

# Use of melatonin, oral and cream, to counteract skin ageing: a controlled trial

<b>Submission date</b>	<b>Recruitment status</b>	<input type="checkbox"/> Prospectively registered
20/01/2025	No longer recruiting	<input type="checkbox"/> Protocol
<b>Registration date</b>	<b>Overall study status</b>	<input type="checkbox"/> Statistical analysis plan
21/01/2025	Completed	<input type="checkbox"/> Results
<b>Last Edited</b>	<b>Condition category</b>	<input type="checkbox"/> Individual participant data
21/01/2025	Skin and Connective Tissue Diseases	<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Skin ageing is a complex process influenced by intrinsic factors, such as genetic predisposition, and extrinsic factors, including UV radiation and environmental pollution. Melatonin, a hormone known for its role in regulating circadian rhythms, has gained attention in dermatology for its potential anti-ageing properties due to its antioxidant and skin-repairing effects. Topical melatonin-based treatments have shown promise in improving signs of skin ageing, including elasticity, wrinkles, and pigmentation. However, no clinical studies have evaluated the combined ("In&Out") approach of using a topical melatonin-based cream alongside a melatonin-containing oral supplement enriched with hyaluronic acid and apigenin, both of which are recognized for their anti-ageing and skin hydration properties. Understanding the synergistic potential of this regimen could offer new insights into more comprehensive anti-ageing strategies.

This study aims to compare the effectiveness of two skin anti-ageing strategies: the use of a melatonin-based topical cream alone and a combined regimen of the same melatonin-based cream and a melatonin-based oral supplement containing hyaluronic acid and apigenin. The primary objective is to assess changes in skin ageing signs over a 12-week period. Secondary objectives include evaluating specific skin parameters and conducting VISIA imaging analysis to further explore the potential added benefit of the combination therapy compared to topical treatment alone.

### Who can participate?

People aged over 50 years with moderate-severe skin ageing (Glogau score >2)

### What does the study involve?

The study involved two melatonin-based products, one melatonin-based cream and a food supplement containing melatonin, apigenin and hyaluronic acid. Participants were randomly allocated to one of two groups. They were instructed to apply the cream twice a day for group A, and the cream twice per day plus one tablet of the food supplement per day for group B. The total duration of the treatment was 12 weeks with three measurements at the start and after 6 and 12 weeks.

What are the possible benefits and risks of participating?

The possible benefit is the improvement of skin health and skin ageing. There are no risks because of the use of already approved cosmetic products using well-known ingredients.

Where is the study run from?

Difa Cooper (Italy)

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

June 2023 to April 2024

Who is funding the study?

The study was founded by an unrestricted grant from Cantabria Labs Difa Cooper (Italy)

Who is the main contact?

Dr Massimo Milani, [massimo.milani@difacooper.com](mailto:massimo.milani@difacooper.com)

## Contact information

### Type(s)

Public, Scientific, Principal investigator

### Contact name

Dr Massimo Milani

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## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### ClinicalTrials.gov (NCT)

Nil known

### Protocol serial number

Nil known

## Study information

### Scientific Title

# Skin anti-aging effect of a melatonin-based in&out strategy in comparison with topical treatment alone: a randomized, assessor-blinded, prospective trial with VISIA evaluation

## Study objectives

To evaluate if an "In&Out" strategy with a melatonin-based dietary supplementation plus melatonin cream-based treatment was superior to melatonin-based cream only on skin aging.

## Ethics approval required

Ethics approval not required

## Ethics approval(s)

The present trial was performed using a cosmetic and a food supplement. Therefore according to the current national legislation, a formal EC approval is not required. However, the present trial was performed according to Helsinki's ethical principles. Each subject signed an informed consent.

## Study design

Randomized prospective assessor-blinded interventional trial

## Primary study design

Interventional

## Study type(s)

Treatment

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

Skin ageing

## Interventions

"Out" strategy: Melatonin-based cream 0.1%

"In" strategy: Mel-based (0.5 mg) dietary supplementation also containing hyaluronic acid (150 mg; HA) and apigenin (0.9 mg)

Participants were randomized in a 1:1 allocation ratio. They were also instructed to apply the cream twice a day using 2 ftu (fingertips units) for group A and the cream twice per day using 2 ftu plus one tablet of the food supplement per day for group B. The total duration of the treatment was 12 weeks with three measurements (baseline, t6 and t12) and two timepoints at 6 and at 12 weeks.

## Intervention Type

Mixed

## Primary outcome(s)

Elasticity, wrinkles, roughness, pigmentation, erythema, and skin pores assessed using the Skin Aging Global Score (SAGS) at baseline, week 6 and week 12

## Key secondary outcome(s)

1. Clinical evaluation of Skin ageing using the Glogau score at baseline, week 6 and week 12
2. Single parameters of SAGS measured at baseline, week 6 and week 12
3. Instrumental skin ageing evaluation using VISIA objective face sculptor analysis performed on a subgroup of 20 participants at baseline, week 6 and week 12

**Completion date**

01/04/2024

## Eligibility

**Key inclusion criteria**

Women with moderate/severe skin ageing defined as a Glogau Score higher than II

**Participant type(s)**

Healthy volunteer

**Healthy volunteers allowed**

No

**Age group**

Senior

**Lower age limit**

50 years

**Upper age limit**

70 years

**Sex**

Female

**Total final enrolment**

46

**Key exclusion criteria**

Skin acute conditions like eczema or skin cancer

**Date of first enrolment**

01/09/2023

**Date of final enrolment**

01/02/2024

## Locations

**Countries of recruitment**

Italy

**Study participating centre**  
**Difa Cooper Medical department**  
Via Milano 160  
Caronno Pertusella  
Italy  
21042

**Study participating centre**  
**Skin Center Clinic Modena**  
Via G. Zattera 130  
Modena  
Italy  
41124

## Sponsor information

**Organisation**  
Difa Cooper (Italy)

**ROR**  
<https://ror.org/044sr7e96>

## Funder(s)

**Funder type**  
Industry

**Funder Name**  
Difa Cooper

## Results and Publications

### Individual participant data (IPD) sharing plan

Dataset will be available on request from Dr Massimo Milani (massimo.milani@difacooper.com)

**IPD sharing plan summary**  
Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#"><u>Participant information sheet</u></a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes