STUDY PROTOCOL

PROTOCOL TITLE:

Effects of fixed meals with special formulated rice on blood glucose levels of healthy volunteers

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TABLE OF CONTENTS

STUDY PROTOCOL

1. BACKGROUND AND RATIONALE

In Singapore, the Ministry of Health has declared a "War on Diabetes" and major efforts will be made to develop and deploy programs to prevent diabetes. One of the cornerstones of diabetes management involves dietary modifications to reduce postprandial hyperglycaemia. However, implementation of a low GI diet is highly complex requiring the individual to choose foods from a long list which are primarily based on western consumption patterns. Many foods in the Asian diet, which largely consist of carbohydrates such as white rice, noodles and other flour based products, are not represented. An alternative solution will require innovative ways to alter commonly available food products that will not only help reduce postprandial glycaemia but also preserve the sensory characteristics of the foods to create a new generation of food products both functional and palatable.

1.1. General Introduction

Lifestyle modification, in particular adopting an appropriate dietary pattern, is generally accepted as the cornerstone for the treatment of people with type 2 diabetes. Consumption of low GI food has shown to improve glycemic control, lipid profile and reduce systemic inflammation. However, there are few dietary intervention studies attempting to change the GI of food by changing the staple carbohydrates. In this study, formulated rice with special fibre enrichment, Diabetec® Fibre Grain (Fibre Grain), was used to replace rice as the staple carbohydrates in one's diet. This fibre enriched rice has been previously tested to have a lower GI than normal rice while still able to preserve all the sensory characteristics of normal rice. With rice being a staple to many Singaporeans, this specially formulated fibre enriched rice offers a lower GI alternative to the conventional rice without affecting the people dietary preference.

1.2. Rationale and justification for the Study

a. Rationale for the Study Purpose

Research has confirmed that a food's glycemic effect cannot be accurately predicted from the type and amount of carbohydrates it contains, as the rate at which the carbohydrates is digested and released into the bloodstream is influenced by many factors such as the food's physical form, its fat, protein and fibre content, and the chemical structure of its carbohydrates. For these reasons, it is possible to produce food from the same group with different effects on blood glucose.

b. Rationale for Test food

Previously, specially formulated Diabetec® Fibre Grain (Fibre Grain) was tested to have a lower GI as compare to normal rice grains. Thus, clinical trial is proposed to test the effect of rice in a mixed meal setting where side dishes are prepared and served in combination with the rice.

c. Rationale for Study Population

We have chosen generally healthy individuals in Singapore as the trial aim to produce rice with lower GI and better glycemic response for the general population.

d. Rationale for Study Design

A within-subject cross-over trial is proposed to investigate the glycemic response of incorporating fibre enriched rice into a mixed meal containing a protein source and vegetables. This is to investigate whether the fibre enriched rice is able to lower the glycemic response in a mixed meal setting. The results of this study would be useful in determining short and intermediate effects of alterations in the type of carbohydrate over a short or intermediate period. If initial benefits are identified, this will strengthen the reasons to evaluate this intervention over a longer period of time. This specially formulated rice can also be an alternative solution to manage the problem of diabetes without the need for change in dietary preference.

2. HYPOTHESIS AND OBJECTIVES

2.1.Hypothesis

Partial replacement of white rice with Fibre Grain will have a lower glycemic response than normal white rice in a mixed meal setting.

2.2.Primary Objectives

The primary aim of the study is to investigate the effects of partial replacement of white rice with Fibre Grains in a mixed meal setting commonly consumed by Asian Singaporeans.

2.3.Potential Risks and benefits:

a. End Points - Efficacy

The anticipated benefit is contribution to knowledge of diabetes management which may help mitigating the disease in the future.

b. End Points - Safety

Minimal risk is anticipated. Some discomfort, pain, bleeding or bruising at the site of the needle stick may occur during collection of blood samples.

3. STUDY POPULATION

3.1.List the number of subjects to be enrolled.

The number of subjects to be enrolled is 25.

3.2.Criteria for Recruitment

Potential subjects will be called up and screened for eligibility by personnel according to the inclusion and exclusion criteria. The research staff will identify potential candidates and will explain the purpose, reason and study protocol. In addition, the participant information sheet will be provided for the candidates to read prior to their decision to participate in the study. The candidates will be encouraged to ask question about the study and have adequate time to make a decision. All subjects are to give informed consent before enrolling into the research. The subsequent visit and any other administrative details will be arranged between the research staff and participant.

3.3.Inclusion Criteria

1 Ability to give informed consent

2 Age between 21-65 years old

3 Overtly healthy males or females, as determined by medical history, physical examination and laboratory results within normal reference range for the population or investigator site, or results with acceptable deviations that are judged to be not clinically significant by the investigator

4 Males and females with stable medical problems that, in the investigator's opinion, will not significantly alter the performance of the biomarker panel, will not place the subject at increased risk by participating in the study, and will not interfere with interpretation of the data.

5 Not on any regular medications (western / traditional medicine). Nutritional supplements with established chemical composition that can be ascertained and clearly recorded is acceptable.

However, subjects using traditional medicine (with compositions that cannot be ascertained) will be excluded in this study.

6 Have venous access sufficient to allow for blood sampling as per the protocol

7 Reliable and willing to make themselves available for the duration of the study and are willing to follow study procedures

8. Family history of diabetes (Parents and/or grandparents with history of diabetes).

3.4.Exclusion Criteria

1 History or presence of current cardiovascular, respiratory, hepatic, renal, gastrointestinal, endocrine, hematological, malignancy or neurological disorders capable of significantly altering the performance of the biomarker panel; or of interfering with the interpretation of data

2 Known or ongoing psychiatric disorders within 3 years

3 Regularly use known drugs of abuse within 3 years

4 Women who are pregnant or lactating

5 Have donated blood of more than 500 mL within 4 weeks of study enrolment

6 Have an average weekly alcohol intake that exceeds 21 units per week (males) and 14 units per week (females):

- 1 unit = 12 oz or 360 mL of beer;
- 5 oz or 150 mL of wine;
- 1.5 oz or 45 mL of distilled spirits

7 Uncontrolled hypertension (blood pressure [BP] >160/100mmHg

8 Active infection requiring systemic antiviral or antimicrobial therapy that will not be completed prior to Study Day 1

9 Treatment with any investigational drug, or biological agent within one (1) month of screening or plans to enter into an investigational drug/ biological agent study during the duration of this study

10 Known allergy to insulin

11 History of bleeding diathesis or coagulopathy

12 Any of the following laboratory values at screening:

Fasting glucose >=126mg/dL(>=7mmol/L) or 2 hour post-prandial glucose >=200mg/dL (>=11.1mmol/L)

13 Clinically significant (as determined by investigator) abnormalities on laboratory examination that will increase risk to the patient or interfere with data integrity

14 Have any other conditions, which, in the opinion of the Investigator would make the subject unsuitable for inclusion, or could interfere with the subject participating in or completing the study

15 Significant change in weight (+/- 5%) during the past month

3.5.Withdrawal Criteria

1. Any serious adverse events.
2. Participants may withdraw from the study if they decide to do so, at any time and irrespective of the reason. The reasons given will be documented.
3. Study site participation may be discontinued if the investigator judges it necessary for medical, safety, regulatory or other reasons consistent with applicable laws, regulations and good clinical practice.

3.6.Subject Replacement

To account for the dropout rate, 25 participants will be recruited for minimal sample size of 20 subjects. A new subject will only be recruited if number of subjects drop below 20.

4. TRIAL SCHEDULE

4.1. Study Visits and Procedures

(a) Visit 1 - Screening

Volunteers will be interviewed and screened by study personnel. If the volunteer satisfies the inclusion and exclusion criteria, a written informed consent will be obtained from all selected volunteers prior to their participation in the study. Volunteers will have the study explained to them by a study personnel, will read the consent form, have the opportunity to ask questions, and then sign the approved written Informed Consent form and keep a copy. The study personnel will then proceed to schedule visit 2 and 3 with the participant.

(b) Visit 2 - Installation of CGMS (Day 1)

Upon arrival, the participant will be educated on how to maintain and care for a CGMS and to keep a food and activity diary for the duration of the CGM. During this period (Day 1-14), participants will receive SMS to check on the CGMS. If there is a need, the research personnel will arrange for a mutually convenient time and place to review and replace the CGMS. Then, the participants will proceed to take the first MMTT.

Mixed meal tolerance test (MMTT)

Before the test, measurement of participants' height, BMI, waist and hip circumference, will be done and recorded. Next, participants will be asked to attend the MMTT protocol. The participant will need to fast (no food or drinks, except plain water) from 10 pm the night before or for approximately 10-12hr prior to the study visit. No food except clear water should be

consumed. A cannula will be inserted into the participant's forearm and the cannula will remain for blood sampling only. A fasting sample will be taken for the immediate measurement of glucose while other samples for insulin, gut hormones (GLP-1, GIP, Peptide YY, Ghrelin, and Glucagon), and other metabolites will be taken, processed, stored and analysed in batches at a later stage. Then, the participant will be given either mixed meal with controlled rice or mixed meal with test rice. At 0, 15, 30, 45, 60, 90, 120 minutes, blood will be sampled through a cannula from one of the arms. Subjects will be asked to remain seated throughout the visit and only minimal movement is allowed. Blood-taking will be conducted in room designated and approved for phlebotomy purposes. Only trained personnel and/or trained nurses will be conducting the blood drawn.

At each time point, the participant will also be given a visual analogue scale (VAS) to indicate how they feel in response to given statements by marking an "X" on a 100-mm line. For example, "How strong is your desire to eat? " Response: Very weak (0 mm) to very strong (100 mm). Appetite was evaluated using a 100 mm VAS. At time 15 min, palatability of the treatment will be assessed by five characteristics, from bad (0 mm) to good (100 mm). These characteristics were visual appeal, smell, taste, texture, and overall pleasantness of the meal given. Scores were determined by measuring the distance (in mm) from the let starting point of the line to the intersection of the "X". The average scores and AUC will be calculated and compared between the two meals

(c) Continuous glucose monitoring (Day 1 - 14)

For the next 14 days, participants will be provided with lunch and dinner from the research team through delivery. They will be randomized to receive either mixed meal with controlled rice or mixed meal with Fibre Grain rice for day 1 to 7 and received the alternative for the day 8- 14. Participants will not be told whether they are receiving the Fibre Grain rice or control rice

(d) Visit 3 (Day 14 of CGM) – MMTT2 and removal of CGMS

On day 14, participants will return to undergo the second MMTT. Their height, BMI, waist and hip circumference will be measured and recorded. Participants will be asked to attend the same MMTT protocol (refer to Day 1 – MMTT protocol). Lastly, they will return the CGMS, and your 14-day food and activity diary

5. STUDY DESIGN

This study is a within-subject cross-over trial design to assess the glycemic response of fibre enriched rice consumer by human subjects as compared to normal non-enriched rice in a mixed meal setting. The approximate time to complete study recruitment will be 4 weeks. Generally healthy population will be recruited in this study. There will be 3 visits in total (including screening). Each visit last from 3-4 h. During the visit, the participants are required to undergo a mixed meal tolerance test and carry a continuous glucose monitoring system for the next 14 days. The meals will be prepared by caterer in the morning of the test and send to the participants. The participant's glycemic response to control (normal rice) will be compared to their response after consumption of fibre enriched rice in a mixed meal setting. A reduction in postprandial blood glucose response will show that Fibre Grain rice is effective in improving the glycemic response of a meal.

6. STATISITCAL METHODS

The sample size was calculated based on Glycaemic Index Research Report #1719 conducted by Sydney University's Glycaemic Index Research Service on the 30% Fibre Grain replacement. Based on the primary outcome of detecting a difference of 27 units in incremental area under the curve (iAUC) from 0 to 120 minutes (iAUC 0-120min) between control and 30% fibre enriched rice and a standard deviation of 25 units in iAUC 0-120min, calculations showed that with $\alpha = 0.05$, and power of 0.9, at least 21 subjects were needed. To account for possible subject attrition during the study, 25 subjects were recruited.

All data will be analyzed using statistical software (eg. SPSS/Stata), with significance defined as a p value of less than 0.05 on a 2-sided paired t-test. Other variables will be presented as mean ± SE with differences between groups assessed by mixed model for categorical variables and continuous variables. Data will be explored for assessment of errors, missing values, and distribution of the variables. Evaluable subjects will be those who meet eligibility and have no missing values for calculating area under the curve (AUC). Variables that will be obtained include:

For CGM profile, paired t-test will be used to compare the fibre enriched rice meal and normal rice meal group in the following:

a. Mean of interstitial glucose (IG) per 24 hours

b. Postprandial peak IG (highest level after meal at breakfast, lunch and dinner)

c. Postprandial time to peak IG (at breakfast, lunch and dinner)

d. Mean amplitude of glycamic excursion (MAGE) to assess variability. This is determined by calculating arithmetic mean of the difference between qualifying consecutive peak and nadirs. Glucose excursions > 1 SD of the mean glucose concentrations will be included.

For postprandial glucose profile after the single meal:

a. Plasma fasting and postprandial glucose (mmol/l), insulin (mU/l) and gut hormones.

b. The incremental AUC (0-2h) will be derived from the glucose concentration profile during the meal test (defined as the area under the glucose curve that is over the basal value taken at time. Differences between the two meals will be analyzed by paired t-test

6.1.Randomisation and Blinding

Participants will be randomized to receive either mixed meal with Fibre Grain or mixed meal

with control rice for the first MMTT (visit2) and the alternative for the second MMTT (visit3). They will also be randomized to receive either Fibre Grain meal or Jasmine rice in mixed meal during CGM. It will be a single blinded trial as participants will not be told whether they are receiving the Fibre Grain or control white rice.

6.2.Contraception and Pregnancy Testing

Research assistants will screen for non-pregnant females for participation in this study.

7. TRIAL MATERIALS

7.1.Trial Product

Research collaborator, Alchemy Foodtech Pte Ltd, will be providing the fibre grains to be used in the clinical studies. Diabetec® Fibre Grains are extruded rice-shaped grains made from Alchemy's patent glycemic lowering composition. The relevant patent title is 'GLYCEMIC REDUCING COMPOSITION' with application number 'PCT/SG2017/000003' claiming priority from 'GB 1602626.2'.The patent is under the inventor: 'Alchemy Foodtech Pte Ltd' and 'Verleen Goh Zhi Min'. Material safety data sheets are attached.

8. SAFETY MEASUREMENTS

8.1.Definitions

Serious adverse event

Any adverse event that:

- Results in death
- Is life-threatening
- Requires hospitalization or prolongs existing hospitalization
- Results in a congenital anomaly
- Causes permanent disability or requires medical or surgical intervention to prevent permanent disability
- An important medical event that, based upon appropriate medical judgment, requires medical or surgical intervention to prevent one of the outcomes listed above.

Non-serious adverse event

Any undesirable symptom or occurrence a subject experience during participation in a clinical

study that does not meet the "serious" criteria.

Anticipated event

This refers to any event attributed to the underlying condition of the patient being studied, or event attributed to the patient population being studied, or an adverse event anticipated on the basis of prior experience with the procedure and medication.

Unanticipated event

This refers to any unanticipated event that cannot be attributed to the underlying condition of the subject being studied or to the subject population, expected events whose frequency or severity exceeds what was anticipated, an event that cannot be attributed to a co-morbid condition or concomitant medication, or an adverse event that was not anticipated on the basis of prior experience with the procedures or drugs used in the study.

Related or possibly related event

Possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.
Related means: events directly or indirectly attributed to the procedure, medication and/or study participation; events occurring with sufficient frequency to suggest that they are not random.

Unrelated event

This is defined as events that would occur regardless of study participation or events that are clearly random occurrences. If the frequency of the event suggests a possible connection to the study procedure, then it should be considered related.

8.2. Collecting, Recording and Reporting of "Unanticipated Problems Involving Risk to Subjects or Others" – UPIRTSO events to the NHG Domain Specific Review Boards (DSRB)

Collecting, Recording and Reporting of Adverse Events

In the occurrence of an adverse event

• All adverse events will be reported to any physician in the study team who will assess and classify the event according to the above. Adverse event reporting form must then be completed.

• Urgent reporting to the DSRB of serious adverse events (SAE) that are unexpected or possibly related occurring between the time that a subject is participating on a protocol and for 30 days following the active procedural phase of the protocol, are required for all problems involving local deaths, whether related or not, and should be done within 24 hours after first knowledge by the investigator.

•Expedited reporting to DSRB is required for all other SAE and must be done as soon as possible but not later than 7 calendar days after first knowledge by the investigator.

• In the event that the trial is still ongoing, the co-PIs will make a decision regarding discontinuation of the study after discussion with the study team within 24 hours of reporting to the PI.

• Reporting to the DSRB to be done using DSRB UPIRTSO report form and to include the facts of the case, including subject identifier, adverse event or problem description, the event relationship to the study or underlying condition, seriousness assessment, whether the event was anticipated or unanticipated, type of report, date of injury, whether the procedure was stopped, and if so, whether it was re-started, and whether the event provides new risk information that alters the risk-benefit assessment and /or should be added to the informed consent disclosure document.

Reporting SAEs to HSA

• All SAEs that are unexpected and related to the study drug to be reported to HSA.

• The investigator is responsible for informing HSA no later than 15 calendar days after first knowledge that the case qualifies for expedited reporting.
Follow-up information will be actively sought and submitted as soon as it becomes available
.

• For fatal or life-threatening cases, the co-PIs are responsible for notifying HSA as soon as possible but no later than 7 calendar days after first knowledge that a case qualifies,

8.3. Collecting, Recording and Reporting of Serious Adverse Events (SAEs) to the Health Science Authority (HSA)

1. **For Industry sponsored Trials**

   All SAEs will be reported to HSA according to the HSA Guidance for Industry "Safety Reporting Requirements for Clinical Drug Trials."

2. **For Principal Investigator initiated Trials**

   All SAEs that are unexpected and related to the study drug must be reported to HSA.

   "A serious adverse event or serious adverse drug reaction is any untoward medical occurrence at any dose that:

- Results in death.
- Is life-threatening (immediate risk of death).
- Requires inpatient hospitalization or prolongation of existing hospitalization.
- Results in persistent or significant disability/incapacity.
- Results in congenital anomaly/birth defect.
- Is a Medically important event.

Medical and scientific judgment should be exercised in determining whether an event is an important medical event. An important medical event may not be immediately life threatening and/or result in death or hospitalization. However, if it is determined that the event may jeopardize the subject and/or may require intervention to prevent one of the other adverse event outcomes, the important medical event should be reported as serious."

All SAEs that are unexpected and related to the study drug will be reported. The investigator is responsible for informing HSA no later than 15 calendar days after first knowledge that the case qualifies for expedited reporting. Follow-information will be actively sought and submitted as it becomes available. For fatal or life-threatening cases, HSA will be notified as soon as possible but no later than 7 calendar days after first knowledge that a case qualifies, followed by a complete report within 8 additional calendar days.

8.4.Data Safety Monitoring Plan

Data will be stored both on paper and electronically. Electronic data will be stored in a standalone-unshared personal computer belonging to the PIs located in the PIs' office with access code required for entry. Only the PI will have immediate access to the research data with sharing of data only to the co-investigators and research assistants.

8.5.Complaint Handling

Complaints will be handled initially by research personnel and PI. If the complaint is medical in nature or if it cannot be resolved at that level, a member of the study team will take over. All data will remain confidential and may still be used in the final analysis of the trial.

9. DATA ANALYSIS

9.1.Data Quality Assurance

All biochemical investigation will be performed at accredited hospital laboratory.

9.2.Data Entry and Storage

Data will be stored both on paper and electronically. Electronic data will be stored in a standalone-unshared personal computer belonging to the PIs located in the PIs' office with access code required for entry. Only the PI will have immediate access to the research data with sharing of data only to the co-investigators and research assistants.

10. SAMPLE SIZE AND STATISTICAL METHODS

10.1. Determination of Sample Size

A power based (90%) sample size calculation using statistics from published GI studies indicated that a group of at least 10 people would be needed for this study in order to find a significant difference among the GI values of the reference and test foods, if a significant difference truly exists (a difference of 1.0 standard deviation units in GI). A group of 24 healthy, non-smoking people, aged between 18-65 years, were recruited.

Null hypothesis: Anthocyanin fortified bread will not change the GI of bread.
Alternate hypothesis: Anthocyanin fortified bread will lower the GI of bread.

10.2. Statistical and Analytical Plans

a. General Considerations

All data will be analyzed using statistical software (eg. SPSS/Stata), with significance defined as

a p value of less than 0.05 on a 2-sided unpaired t-test. Other variables will be presented as mean ± SE with differences between groups assessed by mixed model for categorical variables and continuous variables. Data will be explored for assessment of errors, missing values, and distribution of the variables.

b. Safety Analyses

Safety analysis for adverse events will be performed every visit.

c. Interim Analyses

No interim analysis has been planned for this study.

d. Describe the types of statistical interim analyses and stopping guidelines (if any) that are proposed, including their timing.

All data taken up to that time point will be analysed including incidence of adverse events. Decision for stopping of study will be in accordance with the adverse events reporting.

11. ETHICAL CONSIDERATIONS

11.1. Informed Consent

Informed consent will be taken during screening with the aid of the NUS-IRB approved version of the Participant Information Sheet and Consent Form. Illiterate subjects have the option to have a family member present during the consent taking process. Vulnerable subjects will not be recruited for this study.

11.2. IRB review

This protocol and the associated informed consent documents will be submitted to NUS-IRB for review and approval before the subject recruitment and the study starts.

11.3. Confidentiality of Data and Patient Records

Hardcopy data will be kept under lock and key at the co-PIs' work-station located in the co-PIs' office with access code required for entry. Electronic data will be stored in a standalone unshared password protected PC belonging to the PI located in the same place. There will be scheduled changes to passwords. There will be encryption of all email or protection by password of all data with patient identifiable information. Only the PIs will have immediate access to the

research data with sharing of data available only to the co-investigators on an “as needed” basis. Biological samples will remainss coded and stored with the laboratories.

12. PUBLICATIONS

The study team will not enter into or renew any grant, contact, or agreement that would restrain its freedom to disclose the existence of the research document or the purpose and scope of the proposed research. The study team normally does not accept grants, contracts, or agreements for research which unreasonably restrict its members from publishing or otherwise disseminating the results of this research. The responsibility for compliance with these policies rests with the principal investigator.

13. RETENTION OF TRIAL DOCUMENTS

Records for all participants, including CRFs, all source documentation (containing evidence to study eligibility, history and physical findings, laboratory data, results of consultations, etc.) as well as IRB records and other regulatory documentation will be retained by the PI in a secure storage facility. The records should be accessible for inspection and copying by authorized authorities. These records will be stored at the PI’s workstation under lock and key that is located in the PI’s office with access code required for entry.

INFORMED CONSENT FORM

1. Study Information

Protocol Title:

Effects of fixed meals with special formulated rice on blood glucose levels of healthy volunteers.

Principal Investigator & Contact Details:

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Point of contact from Alchemy FoodTech Pte. Ltd.:

Ms. Verleen Goh

Alchemy Foodtech Pte. Ltd.

53 Li Hwan Terrace Singapore 556981

2. Purpose of the Research Study

3. What procedures will be followed in this study

If you take part in this study, you will be randomized to receive a mixed meal tolerance test (MMTT) with Diabetec® lower GI rice or mixed meal with control white rice for the first MMTT and the alternate for the second MMTT. Randomization means assigning you to one of 7 groups by chance, like tossing a coin or rolling dice.

If you take part in this study, you will be asked to wear a continuous blood glucose monitoring system (CGMS) for 14 days, attend 2 MMTT visits, assessed the meals using a visual analogue scale and keep a food diary during the 14 days of participation. Your participation in the study will last 14 days and you will use the CGMS for about 14 days. You will need to visit the NUS Investigational Medical Unit 2 times during the study.

If you agree to take part in this study, the following will happen to you:

(a) Visit 1 - Screening

To validate your eligibility for the study, the trained research staff will walk you through a screening checklist. You will have the study explained to you, read the consent form, have the opportunity to ask questions, and then sign the approved written Informed consent form and keep a copy. Upon confirming that you are a suitable candidate and signing of the informed consent, a trained research staff will proceed to schedule an appointment for you to return for the subsequent study visit.

(b) Visit 2 - Installation of CGMS (Day 1)

During this visit, you will be educated on how to maintain and care for a continuous glucose monitoring system (CGMS) and to keep a food and activity diary for the duration of the CGM. During this period (Day 1-14), you will receive SMS to check on the CGMS. If there is a need, the research personnel will arrange for a mutually convenient time and place to review and replace the CGMS. You will have to wear the CGMS for the next 14 days. During the period, meals (lunch and dinner) will be prepared and delivered to you. You will also need to record down what you have eaten in between the meals and the activities you have done.

Mixed meal tolerance test (MMTT)

After installation of CGMS, you will undergo a MMTT. You will be randomized to receive either mixed meal with Diabetec® lower GI rice or mixed meal with control rice for the first MMTT (visit 2) and the alternative for the second MMTT (visit 3). The study visit, which will take about 2hr to 3hr, will be carried out within the premises of NUHS. You will need to fast (no food or drinks, except plain water) from 10 pm the night before or for approximately 10-12hr prior to the study visit. You should avoid fat-rich foods for at least 3 days prior to the study, and should not engage in strenuous exercises (eg. swimming or long distance walking) 24 hours before the study. During this study visit, you will be given a prepared meal. At 0, 15, 30, 45, 60, 90, 120 minutes, blood will be sampled through a cannula from one of the arms. You will be asked to remain seated throughout the visit and only minimal movement is allowed.

c) Continuous glucose monitoring (Day 1 - 14)

For the next 14 days, you will be provided with lunch and dinner from the research team through delivery. You will be randomized to receive either mixed meal with controlled rice or mixed meal with Diabetec® lower GI rice for day 1 to 7 and received the alternative for the day 8- 14. You will not be told whether you are receiving the Diabetec® lower GI rice or control rice.

(d) Visit 3 (Day 14 of CGM) – MMTT and removal of CGMS

On day 14, you will return to undergo the second MMTT. Your height, BMI, waist and hip circumference will be measured and recorded. You will be asked to attend the same MMTT protocol (refer to Day 1 – MMTT protocol). Lastly, you will return the CGMS, and your 14-day

food and activity diary

In total, approximately 42 teaspoons of blood(approximately 210ml) will be taken as part of this study.. When your participation in the study ends, you will no longer have access to Diabetec® lower GI rice or CGMS unless special additional arrangements are made by the Principal Investigator. Any blood or tissue specimens obtained during the course of this study will be stored and analyzed only for the purposes of this study for a period not exceeding 6 months and will be destroyed after completion of the study.

4. Your Responsibilities in This Study

If you agree to participate in this study, you should follow the advice given to you by the study team. You should be prepared to visit the Investigational Medical Unit 2 times and undergo all the procedures that are outlined above.

5. What Is Not Standard Care or is Experimental in This Study

The study is being conducted because Diabetec® lower GI rice is not yet proven to have a lower glycemic response than normal white rice. We hope that your participation will help us to determine whether Diabetec® lower GI rice is equal or superior to existing white rice.

Use of a placebo (normal white rice), blinding (participant will not be told which rice is given during the visit), and randomization (Diabetec® lower GI rice and white rice are randomized between visit 1 and 2) are only done for research studies.

6. Possible Risks and Side Effects

a. Slight pain and bruising due to blood drawing procedure. You can lie down when you feel sign of dizziness. In the unlikely event that subject is injured while giving a blood sample, first aid will be provided, and you will be directed to proper health treatment.

b. You might encounter allergic reactions and/or intolerances to the foods given in the study. To avoid this situation, you will be asked about food allergies before entering the study during the screening. The ingredients of the meal provided will also be made known to you and you will be asked for allergic reaction or intolerance to the meal before you can participate in the study. Rarely, a severe and possibly life-threatening allergic reaction can occur. Symptoms of a severe reaction include: swelling of the face, difficulty breathing, or a sudden drop in blood pressure that may cause dizziness. If you have any of these symptoms, call your doctor at once.

c. Possible infective acute gastroenteritis. In case of unlikely event, medical attention will be given immediately. You will be directed to proper health treatment or admitted to hospital for treatment.

Diabetec® lower GI rice is still being tested; therefore, you may experience other side effects that have not yet been reported. However, you will be kept informed of any significant new

findings that may relate to your willingness to continue to take part in this study.

If you experience any new symptoms, you should contact your doctor or the Principal Investigator as soon as possible.

7. Possible Benefits from Participating in the Study

There is no known benefit from participation in this study. However, your participation in this study may add to the knowledge about the use of this Diabetec® lower GI rice in management of diabetes.

8. Important Information for Women Subjects

The effect of Diabetec® lower GI rice on a baby's development is not known. Therefore, pregnant and breast-feeding women may not take part in this study. Women who have a chance of becoming pregnant must have a negative pregnancy test at study entry and use birth control during the study. If you become pregnant during this study, you must stop the trial and call your doctor or the Principal Investigator immediately.

9. Alternatives to Participation

No standard of care treatment will be provided as this is clinical trial on food items.

10. Costs & Payments if Participating in the Study

If you take part in this study, the following will be performed at no charge to you: 2 mixed meal tolerance tests and continuous blood glucose monitoring for 14 days. These costs will be borne by Alchemy Foodtech Pte. Ltd.

You will be reimbursed for your time, inconvenience and transportation costs as follows:

- If you complete the study, you will be paid $250.
- If you do not complete the study for any reason, you will be paid for each visit you completed with reference to table below.

Visit	Reimbursement
Screening	$10
Mixed meal tolerance test 1 and 2	$50 per visit
CGM for a total of 14 days	$10 per day
Total reimbursement for completion of whole study	$250

11. Voluntary Participation

Your participation in this study is voluntary. You may stop participating in this study at any time. Your decision not to take part in this study or to stop your participation will not affect your medical care or any benefits to which you are entitled. If you decide to stop taking part in this study, you should tell the Principal Investigator. If you withdraw from the study, you will be required to inform the Principal Investigator and/or Research assistant at least 3 days before the visit. However, the data that have been collected until the time of your withdrawal will be kept and analysed. The reason is to enable a complete and comprehensive evaluation of the study.

The biological samples collected for the study will be deemed to be gifted to NUS/Alchemy Foodtech Pte. Ltd. and will not be returned to you. You will also not have any right or claim to any share in the commercial gain derived from the research (if any). However, you retain your right to ask the Principal Investigator to discard or destroy any remaining samples if the biological sample(s) is individually-identifiable and has not been used for the research or it has been used for research, but it is practicable to discontinue further use of the biological sample(s) for the research.

Your doctor, the Investigator and/or the Sponsor of this study may stop your participation in the study at any time if they decide that it is in your best interests. They may also do this if you do not follow instructions required to complete the study adequately. If you have other medical problems or side effects, the doctor and/or nurse will decide if you may continue in the research study.

In the event of any new information becoming available that may be relevant to your willingness to continue in this study, you will be informed in a timely manner by the Principal Investigator or his/her representative.

12. Compensation for Injury

If you follow the directions of the doctors in charge of this study and you are physically injured due to the trial substance or procedure given under the plan for this study, the Alchemy Foodtech Pte. Ltd. will pay the medical expenses for the treatment of that injury. Payment for management of the normally expected consequences of your treatment will not be provided by the Alchemy Foodtech Pte. Ltd.
Compensation for the research related injury shall be paid by Alchemy Foodtech Pte. Ltd. according to the Association of the British Pharmaceutical Industry's Clinical Trial Compensation Guidelines. Broadly speaking, the ABPI guidelines recommend that without legal commitment, subjects should be compensated by Alchemy Foodtech Pte. Ltd. without having to prove that Alchemy Foodtech Pte. Ltd. is at fault. There are limitations to compensation in the ABPI guidelines. A copy of the ABPI guidelines will be provided to you upon request.

By signing this consent form, you will not waive any of your legal rights or release the parties involved in this study from liability for negligence.

13. Confidentiality of Study and Medical Records

Information collected for this study will be kept confidential. Your records, to the extent of the applicable laws and regulations, will not be made publicly available.

However, the Sponsoring company Alchemy Foodtech Pte Ltd and NHG Domain Specific Review Board and Ministry of Health will be granted direct access to your original medical records to check study procedures and data, without making any of your information public. By signing the Informed Consent Form attached, you are authorizing (i) collection, access to, use and storage of your "Personal Data", and (ii) disclosure to authorised service providers and relevant third parties.

"Personal Data" means data about you which makes you identifiable (i) from such data or (ii) from that data and other information which an organisation has or likely to have access. This includes medical conditions, medications, investigations and treatment history.

Research arising in the future, based on this "Personal Data", will be subject to review by the relevant institutional review board.

Data collected and entered into the Case Report Forms are the property of *Alchemy Foodtech Pte Ltd*.In the event of any publication regarding this study, your identity will remain confidential.

By participating in this research study, you are confirming that you have read, understood and consent to the Personal Data Protection Notification available at http://www.nuhs.edu.sg/personal-data-protection/nuhsnuh-data-protection-policy.html.

14. Who To Contact if You Have Questions

If you have questions about this research study and/or any injuries during the course of this study you may contact the Principal Investigator,

Dr Khoo Chin Meng

Department of Medicine

National University Hospital

5 Lower Kent Ridge Road, Singapore 119074

Tel: 67726174

The study has been reviewed by the NHG Domain Specific Review Board (the central ethics committee) for ethics approval.

If you want an independent opinion to discuss problems and questions, obtain information and offer inputs on your rights as a research subject, you may contact the NHG Domain Specific Review Board Secretariat at 6471-3266. You can also find more information about participating in clinical research, the NHG Domain Specific Review Board and its review processes at www.research.nhg.com.sg.

If you have any complaints or feedback about this research study, you may contact the Principal Investigator or the NHG Domain Specific Review Board Secretariat.

15. Consent to be Contacted for Future Research

You are being asked for permission to be contacted in the future for participation in research studies that you may be suitable for. If you agree to be contacted, your information and contact details will be entered and stored in a secured database in NUS. Your information and contact details will not be released to any parties outside *NUS* without your permission. When investigators from NUS identify you to be suitable for a particular research study, the investigators or authorized personnel from NUS will contact you to inform you about the research study. Your decision to be contacted for future research studies is completely voluntary and separate from your decision to participate in this study. Your decision will not affect your medical care or any benefits to which you are entitled. You may change your mind at any time by contacting Ms.Yang Dimeng (92717488).

CONSENT FORM

Protocol Title:

Effects of fixed meals with special formulated rice on blood glucose levels of healthy volunteers.

Principal Investigator & Contact Details:

Dr Khoo Chin Meng
Department of Medicine
National University Hospital
5 Lower Kent Ridge Road, Singapore 119074
Tel: 67726174

I voluntarily consent to take part in this research study. I have fully discussed and understood the purpose and procedures of this study. This study has been explained to me in a language that I understand. I have been given enough time to ask any questions that I have about the study, and all my questions have been answered to my satisfaction. I have also been informed and understood the alternative treatments or procedures available and their possible benefits and risks.

By participating in this research study, I confirm that I have read, understood and consent to the NUH Personal Data Protection Notification.

Consent to be Contacted for Future Research

☐ Yes, I agree to be for contacted for future research that I may be eligible for.
I agree to be contacted via:

Phone _____

Mail _____

_____

Email _____

Others _____

☐ No, I do not agree to be contacted for future research.

_____	_____	_____
Name of Participant	Signature	Date

Witness Statement

I, the undersigned, certify that:

- I am 21 years of age or older.
- To the best of my knowledge, the participant/ the participant's legally acceptable representative signing this informed consent form has the study fully explained in a language understood by him/ her and clearly understands the nature, risks and benefits of his/ her participation in the study.
- I have taken reasonable steps to ascertain the identity of the participant/ the participant's legally acceptable representative giving the consent.
- I have taken steps to ascertain that the consent has been given voluntarily without any coercion or intimidation.

_____	_____	_____
Name of Witness	Signature	Date

1. In accordance with Section 6(d) of the Human Biomedical Research Act and Regulation 25 of the Human Biomedical Research Regulations 2017, appropriate consent must be obtained in the presence of a prescribed witness who is 21 years of age or older, and has mental capacity. The witness must be present during the entire informed consent discussion, and must not be the same person taking the appropriate consent. The witness may be a member of the team carrying out the research.
2. However, if the participant/ the participant's legally acceptable representative is unable to read, and/ or sign and date on the consent form, an impartial witness should be present instead. The impartial witness should not be a member of the study team.

Investigator Statement

I, the undersigned, certify that I explained the study to the participant and to the best of my knowledge the participant signing this informed consent form clearly understands the nature, risks and benefits of his / her participation in the study.

_____	_____	_____
Name of Investigator / Person administering consent	Signature	Date