**Investigation of a new caffeine cream on cellulite appearance**

Objective

The objective of this study is to determine the effect of a caffeine cream on cellulite appearance, thigh circumference and skin fold thickness. Participants’ perception of the sensorial qualities of the caffeine cream will be recorded in a personal diary and by questionnaire.

Rationale

Cellulite (gynoid lipodystrophy) is common in women after puberty, particularly in the area of the hips, thighs and abdomen (2-3, 5-8). It manifests as an “orange peel” appearance on the skin surface and is associated with microcirculation alterations (3, 5). Whilst there are many predisposing factors for cellulite appearance such as weight change, race and heredity (4), there is little consensus about its cause (1). Many women consider cellulite to be unsightly and seek topical products to improve the dimply skin appearance.

Caffeine has been incorporated in cosmeceutical products indicated for reducing cellulite (10-11). However, caffeine is a hydrophilic compound that penetrates the skin poorly. A number of methods have been investigated to improve its skin permeation (2, 5, 14-15). We have developed a novel cream containing caffeine that has demonstrated good skin permeation in our in vitro experiments. This study will examine the efficacy of the caffeine creams for cellulite reduction in healthy women.

Study design

A double blind, randomised placebo-controlled paired trial where each volunteer will apply active and placebo cream (containers will be coded by a blinded person) to regions on each of the upper thighs, twice daily for 12 weeks. The effect of the cream on skin appearance will be monitored over 12 weeks. The treatment site will be an approximately 150 x 250 mm area on the anterior surface of each thigh, midway between the proximal border of the patella and the inguinal crease.

Participants

Eligible participants will be healthy, female volunteers aged between 18 to 55 years, with a BMI > 22, recruited via advertisements on noticeboards around the Bentley campus and online advertising via Curtin Weekly and the School of Pharmacy and Biomedical Sciences Facebook pages. Participants will be excluded if they have used anti-cellulite treatment in the past 3 months or had major surgery in the past year including liposuction, or have any scarring of the skin tissues in the upper thigh area. Participants will receive a $20 voucher for participation in the study.

Twenty-four participants will be recruited for the proposed studies. All participants will provide written informed consent.

Cream formulations

A batch of caffeine cream (containing 2% caffeine) and placebo cream (cream base with no caffeine) will be prepared and packaged into containers by TP in the Skin Delivery laboratory (306:102) at the School of Pharmacy and Biomedical Sciences, Curtin University. The containers will be labelled by HB, who will also prepare the randomization schedule. Participants will be provided sufficient cream for 4 weeks application period. All ingredients used in the creams will be pharmaceutical grade and are categorised as GRAS (generally regarded as safe) by the U.S. FDA.

Study site

The study will be conducted in the CHIRI clinical research facility (Building 305) which is equipped with individual rooms with a treatment plinth. The temperature and humidity of the facility is controlled, and the light is suitable for photographic assessments.

Cream effect testing protocols

At day 0 (baseline), and at 4, 8 and 12 weeks, a standardised group of testing procedures will be conducted:

1. Standardized cellulite photographs and scoring

The participant will put on a thong supplied for the measurement process. The participant will then stand with feet placed on a marked position on the floor. A standardised series of photographs will be taken using a digital SLR camera and light source placed on a tripod at a predetermined height and distance from the treatment site. Images will be coded and stored for later data analysis. Images will be analysed by visual grading by three blinded, independent assessors, who will grade the cellulite based on a Cellulite Severity Scale (photonumeric validated visual) based on Hexsel, dal’Forno and Hexsel Celulite Severity Scale (CSS) (12-13). Images will also be analysed by a digital image analysis software system.

1. Thigh circumference

The thigh circumference will be measured at a distance (150mm proximal to the patella), which will be a mid-way point in the treatment site, using a cloth measuring tape. Triplicate measurements will be conducted by an assessor (TP).

1. Cutaneous-fold thickness

The skin fold thickness will be measured at a mid-way point within the treatment site (as described in 2. above). Each skin-fold measurement will be taken by gripping the skin with the thumb and index finger, 1 cm away from the measurement point, then measuring the skin fold thickness with a plicometer. Triplicate measurements will be conducted by a same blinded assessor.

1. Questionnaire

At the start of the study (week 0), TP will collect participant’s information such as name, age, height and their daily food routine and physical exercise, in general terms (to monitor for any substantial change during the study period). On week 4, 8 and 12 the participant will complete a series of questions to assess their perception of the cream products (see Data Collection sheet 1) and will also be asked if there has been any substantial change of their daily diet and exercise.

At week 12, participants will also be asked for the overall perception of the cream products and their effects on their skin.

Study Procedure

At the start of the study, participants will be screened to ensure they are suitable. They will be advised not to change their normal daily routine (diet, exercise, tea and coffee consumption) during the 12-week study period. The daily cream application and diary process will be explained, and they will be advised of the 4-weekly assessment protocols. An initial study data sheet will be completed in conjunction with the study coordinator (TP).

Participants will be advised that the study is testing two cream formulations applied twice daily, in the morning and at night, to the anterior thigh areas. They will be supplied with two cream jars and two separate spatulas, and shown the amount of cream to be removed by the spatula and applied to the treatment area. Each application should be applied with approximately 30 sec rubbing into the area. They will be provided with a diary and asked to record each application. The diary will also contain some questions about their perception of the cream that they should complete. The diary will be collected on the completion of the study. Participants will be given a $20 gift voucher when the complete the study.

Baseline measurements (including height, weight, thigh circumference) and photos will then be taken. A time will be arranged for the 4 week measurement sessions and TP will contact via social media as a reminder prior to the session. This will be repeated at 8 and 12 weeks.



Data analysis

Analysis of variance will be used to evaluate differences in cellulite between the formulations over time. Any adverse events will be recorded and summarised.

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