GLU(predict)} = aAUC_{INS} + b$. $CL_{GLU(ref)} = aAUC_{INS(ref)} + b$. Equation 11 is rearranged to Eq. 12 as follows.

$$U_{GLU} = GI \times II'$$  \hspace{1cm} (12)

The $U_{GLU}$ value includes the values of glucose absorption (GI) and glucose disappearance which is regulated by insulin (II'). In fact, there was a significantly positive correlation between $U_{GLU}$ and II ($r^2 = 0.657, p < 0.05$) (Fig. 7B).

In conclusion, the results of this study have indicated that the values of GI and $U_{GLU}$ in the RV products were calculated from the observed clearance ($CL_{GLU}$), and the predicted clearance ($CL_{GLU(predict)}$), respectively, which were estimated using the standard curve of $AUC_{INS(ref)}$ vs. $CL_{GLU(ref)}$. The RV products were lower GI foods (35—62%). Resulting values of $U_{GLU}$ in the RV products (20—57%) were lower than those of GI. These results suggest that RV products play beneficial effects in the prevention and treatment of type 2 diabetes and the metabolic syndrome.

Acknowledgements This work was supported by a Grant-in-Aid for Scientific Research (category C) from the Japan Society for the Promotion of Science (#19500695) (SS), Institute for Food and Health Science, Yazuya Co., Ltd. (SS), and the Promotion and Mutual Aid Corporation for Private Schools of Japan (SS).

REFERENCES