

# Effect of omeprazole or resveratrol on iron status in thalassemia

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<b>Registration date</b> 08/01/2025	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
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## Plain English summary of protocol

### Background and study aims

Thalassemia is a common hereditary disorder affecting about 1% of the population in Thailand. It results from the defective production of globin chains, leading to symptoms like anemia, jaundice, and growth issues. There are two types: transfusion-dependent thalassemia (TDT) and non-transfusion-dependent thalassemia (NTDT). TDT patients often develop iron overload from regular blood transfusions, while NTDT patients absorb too much iron from their diet. This iron overload can cause various health problems. Current treatments include iron chelation therapy, but they have limitations. This study will investigate if using omeprazole (a proton pump inhibitor) and resveratrol (an antioxidant) can help reduce iron absorption and improve treatment for NTDT patients.

### Who can participate?

NTDT patients at Maharaj Nakorn Chiang Mai Hospital in Thailand

### What does the study involve?

Participants will be divided into three groups of 20, each receiving either a placebo (20 mg maltodextrin), 20 mg omeprazole, or 250 mg resveratrol, taken twice daily before meals for 6 months. All groups will continue with standard treatments like iron chelators, folic acid, vitamin D, calcium supplements, and lifestyle changes. Patients will have appointments at the start, 3 months, and 6 months to monitor clinical signs and blood parameters. Blood tests will measure various health indicators. The study compounds will be prepared in identical gelatin capsules and distributed in labeled bottles. Group 1 will take omeprazole, Group 2 will take resveratrol, and Group 3 will take a placebo, all twice daily for 6 months.

### What are the possible benefits and risks of participating?

Possible benefits: Patients may not benefit from this study because the study drugs may not further decrease serum ferritin. However, the information from this study will be helpful for the treatment of thalassemia patients with iron overload in the future.

### Risks of participants:

- Risk from blood drawing that may be pain, bruising, or a less common side-effect which is vasovagal syncope.

- Risk from study drugs: omeprazole may cause you to feel nausea, vomiting, diarrhea, abdominal pain, bloating, constipation, back pain or fewer side effects which are chest pain, myocardial infarction, intraabdominal infection, lower respiratory tract infection, pancreatitis, osteoporosis or other unexpected side effects.
- Risk from resveratrol is nausea, vomiting, diarrhea or fewer common side-effect is pancreatitis or other unexpected side effects.

Where is the study run from?

Adult thalassemia clinic, Maharaj Nakorn Chiang Mai Hospital, Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

When is the study starting and how long is it expected to run for?

July 2024 to May 2026

Who is funding the study?

1. National Research Council of Thailand
2. Faculty of Medicine Fund, Chiang Mai University, Chiang Mai Thailand (under processing)

Who is the main contact?

Dr. Thanapong Chopetgool, M.D., Resident Hematologist, chopetgoolden@gmail.com

## Contact information

### Type(s)

Public, Scientific, Principal investigator

### Contact name

Dr Thanapong Chopetgool

### Contact details

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## Additional identifiers

### Protocol serial number

National Research Council of Thailand Grant number: N42A670732

## Study information

### Scientific Title

Adjunct omeprazole or resveratrol in non-transfusion dependent thalassemia patients with secondary hemochromatosis: a randomized, double-blind, placebo-controlled trial

### Study objectives

Adjunctive omeprazole or resveratrol in combination with iron chelators could reduce serum ferritin compared with placebo in thalassemia patients with iron overload.

The primary study objective:

To evaluate the efficacy of adjunct omeprazole or resveratrol in combination with iron chelators in reducing serum ferritin compared to placebo in non-transfusion-dependent thalassemia patients.

Secondary objectives are:

1. Evaluate the efficacy of adjunct omeprazole or resveratrol in combination with iron chelators in reducing labile plasma iron (LPI), non-transferrin bound iron (NTBI) and serum iron (SI) compared to placebo
2. Study the association between adjunct omeprazole or resveratrol in combination with iron chelators and the levels of ERFE and hepcidin (Hcd)
3. Study the association between resveratrol and changes in HbF levels
4. Assess the adverse effects of adjunct omeprazole or resveratrol with iron chelators

### **Ethics approval required**

Ethics approval required

### **Ethics approval(s)**

approved 17/12/2024, Office of Research Ethics (Faculty of Medicine, Chiang Mai University, Chiang Mai, 50200, Thailand; +66 53936643; researchmed@cmu.ac.th), ref: 476/2024

### **Study design**

Single-center interventional randomized placebo-controlled clinical trial

### **Primary study design**

Interventional

### **Study type(s)**

Efficacy

### **Health condition(s) or problem(s) studied**

A decrease in serum iron levels in non-transfusion-dependent thalassemia patients

### **Interventions**

The study will be conducted in non-transfusion-dependent thalassemia patients at the Out-patient department numbers 9 or 23 in Maharaj Nakorn Chiang Mai Hospital, Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand.

Using the stratified random sampling technique, sixty-three transfusion-dependent thalassemia (TDT) subjects were enrolled in the study, but three dropped out. The sample size was calculated using G\*Power software version 3.1.9.7, allowing for comparison between the three groups. A repeated measures analysis of variance (ANOVA) F test was employed, incorporating within-between interaction mode. The anticipated effect size for the new compound is 0.50, which is considered large. The statistical power is set at 95% with a significance level ( $\alpha$ ) of 0.05. Measurements were taken at three points: baseline (month 0), during the first intervention (month 3), and at the end of intervention (month 6). Consequently, the total sample size determined by G\*Power is 60, with 20 participants allocated to each group.

The three groups involve taking 20 mg maltodextrin (placebo), 20 mg omeprazole capsule, and 250 mg resveratrol capsule orally twice daily before meals for 6 months. All groups will receive standard treatments including iron chelators, folic acid supplementation, vitamin D supplementation, calcium supplementation, and lifestyle modifications throughout the study. The patients will be appointed at the first visit, 3 months, and 6 months to evaluate clinical signs and blood parameters levels. Blood samples will be analyzed for complete blood count, hemoglobin types, serum levels of blood urea nitrogen (BUN), creatinine (Cr), electrolytes (e.g., Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>2+</sup>, Mg<sup>2+</sup> and phosphates), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), soluble ferritin (sFt), iron (SI), total iron-binding capacity (TIBC), non-transferrin bound iron (NTBI), labile plasma iron (LPI), hepcidin (Hcd), and erythroferrone (ERFE).

The three study compounds, including omeprazole, resveratrol, and placebo, will be prepared and filled in gelatin capsules with the same appearance: 20 mg omeprazole capsule, 250 mg resveratrol capsule, and 20 mg maltodextrin. The capsules will be packed in a white plastic bottle (30 capsules each) and labeled with codes under the bottles. The patients in Group 1 will take an omeprazole capsule orally twice daily (total 40 mg/day) in the morning and evening before meals for 6 months. The patients in Group 2 will take a resveratrol capsule orally twice daily (total 500 mg/day) in the morning and evening before meals for 6 months. The patients in Group 3 will take a placebo capsule orally twice daily in the morning and evening before meals for 6 months.

Before the commencement of the trial, the results of genotyping and physical assessments were recorded. They documented participants' age, height, body weight (BW), body mass index (BMI), and the palpability of the liver and spleen. For 60 days, all participants consumed the product daily and were advised to avoid meals rich in polyphenolic components. Blood samples were taken on days 0, 30, and 60 after a 72-hour pause from their iron chelation therapy and just before their subsequent blood transfusion.

## **Intervention Type**

Supplement

## **Primary outcome(s)**

Changes in serum ferritin measured using an automated Biochemical Analyzer (immuno-chemiluminescence) at baseline, 3 and 6 months

## **Key secondary outcome(s)**

The following secondary outcome measures are assessed at baseline, 3 and 6 months unless stated:

1. A CBC measured using an automated cell counter
2. Hemoglobin typing measured using cationic-exchange HPLC/DAD at baseline and 6 months.
3. Blood urea nitrogen measured using an automated biochemical analyzer
4. Creatinine measured using an automated biochemical analyzer
5. Electrolytes measured using an automated biochemical analyzer (ion selective method)
6. Aspartate aminotransferase measured using an automated biochemical analyzer (colorimetry)
7. Alanine aminotransferase measured using an automated biochemical analyzer (colorimetry)
8. Alkaline phosphatase measured using an automated biochemical analyzer (colorimetry)
9. Serum iron measured using an automated biochemical analyzer (ferrozine colorimetry)
10. Total iron-binding capacity measured using an automated biochemical analyzer (ferrozine colorimetry)
11. Labile plasma iron measured using Rhodamine B fluorochrome/spectrofluorometry

12. Non-transferrin bound iron measured using NTA/fluorescence chelator beads/flow cytometry a
13. Hepcidin measured using a sandwich enzyme-linked immunoassay
14. Erythroferrone measured using a sandwich enzyme-linked immunoassay
15. Vitamin B12 measured using reversed-phase HPLC/DAD
16. Vitamin D3 measured using a competitive enzyme-linked immunoassay

**Completion date**

05/05/2026

## Eligibility

**Key inclusion criteria**

1. Aged 20-65 years old
2. Non-transfusion dependent thalassemia [alpha or beta] diagnosis by HPLC, PCR or gene mutation
3. Hemochromatosis with serum ferritin 300-1000 ng/mL or > 1000 ng/mL with a maximum iron chelator (DFP at 75 mg/kg/day or DFX at 20 mg/kg/day)
4. Concurrent iron chelators without changing dose during 3 months before enrollment and no tendency to adjust the dose of iron chelators between study
5. Inform consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

20 years

**Upper age limit**

65 years

**Sex**

All

**Key exclusion criteria**

Not meeting the participant inclusion criteria

**Date of first enrolment**

10/02/2025

**Date of final enrolment**

30/04/2026

## Locations

## Countries of recruitment

Thailand

## Study participating centre

### Out-patient department numbers 9 or 23 (Adult thalassemia clinic)

11th Floor, Sriphat Building, Maharaj Nakorn Chiang Mai Hospital, Division of Hematology,  
Department of Internal Medicine, Faculty of Medicine, Chiang Mai University  
Chiang Mai  
Thailand  
50200

## Sponsor information

### Organisation

National Research Council of Thailand

### ROR

<https://ror.org/018wfhg78>

### Organisation

Chiang Mai University

### ROR

<https://ror.org/05m2fq25>

## Funder(s)

### Funder type

Research council

### Funder Name

National Research Council of Thailand

### Alternative Name(s)

NRCT

### Funding Body Type

Government organisation

## Funding Body Subtype

National government

## Location

Thailand

# Results and Publications

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analyzed during the current study will be available after the study finishes upon request from Dr. Thanapong Chopetgool, MD. from the Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand. Telephone numbers (Office) +66 53935482 and (Mobile): +66 930748844. Email: chopetgoolden@gmail.com

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>			03/01/2025	No	Yes
<a href="#">Protocol file</a>			03/01/2025	No	No