RESEARCH REPORT

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DETERMINATION OF THE POSTPRANDIAL GLUCOSE AND INSULIN RESPONSES OF WHITE RICE ALONE AND WHITE RICE CONSUMED WITH SUGARDOWN™

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DETERMINATION OF THE POSTPRANDIAL GLUCOSE AND INSULIN RESPONSES OF WHITE RICE ALONE AND WHITE RICE CONSUMED WITH SUGARDOWN™

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SYNOPSIS

Study title:	Determination of the postprandial glucose and insulin responses of white rice alone and white rice consumed with SUGARDOWN™.
Sponsor:	Boston Therapeutics, Inc - 33 S. Commercial St, Manchester, NH 03101, USA and Advance Pharmaceutical Company Limited - Rm.L 3/F, 12 Dai Fu St, Tai Po Industrial Estate, Tai Po, N.T, Hong Kong
Investigator:	Prof. Jennie Brand-Miller, Human Nutrition Unit, School of Molecular Bioscience GO8, Sydney University, NSW, 2006, Australia
Type of research:	Repeated-measures, open cross-over design: 10 subjects consumed three different test meals comprising of white rice or white rice consumed with SUGARDOWN™ (2 different doses). Each of the three test meals was consumed twice by each of the subjects. Each test meal was consumed on a separate morning and was served in a random order. The Human Research Ethics Committee of the University of Sydney approved the experimental procedures used in this study.
Subjects:	10 healthy voluntary subjects (4 females and 6 males) with a mean age of 29.2 years and a mean BMI value of 27.3 kg/m^2.
Inclusion Criteria:	Healthy non-smokers; aged between 25 – 65 years; stable body weight within the overweight range for height (BMI values > 25 kg/m^2); normal dietary and physical activity habits; no history of dieting for the past 3 months; able to fast overnight for ≥ 10 hours before each test session; able to refrain from consuming alcohol the day before a test session; not pregnant or breast-feeding or trying to become pregnant; not taking any medication known to affect blood glucose levels.
Study objectives:	1. To determine the postprandial glucose responses of the three test meals. 2. To determine the postprandial insulin responses of the three test meals.
Study period:	Duration of study period: 10 weeks: March – June 2011. First subject commenced study on the 28th March 2011. Last subject completed their last test session on the 3rd June 2011.
Methodology:	Standard postprandial response methodology: Fasting subjects consumed equal-carbohydrate portions of the three test meals (repeated twice) containing 50 grams of available carbohydrate from the white rice. Each meal was tested on a separate occasion. Finger-prick blood samples were obtained at –10, 0, 15, 30, 45, 60, 90, 120 min. Plasma glucose and insulin concentrations were measured and the incremental areas under the 120-minute plasma glucose and plasma insulin response curves (iAUC) were calculated.
Test Meals:	• White Rice: 63.0 g (dry) Jasmine rice consumed together with 250 mL water • White Rice: 63.0 g (dry) Jasmine rice + 3 SUGARDOWN™ tablets consumed together with 250 mL water • White Rice: 63.0 g (dry) Jasmine rice + 6 SUGARDOWN™ tablets consumed together with 250 mL water • Each test meal was repeated twice by each subject.
Results:	There were no serious adverse events reported during the study (before, during or after the test sessions) and none of the subjects withdrew from the study. The addition of 3 and 6 SUGARDOWN™ tablets reduced the postprandial glucose responses to the white rice by 19% and 32%, respectively. The addition of 3 and 6 SUGARDOWN™ tablets reduced the postprandial insulin responses to the white rice by 16% and 24%, respectively. Plasma glucose responses were significantly associated with their corresponding insulin iAUC responses (r = 0.78, p = 0.0001).

1. INTRODUCTION

Nutrition research conducted in the 1970's showed that different carbohydrates did not have the same effects on blood glucose (sugar) levels after eating. These findings challenged the general assumption that all complex carbohydrates (starches) produce lower blood glucose responses than simple sugars, and questioned the clinical significance of carbohydrate exchange lists that have regulated the diets of people with diabetes for over three decades. These exchange lists are based on the assumption that portions of different foods containing equal amounts of carbohydrate will produce the same blood glucose response. Consequently, **the glycemic index (GI)** method was developed in order to rank equal carbohydrate portions of different foods according to the extent to which they increase blood glucose levels after being eaten (1). Foods with a high GI value (≥ 70) contain rapidly digested carbohydrate, which produces a large rapid rise and fall in the level of blood glucose. In contrast, foods with a low GI value (≤ 55) contain slowly digested carbohydrate, which produces a gradual, relatively low rise in the level of blood glucose (Figure 1).

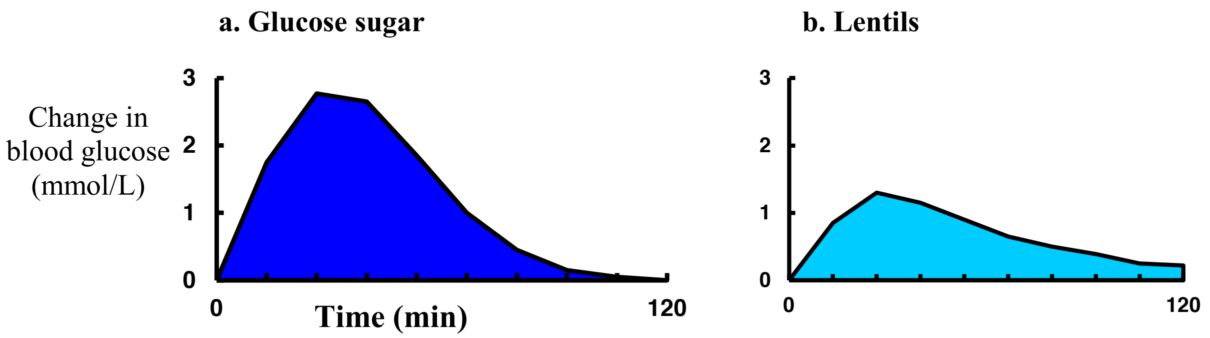

Figure 1. The two-hour incremental blood glucose responses to a high-GI food (a. glucose: GI value = 100) and a low-GI food (b. lentils: GI value = 29).

Over two decades of research has confirmed that a food's effect on blood glucose levels can not be accurately predicted on the basis of the type and amount of carbohydrate it contains. This is because the rate at which carbohydrate is digested and released into the bloodstream is influenced by many food factors, such as the food's physical form, its fat, protein and fibre content, and the chemical structure of its carbohydrate (2, 3). For these reasons, apparently similar foods within the same food group can produce widely different blood glucose responses. Therefore, it's necessary to measure the GI values of foods on an individual basis.

GI research has important implications for the food industry and people's health. Scientists now agree that the terms 'complex carbohydrate' and 'sugars', which commonly appear on food labels, have little nutritional or physiological significance. Recently, a committee of experts was brought together by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organisation (WHO) to review the available research evidence regarding the importance of carbohydrates in human nutrition and health (4). The committee endorsed the use of the GI method for classifying carbohydrate-rich foods and recommended that GI values of foods be used in conjunction with information about food composition to guide food choices. Currently, GI values are being used to construct dietary plans for people with diabetes, and are being used in scientific research, which is examining the association between the glycemic impact of diets and the risk of certain diseases. Over the last decade, a growing body of research has shown that the overall glycemic impact of people's diets can influence the development of insulin resistance and the risk of associated diseases (heart disease, diabetes), independently of the total carbohydrate content of the diet (4). To date, the available evidence suggests that diets based on low-GI carbohydrate-rich foods improve insulin sensitivity and blood glucose control in people with diabetes; reduce high blood fat levels; and may help prolong peak physical performance during endurance events (4, 5). In addition, low-GI foods tend to be less refined and relatively filling and are therefore useful for weight control diets (6, 7). Given that non-insulin-dependent diabetes (NIDDM) and coronary heart disease continue to be major causes of illness and death in all industrialised countries, the extent to which the glycemic impact of people's diets influences both the onset and progression of these diseases is an issue of great importance. Therefore, further research is required to determine the GI values of a greater range of carbohydrate-rich foods and to examine the effects of different processing methods. GI values of new foods and ingredients can be determined before they are released into the marketplace and their GI value can be stated on the food's nutrition panel to assist consumers in their efforts to lower the glycemic impact of their diet.

To date, few studies have measured postprandial blood glucose and insulin responses concurrently. This is due to the expensive cost of measuring insulin levels in blood samples and also reflects the widespread belief that glycemia is the only relevant postprandial factor to consider in the dietary therapy of people with diabetes mellitus. However, available research indicates that postprandial insulin responses to some foods are disproportionately greater than their blood glucose responses (8, 9). A growing body of research results from dietary trials and large epidemiological studies indicates that the long-term consumption of a diet with a high glycemic load that induces recurring and high blood glucose and insulin levels is associated with an increased risk of developing insulin resistance, non-insulin-dependent diabetes mellitus, dyslipidemia, and cardiovascular disease (4, 10-13). It may be possible to show a more direct link between diet and the risk of certain chronic diseases if a large database of the insulin index values of common foods was available.

Although dietary carbohydrate is a major stimulus for insulin secretion, other food factors such as certain amino and fatty acids also enhance insulin secretion. Foods rich in protein, but low in carbohydrate, such as meat or fish, induce relatively high levels of insulin secretion compared to their low blood glucose responses. In addition, foods rich in refined carbohydrate and fat, such as chocolate and certain bakery products, can produce insulin responses that are much greater than their postprandial glycemic responses. Recently, best-selling diet books in the USA have popularised the concept that carbohydrate-rich foods that trigger high insulin responses are particularly fattening. Unfortunately, the authors do not always correctly identify low- or high-insulinemic foods. Therefore, it would be valuable to determine the insulin scores and glycemic index scores of all commercially available foods.

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2. OBJECTIVES OF THE STUDY

a. The primary objective of the study was to determine the postprandial glucose responses to the three test meals.
b. The secondary objective of the study was to determine the postprandial insulin responses to the three test meals.

3. METHODS

This study was conducted using internationally recognised GI methodology in line with international standards for conducting ethical human research. The experimental protocol used in this study was approved by the University of Sydney Human Research Ethics Committee.

3.1 STUDY DESIGN

This study was a partly controlled laboratory-based study comparing the short-term postprandial blood glucose and insulin responses produced by two test meals containing SUGARDOWN™, compared to the effects produced by an equal-carbohydrate portion of plain white rice (the control meal). The study used a repeated-measures design, such that every subject consumed each meal on two separate occasions, completing a total of six separate test sessions. Each subject completed their test sessions on separate weekday mornings at a similar time of day, as close as possible to the time they would normally eat breakfast.

3.2. SUBJECTS

3.2.1 Type of subjects

Ten healthy, non-smoking, overweight or obese subjects (4 females, 6 males) voluntarily participated in this study. The mean ± SD age of the subjects was 29.2 ± 3.3 yr (range: 25.6 – 36.8 yr), and their mean ± SD body mass index value was 27.3 ± 1.1 kg/m^2 (range: 25.5 – 28.7 kg/m^2). The subjects' relevant details are listed in Appendix I.

3.2.2 Recruitment procedures

The subjects were recruited from the staff and student population of the University of Sydney. Interested volunteers were given detailed written and verbal information about all of the study's inclusion criteria and experimental procedures. If the volunteers decided that they would like to participate in the study, they were asked to come to the research centre on another morning, where they completed a detailed screening questionnaire that assessed their current health status and medical history. In order to participate in the study, the volunteers had to meet the inclusion criteria listed below. All suitable volunteers that were invited to participate in the study were required to sign a detailed subject information sheet and a consent form before commencing any experimental procedures.

3.2.2.1 Inclusion criteria

1. Aged between 25-65 years.
2. Non-smoker.
3. Stable body weight within the overweight weight range for their height (BMI values > 25 kg/m^2).
4. Normal dietary habits; not dieting or eating in an overly restrictive fashion in the past 3 months.
5. A regular pattern of low to moderate physical activity.
6. Able to fast for ≥ 10 hours the night before each test session.
7. Able to refrain from eating a legume-based evening meal or drinking alcohol the day before each test session.
8. Finds the test foods suitable for consumption within 12 minutes.
9. Participant covered by social security or a similar system.
10. Not taking any treatment for anorexia, weight loss, or any form of treatment or medication likely to interfere with metabolism or dietary habits.
11. Signed the informed consent form for the study.

3.2.2.2 Exclusion criteria

1. Currently following a restrictive diet (low-calorie, low-carbohydrate, vegan).
2. Any clinically significant physical or mental illness.
3. Suffering from a food allergy or serious food intolerance.
4. Regularly taking prescription medication other than standard contraceptive medication.
5. Females who are currently pregnant, breast-feeding, trying to become pregnant or not using an acceptable contraceptive.
6. Participating in another clinical trial or participated in another clinical trial within the last week.
7. Undergoing general anaesthesia in the month prior to inclusion.
8. Subject in a situation, which in the investigator's opinion could interfere with optimal participation in the present study or could constitute a special risk for the subject.

3.3 TEST FOODS

3.3.1 Description of the test meals

Each rice-based test meal was served to a subject in a fixed portion containing 50 grams of available carbohydrate. All three test meals consisted of the same portion of cooked Jasmine rice (Sun Rice® Jasmine Fragrant Rice, Ricegrowers Limited, NSW, Australia) served with 250 mL of plain water. Two of the test meals also included the consumption of either 3 or 6 SUGARDOWN™ tablets with 250 mL plain water 10 minutes prior to the consumption of the rice-based meal. A glass of 250 mL of water was consumed 10 minutes prior to the consumption of the rice meal for the control meal (Rice). The macronutrient contents of the equal-carbohydrate portions of the test meals are listed in Table 1 below, calculated using the manufacturer's data. The primary ingredients of each SUGARDOWN™ tablet were 2.0 g Mannan Polysaccharide and 1.5 g Sorbitol. Therefore, the RICE + 3 SUGARDOWN™ and RICE + 6 SUGARDOWN™ tablet test meals contained 6.0 g Mannan and 4.5 g Sorbitol and 12 g Mannan Polysaccharide and 9 g Sorbitol, respectively.

Table 1. The weight and macronutrient content of the test portions of the three rice test meals.

Test food ID code	RICE	RICE + 3	RICE + 6
Portion size (g)	**63.0 g (dry)**	**63.0 g (dry)**	**63.0 g (dry)**
Protein (g)	4.6	4.6	4.6
Fat (g)	0.3	0.3	0.3
Available Carbohydrate (g)	50.0	50.0	50.0
Fibre (g)	0.4	0.4	0.4
Energy (kJ)	932	932	932

3.3.2 Methods of test food administration

The three rice test meals were each consumed by the 10 subjects on two separate occasions. Therefore, each subject completed six separate test sessions. Each of the six test meals was presented to the subjects in a random order according to the list shown in Appendix II. Ten minutes prior to the consumption of the rice test meal, the subjects were required to consume either 250 mL of water (control RICE meal), 3 SUGARDOWN™ tablets with 250 mL water (RICE + 3 meal) or 6 SUGARDOWN™ tablets with 250 mL water (RICE + 6). The SUGARDOWN™ tablets are not commercially available in Australia. Therefore, it's unlikely that any of the Australian subjects would have known the identity of the tablets from their appearance alone. The test meals were all served to the subjects on standard white china plates without any commercial packaging. Therefore, the Australian subjects can be considered to have been blind to the exact identity of rice or tablets included in the test meals.

Each rice portion was prepared shortly before required according to the manufacturer's instructions. A test portion of dry rice was individually cooked on the stovetop using a gentle boil method in excess water. The rice portion was stirred occasionally during the cooking process, before being drained and served to a subject in a white china bowl. Each rice portion was served together with 250 mL of plain water. As soon as the subjects commenced eating, a stopwatch was started to time the progress of the two-hour experimental session. The subjects were instructed to consume all of the food and fluid served to them at a comfortable pace within 12 minutes.

3.4 EXPERIMENTAL PROCEDURES

3.4.1 Experimental protocol

The day before each test session, the subjects were required to refrain from drinking alcohol for the entire day and to avoid unusual levels of food intake and physical activity. In the evening, they were required to eat an evening meal based on a low-fat, carbohydrate-rich food, other than legumes, after which the subjects were required to fast for at least 10 hours overnight until the start of their test session the next morning. During the fasting period, they were allowed to drink only water.

The next morning the subjects reported to the research centre in a fasting condition. The researchers first checked that each subject was feeling well and had not taken any medication since the previous test session, and had been able to comply with all of the preceding experimental requirements. Each subject's body weight was then recorded (subjects clothed but without jackets and shoes), after which they warmed a hand in a bucket of hot water for 1-2 minutes. The first of two fasting finger-prick blood samples (- 10 min) was then obtained from a fingertip (≥ 0.7 mL of capillary blood – depending on blood flow and haematocrit level) using a sterile automatic lancet device (Safe-T-Pro®, Boehringer Mannheim, Germany). The subject was then given either 250 mL of water (control RICE meal), 3 SUGARDOWN™ tablets with 250 mL water (RICE + 3 meal) or 6 SUGARDOWN™ tablets with 250 mL water. They were required to consume this test portion within 5 minutes. After 10 minutes, the subjects reheated their hand in hot water for another minute, after which another fasting blood sample was taken (0 min).

After this fasting blood sample was obtained, the subjects were seated at a large table in a quiet room and they were served a fixed portion of white rice, which they consumed together with 250 mL of water at a comfortable pace within 12 minutes. A stopwatch was started for each subject as soon as they began eating (0 min). The subjects were instructed to consume all of the water and food served to them, after which they were required to remain seated at the research centre and refrain from additional eating and drinking for the next two hours. Additional finger-prick blood samples were collected 15, 30, 45, 60, 90 and 120 minutes after eating had commenced. The subjects reheated their hands for 1-2 minutes in hot water before each blood sample was required. Therefore, a total of eight blood samples were collected from each subject during a test session. After completing the 120-minute test session, the subjects were free to consume some refreshments before leaving the research centre.

3.4.2 Criteria of judgement

1. The postprandial glucose responses of three rice test meals.
2. The postprandial insulin responses of three rice test meals.

3.4.3 Determination of plasma glucose and insulin concentrations

Each blood sample was collected into a 1.5-mL plastic micro-centrifuge tube containing 10 IU of the anticoagulant, heparin sodium salt (Grade II, Sigma Chemical Company, Castle Hill, NSW, Australia). Immediately after collection, the blood sample was mixed with the anticoagulant by gently inverting the tube, and then centrifuged at 12,500 x g for 0.5 - 1.0 minute at room temperature. The plasma was then immediately transferred into a labelled, uncoated plastic micro-centrifuge tube and then stored at – 20 ºC until analysed.

3.4.3.1 Measurement of plasma glucose concentrations

Plasma glucose concentrations were measured in duplicate using a Roche/Hitachi 912® automatic spectrophotometric centrifugal analyser (Boehringer Mannheim Gmbh, Mannheim, Germany) employing the glucose hexokinase / glucose-6-phosphate dehydrogenase enzymatic assay (Boehringer Mannheim Australia, Castle Hill, NSW, Australia). All of the eight blood samples for an individual subject's test session were analysed within the same assay run. Each run was performed with standard calibrators and internal controls (CFAS, Precinorm S, and Precinorm U, Boehringer Mannheim, Australia). If the duplicate values for a blood sample differed by more than 0.3 mmol/L, the sample was reanalysed another 2 times, and the 2-3 most similar concentrations were used to calculate an average plasma glucose concentration for that sample.

3.4.3.2 Measurement of plasma insulin concentrations

Plasma insulin concentrations were measured using a solid phase antibody-coated tube radioimmunoassay kit (Diagnostic Products Corporation, Los Angeles, CA, USA). The insulin assay was performed at the School of Molecular Bioscience of the University of Sydney. All of the blood samples collected from each individual subject throughout the entire study were analysed within the same assay run using internal controls. The final insulin concentration of each plasma sample was calculated by converting the radioactive counts observed, using a calibration curve created by standards of known insulin concentrations. Two sets of standards were used in each assay run.

3.5. DATA ANALYSIS

3.5.1 Calculating postprandial glucose and insulin responses

The average value of the two duplicate plasma glucose concentrations recorded for each blood sample was used as subjects' blood glucose concentrations for the eight time points of each two-hour test session. For each subject, the incremental area under the two-hour plasma glucose response curve (iAUC) for each test meal was calculated using the trapezoidal rule with the baseline, fasting value truncated at zero. The baseline value was the average concentration of the two fasting blood samples (-10 and 0 minutes). Any negative area below the fasting level was ignored. The iAUC values allow the comparison of the integrated effects of the test meals over a fixed time period. The incremental area under the plasma insulin response curve for each subject's test meals was calculated using the same method listed above for the plasma glucose iAUC.

3.5.3 Data management, descriptive statistics, and analysis of variance

The raw plasma glucose and plasma insulin results were typed into a spreadsheet (Microsoft® Excel 2004 software, Microsoft Corporation) as they were obtained during the course of the study (double-entry typing and then rechecked at least twice). Once data entry was completed, the incremental areas under the curve for the plasma glucose and insulin responses were calculated. The data in the spreadsheets were then transferred to another computer programme file (Statview® software, version 4.02, 1993, Abacus concepts Inc, Berkley, CA, USA), in order to calculate descriptive statistics for the glucose and insulin iAUC responses (mean, median, SD, SEM).

Repeated-measures analysis of variance (ANOVA) was used to determine whether there were any significant differences amongst the mean glucose and insulin iAUC responses of the three rice test meals. If a statistically significant product-effect was found, a post-hoc multiple comparisons test was performed in order to identify the specific significant differences. For normally distributed data, the Fisher PLSD test was used as the post-hoc test.

4. RESULTS

4.1 Adverse effects, untimely stops or premature departure of subjects

No serious adverse effects were reported or observed during the study and none of the subjects reported taking any medication. Each two-hour experimental session proceeded without incident. Similarly, none of the subjects prematurely departed the study. Two subjects reported minor gastrointestinal discomfort following a 2-hour experimental session containing the highest (6 tablets) dose of SUGARDOWN™ tablets. These subjects reported mild stomach pain and/or diarrhoea on the afternoon of the test session containing the 6 tablet dosage of SUGARDOWN™. All ten subjects reported that the larger dose of SUGARDOWN™ tablets was difficult to consume due to the taste and size of the tablets.

4.2 The test foods' plasma glucose responses

The 10 subjects' individual blood glucose concentrations for each test meal and their corresponding plasma glucose iAUC values are shown in Appendix III. The average 120-min incremental plasma glucose response curves for the foods are shown in Figure 2, depicted as the change in plasma glucose from the fasting baseline value (i.e. actual plasma glucose concentration minus the fasting plasma glucose concentration). The average plasma glucose concentrations at each time point for the three test meals are listed in Table 2.

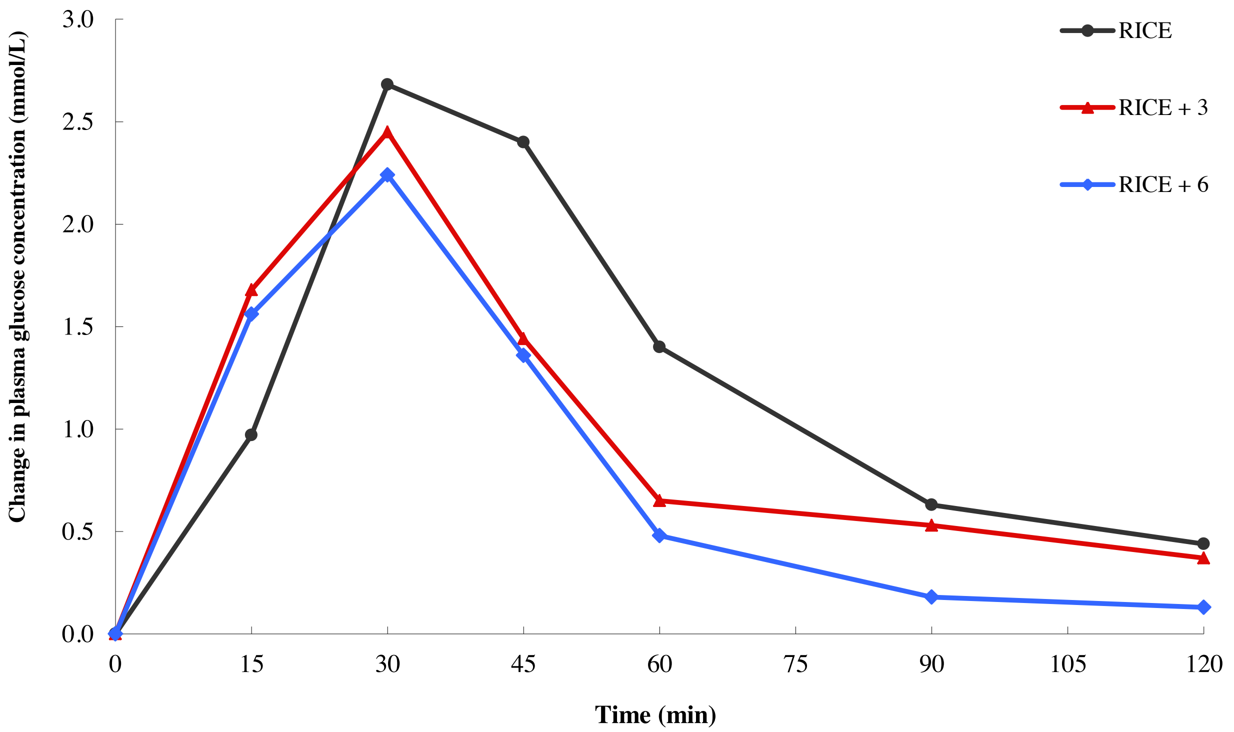

Figure 2. The average two-hour plasma glucose response curves for the three rice test meals, depicted as the change in plasma glucose concentration from the fasting baseline level (n = 20 for each meal).

The control meal (RICE) produced the highest peak plasma glucose concentration at 30 minutes and the greatest overall glycemic response (refer to glucose iAUC values in Table 2). The overall shape of the glycemic response curves produced by the two test meals containing Rice and SUGARDIOWN™ tablets was similar throughout the 120-minute experimental period. Both Rice + SUGARDOWN™ test meals produced a steady rise in plasma glucose to a moderate peak response at 30 minutes, followed by a gradual decline in glucose response between 30 – 120 minutes. The RICE + 6 SUGARDOWN™ tablets meal produced a smaller plasma glucose concentration at each timepoint throughout the 120-minute experimental period, resulting in a lower overall glycemic response compared to the RICE + 3 SUGARDOWN™ tablets meal.

Table 2. The mean ± SEM absolute plasma glucose concentrations for the eight blood samples (mmol/L) collected during the two-hour test sessions for the three test meals (repeated twice) and the mean incremental areas under the foods' two-hour plasma glucose response curves (iAUC). The results listed at 0 minutes are the mean values of two fasting blood samples (-10 and 0 min) (refer to Appendix III)).

Time (min)	**RICE** (n = 20)	**RICE + 3** (n = 20)	**RICE + 6** (n = 20)
0	5.34 ± 0.09	5.34 ± 0.11	5.36 ± 0.12
15	6.31 ± 0.13	7.02 ± 0.09	6.92 ± 0.25
30	8.02 ± 0.21	7.79 ± 0.28	7.61 ± 0.27
45	7.74 ± 0.37	6.78 ± 0.36	6.72 ± 0.27
60	6.74 ± 0.37	5.99 ± 0.27	5.84 ± 0.21
90	5.97 ± 0.21	5.87 ± 0.10	5.54 ± 0.19
120	5.78 ± 0.19	5.71 ± 0.14	5.49 ± 0.22
iAUC	149.74 ± 18.66	120.58 ± 11.06	101.96 ± 12.09

4.3 The test foods' plasma insulin responses

The 10 subjects' individual plasma insulin responses and insulin iAUC values for the test meals are presented in Appendix IV. The average two-hour incremental plasma insulin response curves for the meals are shown in Figure 3, illustrated as the change in plasma insulin from the fasting baseline value (i.e. actual plasma insulin concentration minus the fasting plasma insulin concentration). The average plasma insulin concentrations for the three rice meals are listed in Table 3.

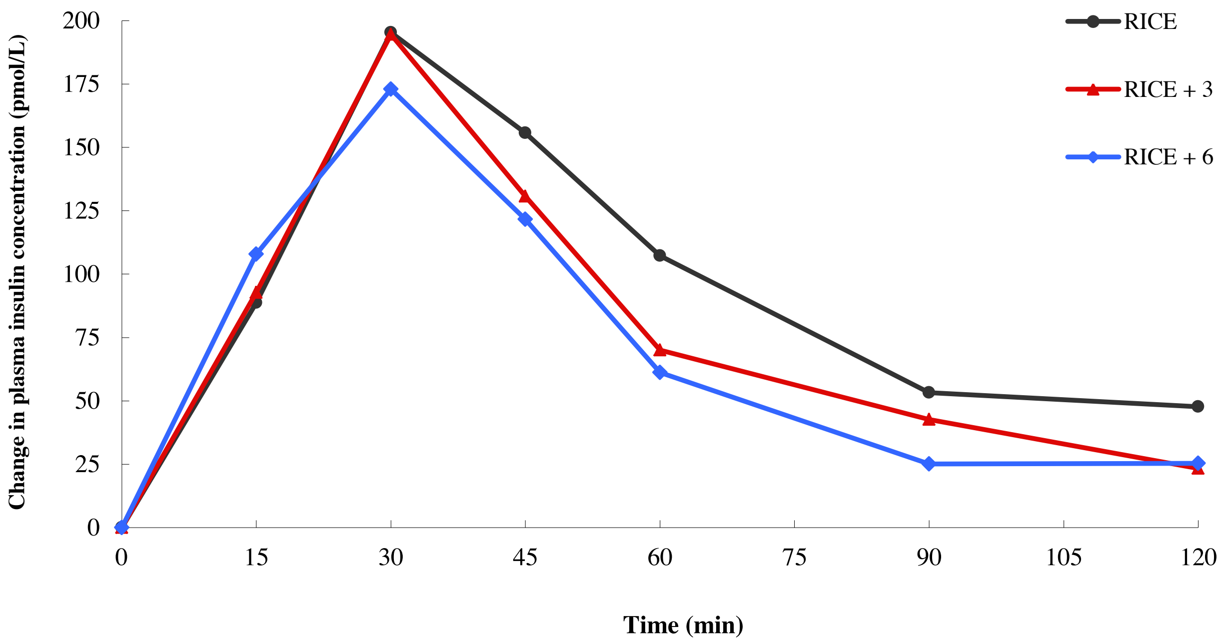

Figure 3. The average two-hour plasma insulin response curves for the three test meals, depicted as the change in plasma insulin concentration from the fasting baseline level (n = 20 for each meal).

As expected due to its high glycemic response, the control food (RICE) produced a large rise in plasma insulin concentration and the largest overall plasma insulin response (refer to insulin iAUC values in Table 3). The overall shape and magnitude of the insulinemic response curves produced by the two Rice + SUGARDOWN™ test meals was similar throughout the experimental period. The two meals both produced a steady rise in plasma insulin concentration to a peak response at 30 minutes followed by a gradual decline in insulin concentration between 30 -120 minutes. Similar, to the corresponding glycemic response curves, the RICE + 6 SUGARDOWN™ tablets produced a lower peak and overall insulin response compared to the RICE + 3 SUGARDOWN™ tablets. The average plasma insulin levels for all three rice meals remained above the fasting baseline level at the completion of the 120-minute experimental period.

Table 3. The mean ± SEM absolute plasma insulin concentrations for the eight blood samples (pmol/L) collected during the two-hour test sessions for the test meals and the mean incremental areas under the two-hour plasma insulin response curves (iAUC). The results listed at 0 minutes are the mean values of two fasting blood samples (-10 and 0 min) (Appendix IV).

Time (min)	**RICE** (n = 20)	**RICE + 3** (n = 20)	**RICE + 6** (n = 20)
0	25.80 ± 3.93	29.51 ± 4.59	27.96 ± 5.63
15	114.49 ± 16.07	122.21 ± 19.70	135.79 ± 24.94
30	221.03 ± 26.97	224.10 ± 41.63	200.89 ± 36.46
45	181.54 ± 41.29	160.19 ± 39.07	149.55 ± 30.33
60	133.01 ± 44.22	99.54 ± 25.98	89.14 ± 23.55
90	78.98 ± 20.00	72.21 ± 18.82	53.01 ± 17.17
120	73.50 ± 20.32	52.81 ± 14.39	53.36 ± 17.12
iAUC	11335.95 ± 2529.91	9546.28 ± 2262.07	8590.22 ± 1982.35

4.4 The test foods' average iAUC responses

The postprandial glucose and insulin iAUC responses varied among the subjects that participated in the study (Appendices III and IV). This variation between different peoples' responses to the same food is normal and is due to a number of factors, such as different rates at which the subjects ingested the food, differences in the nutrient content of the individual test food portions, differences in the subjects' carbohydrate metabolism, and lifestyle and genetic factors. The mean glucose and insulin iAUC responses for the three rice test meals are illustrated in Figure 4.

Parametric statistical tests (repeated-measures ANOVA and the Fisher PLSD test) were used to determine whether there were any significant differences among the plasma glucose and insulin iAUC responses for the rice test meals.

The one-factor repeated-measures ANOVA of the rice meals' average plasma glucose iAUC responses indicated that a significant difference existed amongst the mean iAUC values ($p = 0.0001$). The results of the post-hoc test (Fisher PLSD test) showed that the mean iAUC response for the control meal (RICE) was significantly greater than the mean glucose responses for the RICE + 3 tablets ($p<0.01$) and the RICE + 6 tablets ($p < 0.001$). The mean plasma glucose iAUC response for the RICE + 3 tablets meal was also found to be significantly higher than the mean glucose response for the RICE + 6 tablets ($p<0.05$).

The one-factor repeated-measures ANOVA of the rice meals' average plasma insulin responses indicated that a significant difference existed amongst the mean iAUC responses ($p = 0.0009$). The mean plasma insulin iAUC response of the RICE meal was significantly greater than the mean insulin responses of the RICE + 3 tablets meal ($p<0.05$) and the RICE + 6 tablets meal ($p<0.001$). No significant difference was detected between the mean plasma insulin responses of the two test meals containing the SUGARDOWN™ tablets.

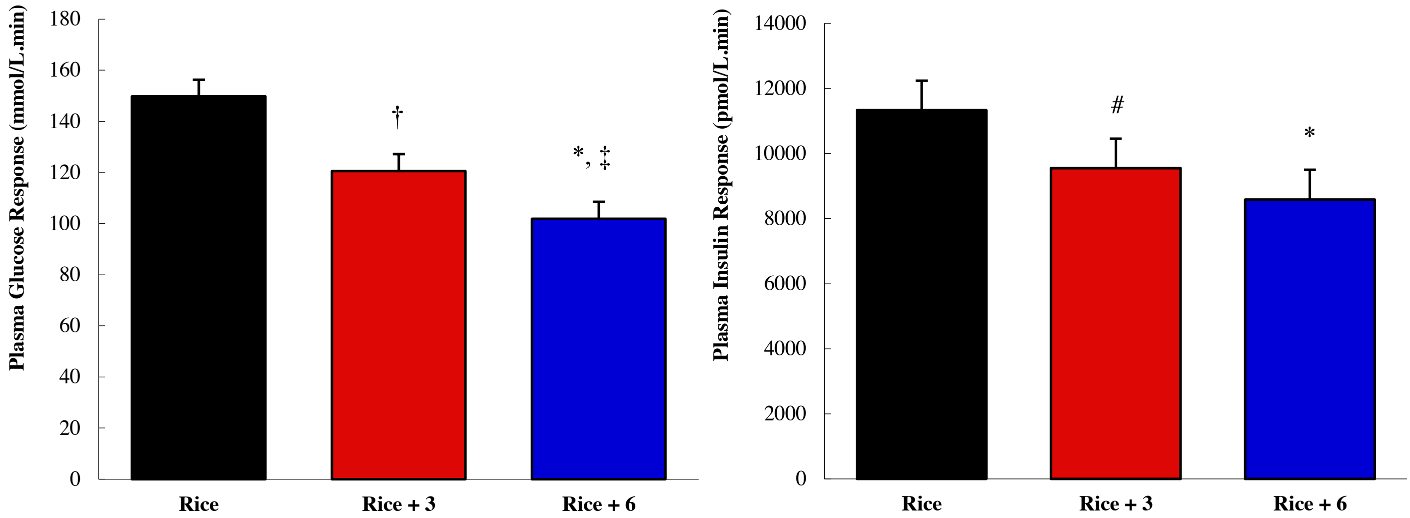

Figure 4. The mean (±SEM) plasma glucose and insulin iAUC responses to the three test meals (n = 20 for each meal). Significantly different from RICE: *p<0.001, † p<0.01, # p<0.05. Significantly different from RICE + 3 SUGARDOWN™ tablets: ‡ p<0.05.

4.4.1 The relationship between the test foods' glucose and insulin iAUC responses

Linear regression analysis was used to determine the degree to which the individual subjects' plasma glucose and insulin responses for the test meals were associated. As shown in Figure 5 below, the rice test meals' glucose responses were significantly associated with their corresponding insulin responses (r = 0.78, n = 60, p = 0.0001).

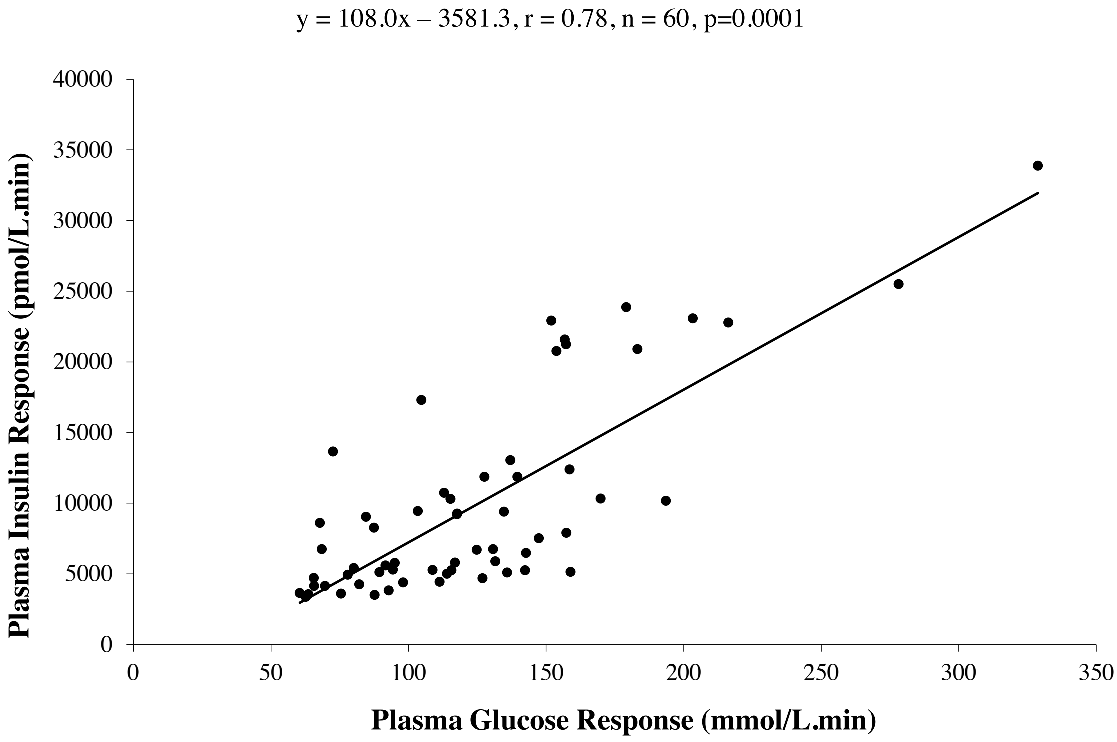

Figure 5. The relationship between the individual subjects' glucose and insulin iAUC responses for the rice test meals.

5. CONCLUSION

This study shows that the consumption of SUGARDOWN™ tablets prior to a high carbohydrate food significantly reduce the postprandial glucose and insulin responses to that meal. The lower dose of SUGARDOWN™, 3 tablets containing 6 g Mannan Polysaccharide and 4.5 g Sorbitol, resulted in a 19% reduction in postprandial glucose and 16% decrease in postprandial insulin response compared to the white rice consumed alone. The higher 6 tablet dose of SUGARDOWN™, containing 12 g Manna Polysaccharide and 9 g Sorbitol, produced a 32% reduction in the 2-hr glucose response and a 24% reduction in the postprandial insulin response compared to the white rice control meal.

APPENDIX I

THE SUBJECTS' RELEVANT CHARACTERISTICS

Number	ID Code	Gender	Age (yr)	BMI (kg/m^2)	Ethnicity
1	S0913	F	25.6	28.5	Caucasian
2	S0941	M	30.8	26.2	Caucasian
3	S0939	M	30.1	26.5	Caucasian
4	S0928	F	26.5	27.3	Caucasian
5	S0914	M	29.2	28.7	Caucasian
6	S0900	M	36.8	25.5	Caucasian
7	S0896	M	26.3	27.2	Caucasian
8	S0942	M	28.0	28.4	Caucasian
9	S0931	F	27.5	27.8	Caucasian
10	S0704	F	31.6	26.7	Caucasian

APPENDIX II

THE RANDOM ORDER OF PRESENTATION OF THE TEST MEALS

Subject	1	2	3	4	5	6
1	RICE	RICE + 3	RICE + 6	RICE	RICE + 3	RICE + 6
2	RICE	RICE + 3	RICE	RICE + 6	RICE + 3	RICE + 6
3	RICE + 3	RICE + 6	RICE + 3	RICE	RICE + 6	RICE
4	RICE + 6	RICE + 3	RICE	RICE + 3	RICE	RICE + 6
5	RICE	RICE	RICE + 6	RICE + 6	RICE + 3	RICE + 3
6	RICE	RICE + 6	RICE + 6	RICE	RICE + 3	RICE + 3
7	RICE + 3	RICE + 6	RICE	RICE	RICE + 3	RICE + 6
8	RICE + 3	RICE	RICE	RICE + 6	RICE + 6	RICE + 3
9	RICE	RICE	RICE + 6	RICE + 3	RICE + 6	RICE + 3
10	RICE	RICE + 6	RICE	RICE + 6	RICE + 3	RICE + 3

Subjects were progressively allocated to the rows in the table above after they completed their screening.

APPENDIX III

THE INDIVIDUAL SUBJECTS' PLASMA GLUCOSE RESULTS

White Rice and SUGARDOWN™ Study 2011

PLASMA GLUCOSE RESULTS (mmol/L)

Food: White Jasmine Rice

Time (min)	Subject										MEAN	SEM
	1	2	3	4	5	6	7	8	9	10		
-10	5.76	5.34	5.64	5.17	5.67	5.27	5.28	5.64	5.44	4.80	**5.40**	**0.09**
0	5.73	5.22	5.69	5.09	5.72	5.35	5.15	5.63	5.42	4.78	**5.38**	**0.10**
0	5.75	5.28	5.66	5.13	5.69	5.31	5.22	5.63	5.43	4.79	**5.39**	**0.10**
15	6.04	6.80	7.53	5.72	7.13	5.76	5.79	5.81	6.40	6.24	**6.32**	**0.20**
30	8.08	8.75	8.36	7.50	9.14	8.57	6.37	8.37	8.07	6.97	**8.02**	**0.27**
45	10.88	8.04	8.79	7.15	7.11	8.16	6.53	9.20	7.65	6.15	**7.96**	**0.44**
60	11.27	6.49	7.25	6.44	6.52	7.42	6.29	7.23	7.16	5.69	**7.17**	**0.49**
90	7.69	5.78	6.47	6.38	6.19	5.00	5.38	6.02	6.39	5.85	**6.11**	**0.23**
120	7.76	5.20	6.87	6.28	6.12	5.16	5.47	5.45	6.45	5.07	**5.98**	**0.28**
iAUC	**328.84**	**156.88**	**193.65**	**158.61**	**134.78**	**142.44**	**78.05**	**142.82**	**169.95**	**130.80**	**163.68**	**20.7**

White Rice and SUGARDOWN™ Study 2011

PLASMA GLUCOSE RESULTS (mmol/L)

Food: White Jasmine Rice

Time (min)	Subject 1	2	3	4	5	6	7	8	9	10	MEAN	SEM
-10	5.59	5.19	5.44	4.95	5.72	5.58	5.23	5.28	5.01	4.79	**5.28**	**0.10**
0	5.61	5.22	5.43	5.04	5.94	5.61	5.29	5.31	5.00	4.84	**5.33**	**0.10**
0	5.60	5.20	5.43	4.99	5.83	5.59	5.26	5.29	5.00	4.81	**5.30**	**0.10**
15	7.04	6.26	6.44	6.48	6.27	7.20	5.83	5.52	6.14	5.93	**6.31**	**0.16**
30	10.02	7.73	7.97	7.63	7.90	8.89	7.56	7.40	7.73	7.46	**8.03**	**0.26**
45	10.31	7.87	7.35	6.36	7.01	8.50	7.34	6.46	7.17	6.83	**7.52**	**0.37**
60	8.58	6.81	6.43	5.64	5.37	5.54	6.67	5.84	6.24	5.97	**6.31**	**0.29**
90	7.15	5.69	5.77	6.12	6.38	4.68	5.59	5.71	5.74	5.47	**5.83**	**0.20**
120	5.98	5.81	5.66	5.57	5.92	5.49	5.05	5.46	6.17	4.75	**5.59**	**0.14**
iAUC	**278.25**	**153.86**	**117.71**	**139.73**	**67.87**	**117.04**	**114.10**	**80.21**	**157.54**	**131.64**	**135.80**	**18.3**

White Rice and SUGARDOWN™ Study 2011

PLASMA GLUCOSE RESULTS (mmol/L)

Food: White Jasmine Rice + 3 SUGARDOWN™ tablets

Time (min)	Subject										MEAN	SEM
	1	2	3	4	5	6	7	8	9	10		
-10	5.59	5.22	5.74	5.08	5.86	5.43	5.49	5.42	5.04	4.71	**5.36**	**0.11**
0	5.55	5.15	5.70	5.04	6.02	5.33	5.59	5.53	5.14	4.86	**5.39**	**0.11**
0	5.57	5.18	5.72	5.06	5.94	5.38	5.54	5.47	5.09	4.78	**5.37**	**0.11**
15	7.01	6.72	7.27	6.89	7.54	6.78	7.09	6.84	7.76	6.93	**7.08**	**0.11**
30	8.96	7.97	8.11	7.42	9.01	7.40	8.13	8.34	6.36	6.62	**7.83**	**0.28**
45	8.31	7.28	7.03	6.06	7.86	7.17	6.76	7.20	4.80	5.52	**6.80**	**0.34**
60	7.46	6.43	6.35	5.92	6.82	6.69	5.99	5.54	5.18	5.33	**6.17**	**0.23**
90	6.02	6.11	6.21	6.02	6.24	6.10	5.18	5.94	5.64	5.99	**5.94**	**0.10**
120	6.48	5.56	6.25	5.81	5.91	5.85	5.29	5.73	5.43	5.13	**5.74**	**0.13**
iAUC	**183.26**	**157.43**	**115.73**	**137.18**	**127.76**	**135.91**	**87.82**	**108.90**	**65.83**	**124.88**	**124.47**	**10.51**

White Rice and SUGARDOWN™ Study 2011

PLASMA GLUCOSE RESULTS (mmol/L)

Food: White Jasmine Rice + 3 SUGARDOWN™ tablets

Time (min)	Subject 1	2	3	4	5	6	7	8	9	10	MEAN	SEM
-10	5.77	5.05	5.63	5.05	5.78	5.58	5.29	5.19	4.90	4.78	**5.30**	**0.12**
0	5.89	5.25	5.38	5.20	5.78	5.34	5.45	5.38	4.73	4.77	**5.31**	**0.12**
0	5.83	5.15	5.51	5.12	5.78	5.46	5.37	5.28	4.81	4.78	**5.31**	**0.11**
15	8.21	6.96	7.03	6.75	6.72	7.56	6.89	6.35	6.41	6.65	**6.95**	**0.18**
30	9.89	7.94	8.38	7.19	7.90	7.12	7.41	8.30	6.53	6.79	**7.74**	**0.31**
45	8.70	7.20	8.07	5.42	8.21	6.00	6.67	7.02	5.24	5.11	**6.76**	**0.41**
60	7.14	6.45	7.20	5.50	6.50	5.56	6.17	4.74	4.36	4.62	**5.82**	**0.33**
90	6.61	5.78	5.94	6.31	6.08	5.45	5.44	5.41	5.19	5.80	**5.80**	**0.14**
120	6.52	5.36	5.80	5.87	6.12	5.27	5.24	6.02	5.72	4.83	**5.67**	**0.16**
iAUC	**203.40**	**152.03**	**159.00**	**115.43**	**113.03**	**65.70**	**92.93**	**98.13**	**75.52**	**91.80**	**116.70**	**13.50**

White Rice and SUGARDOWN™ Study 2011

PLASMA GLUCOSE RESULTS (mmol/L)

Food: White Jasmine Rice + 6 SUGARDOWN™ tablets

Time (min)	Subject 1	2	3	4	5	6	7	8	9	10	MEAN	SEM
-10	5.82	5.36	5.48	5.14	5.84	5.31	5.07	5.35	5.06	4.84	**5.32**	**0.10**
0	5.81	5.25	5.65	5.06	5.87	5.27	4.97	5.38	5.23	4.81	**5.33**	**0.11**
0	5.82	5.30	5.56	5.10	5.85	5.29	5.02	5.36	5.14	4.83	**5.33**	**0.11**
15	8.07	6.11	8.36	6.65	6.91	6.73	5.14	6.35	7.57	6.83	**6.87**	**0.30**
30	9.79	7.34	7.68	6.55	8.16	7.88	5.77	8.08	6.50	7.25	**7.50**	**0.35**
45	8.83	6.75	7.07	5.17	7.42	6.80	6.10	7.98	5.84	5.80	**6.77**	**0.35**
60	7.51	5.75	6.23	5.09	6.15	5.15	5.64	6.37	5.67	5.01	**5.85**	**0.24**
90	6.57	5.19	6.67	6.01	5.94	5.33	5.51	4.68	5.45	5.17	**5.65**	**0.20**
120	6.97	5.33	5.74	6.07	5.93	4.90	5.36	5.05	5.52	4.82	**5.57**	**0.20**
iAUC	**216.34**	**72.61**	**147.49**	**87.52**	**84.68**	**82.17**	**62.81**	**111.41**	**94.43**	**95.07**	**105.45**	**14.34**

White Rice and SUGARDOWN™ Study 2011

PLASMA GLUCOSE RESULTS (mmol/L)

Food: White Jasmine Rice + 6 SUGARDOWN™ tablets

Time (min)	Subject 1	2	3	4	5	6	7	8	9	10	MEAN	SEM
-10	6.18	5.14	5.67	4.93	6.01	5.25	5.47	5.28	5.31	4.71	**5.39**	**0.14**
0	6.14	5.20	5.68	5.04	5.87	5.39	5.55	5.18	5.30	4.79	**5.41**	**0.13**
0	6.16	5.17	5.67	4.98	5.94	5.32	5.51	5.23	5.31	4.75	**5.40**	**0.14**
15	9.18	6.55	7.51	7.11	7.24	5.31	7.32	7.31	6.02	6.19	**6.97**	**0.33**
30	9.77	7.70	7.99	7.28	7.89	7.37	8.16	7.06	7.47	6.49	**7.72**	**0.28**
45	7.71	7.05	7.12	5.90	7.33	7.39	5.74	5.64	7.44	5.45	**6.67**	**0.28**
60	7.04	6.09	6.53	5.55	5.88	5.09	4.96	5.12	6.78	5.25	**5.83**	**0.24**
90	7.02	4.95	5.63	5.46	5.56	4.43	5.13	5.07	5.70	5.43	**5.44**	**0.21**
120	6.88	5.03	5.77	5.66	5.84	4.91	5.60	4.00	5.78	4.67	**5.41**	**0.25**
iAUC	**179.29**	**104.80**	**103.53**	**117.79**	**68.59**	**60.56**	**69.75**	**63.71**	**127.05**	**89.55**	**98.46**	**11.66**

APPENDIX IV

THE INDIVIDUAL SUBJECTS' PLASMA INSULIN RESULTS

White Rice and SUGARDOWN™ Study 2011

PLASMA INSULIN RESULTS (pmol/L)

Food: White Jasmine Rice

Time (min)	Subject 1	2	3	4	5	6	7	8	9	10	MEAN	SEM
-10	48.21	22.92	12.62	35.13	40.78	21.01	18.26	17.70	19.05	12.09	**24.78**	**3.89**
0	50.09	37.48	14.38	44.29	54.48	9.88	16.44	12.22	30.86	15.17	**28.53**	**5.39**
0	49.15	30.20	13.50	39.71	47.63	15.44	17.35	14.96	24.96	13.63	**26.65**	**4.50**
15	91.08	123.16	172.09	205.55	154.71	61.99	71.63	22.60	92.80	146.87	**114.25**	**17.77**
30	279.60	277.24	127.87	376.93	267.73	163.23	136.91	130.64	202.06	197.84	**216.00**	**26.03**
45	553.19	396.93	89.41	72.63	188.87	154.21	88.38	190.92	158.85	62.52	**195.59**	**50.24**
60	607.89	200.99	102.82	59.92	113.23	28.04	58.55	61.36	101.85	53.40	**138.81**	**54.31**
90	252.91	179.34	83.66	142.65	47.49	11.09	28.99	49.21	77.20	19.31	**89.18**	**24.92**
120	284.13	207.23	67.66	91.36	106.74	10.45	15.57	5.70	113.14	25.17	**92.71**	**29.03**
iAUC	**33855.17**	**21573.29**	**10160.14**	**12357.70**	**9384.64**	**5231.63**	**4926.00**	**6451.61**	**10302.56**	**6733.14**	**12097.59**	**2861.3**

White Rice and SUGARDOWN™ Study 2011

PLASMA INSULIN RESULTS (pmol/L)

Food: White Jasmine Rice

Time (min)	Subject										MEAN	SEM
	1	2	3	4	5	6	7	8	9	10		
-10	41.33	22.45	13.99	22.92	46.33	16.25	11.62	11.32	32.14	10.49	**22.88**	**4.10**
0	42.87	38.85	15.44	31.38	37.22	19.19	18.58	16.80	27.14	22.56	**27.00**	**3.17**
0	42.10	30.65	14.71	27.15	41.77	17.72	15.10	14.06	29.64	16.52	**24.94**	**3.46**
15	194.12	192.59	18.86	147.89	173.87	31.89	66.08	63.63	94.52	163.86	**114.73**	**21.30**
30	421.06	241.49	227.33	374.45	233.14	97.84	156.67	221.07	135.33	152.21	**226.06**	**32.54**
45	407.44	291.67	107.21	172.40	155.85	127.87	75.11	81.02	187.48	68.89	**167.49**	**34.07**
60	343.61	372.29	112.99	63.36	62.85	103.21	61.05	34.18	92.82	25.73	**127.21**	**39.50**
90	188.77	95.41	70.91	79.54	102.48	33.20	16.62	17.75	48.70	34.36	**68.77**	**16.51**
120	98.96	138.18	58.38	44.72	14.37	38.58	22.23	9.68	94.67	23.14	**54.29**	**13.58**
iAUC	**25481.81**	**20749.55**	**9191.21**	**11849.43**	**8575.42**	**5767.04**	**4974.91**	**5386.77**	**7894.80**	**5872.26**	**10574.32**	**2221.0**

White Rice and SUGARDOWN™ Study 2011

PLASMA INSULIN RESULTS (pmol/L)

Food: White Jasmine Rice + 3 SUGARDOWN™ tablets

Time (min)	Subject										MEAN	SEM
	1	2	3	4	5	6	7	8	9	10		
-10	33.08	47.05	26.26	27.26	50.39	17.08	26.63	15.73	31.18	16.00	**29.07**	**3.81**
0	56.56	46.33	14.12	18.34	52.39	12.62	20.43	10.96	24.19	28.31	**28.43**	**5.41**
0	44.82	46.69	20.19	22.80	51.39	14.85	23.53	13.35	27.69	22.16	**28.75**	**4.35**
15	170.28	174.73	87.07	134.54	123.95	81.94	71.57	59.02	151.06	143.90	**119.81**	**13.28**
30	421.77	486.51	163.08	174.47	399.62	134.79	130.92	132.16	136.86	191.38	**237.16**	**44.35**
45	386.69	325.18	94.94	193.30	201.70	60.29	76.56	54.85	68.60	44.32	**150.64**	**38.67**
60	234.37	189.95	66.10	154.94	172.46	55.88	40.96	16.27	15.46	28.73	**97.51**	**25.86**
90	117.52	200.89	14.97	137.31	48.23	31.67	21.14	68.16	36.52	58.21	**73.46**	**18.98**
120	162.61	91.97	20.17	29.75	94.24	25.17	13.09	43.23	12.48	72.03	**56.47**	**15.35**
iAUC	**20876.49**	**21223.74**	**5230.49**	**13021.42**	**11842.66**	**5069.82**	**3487.55**	**5248.31**	**4135.57**	**6674.74**	**9681.08**	**2142.87**

White Rice and SUGARDOWN™ Study 2011

PLASMA INSULIN RESULTS (pmol/L)

Food: White Jasmine Rice + 3 SUGARDOWN™ tablets

Time (min)	Subject 1	2	3	4	5	6	7	8	9	10	MEAN	SEM
-10	43.29	46.02	20.33	21.39	55.55	10.75	24.19	10.02	26.16	26.04	**28.37**	**4.79**
0	67.97	52.67	16.61	26.86	44.98	16.39	29.41	20.93	22.58	23.39	**32.18**	**5.46**
0	55.63	49.35	18.47	24.13	50.27	13.57	26.80	15.48	24.37	24.72	**30.28**	**4.90**
15	238.97	291.43	38.33	114.99	103.43	68.59	55.35	43.10	117.94	173.92	**124.60**	**27.07**
30	487.55	347.18	133.96	169.29	323.07	144.16	120.21	143.41	109.51	132.19	**211.05**	**40.70**
45	379.58	364.21	73.46	184.20	284.61	86.69	95.98	95.85	84.48	48.38	**169.74**	**40.04**
60	230.34	279.60	76.30	114.39	106.97	42.80	73.88	48.33	5.74	37.24	**101.56**	**27.79**
90	174.51	186.10	52.85	91.40	83.43	17.70	16.45	11.78	15.88	59.47	**70.96**	**20.37**
120	153.71	102.92	13.98	43.61	52.19	16.04	16.43	27.26	37.25	28.10	**49.15**	**14.27**
iAUC	**23056.67**	**22908.64**	**5128.52**	**10282.99**	**10704.44**	**4699.21**	**3799.34**	**4362.77**	**3592.16**	**5580.07**	**9411.48**	**2396.47**

White Rice and SUGARDOWN™ Study 2011

PLASMA INSULIN RESULTS (pmol/L)

Food: White Jasmine Rice + 6 SUGARDOWN™ tablets

Time (min)	Subject										MEAN	SEM
	1	2	3	4	5	6	7	8	9	10		
-10	70.07	25.77	16.80	20.12	66.67	6.38	15.08	12.48	26.10	16.31	**27.58**	**7.05**
0	68.86	29.55	24.34	29.31	70.70	9.64	23.59	11.61	29.48	13.36	**31.04**	**6.88**
0	69.47	27.66	20.57	24.71	68.68	8.01	19.33	12.05	27.79	14.83	**29.31**	**6.93**
15	315.41	172.86	72.56	149.05	173.66	46.68	40.91	31.97	111.60	175.12	**128.98**	**27.62**
30	445.39	302.21	204.09	164.95	304.78	101.53	148.27	145.05	117.01	107.53	**204.08**	**35.52**
45	300.68	215.57	134.11	130.78	214.77	107.03	64.55	87.85	75.06	73.40	**140.38**	**24.81**
60	245.65	156.18	74.92	33.77	119.82	18.97	41.00	56.70	46.70	42.49	**83.62**	**22.40**
90	199.10	70.17	24.95	97.25	89.51	18.37	13.84	8.88	54.00	20.53	**59.66**	**18.56**
120	210.10	50.65	81.57	45.10	63.29	22.32	16.76	16.45	78.65	33.53	**61.84**	**18.11**
iAUC	**22758.91**	**13626.59**	**7504.40**	**8245.39**	**9018.47**	**4240.17**	**3357.66**	**4429.65**	**5279.60**	**5746.86**	**8420.77**	**1855.83**

White Rice and SUGARDOWN™ Study 2011

PLASMA INSULIN RESULTS (pmol/L)

Food: White Jasmine Rice + 6 SUGARDOWN™ tablets

Time (min)	Subject										MEAN	SEM
	1	2	3	4	5	6	7	8	9	10		
-10	45.62	54.89	21.49	14.09	39.73	14.54	8.66	14.00	22.32	25.33	**26.07**	**4.90**
0	49.97	69.75	11.18	22.08	41.60	14.96	17.46	11.72	16.25	16.69	**27.17**	**6.27**
0	47.80	62.32	16.34	18.08	40.66	14.75	13.06	12.86	19.28	21.01	**26.62**	**5.48**
15	208.87	308.41	255.31	259.97	71.77	105.02	54.50	43.81	96.50	21.79	**142.59**	**33.17**
30	356.91	456.16	158.86	144.36	296.39	93.63	133.28	63.48	129.37	144.51	**197.69**	**40.38**
45	409.16	337.57	78.43	115.13	174.35	71.57	74.34	134.91	88.10	103.63	**158.72**	**37.51**
60	276.31	207.56	74.51	76.16	64.44	25.63	48.71	39.40	52.67	81.21	**94.66**	**25.66**
90	187.18	75.26	47.38	38.04	28.21	14.81	10.94	3.18	17.09	41.61	**46.37**	**17.02**
120	184.92	48.96	51.04	41.57	42.87	3.44	10.16	13.93	28.77	23.13	**44.88**	**16.43**
iAUC	**23853.11**	**17284.82**	**9414.47**	**9235.84**	**6725.09**	**3635.50**	**4115.74**	**3546.59**	**4677.59**	**5107.88**	**8759.66**	**2135.11**