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| **Pamantasan ng Lungsod ng Maynila(PLM)-Ospital ng Maynila Medical Center (OMMC) Department of Internal Medicine and ICU****Quirino Avenue, Corner Roxas Boulevard, Malate, Manila** |
| The Effects of Malunggay (Moringa oleifera) leaves capsule supplements on High Specificity C-Reactive Protein (hsCRP) and Hemoglobin A1c (HgbA1c) Levels of Diabetic Patients in Ospital ng Maynila Medical Center Internal Medicine Department Diabetic Clinic: A Prospective Cohort Study |
| Clinical Trial |
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| **Rainier Nery Mozo, MD;Imelda Caole-Ang, MD, FPCP, FPCC** |
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**MAIN AUTHOR: Rainier Nery Mozo MD Email Address:** **rainiermozomd@yahoo.com** **Contact Number: 0932-844-9951**

**The Effects of Malunggay (*Moringa oleifera*) leaves capsule supplements on High Specificity C-Reactive Protein (hsCRP) and Hemoglobin A1c (HgbA1c) Levels of Diabetic Patients in Ospital ng Maynila Medical Center Internal Medicine Department Diabetic Clinic: A Prospective Cohort Study**

Rainier Nery Mozo, MD; Imelda Caole-Ang, MD

**Abstract**

**Introduction:**

 Current evidence supports a central role of inflammation in the pathogenesis of atherosclerosis and diabetes.[1-3] DM type 2 is an inflammatory atherothrombotic condition associated with high prevalence of thrombotic cardiovascular disease. In patient with DM, this inflammation is reflected by elevated plasma C-reactive protein (CRP) levels. [4-8] HsCRP is considered as a strong predictive of cardiovascular risks and death. [6, 61-72] Some evidence showed that CRP may represent an active participant in atherogenesis. [7]

Among the DM risk factors (like hypertension, atherogenic dyslipidemia, insulin resistance, impaired fibrinolysis, inflammatory profile), definitely, inflammation is the neglected one.

**Moringa oleifera** has been suggested to exert anti-inflammatory[42-45] and hypoglycemic property. [80]

**Objective:** To determine the effect of *Moringa oleifera* leaves supplementation on the hsCRP, and HgbA1c levels of diabetics of OMMC DM clinic

**Methods:** We performed a prospective cohort study of 56 adult diabetics who were given 12-weeks supplementation of *Moringa oleifera*. Plasma hsCRP and serum HgbA1c were compared before and after treatment with M. oleifera.

**Results:** The over all population mean prehsCRP is 3.38 mg/dl (95% CI 2.77-3.99). Supplementation of M. oleifera decreased significantly(p<0.0001) the posthsCRP to 1.69 mg/dl (95% CI 1.28-2.09). The mean preHgba1c is 6.96% (95% CI 6.64-7.09) was reduced postHgbA1c to 6.06% (95% CI 5.88-6.24). The mean reduction of 0.6% in HgbA1c was significant (p-value <0.0001).

**Conclusion:** Our study confirms that diabetics may have additional benefit from intake of Moringa oleifera leaves by reducing hsCRP and by improving blood sugar control as evidenced by the reduction of Hgba1c.

**Review of Literature**

***Diabetes Mellitus and inflammation***

*Hyperglycemia, is the most obvious abnormality in DM. However it is only the tip of the 'metabolic syndrome iceberg’. Among the abnormalities in DM like hypertension, atherogenic dyslipidemia, insulin resistance, impaired fibrinolysis,* ***definitely it is the******generalized inflammation which is the most neglected one.***

**The understanding of the pivotal role of inflammation in the pathogenesis of atherosclerosis has opened the opportunities for a better future for management of DM and prevention of its complications. So risk assessment, prediction of cardiovascular events in DM and prevention of inflammation by add-on therapy are the needs of the present day.** [57]

**C-Reactive Proteins (CRP)**

C-reactive protein, an acute-phase reactant produced by liver, is an extreme sensitive marker of systemic inflammation.[51]

**Circulating CRP concentration**

Figure . C-Reactive Protein [102]

In healthy young adult volunteer blood donors, the median concentration of CRP is 0.8 mg/l, the 90th percentile is 3.0 mg/l, and the 99th centile is 10 mg/l, [75] but, following an acute-phase stimulus, values may increase from less than 50 μg/l to more than 500 mg/l, that is, 10,000-fold.

The attention focused on CRP reflects in part the fact that it is **an exceptionally stable analyte in serum or plasma and those immunoassays for it are robust, well standardized, reproducible, and readily available**. [61]

**HsCRP determination should be performed in a metabolically stable individual without obvious inflammatory or infectious conditions in order to reduce within-individual variability**.

Interpreting CRP results is straightforward (Figure 2 below).[62] If a level of >10 mg/L is identified, there should be a search initiated for an obvious source of infection or inflammation, which could obscure any prediction of coronary risk that might be attributed to the elevated level. **That result of more than 10 mg/L should be then discarded** and the hsCRP be measured again after 2 weeks. [62]

 Figure . Clinical Interpretation of hsCRP for cardiovascular risk prediction [100]

Several factors have been identified as being associated with increased or decreased levels of hsCRP (Table I). [62]

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| TABLE I. Patient Characteristics and Conditions Associated with Increased or Decreased Levels of hsCRP |
| Increased Levels | **Decreased Levels** |
| * Elevated Blood Pressure
* Elevated Body Mass Index
* Cigarette Smoking
* Metabolic syndrome/ DM
* Low HDL/High Triglycerides
* Estrogen/Progesterone hormone use
* Chronic Infections (gingivitis, bronchitis)
* Chronic Inflammation (rheumatoid arthritis)
 | * Moderate alcohol consumption
* Increased activity/ endurance exercise
* Weight loss
* Medications: Statins, Fibrates, Niacin
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***C-Reactive Protein, Diabetes Mellitus and Cardiovascular Disease***

It is perceived that **chronic low-grade inflammation as shown by elevated CRP** might potentially be **a cause underlying the etiology and disease progression of DM, although the exact mechanisms are still not well understood.** [52]

It was found out that CRP levels were higher in diabetics than non-diabetics. [52] In addition, C-reactive protein was noted to be a strong and better independent predictor of thrombotic cardiovascular events and death in DM than traditional risk factors [61-72] or parameters of metabolic control in DM at high risk for cardiovascular endpoints.[53]

Besides its predictive role in determining thrombotic cardiovascular risk, there is some evidence that CRP may represent an active participant in atherogenesis.[54,78-79]

***Moringa oleifera***

*****Moringa oleifera* (of the family Moringaceae and synonymous with Moringa pterygosperma[2] ) is a drought-resistant wispy tree. Any reader who is familiar with M. *oleifera* will recognize the oft-reproduced characterization made many years ago by the Trees for Life organization, that **“ounce-for-ounce,** ***M. oleifera leaves contain more Vitamin A than carrots, more calcium than milk, more iron than spinach, more Vitamin C than oranges, and more potassium than bananas,” and that the protein quality of M. oleifera leaves rivals that of milk and eggs***. [5]

Figure . *Moringa oleifera*

**Phytochemistry of Moringa oleifera**

Moringa family is rich in compounds containing the simple sugar, rhamnose, and it is rich in a fairly unique group of compounds called glucosinolates and isothiocyanates. [13,14] In an analysis, it was noted that ***the leaf extracts appear to have the most level of all bioactives of interest which supports its usage.*** [49-50]

**Anti hyperglycemic Property & Effect on HgbA1c**

 ***HgbA1c is a very sensitive index for glycemic control in DM.*** [82] ***It was noted in studies that every 1% drop in HgbA1c reduces the risk of microvascular complications by 40%, and death by 21%.* [84,85]**A review on Moringa oleifera where supplementation of the leaf powder daily noted significant reductions in fasting glucose (28%) and postprandial glucose (26%) relative to baseline.[81,82,92,93]

**Methods**

1. **Study Participants**

**A.1 Inclusion Criteria**

Participants for the study will be the following:

1. Male or female participants aged between 19 and 65 years of age.
2. They were diagnosed by the Internal Medicine resident or other physician as having Diabetes Mellitus using the following criteria stated by American Diabetes Association (ADA)

Participants presents with 1 or more of the following:

* FPG more than or equal 126 mg/dl (7.0 mmol/L). Fasting is defined as no caloric intake for atleast 8. OR
* 2-h plasma glucose more than or equal to 200 mg.dl (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using glucose load containing the equivalent of 75g anhydrous glucose dissolved in water OR
* In pa patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose of more than or equal to 200 mg/dl (11.1 mmol/L)
1. Participants should be willing to have their blood extracted for hsCRP and Hgba1c measurement before and after 12 weeks supplementation of *M. oleifera*.
2. Participants have available treatment partner.
3. Participants with their treatment partners should be willing to stay in Metro Manila during the course of the trial, and must be easily contacted by phone.

Treatment partners were relatives of the participants who are living with them and are able to monitor participants’ intake of supplements, maintenance medications and activities (smoking, alcohol intake, exercise).

Treatment partners are contacted every week for monitoring of any morbidity to any medical condition, mortality and presumed adverse effects of M. oleifera. They monitor the compliance of the participants to supplementation and their maintenance medications. All participants and treatment partner are advised to notify the investigator for any additional drugs that will be taken or prescribed by any physicians. At home, treatment partner were given the responsibility to advise the participants to abstain from smoking, alcoholic beverage intake and endurance exercise a day before the blood extractions.

Subjects who have been diagnosed with other diseases such as asthma, stroke, or hypertension was included in the trial provided since they are already medically stable and that these diseases are not listed as part of the exclusion criteria.

All eligible subjects signed a consent form and agreed with aforementioned conditions.

**A.2 Exclusion Criteria**

The subjects with the following conditions were excluded in the study:

1. Subjects who are suspected to have psychiatric disorders, mentally challenged, or confirmed to be pregnant
2. Subjects who are not medically stable or those confirmed to be afflicted with communicable or life threatening diseases such as but not limited to the following:
	1. ongoing infection (Pulmonary Tuberculosis, DM foot infection, cellulitis, pneumonia, Urinary Tract Infections, ear infections or dental/gum Infections)
	2. decompensated heart failure ( CHF III-IV)
	3. chronic liver disease in decompensated state
	4. stroke in evolution,
	5. acute coronary syndrome within 6 months,
	6. systemic or pulmonary inflammatory condition (including rheumatoid arthritis, systemic lupus erythematosus,
	7. chronic obstructive pulmonary disease in exacerbation,
	8. bronchial asthma in exacerbation,
	9. history of renal or other organ transplant and/or
	10. immunocompromised state
3. Subjects with anemia (hemoglobin value of less than 13.0 g/dl in males; 12.0 g/dl in females)
4. Subjects with undergoing Moringa oleifera, fish oil or any vitamins or multivitamins supplementation within the past 8 weeks are excluded in the study.
5. Subjects with the use of estrogen/progesterone hormone.
6. Subjects with plan or anticipated by their physicians to be initiated with renal replacement therapy (dialysis) during the study.
7. Subjects who are pregnant or plan to be pregnant.
8. Subjects with known or suspected allergy to *M. oleifera* or any other component to the drug preparation.

Subjects with plasma hsCRP more than or equal 10 mg/dl will also be excluded. Subjects who refused to agree to the terms of the study’s protocols including, but not limited to, subject selection, treatment program, follow-up schedule, consent, indemnity clause, and/or honorariums were excluded.

**A.3 Withdrawal**

Participants was considered withdrawn if they are lost to follow-up after attempts to contact them through the Principal Investigator’s best effort.

1. **Moringa *oleifera* powdered leaves capsule supplementation**

 M. *oleifera* powdered leaves capsule contains 500mg of pure malunggay leaves encapsulated in vegetable capsule. These capsules were manufactured for Atienza Naturale by Greenplus Corporation under FDA registration number 17069452532. Manufacturing process was approved by DOST.

The capsules used in this study were manufactured last June 2014 with expiration date of June 2016. The capsules were taken by every participants, 1 capsule thrice a day for 12 weeks.

1. **Determination of High Specific C-Reactive Protein (hsCRP) level**

High Specificity CRP was measured by licensed medical technologist at Asia Pacific Laboratory via an automated high-sensitivity immune-nephelometric assay in COBAS INTEGRA 400 Analyzer developed in Germany by ROCHE diagnostics. The equipment is calibrated every 6 months.

1. **Determination of Hemoglobin A1c (hgbA1c) level**

Hemoglobin A1c serum level was also measured by licensed medical technologist at Asia Pacific Laboratory using Quo-test HgbA1c analyser. All anemic participants as defined by the exclusion criteria will be eliminated. The equipment is calibrated every 6 months.

1. **Setting**

The study was administered to participants of a single DM clinic in a single university tertiary hospital in Manila, Philippines. All participants had plasma high specific CRP and HgbA1c initial measurement. After taking *up Moringa oleifera* powdered leaves capsule, 1 capsule thrice a day, participants were followed up for 12 weeks for post treatment measurement of plasma CRP and HgbA1c.

1. **Intervention**

All screened participants had plasma high specificity CRP ang HgbA1c initial measurement. Participants were instructed to take a capsule of powdered *Moringa oleifera* leaves thrice a day for 12 weeks. After which, participants were required to come back for post treatment measurement of plasma high specific CRP and HgbA1c. Initial and final body weight measurments were noted

 Reminders were given to the participants to avoid taking any multivitamins, smoking and alcoholic beverages. Avoidance of endurance exercise a day prior to blood extractions was advised. All participants and treatment partners were advised to notify the investigator for any additional drugs that will be taken or prescribed by any physicians.

1. **Assessment & Follow-up**

Phone calls were done every week to treatment partners by the investigator to monitor the compliance of the participants to their supplementation and other maintenance medications.

Besides weekly phone calls to treatment partners, participants with their treatment partners were seen monthly by the clinical investigator were done to assess participants. Patients were assessed for any adverse reactions to the supplements.

After taking a capsule of*Moringa oleifera* thrice a day for 12 weeks, the participants were instructed to have their follow-up visit for repeat measurement of plasma high specific CRP and HgbA1c.

1. **Procedure**

G.1. Before administering the supplementation, necessary permits were obtained, and from the regulatory requirements stipulated in the Regulatory considerations portion of this document.

 G.2. All participants volunteered for the study. They signed a consent form after reading the Patient Information Table. Participants were then seen by the investigator who will give them clearance for the trial. Physical examination was done to assess the initial status of every participant. List of maintenance medications was obtained.

 G.3. Participants was given a letter which explains the study procedure which they can present to their physicians in the event that they will need hospitalization or emergency room consultation during the course of the study.

 G.4. Initial body weigth of every participant was measure and used to calculate for the BMI. Recent measurement of serum HDL and Tg level were noted from the patients’ DM clinic chart. Recent serum creatinine of patient was also noted from the patients’ DM clinic chart and was used to compute for their estimated clearance using the Cockcroft-Gault formula. Maintenance medications were noted especially the presence of statins, niacin, fibrates and multivitamins.

G.5. Participants had blood extractions for initial measurement of plasma CRP and HgbA1c level. All patients with HsCRP of more than 10 mg/L were excluded.

 G.6. Participants were asked to take capsule of*Moringa oleifera* thrice a day for 12 weeks. This will be guided by their treatment partners.

G.7. Treatment partners were contacted weekly via phone calls by the investigator to monitor the participants on their compliance to their supplementation and maintenance medications.

G.8. Patients were asked to have follow-up check up monthly for assessment of any adverse reaction of supplementation, to check for the presence of hypertension, and check if there is any drug added to patient maintenance medications.

 G.9. Participants had follow-up visit to have post treatment measurement of plasma CRP and HgbA1c level. Final body weight was noted.

G.10. Participants were considered as having withdrawn from the trial if they fail to do follow-up visit within 2 weeks.

 G.11. Data from pre and post supplementation of *Moringa oleifera* powdered leaves capsules were statistically analyzed using appropriate software and techniques.

1. **Procedural Chart**

**Ethical Considerations**

1. **Securing Permits to undergo the study at the required institution**

 This study was approved by the Ospital ng Maynila Medical Center Medical Education and Research committee and Ospital ng Maynila Medical Center Department of Internal Medicine Research Committee.

1. **Disclosure of Research objectives and Inform Consent**

 Participants were informed of the research objective both verbally and in writing in a language they can understand before they underwent informed consent process.

Participants were informed of the details of the study and provided a copy of **“Talaan ng Impormasyon Para sa Pasyente” (APPENDIX A).**

**Statistical Analysis**

All statistical analyses were performed on a personal computer running Stata 12.0 on a Microsoft window version 7 operating system. Mean and percentages were computed. Wilcoxon signed-Rank test was used to analyze the difference between pre and post mean plasma hsCRP and HgbA1c values.

**Results**

Of the 73 patients enrolled at the DM Clinic, 60 of which met the inclusion criteria for this study. Of the 60 patients who met the inclusion criteria, 4 participants were excluded. Of the 4 excluded participants, 3 patients did not complete their screening requirements while one hospitalized due to pneumonia and exacerbation of chronic obstructive pulmonary disease a week after the screening period (before the supplementation started).

Majority of participants were female (80%). The mean age of the study population is 61.21+8.01 years. The mean BMI is 20+1.96.

All participants are noted to have controlled hypertension. No participant was noted smoker.

In their list of maintenance medications, it was noted that all participants has simvastatin 40mg once a day. No intake of niacin and fibrates was noted.

Two participants were observed to have weight loss of 0.5kg.

The over all population mean pre hsCRP is 3.38 mg/L (95% CI 2.77-3.99) while the post hsCRP is 1.69 mg/L (95% CI 1.28-2.09). Reduction in mean plasma hsCRP was significant (p<0.0001) shown in table II.

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| Table II. Measurement of mean hsCRP and HgbA1c  before & after Supplementation of *Moringa oleifera*  (n=56) |  |
|  | Mean Pretreatment | Mean Posttreatment | Difference | p-value |
| hsCRP | **3.38 mg/l** | **1.69 mg/l** | **1.69** | **<0.0001** |
| Hgba1c | **6.69 %**  | **6.06%** | **0.63** | **<0.0001** |

In the measurement of Hgba1c, it was noted that mean pre Hgba1c is 6.96% (95% CI 6.64-7.09) and was reduced to post hgbA1c is 6.06% (95% CI 5.88-6.24). The mean reduction of 0.6% was noted to be significant at p-value less than 0.0001.

Controlling the Hgba1c, weight and age, multilinear regression was utilized showing the mean pre hsCRP is 1.5 times (95% CI 0.68-2.35) elevated compared to mean post hsCRp.

**Discussion**

C-reactive protein, a member of the pentraxin family, is the prototypic marker of inflammation. In addition to being a risk marker for atherosclerosis, it promotes tissue factor release from monocytes, phagocytosis and shedding of cell adhesion molecules. Furthermore, CRP co-localizes with complement in the atherosclerotic lesion. [86-89] C-reactive protein is one of many proteins produced by the liver in response to cellular injury due to trauma, infarction or infection [90]. Release of CRP from the liver into the circulation after cell injury is stimulated by the proinflammatory cytokine interleukin-6 (IL-6). [91]

Diabetes Mellitus type 2 is an inflammatory atherothrombotic condition associated with high prevalence of cardiovascular disease. In patient with DM type 2, this inflammation is reflected by elevated plasma levels of several biomarkers of inflammation such as C-reactive protein (CRP). [51-55]

In this study, the over all population mean plasma pre hsCRP is 3.38 mg/L (95% CI 2.77-3.99) falling to the high risk category. Treatment of the M. oelifera capsules after 12weeks lead to the mean plasma post hsCRP of 1.69 mg/L (95% CI 1.28-2.09) falling to the moderate risk category. The reduction in mean plasma hsCRP was noted to be significant (p<0.0001).

Since hsCRP reduction was noted in all pariticipants, possible effect of factors causing elevated hsCRP specifically presence of elevated blood pressure, elevated BMI, cigarette smoking, low HDL, high triglycerides, were not analyzed.

Analysis now focuses on the potential contribution of other factors that can decrease hsCRP level. These factors were moderate alcohol consumption, increased activity/ endurance exercise, weight loss and medications like statins, fibrates and niacin. Since participants with their treatment partners were advised to abstain from alcohol intake and endurance exercise prior to extractions, focus was turned to presence of weight loss and presence of medications. However, it was noted that all participants were noted to have simvastatin 40mg per capsule to be taken once a day as part of their maintenance medications. No noted intake on niacin and fibrates. Weight loss of 0.5 kg was noted to only 2 participants.

Hemoglobin A1c is the measure of glycemic control. In our study, the mean pre hgba1c of the over-all population is 6.96% (95% CI 6.64-7.09). Treatment of the *M. oelifera* capsules after 12 weeks lead to the mean post hgbA1c of 6.06% (95% CI 5.88-6.24). The noted mean reduction of 0.6% in hemoglobin A1c was significant(p<0.0001).

This study showed that 12-weeks supplementation of M. oleifera can bring significant reduction in hsCRP and Hgba1c.

The reduction in hsCRP was possibly due to the components of M. oleifera that has anti-inflammatory effect. As reported by Lee Y.M., et al. Benzyl isothiocyanate found in *M. oleifera* leaves exhibits anti-inflammatory effects[40] while benzylisothiocyanate inhibits inflammatory mediator production by lipopolysaccharide-stimulated RAW 264.7 murine macrophage cell lines. [41] Park E.J., et al. reported 4-{(2'-O-acetyl-α-L rhamnosyloxy)benzyl} isothiocyanate from *M. oleifera* or RIBT causes inhibition of lipopolysaccharide-induced cyclooxygenase-2 and inducible nitric oxide synthase expression.[42]

The reduction in Hgba1c was associated to the antioxidant namely the carotenoids, flavonoids, vitamin C and E found in *M. oleifera*. These substances were noted to facilitate improvement in reducing blood glucose of the diabetics by improving glucose metabolism and decreasing insulin resistance.[93] It was stated that the antioxidants and flavonoids control the glycation process, so that decrease in glycated hemoglobin was observed. [101] This was supported by the study done by Gidhari et al [93] in which administration of *M.Oleifera* leaves powder twice daily for 90 days in a 60 patients with type 2 diabetic causes a significant(p<0.0076) mean reduction of 0.41% in Hgba1c.

Several studies have shown that reduction of HgbA1c and weight loss can cause a potential decrease in hsCRP. To eliminate the possible effects of reduction of Hgba1c and weight to the hsCRP reduction, multilinear regression was utilized. Controlling the other variables particularly hgba1c, age and weight it showed that the mean pre hsCRP is 1.5 times (95% CI 0.68-2.35) elevated compared to mean post hsCrp.

This study emphasized that even if an individual has a good glycemic control as shown by the having hgbA1c less than 7%, they can still be at high risks to develop CV events due to high level of inflammation as shown by elevated initial hsCRP of our participants.

 This study showed that in diabetic patients taking *M. oleifera* supplementation for 12 weeks in addition to their maintenance medications may still give additional benefit in terms of sugar control and reduction of inflammation.

**Conclusion**

Our study confirms that diabetic patients may additional benefit from intake of Moringa oleifera leaves by reducing inflammation as shown by decrease in hsCRP and by improving blood sugar control as evidenced by the reduction of Hgba1c.

**Recommendations**

Randomized-control studies with bigger population size should be undertaken to further elucidate the effect of malunggay capsules to hsCRP and Hgba1c. Study with longer duration of supplementation can also be done to further determine the effect of the malunggay capsule.

 A biochemical study of the specific substance of *M. oleifera* that causes the decrease in HgbA1c or blood glucose may be of great focus in the future.

**Limitations**

Limitations inherent to cohort study designs apply to this particular study. Due to absence of randomization and blinding, biases with regards to patients selected for intervention are not controlled. The possibility of bias cannot be excluded since patients gathered were from a DM clinic which may not represent DM patient in general population.

**Conflict of Interest**

The principal author is a senior resident physician of Ospital ng Maynila Medical Center Department of Internal Medicine and ICU. He is a degree holder of Doctor of Medicine in Pamantasan ng Lungsod ng Maynila and Bachelor of Science in Biochemistry in University of the Philippines Manila.

The co-author is a fellow of both Philippine College of Physicians and Philippine College of Cardiology. She is regular consultant of Ospital ng Maynila Medical Center Department of Internal Medicine and ICU. She is both a degree holder of Bachelor of Science in Zoology and Doctor of Medicine in Pamantasan ng Lungsod ng Maynila.

The authors are not affiliated or connected in any way to Greenplus Corporation or Atienza Naturale.

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**Appendix A**

**TALAAN NG IMPORMASYON PARA SA PASYENTE**

**1. Titulo ng Pag-aaral**

 “The Effects of Malunggay (*Moringa oleifera*) leaves capsule supplements on High Specificity C-Reactive Protein (hsCRP) and HgbA1c levels of Diabetic Patients in Ospital ng Maynila Medical Center Internal Medicine Department Diabetic Clinic: A Prospective Cohort Study”

 Pangunahing tagapagsuri:

Rainier Nery Mozo, M.D., Contact No: 09328449951, email: rainiermozomd@yahoo.com

**2. Layunin ng Pag-aaral**

 Kayo ay inaanyayahang sumali sa pag-aaral na ito. Maaari po lamang na basahin ninyo ang impormasyong nakasaad dito. Ang pag-aaral na ito ay ipapaliwanag din ng personal sa inyo kung saan kayo ay bibigyan din ng pagkakataong magtanong. Kung naiintindihan ninyo at nais ninyong lumahok, maaari lang pong pakipirmahan ang 2 kopya ng katibayan ng paghihintulot na nasa dulong pahina ng talaang ito.

Ang “Diabetes Mellitus (DM)” o dyabetis ay isang mahalagang sanhi sa pagkakaroon ng “cardiovascular disease” o atake sa puso o utak. Bagaman maraming pag-aaral na ang naisagawa upang malaman ang mga gamot upang maiwasan ang mga ito, ang mga komplikasyon buhat sa pagkakaroon ng DM ay nangunguna pa rin sa listahan ng sanhi ng “morbidity and mortality” sa buong mundo. Ilan sa listahan ng “DM risk factors” ay ang mataas na “blood pressure”, “atherogenic dyslipidemia”, “insulin resistance”, “impaired fibrinolysis”, at “inflammatory profile”. Sa mga “DM risks factors” na ito ang “inflammation” ang isa sa hindi pa gaanong nabibigyan pansin. Kaya naman, kailangan nating humanap ng paraan upang matutukan at maibsan ito. Ang “inflammation” ay ipinakaita ng mataas na lebel ng “C-reactive protein” o “CRP” sa dugo.

Buhat sa maraming pag-aaral, ang *Moringa oleifera* o malunggay ay napag-alamang may “anti-inflammatory effects”. Ang dahon ng halamang ito kapag ginamit ay maaaring makapagpababa ang “CRP levels” at “HgbA1c”. Sa pagbaba ng “hsCRP at HgbA1c levels” ay maaaring lumiit din ang posibilidad ng pagkakasakit o pagkamatay buhat sa atake sa puso o utak ang pasyenteng may DM.

 Ang layunin ng pagaaral na ito ay upang malaman kung ang pag-inom ba malunggay capsule ay nakapagpapababa ng “HsCRP, HgbA1c levels” at “clinical outcome” sa mga pasyenteng may DM.

 Ang pag-aaral na ito ay gaganapin sa loob ng 12 lingo. Kahit sino na may edad 19 taong hanggang 65 taong gulang at marunong magbasa at sumagot sa wikang Ingles, na nasuring may DM ng “Internal Medicine Resident” o ng isang doctor sa pamamagitan ng “criteria” na nirekomenda ng American Diabetes Association Guideline ay posibleng kandidato para sa nasabing pag-aaral.

Ang pag-diagnose ng pagkakaroon ng diabetes mellitus o DM (Mula sa American Diabetes Association Guideline) ay ang pagkakaroon ng isa o higit pa sa mga sumusunod:

* FPG >126 mg/dl (7.0 mmol/L) Fasting ay ang hindi pagkain ng higit sa 8 oras
* 2-h plasma glucose >200 mg.dl (11.1 mmol/L) OGTT
* Sa isang pasyenteng may mga sintomas ng “hyperglycemia or hyperglycemic crisis”,
* random plasma glucose > 200 mg/dl (11.1 mmol/L)

**Maaari kang di pasalihin kung ikaw ay may kundisyon ng katulad sa mga sumusunod:**

1. Kung ikaw ay babae at may potensyal na maging buntis, hindi ka dapat nagdadalang tao sa pagsimula ng pag-aaral at maaari kang hingan ng pregnancy test ng mga pangunahing tagapagsuri para ito ay kumpirmahin; Kung ikaw ay may “psychiatric disorder” o problema sa pag-iisip.
2. Kung ikaw ay may sakit na katulad sa mga sumunsunod:
	1. Patuloy impeksyon (Pulmonary tuberculosis, DM foot infection, cellulitis, pulmunya , UTI, infection sa tenga, infection sa ngipin/gilagid)
	2. Patuloy na pagpalya ng puso o heart failure
	3. Patuloy na pagpalya ng atay
	4. pasimulang stroke
	5. atake sa puso sa loob ng 6 na buwan,
	6. “systemic or pulmonary inflammatory condition” (katulad ng “rheumatoid arthritis”, “systemic lupus erythematosus”,
	7. Kasalukuyan atake ng “chronic obstructive pulmonary disease”,
	8. Kasalukuyan atake ng hika,
	9. May “history” ng renal or ibang organ transplant
	10. “immunocompromised state”
3. Kung ikaw ay may anemia (hemoglobin value ay mas mababa 13.0 g/dl sa lalake; 12.0 g/dl sa babae)
4. Kung ikaw ay may kasalukuyang umuinom Moringa oleifera, fish oil o kahit anung vitamins o multivitamins sa loob ng 8 lingo ay hindi kasali sa pag-aaral.
5. Kung ikaw ay umiinom ng hormone tulad ng estrogen o progesterone.
6. Kung ikaw ay may hsCRP > 10mg/dl.
7. Kung ikaw ay pinagpaplanuhan na isailalaim sa dialysis.

Ikaw ay maaaring i-disqualify ng “author” o ng “screening doctor” sa mga kadahilanang hindi nakasaad sa listahan sa taas.

**3. Pamamaraan ng Pag-aaral:**

 Kung kayo ay papayag na sumali:

 a. Kayo ay tatanungin ng mga datos tulad ng inyong pangalan, edad, antas ng edukasyon, at kung saan kayo ay maaaring matawagan.

 b. Kayo ay sasailalim sa “physical examination” ng “screening doctor”; Ang inyong chart at mga resulta ng “laboratory” ay sususriin din.

 c. Ikaw ay kukuhaan ng dugo para alamin ang inyong “hsCRP at HgbA1c level”

 d. Ikaw ay aatasan na uminom ng malungay capsule, 1 capsule tatlong beses kada araw sa loob ng tatlong buwan. Ikaw ay inaasahan ipagpatuloy inumin ang inying mga “maintenance” na mga gamot.

 g. Ikaw ay hindi dapat manigarilyo, uminom ng alak o gumawa ng “endurance exercise” isang araw bago ang pagkuha ng dugo.

 f. Pagkalipas ng tatlong buwan, ikaw ay aatasan upang bumalik para sa mulaing pagkuha ng dugo at pagsususri ng inyong “hsCRP at Hgba1c level”

 **4. Mga posibleng panganib at di-inaasahang epekto**

 Ayon sa mga nakaraang pagsubok pangklinikal, wala pang naiulat na panganib o negatibong side-effect ang pag-inom ng malunggay capsule. Gayunpaman, mayroong posibilidad na makakaranas ka ng pagbilis ng pagdudumi na maaaring humantong sa diarrhea sa pag-inum ng Malunggay capsule. Ang mga epektong ito ay pansamantalang at karaniwan ay mawawala agad. Kung sa pagganap ng mga pagsasanay na nakatakda sa pagsusuri nito ay magbibigay ng anumang mga negatibong epekto sa iyo, ang mga pangunahing tagapagsuri ay pagaaralan ito at magbibigay sa inyo ng tulong upang malutas ito. Ang mga sumusunod ay maaaring maisama sa tulong na ito: Maaaring sagutin ng pangunahing tagapagsuri ang bayad na konsultasyon sa Out Patient Department o Emergency Room ng Ospital ng Maynila Medical Center lamang. Para sa konsultasyong out-patient at emergency room, ang pangunahing tagapag-suri ay hindi sasagot sa mga pangangailangang pangiksamen, pagagamot, o panterapeutika. Gayunpaman, ang pangunahing tagapagsuri ay maaaring bimbinin ang kompensasyon para sa mga kalagayang naisulat dito kung matiyakan niya na ang mga kaganapan na nagdulot ng pagospital o kamatayan ay hindi direktang may kinalaman sa mga pagsasanay na ipinapagawa sa pagsusuring ito. May mga kaganapan na hindi maisaalang-alang bilang sanhi ng mga pagsasanay na itinuturo sa pagsusuring ito. Ang mga kaganapan na kasama dito, ngunit hindi limitado lamang sa mga ito, ay mga aksidente na nagaganap sa panahon ng transportasyon papunta o mula sa lugar ng pagsusuri, mga kaganapan dulot ng sakunang natural tulad ng ngunit hindi limitado sa baha, lindol, o tsunamis, side effect at di kanais-nais na reaksyon sa iba pang mga paggagamot na hindi bahagi ng pagsusuring ito, o mga kaganapan na ginawa ng tao tulad ng mga nakawan, o pananakit. Kung ikaw ay lalahok sa pag-aaral na ito, sumasang-ayon ka na ang mga tagapagsuri, ang kanyang mga kawani, ang Ospital ng Maynila Medical Center, ang kanyang mga administrador, mga nars, mga doktor, mga mag-aaral at iba pang mga tauhan nito ay hindi maaaring managot sa mga epektong hindi kanais-nais na maaari mong maranasan.

**5. Benepisyo sa mga paglahok sa pag-aaral**

 Ang mga kalahok sa pag-aaral na ito ay maaaring makakuha ng mga benepisyo mula sa libreng pagpapakuha ng hsCRP at HgbA1c levels. Ang levels ng inyong CRP ay makakatulong sa inyong doktor sa aspeto ng pag-“predict” ng inyong “risk” sa atake sa puso o stroke sa utak. Samantalang ang pagkuha ng HgbA1c ay makakatulong upang malaman kung sapat na ang controlng inyong iniinom na gamot sa inyong sugar.

**6. Pagkapribado ng Impormasyon**

 Ang mga datos na inyong binigay sa amin katulad ng inyong pangalan, edad, contact number, o email address ay hindi ipapakita o ibibigay kanino man. Ito rin ay hindi babanggitin sa huling report na ilalabas ng pagaaral na ito. Sa paglagda sa katibayan ng pagpapahayag, kayo ay pumapayag na tawagan kayo ng may-akda, ng mga taong tumutulong sa kanya sa contact number na inyong binigay upang ipaalala o iabiso sa inyo ang mga susunod na hakbang kailangang ninyong gawin sa pagaaral na ito.

**7. Pagpapahayag sa pagsali sa pagaaral na ito**

 Kung kayo ay sumasang-ayon sa pagsali sa pag-aaral na ito. Maaari lamang isulat ang iyong pangalan sa blangko na nasa katibayan ng pagpapahayag at lagyan ng inyong lagda sa itaas ng inyong pangalan. Pakipirmahan lamang ang 2 kopya para maitago ninyo ang isang kopya. Maaari rin kayong tumanggi sa pagaaral na ito at hindi na ninyo kailangan lagdahan ang katibayan na iyon.

**8. Mga probisyon na magpatigil sa inyong paglahok sa pagaaral na ito**

 Ang inyong paglahok sa pagaaral na nito ay matitigil kapag hindi kayo makapupunta sa follow-up sa katapusan ng pag-aaral. Maaari rin kayong matanggal kung napatunayan na hindi totoo ang inyong mga sinasagot o mga datos na inyong binigay sa amin. Kung sakaling kayo ay matanggal mula sa pagaaral, ang mga benepisyo na maaari rin ninyong matanggap mula sa pagsali sa pagsusuri na ito ay hindi ibibigay sa inyo. Ang mga pangunahing imbestigador ng pagaaral na ito ay may karapatan na tanggalin o idisqualify ang kahit sinong kasapi sa pagsusuring ito dahil sa mga dahilan na hindi nabanggit dito.

**9. Pabuya**

Sa paglahok sa pagsusuring ito, ikaw ay sumasang-ayon na ipagtatanggol, at proprotektahan laban sa pinsala ang Ospital ng Maynila Medical Center, ang mga tagapangasiwa nito,mga doktor, at tauhan ng walang pinsala mula sa at laban sa anumang paghahabol, paghahabla, paglilitis o pagdedemanda, kabilang ang, nang walang limitasyon, aksyong legal o bayaring pangaccounting, na magmumula o nagresulta mula sa iyong paglahok sa pagsusuri na ito. Ang pangunahing tagapagsuri ay magbibigay ng abiso sa iyo ng anumang paghahabol, paghahabla, paglilitis o pagdedemanda at siya rin ay tutulong sa iyo, sa iyong sariling pananagutan, sa pagtatanggol ng anumang naturang paghahabol, paghahabla, paglilits o pagdedemanda. Ang pangunahing tagapagsuri ay may karapatan na akuin ang eksklusibong depensa at kontrol ng anumang bagay na sumasailalim sa mga pabuya sa ilalim ng seksyon na ito. Sa ganoong kaso, sumasang-ayon ka na ikaw ay makikipagtulungan sa anumang mga makatwirang kahilingan sa pagtatanggol sa pangunahing tagapagsuri ng mga naturang bagay na ito.

**10. Pagtatatuwa ng mga garantiya at Limitasyon ng Pananagutan**

Ang pangunahing tagapagsuri, ang kanyang mga kaakibat, at kanilang kaukulang mga opisyal, direktor, empleyado, ahente, mga tagapagtustos, o mga tagapaglisensya ay hindi gumagawa ng garantiya tungkol sa nilalaman ng mga materyales na ibibigay para sa pagsusuri, kabilang ngunit hindi limitado sa kanilang katumpakan, pagiging maaasahan, pagkakumpleto, pagiging maagap, o pagiging akma sa panahon o oras.

Wala sa alinman sa mga pangunahing tagapag-usig, ang kanyang mga kaakibat, at kanilang kaukulang mga opisyal, direktor, empleyado, ahente, mga tagapagtustos, o mga tagapaglisensya ang dapat managot para sa katotohanan, o pagkakumpleto ng anumang impormasyon na lumitis sa mga kalahok ng pagsusuri na ito para sa mga pagkakamali, kakulangan o para sa anumang pagkaantala o pagkagambala ng oras o impormasyon mula sa kahit anong dahilan. Ikaw ay sumasangayon na ang paggamit ng mga materyales na ibinigay at ang kanilang mga nilalaman ay sa iyong sariling peligro.

Ang pangunahing tagapagsuri, ang kanyang mga kaakibat, at kanilang kaukulang mga opisyal, direktor, empleyado, ahente, mga tagapagtustos, o mga tagapaglisensya ay nagbibigay ng mga serbisyo para sa iyo na matutunan, masanay, masukat, masubaybayan, at mangasiwaan ang mga ipinanukalang mga pagsasanay sa pagsusuring ito. Ang mga serbisyong ito ay hindi naglalaman o bumubuo, at hindi dapat na mapapakahulugang payo o opiniong medikal. Ang iyong paglahok sa pagsusuri, at ang iyong mga pakikipag-ugnayan sa mga pangunahing tagapagsuri, ang kanyang mga kaakibat, at kanilang mga kaukulang mga opisyal, direktor, empleyado, ahente, mga tagapagtustos, o mga tagapaglisensya ay hindi lumilikha ng isang relasyong pangdoktor at pasyente sa pagitan mo at ng pangunahing tagapagsuri, ang kanyang mga kaakibat, at kanilang kaukulang mga opisyal, direktor, empleyado, ahente ,mga supplier, o mga tagapaglisensya.

**11. Mga ipinagbabawal na aktibidad**

Sa paglahok sa pagsusuring ito, sumasangayon ka na hindi ka gagawa o sasali sa anumang mga gawaing ipinagbabawal katulad ng mga sumusunod:

a. Ibenta ang mga ipinamigay na libreng malungay capsules

b. Gamitin ang serbisyo para sa anumang mga komersyal na layunin o sa benepisyo ng sinumang ikatlong partido, kung ito ay walang pahintulot ng pangunahing tagapagsuri o sa kahit anong paraan na hindi pinahihintulutan ng aming mga tuntunin.

c. Magpanggap o magsinungaling tungkol sa pakikipagtulungan ninyo sa kahit sinumang tao o entidad

d. lumabag sa anumang nalalapat na batas o regulasyon

e. Hikayatin o paganahin ang sinuman na gawin ang anuman sa mga gawaing ipinagbabawal sa mga tuntunin na ito.

**12. Pagtatatuwa ng mga garantiya at Limitasyon ng Pananagutan**

Ang pangunahing tagapagsuri, ang kanyang mga kaakibat, at kanilang kaukulang mga opisyal, direktor, empleyado, ahente, mga tagapagtustos, o mga tagapaglisensya ay hindi gumagawa ng garantiya tungkol sa nilalaman ng mga materyales na ibibigay para sa pagsusuri, kabilang ngunit hindi limitado sa kanilang katumpakan, pagiging maaasahan, pagkakumpleto, pagiging maagap, o pagiging akma sa panahon o oras.

Wala sa alinman sa mga pangunahing tagapag-usig, ang kanyang mga kaakibat, at kanilang kaukulang mga opisyal, direktor, empleyado, ahente, mga tagapagtustos, o mga tagapaglisensya ang dapat managot para sa katotohanan, o pagkakumpleto ng anumang impormasyon na lumitis sa mga kalahok ng pagsusuri na ito para sa mga pagkakamali, kakulangan o para sa anumang pagkaantala o pagkagambala ng oras o impormasyon mula sa kahit anong dahilan. Ikaw ay sumasangayon na ang paggamit ng mga materyales na ibinigay at ang kanilang mga nilalaman ay sa iyong sariling peligro.

Ang pangunahing tagapagsuri, ang kanyang mga kaakibat, at kanilang kaukulang mga opisyal, direktor, empleyado, ahente, mga tagapagtustos, o mga tagapaglisensya ay nagbibigay ng mga serbisyo para sa iyo na matutunan, masanay, masukat, masubaybayan, at mangasiwaan ang mga ipinanukalang mga pagsasanay sa pagsusuring ito. Ang mga serbisyong ito ay hindi naglalaman o bumubuo, at hindi dapat na mapapakahulugang payo o opiniong medikal. Ang iyong paglahok sa pagsusuri, at ang iyong mga pakikipag-ugnayan sa mga pangunahing tagapagsuri, ang kanyang mga kaakibat, at kanilang mga kaukulang mga opisyal, direktor, empleyado, ahente, mga tagapagtustos, o mga tagapaglisensya ay hindi lumilikha ng isang relasyong pangdoktor at pasyente sa pagitan mo at ng pangunahing tagapagsuri, ang kanyang mga kaakibat, at kanilang kaukulang mga opisyal, direktor, empleyado, ahente ,mga supplier, o mga tagapaglisensya.

**13. Pagpopondo**

 Ang pondo na gagamitin sa pag-aaral na ito ay mula sa pangunahing tagapagsuri ng pag-aaral. Ang ibang pondo ay mula sa Philippine College of Physicians- Manila Chapter

**14. Pagkontak sa Pangunahing Tagapagsuri**

 Para sa iba pang katanungan, maaari niyo pong tawagan ang pangunahing tagapagsuri ng pag-aaral:

 Rainier Nery Mozo, M.D,

Contact No: 0932-8449951

email: rainiermozomd@yahoo.com

**15. Pag-apruba sa pag-aaral**

 Ang par-aaral na ito ay sinuri at sinang-ayunan ng Ospital ng Maynila Medical Center Ethics Committee. Kung may katanungan tungkol sa inyong karapatan o mayroon reklamo ukol sa pag-aaral na ito maaari nyong ipagbigay alam sa sumusunod.

**Name of OMMC Ethics Committee Chair:\_Dr. Carolino Paula Martin**

**Address:** Ospital ng Maynila Medical Center

Quirino Avenue, corner Roxas Boulevard, Malate Manila

**Tel:** (02) 524-6061

**Appendix B**

**TABLE OF INFORMATION FOR THE SUBJECT PARTICIPANT**

**1. Title of the Study**

“The Effects of Malunggay (*Moringa oleifera*) leaves capsule supplements on High Specificity C-Reactive Protein (hsCRP) and HgbA1c levels of Diabetic Patients in Ospital ng Maynila Medical Center Internal Medicine Department Diabetic Clinic: A Prospective Cohort Study”

Primary Author:

Rainier Nery Mozo, M.D, Contact No: 09328449951, email: rainiermozomd@yahoo.com

**2. Goal of the Study**

You are invited to participate in this study. Kindly read the information stated here. This study will be explained to you and you will be given the chance to ask questions as well. There are 2 copies of the consent form on the last page of this table. Please sign them both if you understand the provisions stated here and wish to participate in this study.

Diabetes Mellitus (DM) is a significant risk factor for cardiovascular disease and death. Despite recent advances in therapeutic strategies, DM complications are still one of the leading causes of morbidity and mortality worldwide. Among the DM risk factors (like hypertension, atherogenic dyslipidemia, insulin resistance, impaired fibrinolysis, inflammatory profile); definitely, inflammation is the most neglected one. Therefore, there is an urgent need for further development of novel anti-inflammatory therapy.

*Moringa oleifera* has been suggested to exert anti-inflammatory effects. *Moringa oleifera* leaves supplements may reduce cardiovascular mortality and morbidity in diabetic patient as reflected by reduced HsCRP at HgbA1c levels.

The objective of the study is to determine the effect of *Moringa oleifera* leaves capsule supplementation on the HsCRP and HgbA1c levels of Diabetic patients**.**

Collection of the data for this study will be conducted within one month. Anyone of at least 19 years to 65 years of age, can read and write in both the English language, and is diagnosed with Diabetes mellitus by screening doctor from the Diabetic Mellitus (DM) Clinic of Department of Internal Medicine and ICU of Ospital ng Maynila Medical Center. Subjects for the study will be the following:

1. Male or female participants aged between 19 and 65 years of age.

2. They must be diagnosed by the Internal Medicine resident or other physician as having Diabetes Mellitus using the following criteria stated by American Diabetes Association (ADA): Patient presents with 1 or more of the following:

* FPG more than or equal 126 mg/dl (7.0 mmol/L). Fasting is defined as no caloric intake for atleast 8. OR
* 2-h plasma glucose more than or equal to 200 mg.dl (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using glucose load containing the equivalent of 75g anhydrous glucose dissolved in water OR
* In pa patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose of more than or equal to 200 mg/dl (11.1 mmol/L)
1. Participants should be willing to have their blood extracted for hsCRP and Hgba1c measurement before and after 12 weeks supplementation of *M. oleifera*.
2. Participants have available treatment partner.
3. Participants should be staying in Metro Manila during the course of the trial, and must be easily contacted by phone.

You can be excluded in the study if have one of the following conditions:

1. Patients who are suspected to have psychiatric disorders, mentally challenged, or confirmed to be pregnant
2. Patients who are not medically stable or those confirmed to be afflicted with communicable or life threatening diseases including any of the following:
	1. ongoing infection (Pulmonary Tuberculosis, DM foot infections, cellulitis, pneumonia, urinary tract infections, ear infections, dental or gingivitis Infections),
	2. decompensated heart failure ( CHF III-IV),
	3. chronic liver disease in decompensated state,
	4. stroke in evolution,
	5. acute coronary syndrome within 6 months,
	6. systemic or pulmonary inflammatory condition (including rheumatoid arthritis, systemic lupus erythematosus),
	7. chronic obstructive pulmonary disease in exacerbation,
	8. bronchial asthma in exacerbation,
	9. history of renal or other organ transplant and/or
	10. immunocompromised state
3. Participants with anemia (hemoglobin value of less than 13.5 g/dl in males; 12.0 g/dl in females)
4. Participants with undergoing Moringa oleifera, fish oil or any vitamins or multivitamins supplementation within the past 8 weeks are excluded in the study.
5. Participants with the use of estrogen/progesterone hormone
6. Participants with plan or anticipated by their physicians to be initiated with renal replacement therapy (dialysis) during the study.

You can be disqualified by the trial organizers, their physicians or by physicians of the study due to compelling reasons which may not be listed here. The study is expected to be completed in 12 weeks time.

**3. Methods of the Study**

Should you wish to participate:

1. You will be asked to furnish us with a set of data like your name, age, and contact details as well as your level of education.
2. You will be undergoing physical examination by the screening physicians. Your chart and results of laboratory will be reviewed.
3. Blood will be extracted for hsCRP and Hgba1c determination.
4. You will be asked to take Malunggay capsule, 1 capsule 3 times a day for 1 month. You will be asked to continue taking your maintenance medications.
5. You will be asked not to smoke, take any alcoholic beverages, and not do any endurance exercise a day prior to the exctractions.
6. After 3 months, you will be asked to have your follow-up blood extraction for another HsCRP at HgbA1c measurements.
7. This study requires no less than 45 respondents.

**4. Possible Side Effects and expected discomforts**

As seen in previous clinical trials, there have been no reported dangers or negative side-effects in taking Malunggay capsule. The method of this study does not require the introduction of any medicine or chemicals that might give negative effects, thus the possibility of having side effects or undesireable effects are remote. However, there is a possibility that you will experience some discomfort such as increased bowel movements which may lead to diarrhea. These effects are temporary and will usually disappear. If performing the exercises stipulated in the techniques will give any negative effects on you, the main investigator will study and will give assistance to help you resolve it. This assistance may include following: the main investigator may shoulder your consultation fees at the Out Patient Department or the Emergency Room Department of the Ospital ng Maynila Medical Center only. For out-patient and emergency room consults, the main investigator will not shoulder diagnostics, medicinal, or therapeutic interventional costs. However, the principal investigator may withhold compensation for the above given circumstances if he determines that the events which may have lead to the condition necessitating hospitalization or results in death were not directly related to the trial’s interventions. Events which are not to be considered as due to the treatment include but not limited to accidents occurring during transport to or from the trial site, events caused by natural disasters such as but not limited to floods, earthquakes, or tsunamis, side effects and adverse reactions to other treatments such as but not limited to medications not part of the treatment trial, or man-made events such as robbery, or physical assault. In participating in the study you agree that the authors, his/her research assistants, Ospital ng Maynila Medical Center, its administrators, nurses, doctors, students and other personnel cannot be held liable in the unlikely occurrence of an undesirable effect.

**5. Benefits of participating in the study**

The participants of this study may gain the benefits of taking free hsCRP levels. hsCRP levels may help your physician in estimating your cardiovascular risk.

Beyond this, you will not be compensated for other expenses that you may have acquired during the course of the trial, including expenses for food and drinks, transporations fares, and/or purchase of necessary equipment to participate in the trial.

**6. Confidential Information**

 The personal data that you’ve provided in this study like your name, age, or contact number, or email address will not be given out to anybody else. These will not be indicated or presented in the final reports done on this study. This confidentiality is subject to the laws of the Republic of the Philippines.

**7. Consent to participate in this study**

 Should you agree to participate in this study, kindly write your name and signature on the blank space provided on the consent form. Please fill up 2 copies of the consent form so you can keep one copy for yourself. You also have the option to refuse to participate in this study, for which you do not need to fill-up the consent form.

**8. Refusing to participate or withdrawing from the study**

 You are not obliged to participate in this trial, and you are free to refuse to participate in it. You are also free to withdraw from the study at anytime. You will not be penalized for refusing to participate or for withdrawing from the study.

**9. Provisions to remove you in participating in this study**

 Factor which can be grounds for removal or disqualification from the trial include failure to appear during follow up. Giving fraudulent data or answers will likewise result to your removal as a participant of the study. Once removed from the study, your entitlement to a stipend will also be forfeited. The main investigator reserves the right to disqualify you or remove you from the study for other reasons not mentioned here.

**10. Indemnity**

 In participating in the study, you agree to defend, indemnify, and hold the Ospital ng Maynila Medical Center, its administration, doctors, and staff harmless from and against any claims, actions, or demands, including, without limitation, reasonable legal and accounting fees, arising or resulting from your participation in this trial, and/or the use of the therapies, instruction, instruments, or facilities used in the trial. The main investigator will provide notice to you of any such claim, suit, or proceeding and shall assist you, at your expense, in defending any such claim, suit or proceeding. The main investigator reserves the right to assume the exclusive defense and control of any matter which is subject to indemnation under this section. In such case, you agree to cooperate with any reasonable requests assisting the main investigator’s defense of such matter.

**11. Prohibited activities**

 In participating in the trial, you agree not to engage in any of the following prohibited activities:

1. Selling of the provided malunggay capsule
2. Use the service for any commercial purpose or the benefit of any third party, except otherwise explicitly permitted for you by the main investigator or in any means not permitted by our terms.
3. Impersonate or misrepresent your affiliation with any person or entity
4. Violate any applicable law or regulation
5. Encourage or enable any other individual to do any of the activities prohibited in these terms.

**12. Disclaimer of Warranty and Limitation of Liability**

 The main investigator, his affiliates, and their respective officers, directors, employees, agents, suppliers, or licensors, make no warranties or representations about the content of materials provided for during the trial, including but not limited to their accuracy, reliability, completeness, timeliness, or reliability.

 Neither the main investigator, his affiliates, and their respective officers, directors, employees, agents, suppliers, or licensors shall be subject to liability for truth, or completeness of any information conveyed to participants of this trial for errors, mistakes, or omissions therein or for any delays or interruptions of the data or information stream from whatever cause. You agree that the use of the materials provided and their content is at your own risk.

 The main investigator, his affiliates, and their respective officers, directors, employees, agents, suppliers, or licensors provides the services for you to learn, practice, measure, track, and manage the proposed exercises in the trial. These services do not contain or constitute, and should not be interpreted as medical advice or opinion. Your participation in the trial, and your interaction with the main investigator, his affiliates, and their respective officers, directors, employees, agents, suppliers, or licensors does not create a doctor-patient relationship between you and the main investigator, his affiliates, and their respective officers, directors, employees, agents, suppliers, or licensors.

**13. Funding**

 Fund for this study will be provided by the primary author. Some part of the budget will be coming from the research grant given by the Philippine College of Physicians-Manila Chapter.

**14. Contacting the Primary Investigator**

 For further information, or in case of study-related injuries, you may contact the primary investigator:

 Rainier N. Mozo, M.D,

Contact No: 0932-8449951

email: rainiermozomd@yahoo.com

**15. Approval of the study**

 The study has been reviewed and approved by the Ospital ng Maynila Medical Center Ethics Committee. They may be reached if you have questions on your rights in participating in this trial, grievances and complaints at the contact information below:

 **Name of OMMC Ethics Committee Chair: Dr. Carolina Paula Martin**

**Address:** Ospital ng Maynila Medical Center

Quirino Avenue, corner Roxas Boulevard, Malate Manila

**Tel:** (02) 524-6061

**Appendix C**

**CONSENT FORM / *KATIBAYAN NG PAGHINTULOT***

Dear Doctor Mozo,

*Mahal kong Doktor Mozo,*

 The study entitled “The Effects of Malunggay (*Moringa oleifera*) leaves capsule supplements on High Specificity C-Reactive Protein (hsCRP) and HgbA1c levels of Diabetic Patients in Ospital ng Maynila Medical Center Internal Medicine Department Diabetic Clinic: A Prospective Cohort Study” has been explained to me verbally and/or I have read through the study’s information and consent form. My questions have been answered and I have agreed to participate in the study, agreeing to the terms and regulations of the study.

 *Ang pagaaral na pinamagataang “*The Effects of Malunggay (*Moringa oleifera*) leaves capsule supplements on High Specificity C-Reactive Protein (hsCRP) and HgbA1c levels of Diabetic Patients in Ospital ng Maynila Medical Center Internal Medicine Department Diabetic Clinic: A Prospective Cohort Study*” ay naipaliwanag sa akin at/o binasa ko ang talaan ng impormasyon nito. Ang aking mga tanong ay nasagot na rin at pumapayag akong sumali sa pagaaral na ito, pumapayag ako sa mga tuntunin at regulasyon ng pagsusuring ito.*

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Participant*/Kalahok* Witness/*Saksi*

Signature above printed name Signature above printed name

Lagda sa ibabaw ng pangalan Lagda sa ibabaw ng pangalan

 Date of Signing/*Petsa ng Paglagda*:\_\_\_\_\_\_\_\_\_\_\_\_\_

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Researcher/*Tagapagsuri*

Signature above printed name

Lagda sa ibabaw ng pangalan

Pls provide us a photocopy of a government issued ID for reference.

*Maaari lang pong magbigay sa amin ng isang kopya ng identification card na binigay ng gobyerno sa amin.*

(Note: If this Consent form is used as a source document, it must signed and dated by study personnel.)

Consent form version 1.0

**Appendix D**

Subject number:

**Subject Information Sheet**

Initials:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Age: \_\_\_\_ Sex:\_\_\_\_ Tel/Cellphone Number(s):\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Address: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Email Address (optional): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Treatment Partner:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Tel/Cellphone Number(s):\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Educational Level Attained (please check one):

\_\_\_\_\_\_ None

\_\_\_\_\_\_ Elementary

 Grade:\_\_\_\_\_

\_\_\_\_\_\_ High School

 Year Level: \_\_\_\_\_

\_\_\_\_\_\_ Vocational (TESDA)

 Course: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

\_\_\_\_\_\_ College

 Course: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

 Level Finished: \_\_\_\_\_\_\_\_

\_\_\_\_\_\_ Post-Graduate (Masteral or Doctorate)

 Degree Attained: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

I attest that I am literate in English / Ako ay nakakaintindi at nakakasulat sa wikang Ingles:

\_\_\_\_\_\_\_ Yes / Oo \_\_\_\_\_\_\_ No / Hindi

|  |  |
| --- | --- |
| Confirmed complete by: (Signature over printed name) | Confirmed Accurate by: (Signature over printed name) |
| Date: | Date: |

(Note: If this SIS is used as a source document, it must signed and dated by study personnel.)

Subject Information sheet version 1.0

**Appendix E**

**The Effects of Malunggay (*Moringa oleifera*) leaves capsule supplements on High Specificity C-Reactive Protein (hsCRP), and HgbA1c levels of Diabetic Patients in Ospital ng Maynila Medical Center Internal Medicine Department Diabetic Clinic: A Prospective Cohort Study**

**INCLUSION / EXCLUSION CRITERIA**

|  |
| --- |
| Subject ID: |
| Visit Date (dd/mm/yyyy): |

|  |
| --- |
| INCLUSION CRITERIA |
| Participant must: | YES | NO |
| 1. Age between 19 and 65 years of age |  |  |
| 2. Will stay in Metro Manila during the course of the trial |  |  |
| 3. Can be reached by phone (may be landline or mobile) |  |  |
| 4. Literate in English with at least grade 1 proficiency |  |  |
| 5. Diagnosed as: Diabetes Mellitus (As per ADA Guidelines) |  |  |
| 6. Medically stable |  |  |
| 6. Willing to have their blood extracted for hsCRP and Hgba1c measurement before and after 12 weeks of M. oleifera supplementation |  |  |
| 7. Willing to be followed-up at OMMC or at area designated by the main investigator |  |  |
| 8. Willing to sign Consent form |  |  |
| 9. Willing to commit to the trial’s schedule for pre and post supplementation HsCRP measurment |  |  |
| 10. Have available treatment partner |  |  |
| 11. Will stay in Metro Manila for the whole study period |  |  |
| **NOTE:** All inclusion criteria must be answered **YES** to be included in the study |

|  |
| --- |
| EXCLUSION CRITERIA |
| Participant must not: | YES | NO |
| 1. Diagnosed or suspected to have psychiatric disorders, mentally challenged. |  |  |
| 2. Pregnant at time of subject screening |  |  |
| 3. Have a disability such as blindness, hearing impairment, inability to use either arms, have difficulty in ambulating or balance, muscular dystrophy, or any other condition which may restrict their participation in either treatment arms |  |  |
| 4. Afflicted with communicable or life threatening diseases or any disease associated with  state of inflammation* 1. ongoing infection (Pulmonary Tuberculosis, DM foot, cellulitis, pneumonia, ear infections, gingivitis or dental infections)
	2. decompensated heart failure ( CHF III-IV)
	3. chronic liver disease in decompensated state
	4. stroke in evolution,
	5. acute coronary syndrome within 6 months,
	6. systemic or pulmonary inflammatory condition

 (including rheumatoid arthritis, systemic lupus erythematosus), * 1. chronic obstructive pulmonary disease in exacerbation,
	2. bronchial asthma in exacerbation,
	3. history of renal or other organ transplant and/or
	4. immunocompromised state
 |  |  |
| 5. Presence of anemia (hemoglobin value of less than 13.5 g/dl in males; 12.0 g/dl in females) |  |  |
| 6. Undergoing Moringa oleifera, fish oil or any vitamins or multivitamins supplementation within the past 8 weeks |  |  |
| 7. Use of estrogen/progesterone hormone |  |  |
| 8. With plan or anticipated by their physicians to be initiated with renal replacement therapy (dialysis) during the study. |  |  |
| 9. hs CRP equal or more than 10 mg/dl |  |  |
| 10. Subjects who pregnant |  |  |
| 11. Subjects with known or suspected allergy to M. oleifera or any other component to the drug preparation. |  |  |
| **NOTE:** All exclusion criteria must be answered **NO** to be included in the study |

Did the participant meet the eligibility requirement for this study? \_\_\_\_\_\_\_ YES \_\_\_\_\_\_ NO

|  |  |
| --- | --- |
| Completed by: (Signature over printed name) | Confirmed Accurate by: (Signature over printed name) |
| Date: | Date: |

(Note: If this Inclusion/Exclusion Criteria is used as a source document, it must be signed and dated by study personnel.)

Inclusion/Exclusion Criteria version 1.0

**Appendix F**

**The Effects of Malunggay (*Moringa oleifera*) leaves capsule supplements on High Specificity C-Reactive Protein (hsCRP) and HgbA1c levels of Diabetic Patients in Ospital ng Maynila Medical Center Internal Medicine Department Diabetic Clinic: A Prospective Cohort Study**

 **MEDICAL DATA SHEET**

|  |  |  |
| --- | --- | --- |
| SUBJECT CODE: | Assesment for (Pls. Check one) \_\_\_Pre-treatment \_\_\_Posttreatment | DATE ACCOMPLISHED: |
| Date of Birth (dd/mm/yyyy): | Gender:  \_\_M \_\_F | Race: \_\_\_ Filipino \_\_\_ Other:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
| NAME of Treatment Partner: | Relationship of Treatment Partner | Contact Number: |

**I. Eligibility**

Does the subject meet all of the inclusion eligibility criteria? \_\_\_ Yes \_\_\_No

 If no, specify the unmet inclusion criteria (by number): \_\_\_\_\_\_\_\_\_\_

 Does the subject meet any of the exclusion criteria? \_\_\_ Yes \_\_\_No

 If yes, specify the met exclusion criteria (by number): \_\_\_\_\_\_\_\_\_\_\_

**II. History**

**Diagnosis of DM: Year \_\_\_\_**

**List of Current Medications:**

**\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Compliance: (Y/N) Remarks: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Intake of any multi/vitamins or supplement for the past 8 weeks: (Y/N) pls specify: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Allergy to any food/drugs: (Y/N) pls. specify: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Previous Admissions: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Smoker: (Y/N) how many pack years: \_\_\_\_\_\_\_\_\_\_**

**Alcoholic Beverage Drinker: (Y/N) Dosage & Frequency: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Occupation: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

|  |  |  |
| --- | --- | --- |
| Subjective Complaints at the time of Examination:(you can encircle 1 or more) | Yes | No |
| Fever, Chills, Headache, Dizziness, Nausea, Vomiting |  |  |
| Cough, Colds, Difficulty of Breathing |  |  |
| Chest pain, Palpitations, Paroxysmal Nocturnal Dyspnea, Orthopnea |  |  |
| Easy fatigability |  |  |
| Changes in bowel movement, Melena, Hematochezia, |  |  |
| Dysuria, Hematuria, Increase in frequency |  |  |
| Increase/decrease in urine output |  |  |
| Edema |  |  |
| Others: |  |  |

**III. Physical Examination**

Vital Signs at enrollment: BP \_\_\_\_\_ RR: \_\_\_\_\_ PR:\_\_\_\_\_ T: \_\_\_\_\_

**Weight in kg: \_\_\_\_\_\_\_\_\_\_\_\_\_\_**

|  |  |
| --- | --- |
| EXAMINATION | FINDINGS |
| General |  |
| HEENT |  |
| CHEST AND LUNGS |  |
| CARDIOVASCULAR |  |
| GASTRO |  |
| GUT |  |
| EXTREMITIES |  |
| NEURO |  |

**IV. Diagnostic Studies:**

|  |  |  |  |
| --- | --- | --- | --- |
| **Type of study** | **Date** | **Result** | **Interpretation** |
| **Complete Blood Count** |  |  |  |
| **Serum Creatinine** |  |  |  |
| **Serum Na** |  |  |  |
| **Serum K** |  |  |  |
| **Serum Ca** |  |  |  |
| **Total Cholesterol** |  |  |  |
| **Triglyceride** |  |  |  |
| **LDL** |  |  |  |
| **HDL** |  |  |  |
| **LDL12L-ECG** |  |  |  |
| **Chest Xray** |  |  |  |
| **Urinalysis** |  |  |  |
| **2D-echo** |  |  |  |

**V. Co-Morbidities**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Condition | Diagnosed date (dd/mm/yyyy) | Medication (Generic + Brand Name + dosage and route) | Medication Start Date(dd/mm/yyyy) | Medication Stop Date(dd/mm/yyyy) | Status(Stable, Currently in Exacerbation, etc.) |
|  |  |  |  |  |  |
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**VI. HsCRP DETERMINATION**

|  |  |  |
| --- | --- | --- |
| **TIMING** | **Date of Extraction** | **Resullt** |
| **Pre-supplementation** |  |  |
| **Post-supplementation** |  |  |

**VII. HgbA1c DETERMINATION**

|  |  |  |
| --- | --- | --- |
| **TIMING** | **Date of Extraction** | **Resullt** |
| **Pre-supplementation** |  |  |
| **Post-supplementation** |  |  |

**VIII. CLINICAL OUTCOME**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Date** | **Assessment** | **Outcome/Disposition** |
| **ER Consult** |  |  |  |
| **OPD Consult** |  |  |  |
| **Hospitalization** |  |  |  |

|  |  |
| --- | --- |
| Completed by: (Signature over printed name) | Confirmed Accurate by: (Signature over printed name) |
| Date: | Date: |

(Note: If this Medical Data Sheet is used as a source document, it must be signed and dated by study personnel.)

Medical Data Sheet version 1.0