

## **Proof-of-Concept Research Proposal**

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A Randomised, double-blinded Controlled Trial

**Alterations in skin hydration, moisture and genomic in patients with dry skin conditions following daily oral palm tocotrienol and squalene (STGAIA™) supplementation**

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## **ABSTRACT**

Skin is the soft and flexible outer layer that covers the body. It functions in protection, thermoregulation and sensation. Dry skin, also known as xerosis, is associated with scaling, itching and cracking and can be caused by environmental factors; cold or dry air, harsh soaps, over-scrubbing, or health conditions; eczema, diabetes, genetics, and dehydration. Currently, the recommended treatment options for dry skin are the application of moisturiser, ointment and cream. Recent studies have demonstrated the beneficial effects of the topical application of vitamin E in maintaining healthy skin in cell-based animal models and human trials. However, studies on oral supplements of vitamin E phytonutrients on skin health remain scarce. Therefore, this proof-on-concept study is aimed to investigate the protective effect of palm squalene and tocotrienols oral supplements on human subjects with dry skin-related issues. This study will enable us to understand the effects of palm squalene and tocotrienols on skin sebum content, skin hydration and trans-epidermal water loss in patients with dry skin-related issues.

## **Keywords**

Palm squalene, tocotrienols, dry skin

## **INTRODUCTION**

Skin is the largest organ in the human body. By covering the entire body, it serves as a first-line defence against external perils such as heat, UV radiation, injury and microbial infections. However, the skin-barrier defect can result in skin dryness, and this condition is mainly attributed to a reduction in sebum secretion and excessive water loss from the stratum corneum (SC). Healthy skin forms an intact SC layer with an effective permeability barrier that prevents excessive water loss and penetration of damaging irritants and allergens. Disruption in the skin barrier results in the loss of the tight arrangement between the skin cells, leading to water loss and skin becoming dry and dehydrated. The damaged skin barrier is characterised by dry skin, itching and inflammation (Purnamawati *et al.*, 2017).

Palm tocotrienol (T3) has been widely used as a health supplement to protect against vital organs like the nerves, brain, skin and liver. The benefits of T3 on skin health have been reported in numerous investigations, including cell-based and animal studies (Sen, Khanna and Roy, 2007). On the other hand, squalene is a natural dehydrotriterpenic hydrocarbon, known as an intermediate in the biosynthesis of phytosterol or cholesterol in plants/animals and humans (Popa *et al.*, 2015). In humans, new-borns have the greatest concentration of squalene in their blood, but the reserve begins to decline tremendously between 30 and 40 years. As palm oil contains 250-540 mg/L squalene, it is essential to assess the health benefits of palm squalene, especially on skin health.

The main objective of this randomised control trial (RCT) is to investigate the dietary supplementation of STGaia™, a Phytogaia-exclusive product with a combination of tocotrienol and palm squalene on human subjects with dry, scaly and itchy skin. This proof-of-concept study will be conducted on human subjects with minor skin issues for four weeks. At the end of the fourth week, the changes in skin parameters and feedback from subjects by means of questionnaires will be gathered, evaluated and analysed. The study will be assisted by a qualified dermatologist as clinical collaborators from Pusat Perubatan University Kebangsaan Malaysia (PPUKM).

## **RESEARCH OBJECTIVES**

The proposed proof of concept study investigates the role of the oral supplement of STGaia™ (a combination of palm squalene and tocotrienol) in protecting against skin dryness-related issues in patients.

### **Specific Objectives:**

1. To assess the effect of STGaia™ on the sebum content
  - i. Using a sebumeter (expressed in  $\mu\text{g}/\text{cm}^2$ ) to categorize skin type – dry, normal, oily.
  - ii. Quantitation of tocotrienol and squalene levels in sebum and plasma using LCMS technique
2. To measure the effect of STGaia™ on the skin (stratum corneum) hydration level by measuring skin dielectric properties
3. To quantify the transepidermal water loss following oral supplementation of STGaia™ to assess the density gradient of the water evaporation from skin stated in  $\text{g}/\text{h}/\text{m}^2$ .
4. To evaluate physical changes in skin textures using the XASI scoring tool and clinical assessment
5. To evaluate the physical and structural changes of nail and hair textures
6. To investigate the nutrigenomic alterations in subjects

### **Research questions:**

- 1 Does the oral supplement of palm squalene and tocotrienol protects against skin dryness in human subjects?
- 2 Do palm squalene and tocotrienol improves skin textures and hydration?
- 3 Does oral palm squalene and tocotrienol supplement improve nail and hair health?

### **Hypothesis**

H1: STGaia™ (Palm squalene and tocotrienol) protects human skin from dryness-related conditions.

H2: STGaia™ (Palm squalene and tocotrienol) improves nail and hair health

## RESEARCH DESIGN

The patients will be recruited based on the following inclusion and exclusion criteria.

### Inclusions and Exclusion Criteria

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#### Inclusion criteria

1. Provision of a signed and dated informed consent form
2. Stated willingness to comply with all study procedures and availability to attend study visits for the duration of the study
3. English or Malay-speaking
4. Both sexes who are 25-45- years of age
5. Score of a 10 or higher in the Xerosis Area and Severity Index (XASI).

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#### Exclusion criteria

1. Current self-reported lactation, pregnancy or active intent to conceive
2. Fever within seven days of study enrolment
3. Self-reported systemic antibiotics (oral or injectable) use in the past six weeks.
4. On treatment or medication
5. Menopause and/or taking hormone replacement therapy
6. Consuming hair, skin and nail supplements or prescribed medicine
7. Have some health-related problem (e.g, flu, fever, allergy)

A total of 36 human subjects with dry skin issues will be shortlisted after considering the inclusion and exclusion criteria. Then, the subjects will undergo prescreening tests to obtain the baseline readings. Subsequently, subjects will be randomly grouped into placebo and treatment groups. The study approach is briefly described in **Table 1**.

**Table 1: Study plan and grouping**

Skin, Nail and Hair assessments	Study Groups		
	Placebo	Low Dose STGAIA	High Dose STGAIA
<b>Evaluation of baseline values (Pre-screening, Day 0)</b>			
<p><b><u>Skin evaluation</u></b></p> <ul style="list-style-type: none"> <li>• Xerosis Area and Severity Index (XASI)</li> <li>• Sebum content (Sebumeter)</li> <li>• Skin hydration measurement (Corneometer)</li> <li>• Trans-epidermal water loss measurement (Tewameter)</li> <li>• Skin surface observation (Wrinkling)</li> <li>• Tocotrienol and squalene levels in sebum and plasma (LCMS technique) (<i>Sebum and Blood collection</i>)</li> </ul> <p><b><u>Nail examination</u></b></p> <ul style="list-style-type: none"> <li>• Oxford Nail Appearance Score (photos) <ul style="list-style-type: none"> <li>○ Horizontal and lateral ridging</li> <li>○ Nail surface appearance</li> <li>○ Nail bed color</li> <li>○ Brittleness</li> </ul> </li> </ul> <p><b><u>Hair examination</u></b></p> <ul style="list-style-type: none"> <li>• Hair density</li> <li>• Hair diameter</li> <li>• Hair structure (split ends)</li> </ul>	12 subjects	12 subjects	12 subjects
<b>Nutrigenomic study (<i>Blood collection</i>)</b>			6 subjects
<b>4 weeks of supplementation with STGaia™ (Visit 1, Day 28)</b>			
<p><b><u>Skin evaluation</u></b></p> <ul style="list-style-type: none"> <li>• Xerosis Area and Severity Index (XASI)</li> <li>• Sebum content (Sebumeter)</li> <li>• Skin hydration measurement (Corneometer)</li> <li>• Trans-epidermal water loss measurement (Tewameter)</li> <li>• Skin surface observation (Wrinkling)</li> <li>• Tocotrienol and squalene levels in sebum and plasma (LCMS technique) (<i>Sebum and Blood collection</i>)</li> </ul> <p><b><u>Nail examination</u></b></p> <ul style="list-style-type: none"> <li>• Oxford Nail Appearance Score (photos) <ul style="list-style-type: none"> <li>○ Horizontal and lateral ridging</li> <li>○ Nail surface appearance</li> <li>○ Nail bed color</li> <li>○ Brittleness</li> </ul> </li> </ul> <p><b><u>Hair examination</u></b></p> <ul style="list-style-type: none"> <li>• Hair density</li> <li>• Hair diameter</li> <li>• Hair structure (split ends)</li> </ul>	12 subjects	12 subjects	12 subjects



<b>Groups</b>	<b>Placebo</b>	<b>Treatment 1 (Oral supplement-low dose)</b>	<b>Treatment 2 (Oral supplement - high dose)</b>
<b>8 weeks of supplementation with STGaia™ (Visit 2, Day 56)</b>			
<p><b><u>Skin evaluation</u></b></p> <ul style="list-style-type: none"> <li>• Xerosis Area and Severity Index (XASI)</li> <li>• Sebum content (Sebumeter)</li> <li>• Tocotrienol and squalene levels in sebum and plasma (LCMS technique) (<i>Sebum and Blood collection</i>)</li> <li>• Skin hydration measurement (Corneometer)</li> <li>• Trans-epidermal water loss measurement (Tewameter)</li> <li>• Skin surface observation (Wrinkling)</li> </ul> <p><b><u>Nail examination</u></b></p> <ul style="list-style-type: none"> <li>• Oxford Nail Appearance Score (photos)               <ul style="list-style-type: none"> <li>○ Horizontal and lateral ridging</li> <li>○ Nail surface appearance</li> <li>○ Nail bed color</li> <li>○ Brittleness</li> </ul> </li> </ul> <p><b><u>Hair examination</u></b></p> <ul style="list-style-type: none"> <li>• Hair density</li> <li>• Hair diameter</li> <li>• Hair structure (split ends)</li> </ul>	12 subjects	12 subjects	12 subjects
<ul style="list-style-type: none"> <li>• <b>Nutrigenomic study</b> (<i>Blood collection</i>)</li> </ul>			6 subjects
<b>10 Weeks – 2 Weeks Post-supplementation of STGAIA™ (Visit 3, Day 70)</b>			
<p><b><u>Skin evaluation</u></b></p> <ul style="list-style-type: none"> <li>• Xerosis Area and Severity Index (XASI)</li> <li>• Sebum content (Sebumeter)</li> <li>• Skin hydration measurement (Corneometer)</li> <li>• Trans-epidermal water loss measurement (Tewameter)</li> <li>• Skin surface observation (Wrinkling)</li> <li>• Tocotrienol and squalene levels in sebum and plasma (LCMS technique) (<i>Sebum and Blood collection</i>)</li> </ul>	12 subjects	12 subjects	12 subjects
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