Efficacy of ASIMOMMY® Compared to Domperidone and Placebo in Increasing Breastfeeding: Randomized Single-Blind Controlled Trial in Indonesia

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1. LIST OF ABBREVIATIONS
   GCP: *Good Clinical Practice*
   DSMB: *Data Subject Monitoring Board*
   ASI: Air Susu Ibu
   RCT: *Randomized Control Trial*
   CTP: *Computed Tomography Perfusion*

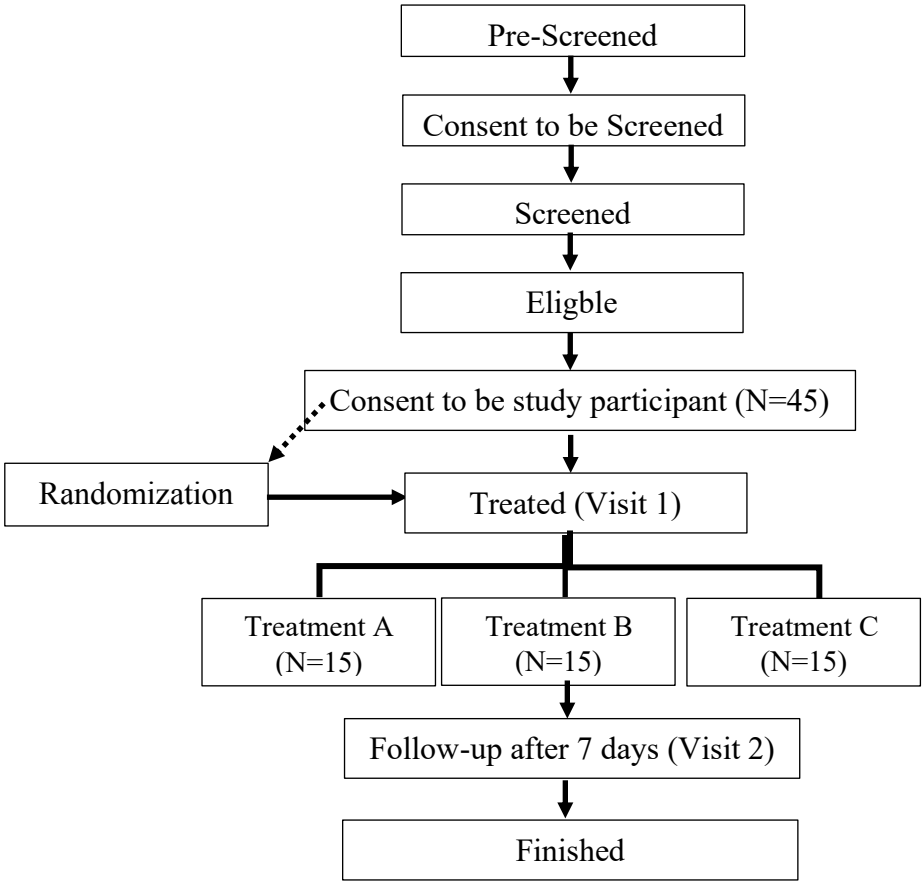
2. STUDY SYNOPSIS AND SCHEMA
   Study Synopsis

Title	Efficacy of ASIMOMMY® Compared to Domperidone and Placebo in Increasing Breastfeeding: Randomized Single-Blind Controlled Trial in Indonesia.
Purpose	Assessing the efficacy of ASIMOMMY® in increasing breast milk production in postpartum mothers.
Hypothesis	ASI MOMMY® increases milk production in postpartum mothers.
Methodology	
Study Design	*Randomized Controll Trial* (RCT).
Study Time	October 2022 until March 2022.
Study Location	Tegalrejo and Jetis Primary Health Care, Yogyakarta.
Study Product	
Treatment group	ASI MOMMY®.
Control group:	Domperidone and placebo.
Subject Criteria:	
Inclusion Criteria:	• Mothers 20-35 years old. • Gestational age at delivery 37-40 weeks. • Vaginal delivery. • Normal body mass index (BMI 18.5-24.9 kg/m^2). • Not taking drugs or breast milk enhancement supplements. • Healthy mother's condition with normal nipples (protruding). • Healthy baby condition with good suction reflex. • The baby consumes only breast milk.
Exclusion criteria:	• Allergy to ASI MOMMY® and Domperidon. • The mother is taking medications that affect the effects of domperidone (such as antacids, cimetidine, ranitidine, famotidine and nizatidine) or medications that interact with domperidone (such as haloperidol, lithium). • The mother is in a state of illness requiring hospitalization. • Mother has HIV AIDS, heart problems, mastitis, and had undergone breast surgery. • Underweight, overweight and obese mothers. • Giving birth to twins. • The baby has a congenital defect that affects the suctioning process of breast milk

	• Infants and mothers who did not participate in the treatment until completion (day 7 of the intervention).
Sampel size	The sample size was 15 subjects per group. The total sample size was 45 subjects.
Subject Allocation Method	Randomization with a randomization list.
Intervention	• Beginning of the study is on day 3 postpartum, the initial baby weight was weighed before the start of the intervention. • The weighing was conducted at Tegalrejo and Jetis Primary Health Center, at 08.00-10.00 WIB using Onemed OD-231 digital baby scales with an accuracy of 0.01 kg. When weighing the baby did not wear clothes or pampers. • Body weight weighing was carried out at Tegalrejo and Jetis Primary Health Center, at 08.00-10.00 WIB using Onemed OD-231 digital baby scales with an accuracy of 0.01 kg. When weighing babies do not wear clothes or pampers. • Intervention starts on the 3rd day postpartum until the next 7 days (10th day postpartum) with drug administration. • The intervention provided will be single-blind, the packaging will be similar, and neither the research assistant nor the subject will know the type of intervention provided. Administration of domperidone in capsule preparation at a dose of 10 mg orally taken every 8 hours, 3 times a day, for 7 days, at 06.00, 14.00, and 22.00 WIB. ASIMOMMY® and placebo in capsule preparation were taken once a day, at night, as much as 2 capsules, for 7 days. Each subject will get all capsules on the first day to be taken for 7 days. • Evaluation of the baby's weight was done by re-weighing the baby's weight on the 7th day of the intervention. Then the baby's weight gain was assessed, which was obtained from the difference between the baby's weight on day 7 of the intervention and the baby's weight on day 0 (before the intervention).
Duration of intervention	7 days.
Study Outcomes	Breast milk production was measured by assessing the infant's weight gain, which was obtained from the difference between the infant's weight on day 7 of the intervention and the infant's weight on day 0 (before the intervention).
Statistical Analysis	Statistical data analysis in this study used the SPSS version 24.0 program. Data were tested for normality first to determine the statistical analysis test used next. Research results with categorical data (nominal and ordinal) are displayed in the form of number/frequency and percentage of each group. Numerical data that is normally distributed (parametric) will be displayed in the mean and standard deviation, while if the data is not normally distributed (non-parametric) it is displayed with the median, minimum and maximum values.

	Chi Square test was used for variables with categorical data (nominal and ordinal). The bivariate analysis test used for variables with numerical data (parametric) is One Way Anova with Post Hoc Bonferroni, while for non-parametric is Kruskall Walis with Post Hoc Mann Whitney. The analysis test for external variables with parametric data and dependent variables was carried out with the Pearson correlation test, while for non-parametric data it was carried out with the Spearman correlation test.

Synopsis or Schema:



3. STUDY FLOW CHART OR TIME AND EVENT TABLE

Visit	Screening/ Baseline	Treatment/ Day 0	Day 7	Unscheduled Visit
Visit Window	-14 days	-	+0 –14 days	-
Informed Consent	✓			

Assign subject ID	✓			
Medical History	✓			
Inclusion/ Exclusion Criteria	✓			
Physical Exam (incl. temp, BP, BW)	✓			
Randomization	✓			
Treatment		✓	✓	
Adverse event				

4. INTRODUCTION
    a. BACKGROUND

Breast milk is the first and best source of nutrition for babies that is natural. Breast milk contains a variety of nutrients needed in the growth and development process of the baby. Breast milk also plays a role in enhancing sensory and cognitive development, and protects infants against infectious diseases.

The World Health Organization (WHO) recommends exclusive breastfeeding for the first six months of infancy to achieve optimal growth and development (Kramer and Kakuma, 2012). Exclusive breastfeeding has been shown to reduce infant mortality from common diseases such as diarrhea and pneumonia. In addition, exclusive breastfeeding can help accelerate healing in sick infants (Kramer et al., 2001). Breastfeeding also affects maternal health and well-being, such as reducing the risk of ovarian cancer and breast cancer, and increasing family and national resources.

Various attempts have been done since ancient times to deal with the problem of low breastmilk production in breastfeeding mothers. Pharmacological and non-pharmacological interventions is given to increase breastmilk production. Prescribing drugs that increase breastmilk supply, otherwise known as galactagogues, needs to be considered since breastmilk is important for a baby's health. A modern drug that is indicated as a galactogogue among others is domperidone and metoclopramide. Domperidone is a dopamine D2 receptor antagonist. Metoclopramide falls under the same drug class as domperidone that works as a dopamine D2 receptor antagonist. However, in terms of its traits, domperidone is less permeable than metoclopramide, less soluble in water, and has a higher molecular weight, which in turn causes less extrapyramidal effects in comparison to metoclopramide. By looking at the traits and characteristics, domperidone is more recommended thatn metoclopramide[3].

Several traditional herbs have been used and is well known since a long time ago by Indonesian people to increase the production of breastmilk, such as Katuk leaves (*Sauropus*

androgynous Folium), Fenugreek (*Trigonella foenum-graceum*), and Moringa leaves (*Moringa oleifera Folium)*. These plants have been scientifically proven through preclinical and even clinical research. However, not many have been further developed as phytopharmaceuticals that can be used in formal health services.

In previous research, ASI MOMMY® capsules have been successfully produced in accordance to the traditional method of making good herbal drugs, with each capsule containing extracts of Katuk leaf (300 mg), Fenugreek (150 mg), and Moringa leaf (50 mg). This formulation has gone through pharmacodynamic activity test, and acute and subactute toxicity test. Research has shown that ASI MOMMY® is works actively as a galactogogue and is not toxic, therefore it is safe to be given to humans (unpublished)[4],

No research has been done to test the benefits of ASI MOMMY® in increasinng breastmilk production. Therefore, this research is a clinical trial that intends to see the benefits of ASI MOMMY® for increasing breastmilk production in postpartum women. This research is a part of the previous main research that is still ongoing to this day which aims to develop the formulation of ASI MOMMY® as a phytopharmaceutical.

5. PURPOSE

The aim of this research is to study the benefits of ASI MOMMY® for increasing production of breastmilk in postpartum women.

6. BENEFIT

Benefits of conducting this research are as follows:

a. Theoretical Benefit

This research is hoped to be beneficial for becoming the basis of research and development in knowledge regarding breastmilk enhancing drugs for postpartum women.

b. Academic Benefit (Scientific)

This research is hoped to give contribution to the field of Pharmacology and Medicine, for studying the benefits of ASI MOMMY® traditional medicine formulation in increasing the priduction of breastmilk in postpartum women by looking at the increase in babies' body weight. The data obtained is hoped to provide the basic data for developing future research studies, because there is still a lack of research about phytopharmaceuticals concerning breastmilk in Indonesia.

c. Health Services

Data collected from this research will help citizens in obtaining herbal preparations that is safe and effective, and backed up by scientific evidence. Aside from that, it will also help the government in improving programs concerning exclusively breastfeeding women.

7. INFORMATIONAL RELATED TO THE THERAPHY

ASIMOMMY® is one product produced by PT Swayasa Perkasa Yogyakarta Indonesia which traditionally can increase the production of breastmilk. Instructions for product storage, ingredients and benefits of ASIMOMMY® are enclosed in the leaflet.

ASIMOMMY® contains several different natural components such as *Sauropi folium* extract (Katuk leaf), *Foenigraeci semen* extract (Fenugreek), and *Moringae folium* extract (Moringa leaf). Components in ASIMOMMY® ingredients is beneficial in enhancing breastmilk because it is rich in nutrition that is useful in the growth and development of babies.

The recommended direction for storage is to keep it in a place with temperature below 30 degrees Celsius, in a dry place away from sunlight exposure.

8. STUDY DESIGN

a. Overview of The Study Design

This research is a pilot study, single blind, randomized controlled trial. Subjects are allocated to three groups with a randomized list. The three treatment groups are the intervention group, positive control group, and negative control group. The intervention group is the group of patients that receive ASI MOMMY®, the positive control group are patients that receive domperidone, and the negative control group is the placebo group.

b. Duration of The Study and Visit Schedule

In the beginning of this reasearch, on the third day postpartum, the babies' weights are measured before starting the intervention. There are 3 treatment groups, a group that is given domperidone, ASI MOMMY®, and placebo. The information about which drug intervention given is hidden, where both the researcher and subjects do not know which type of treatment they are receiving. Domperidone is given in the form of tablet with a dosage of 10 mg orally, taken every 8 hours, three times a day at 06.00, 14.00, and 22.00 West Indonesia time for a duration of 7 days. ASI MOMMY® and placebo capsules is taken once a day at nighttime, as much as 2 capsules for a duration of 7 days. The capsule is given to the subjects that have been randomised. All subjects will receive all the drugs in the first day to be taken for the next 7 days. The drug given is not known to the researcher nor the subject. Aside from that, the research asistant and family of the subjects helps monitor the subjects regarding the regularity and adherence of taking the drugs.

9. STUDY POPULATION

a. Subject Recruitment

Data collection is done by healthcare providers on duty. Data collection is conducted starting from July 2022 until December 2022 by finding information about mothers in labor from Jestis and Tegalrejo public health centers. Women in

puerperium who meet the inclusion and exclusion criteria are gathered in the research until the number of samples needed is fulfilled.

The researcher explains the research intent, method, and procedure that will be done to the mother. Then the mother is allowed to sign the informed consent form if they agree to become a research subject. The research subjects are given lactation counseling. Next, the research subjects are randomized by the researcher using the random number table with each group containing 15 subjects. The researcher will allocate each group with one type of treatment, that is drug A, drug B, and drug C, then randomization is conducted. The list of randomizations is kept by the researcher.

b. Populasi

The subject population in this research are postpartum women from Tegalrejo Public Health Center and Jetis Public Health Center in Yogyakarta who plan to breastfeed their baby.

c. Inclusion Criteria
   a. Gestational age 37-40 weeks at labor
   b. Giving birth vaginally
   c. Normal body mass index (BMI 18.5-24.9 kg/m^2)
   d. Does not consume drugs or supplements to enhance breastmilk
   e. Healthy women with normal nipple condition (protrudes)
   f. Condition of baby is health with good suction reflex
   g. Baby currently only consumes breastmilk

d. Exclusion Criteria
   a. Allergy towards ASI MOMMY® and Domperidone
   b. Women who consumes drugs that influences the effects of domperidone (such as antacids, cimetidine, ranitidine, famotidine, and nizatidine) or drugs that interacts with domperidone (such as haloperidol, lithium).
   c. Women who are in sick condition and needs in-hospital treatment
   d. Women with HIV AIDS, heart problems, mastitis, and a history of breast surgery
   e. Underweight, overweight, and obese women
   f. Twin pregnancies
   g. Babies born with a congenital disease that affects the breastfeeding process
   h. Babies and mothers who do not follow the regimen from start to finish (seventh day of intervention)

e. Number of CTP Sites

Site 1 in this research is Jetis Public Health Center Yogyakarta with its address in Pengeran Diponegoro street number 91, Bunijo, Jetis district, Special Region of Yogyakarta 55231. The telephone number that can be contacted is (0274) 554801.

Site 2 in this research is Tegalrejo Public Health Center Yogyakarta with its address in Magelang street number 180, Karangwaru, Tegalrejo district, Yogyakarta city 55242. The telephone number that can be contacted is (0274) 554801.

f. CTP Characteristics

Public Health Centers serves many aspects of basic health in the community, one of which is maternal and child health services.

g. Rationale for CTP Selection

Jetis and Tegalrejo are public health centers that provides this service and have a delivery room with adequate human resource and equipment.

10. CLINICAL TRIAL PROCEDURE

a. Recruitment and Enrollment

The research team will fill the recuiter information log sheet. All subject candidates will receive starting information and disclose their willingness to participate in the clinical trial and consent to give information about their phone number and home address.

b. Recruitment Plan

Research subject candidates are recruited untul the amount of subjects fullfill the minimal sample amount that has been determined by the research team.

c. Initial Subject Screening

During initial screening the screening form will be filled, the researcher will fill the screening log, and if the subject candidate fullfills the inclusion and exclusion criteria of the research, they will be given a subject ID number by the research team.

d. Informed Consent Prosedure

Research subjects will be given starting information and be given the opportunity to ask questions if they still have questions regarding the research. After it is made sure that the research subjects have understood and recerived information about the research, the doctor or midwife on site will ask for the subject's signature for willingness to participate in every step of the research.

e. Baseline Assessment

This study includes interviews related to the demographic data of the subjects.

f. Randomization

Randomization using random numbers that is obtained from the random numbers table. The randomized list is placed inside a non-transparent, sealed envelope and is given serial numbers according to the number of subjects. The envelopes are held by one of the researchers and kept in the Center. Every subject that fullfills the criteria to participate in the research will be reported to the Center and Research Site, and an envelope is taken according to the serial numbers.

g. Treatment

i. Subject Discontinuation Criteria

In this research, the criteria for sample drop out includes subjects/babies who are sick and cannot continue participating in the research, babies who drink baby formula during the intervention, and subjects who consecutively skips consuming the capsules.

Termination of the intervention is done if the subject experiences side effects or serious adverse effects and will be examined by the research doctor for further observation and will receive treatment according to the research flow and placed in the intervention termination form.

ii. Treatment Discontinuation

Drug administration will end when the patient has completed the research process or the subject is placed under the drop out criteria.

iii. Replacement of Subject

Replacement of research subject is done if the number of subjects that is needed in the research does not fulfill the minimum amount due to drop out or termination of intervention.

iv. Follow-up of Withdrawn Subject

Subjects who withdraw due to heavy allergic reactions will receive monitoring by the research doctor and if the subject withdraws due to other dropout factors then the subject is required to give the product back to the research team.

h. Follow Up

Follow up of research subjects will be done by research assistants by giving periodical reminders of when to take the drug through WhatsApp broadcasting that is given to the research assistants by the subjects.

i. Blinding

i. Type(s) of Blinding

The type of blinding done is single blind, where the researcher knows the type of capsule product given to each respondent, however, the respondent and research assistants or operator who administers the product does not know which type or product is given to the respondent

ii. Maintenance of Blinding

To maintain the blinding, the list of randomization is only kept and known by the researcher.

iii. Breaking the Blinding

The list of randomization will be opened at the end of the research when all the research process is finished.

j. Preventions of the Subject Dropout

To prevent dropout of subjects, the research asistants will periodically remind the subjects when to take the capsules and schedule for next visit.

11. STUDY TREATMENT

a. Study Intervention

i. Active Group

The intervention group is the group of patients who receive ASI MOMMY® preparation.

1. Dose, Formulation, Rute, Duration, Hours, etc

ASIMOMMY® formula contains extracts of Katuk leaf (Sauropus androgynous) 300 mg, Fenugreek (Trigonella foenum-graceum) 50 mg, and Moringae oleifera extract (Moringa leaf) 50 mg. The formulation is taken once a day at nightime, as much as 2 capsules for a duration of 7 days (Mustofa et al., 2020). The capsule is taken once a day at nighttime at 20.00 as much as two capsules.

ii. Control group

The positive control group consists of patients who receive domperidone

1. Dose, Formulation, Route, Duration, Hours, etc

Domperidone that is used is 10 mg dosage, taken every 8 hours for 7 days (Paul et al., 2015). The drug is taken three times a day at 06.00, 14.00, and 22.00 West Indonesia Time.

iii. Placebo group

The negative control group consists of patients who receive placebo.

1. Dose, Formulation, Route, Duration, Hours, etc

Sugar inside the capsule does not give any therapeutic effect, is taken once a day, as much as 2 capsules, for duration of 7 days.

b. Dispense of Study Medications

At the first visit, research subjects are given all the drugs equivalent to the number of capsules that will be consumed for a week.

c. Drug Packaging/handling/Storage/Accountability

ASI MOMMY® is a polyherbal formula that is made in a capsule form by the herbal drug industry (PT Swayasa Prakarsa, Yogyakarta, Indonesia). This drug preparation is kept under 30 degrees celsius in a dry place away from sunlight.

Each capsule contains extracts of Katuk leaf 300 mg, Fenugreek 150 mg, and Moringa leaf 50 mg. ASI MOMMY® has undergone activity testing and acute and subchronic toxicity testing. Research has shown that ASI MOMMY® formula works actively as an herbal galactogogue drug and does not have give any toxic effects, therefore it is safe to be given to humans (unpublished data).

d. Training procedure

Training will be given by experts provided by the research team to the research members in two sites which includes materials about the SOP, protocols, and entire research flow.

12. CONCOMITANT THERAPHY

a. General Considerations

The subjects are prohibited from consuming drugs other than what is provided by the researchers, because it may affect the mechanism or interaction of the intervention drug.

b. Medications Prohibited Before or During the Trial

The types of drugs prohibited during the research among others are antacids, cimetidine, ranitidine, famotidine and nizatidine, or drugs that interact with domperidone such as haloperidol and lithium.

13. STUDY ASSESSMENT

In this research, the assessments done are regarding physical examination, measurement of blood pressure, along with the baby's body weight prior to and after the intervention.

14. STATISTICAL ANALYSIS

a. General Design

The method used in this research is a single blind, Randomized Control Trial (RCT). The benchmark of this study is the measurement of the babies' weight before and after the intervention therapy that is given (the research product).

i. Hypothesis

H0: The traditional drug preparation ASIMOMMY® does not increase breastmilk production in postpartum women.

H1: The traditional drug preparation ASIMOMMY® increases breastmilk production in postpartum women.

ii. Output (*Endpoint*)

The output expected is that ASI MOMMY® is able to increase the production of breastmilk which in turn increases the weight of the baby after the mother receives the intervention.

b. Rationale for Sample Size and Statistical Power

Sample size is calculated using sample size formula for hypothesis testing on the average of more than two groups, unpaired numeric comparative in one measurement, are as follows (Dahlan, 2016):

$$z_\beta = \frac{\sqrt{v_{2(2[v_1+\delta^2]^2-[v_1+2\delta^2])}} - \sqrt{v_1(v_1+\delta^2)\,(2v_2-1)F}}{\sqrt{v_1}(v_1+\delta^2)F + v_2(v_1+\delta^2)}$$

Information:
n = number of subjects in one group
Z_β = beta standard value 20 % which is 0,84
V_1 = degree of freedom from the number of = k-1. V_1 = 3-1 = 2
V_2 = degree of freedom from the number of groups k (n-1). V_2 = 3(n-1)
K = number of groups = 3

$$\delta^2 = \frac{n\sum_{(x_i-x)} 2}{s^2}$$

X_i = average of baby body weight in a group

X_1 = average of baby body weight in the domperidone and placebo group which is 3426,6 (Amri *et al*., 2020)

X_2 = average of baby body weight in the placebo group which is 3221,1 (Amri *et al*., 2020)

X_3 = average of three groups is 3000

X = overall average (3 group)

S = combined standard deviationn

F = Anova table value as function of type 1, V_1, V_2

Alpha = type 1 error 0,05.

i. Projected Number of Site
Locations used in this study are two sites which are Jetis and Tegalrejo Public Health Centers in Yogyakarta.

ii. Projected Number of Participant per site
Total number of subjects in one place is around 22 or 23 subjects.

c. Statistical Methods for primary and Secondary Outcomes

Statisical data anlysis in this study is done using SPSS 24.0 program. The data undergoes normality testing first to determine which statistical analysis test will be used. The result of research with categoric data will be presented in the form of quantity/frequency and percentage from each group. Numeric data with normal distribution (parametric) will be presented in the form of average and standard deviation, whereas if the data is not distributed normally (non-parametric) then it will be presented using median, minimal value and maximum value.

d. Significance Testing

Chi-squared test is used for variabels with categoric data (nominal and ordinal). Bivariate analysis test that is used for variables with numeric data (parametric) is the One Way Anova test with Post Hoc Bonferroni, meanwhile for non parametric data is Kruskall Walis with Post Hoc Mann Whitney.

Analytical test for variables aside from parametric data and dependent variables is using Pearson correlation, while non-parametric data is analysed using Spearman correlation

e. Demographic and baseline Characteristics

Research data with categoric data (nominal and ordinal) is presented in the form of quantity/frequency and percentage from each group.

f. Safety Analysis

The entire data analysis process will be done by a biostatistics expert appointed by the research team.

15. DATA AND SAFETY MONITORING PLAN

a. Data and Safety Monitoring Board

The researchers have appointed an expert if any unwanted occurrence were to happen, in order to conduct further assessment and interventions.

b. Safety Monitoring

Side effects will be noted by the research team starting from when the research subject signs the informed consent until three days after the last day that the subject consumed the research product. All data regarding side effect that arise is collected from the subjects and their daily cards. All side effects is noted in the Case Report Form (CRF).

16. DATA MANAGEMENT AND PROCEDURES

The Principal Investigator is responsible for making sure the research is conducted according to the protocols of Good Clinical Practice (GCP), applicable regulatory requirements, and that the data collected is valid. To reach this goal, this study will be continuously monitored and reviewed each month by the research team.

Monitoring of clinical site is done to make sure that the rights and well-being of human subjects are protected, that the clinical trial data reported is accurate, complete, and able to be verified, and that the trial run is in accordance with the protocols/amendments currently approved, with GCP, and with applicable regulatory requirements.

Clinical Monitoring Plan will be made by the sponsor and will explain in detail who will conduct monitoring, the frequency of monitoring done, at what level detailed monitoring will be done, and distribution of monitoring reports.

Collection of private patient information will be limited by the amount needed to achieve the aim of this study, so that no sensitive information is unecessarily collected.

17. HUMAN SUBJECTS PROTECTION

a. Informed Consent/Assent

Every participant must give written consent with full knowledge regarding the procedures involved in the research. Informed consent, approved by the IRB and in accordance with regulatory guidelines, must be explained thoroughly by the investigator or research team member including the aim of the research, method, benefits and risks, and signed by the subject involved in the researhc, The subjects are informed that participation in this study is voluntary and that they are able to withdraw at any time.

b. Subject Confidentiality/Privacy

Subjects will be informed that chosing to not participate in the research will not affect the treatment that they receive for therapy. Subjects will be informed that they consent to giving staff access to investigate confidential medical records.

Subjects are given enough time to read the consent form and opportunity to ask any questions. After the informed consent form is signed, subjects are given a copy of the document.

c. Compensation for Treatment

Participating mothers in this research will receive transportation replacement cost of 200.000 Rupiah from the researchers. If the subject experiences serious side effects, all cost of treatment for the side effects will be compensated by the research team.

18. REGULATORY AND ADMINISTRATIVE CONSIDERATION

a. IRB Approval

This research has been approved by the ethical committee of the Faculty of Medicine, Public Health, and Nursing UGM with reference number: KE/FK/0191/EC/2022 per 22 February 2022.

Deviation from protocol is non-compliance towards clinical trial protocol or GCP requirements. Non-compliance may come from the participants, investigator, or staff from study location. As a result from deviations, corrective actions must quickly be developed and implemented by the location site.

All deviations/violations of protocol must be documented using CRF Protocol Deviation/Violation and handed over to IRB according to their guidelines for reporting.

b. Law and Regulation

This clinical study will be conducted in accordance to all national laws and regulations where the study is done, along with the applicable guidelines. This study will be registered in www.clinicaltrials.gov

c. Publication and Data Sharing Policy

Preparation and submission of publication manuscript which contains results of research must be according to the process established by the agreement between the participating research sponsor and institution. Publication or presentation of any study results must follow all applicable privacy laws.

d. Conflict of Interest

No conflict of interest to be reported

e. BPOM Registration

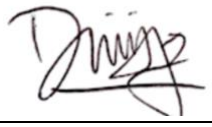
Results of this clinical trial will be reported and submitted to BPOM

f. Reporting to Sponsor

Monitoring and results of this clinical trial will be periodically reported to the sponsor.

19. SIGNATURE

I agree to ensure that all staff members involved in this research are informed of their obligation in fulfilling the commitments above.

Signature of Principal Investigator (PI)	Date
	19 October 2022
Name	
Andini Juwan Prabandari, MD.	
Name of Institution	
Center for Herbal Medicine, Faculty Of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia	

20. APPENDICES

19.1. SERIOUS ADVERsE EVENT REPORT

Log Serious Adverse Event* (SAE) *Report
Uji Klinik ASI MOMMY
Diisi oleh: Principle Investigator

Principal Investigator :

Subjek ID :☐-☐-☐☐☐-☐☐☐

Nomor Site / Nama Site Penelitian: /

No	SAE Number	SAE Description	Adverse Event	SAE Clasifications	Event Start Date	Event End Date	Date Site Became Aware of Event (Reported Date)	Grade	Unexpected (YA atau TIDAK)	Attribution	Outcome

SAE Classification	Grade	Attribution	Outcome
1 - Fatal (resulted in death)	1 - Mild	0 – Definite	0 – Fatal
2 - A life-threatening occurrence	2 - Moderate	1 – Probable	1 – Not recovered/not resolved
3 - Requires inpatient hospitalization or prolongation of existing hospitalization	3 - Severe	2 – Possible	2 – Recovered w/sequelae
4 - Results in persistent or significant disability/incapacity	4 - Life Threatening	3 – Unlikely	3 – Recovered w/o sequelae
5 - Results in congenital anomaly/birth defect	5 – Death (Fatal)	4 – Unrelated	4 – Recovering/Resolving
6 - A significant medical incident that, based upon appropriate medical judgment, may jeopardize the subject and require medical or surgical intervention to prevent one of the outcomes listed above.			