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Effect of a Combination of Extract of *Centella asiatica* L. Leaves and Extract of Green Coffee (*Coffea canephora robusta* P.) Beans in a Cream Preparation for Grade 1-3 Cellulite and Slimming

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Abstract

An accumulation of fat in the subcutaneous tissue causes cellulite and dimpling on the surface of the skin. Although not related to obesity, obesity worsens cellulite. There are abundant topical anticellulite creams on the market, but the efficacy of these creams has not been scientifically proven. A combination of *Centella asiatica* L. leaves extract and green coffee (*Coffea canephora robusta* P.) bean extract in a cream preparation was clinically tested in 30 women for 84 days in the absence of diet and exercise. The descriptive-true experimental before (T-0)-after (T-84) method was used to classify the cellulite (grade 1–3) and to determine the slimming effect. The cellulite appearance and the body circumferences (abdominal and thigh) perimeters were photographed 5cm and 10cm below the navel and below the gluteal fold. The results of before and after the treatment showed that grade 1 cellulite lower ($p < 0.000$), the measurement of abdominal circumference showed reduction ($p < 0.013$), but the measurement of both thigh circumference showed insignificantly reduction ($p < 0.512$). The combination of both extracts reduce cellulite and fat deposits in the abdominal area, making the volunteers look slimmer.

Abstrak

Efek Kombinasi Ekstrak Daun Pegagan (*Centella asiatica* L.) dan Ekstrak Biji Kopi Hijau (*Coffea canephora robusta* P.) dalam Sediaan Cream untuk Mengatasi Selulit Tingkat 1-3 dan Pelangsing. Penumpukan lemak pada jaringan subkutan dapat menyebabkan selulit yang membuat permukaan kulit menjadi tidak rata dan bergelombang. Walaupun tidak berhubungan dengan obesitas, namun tidak dapat dipungkiri bahwa obesitas dapat memperburuk kondisi selulit. Krim topikal berbahan aktif dari tanaman untuk mengatasi selulit banyak beredar di pasaran, namun efikasinya belum dibuktikan secara ilmiah. Metode penelitian adalah deskriptif-true *experimental* menggunakan kombinasi ekstrak daun gotu kola (*Centella asiatica* L.) dan ekstrak biji kopi hijau (*Coffea canephora robusta* P.) dalam sediaan krim untuk mengatasi selulit tingkat 1-3 dan dilihat efek pelangsingannya juga. 30 wanita yang masuk dalam kriteria inklusi, tanpa pembatasan kalori dan olah raga, menggunakan krim uji selama 84 hari pada area perut dan paha. Data yang diambil adalah foto untuk melihat perubahan selulit dan pengukuran lingkaran perut (5 cm & 10 cm di bawah pusar) dan kedua paha (5 cm & 10 cm di bawah *gluteal fold*) untuk melihat efek pelangsingan. Foto memperlihatkan selulit berkurang 1 tingkat ($p < 0,000$), berkurangnya lingkaran perut ($p < 0,013$), namun tidak terlihat efek krim pada lingkaran paha ($p < 0,512$). Kombinasi kedua ekstrak terbukti mampu mengurangi selulit dan timbunan lemak pada area perut, sehingga relawan terlihat lebih langsing.

Keywords: cellulite, *Centella asiatica*, *Coffea canephora robusta*

1. Introduction

Fat accumulation in the body can occur in the tissues, organs, or even in the skin layer known as the subcutaneous layer. The fat accumulated in the tissues or organs is called visceral fat. An excess of this type of fat can lead to various diseases, such as type 2 diabetes, high blood pressure, atherosclerosis and heart disease. Subcutaneous fat is located under the skin, specifically

in the hypodermis [1]. This type of fat can undermine the appearance of healthy men or women, even those with a healthy weight.

The difference between visceral fat and subcutaneous fat lies in its resistance to the process of fat burning (thermogenesis or lipolysis). The physiology of visceral fat is linked to beta-adrenoreceptors, which stimulate lipolysis. These are triggered by certain signals, such as

reducing calorie intake or exercising. In contrast, the alpha-2-adrenoreceptors of subcutaneous fat are resistant to lipolysis and standard weight-reduction diet [1]. Thus, a topical formula that directly targets the subcutaneous area is needed.

Cellulite is a skin condition that many people find aesthetically unacceptable. However, 85% of women over 20 years have various stages of cellulite [2]. There are four stages of cellulite [4]: (a) Pre-cellulite condition (grade 0 cellulite) is when the skin feels smooth and firm with neither of accumulation of linked collagen fibres nor elastin nodules. Adipocytes have regular diameter and not yet engorged with lipids. Nourishment and oxygen flow swiftly from a thick blood and lymphatic vessels to subcutaneous tissue. (b) Stage 1 (grade 1 cellulite) occurs in a deep cellular layer without cosmetic implications. Adipocytes are engorge with lipids, going bigger and clump together. The lymphatic circulation start to have a difficulty with removing the accumulation of fluids, because of vessel walls become so permeable that induce loss of fluid into the spaces between adipocytes and cause oedema. (c) Stage 2 (grade 2) of cellulite is visible because the thinning of epidermis and dermis. An accumulation of fluids increases the heterogeneity of the subdermal region and the 'orange peel' phenomenon becomes evident. Clumping of adipocytes and collagen fibres linkage hamper blood circulation and cause homeostasis. (d) Stage 3 (grade 3) is when the skin palpation shows clearly 'orange peel' phenomenon. Adipocytes are cut off from nourishment and oxygen supply and toxin-removing events. They clump together, surrounded by a thick and hard collagen layer and fatty masses become micronodules. (e) Stage 4 (grade 4) is when micronodules clump together forming hard macronodules in dermal layer. Nodules can compress nerves in involved area causing pain and trouble for subjects. This later stage is irreversible and refractory to any cosmetic treatment.

Cellulite described as a fat metabolic disorder where the fat localized in subcutaneous tissue causes changes in body shape. Cellulite occurs in the first subcutaneous layer, which could affect the flow of blood vessels and the lymphatic microcirculation [3]. Unevenly fatty material accumulated in localized part of body cause dimpling skin and increasing over time become nodules. Cellulite is commonly found in pelvis area, lower limbs, around belly and upper arm area [3-4].

Cellulite cannot be equated with obesity because of the localized fat in specific area. Obesity refers to adipocyte hyperplasia or hypertrophy where the fat spread evenly in the body [2]. Cellulite is also not associated with morbidity or mortality, making it difficult to define it as a pathologic condition [3]. Nevertheless, it is a complex condition because it involves the microcirculation, the lymphatic system, the extracellular matrix and the

presence of a prominent subcutaneous fat bulge in the dermis [2].

The treatment for cellulite known these days involves suctioning the excess fat by surgery or called ultrasonic liposuction. These procedures are high cost and therefore only available to those who can afford them. To increase the availability of cellulite treatment, other affordable treatment methods are needed, although it may take longer for the skin to look smooth again with these methods. In the last decade, an improvement in cellulite had reported with the use of mechanical systems, such as massage, with or without the addition of topical creams [5]. Several studies reported that certain plant active compounds, such as xanthine or asiaticoside, in topical cream preparation could accelerate the removal of adipocytes (fat cells) by increasing the process of mitochondrial breakage and burning fat in the target area (thermogenesis) [2,10].

Centella asiatica L. or gotu kola contains asiaticoside as its main component. It can stimulate type 1 human collagen production, a protein that plays role in wound healing process [6] and in a topical cream preparation it repairs the viscoelasticity of the skin [7]. Gotu kola leaves extract [PLE] was chosen as one of the active ingredients in this study of cellulite because of its natural collagen biosynthesis stimulating effect and its ability to protect vascular tissue [8].

Green coffee (*Coffea canephora robusta* P.) beans or raw, unroasted coffee contains polyphenol (5-O-caffeoylquinic acid) as its main component and less than 2% caffeine. The polyphenol, known as chlorogenic acid, is a potent antioxidant. The roasting process breaks down chlorogenic acid into quinic acid and caffeic acid, thus increasing the level of caffeine [9]. Scientific research has indicated that caffeine as one of the active ingredient in anti-cellulite topical cream preparation and slimming [2,10-11]. However, there has been no study of the effectiveness of chlorogenic acid as a slimming factor in topical cream preparation. Green coffee bean extract [GCBE] was chosen in this study based on research conducted by Shimoda *et al.*, who proved that GCBE administered orally to experimental mice reduced body weight effectively and prevented fat accumulation by inhibiting the absorption of fat and activating the metabolism of fat in the liver [12]. Chlorogenic acid in oral dosage suppresses levels of triglycerides and the caffeine acts as a fat absorption suppressor [12].

The combination of PLE with its collagen biosynthesis properties and GCBE with its excess subcutaneous fat reducing effect in cream preparation for cellulite treatment and slimming has not been scientifically investigated yet. If that combination showed a synergistic effect in terms of stimulating the formation of collagen and reducing the subcutaneous fat layer,

then it could be expected to improve the appearance of cellulite and to reduce the circumference of abdominal and thigh area.

2. Methods

The equipment used in making the cream preparation were an analytical balance (*Mettler Toledo*), a 45 cm diameter aluminum tub, a homogenizer, plastic measuring cup and packaging bottles. Cellulite appearance and abdominal-thigh measurement data were collect with a ruler, a measuring tape, a camera with a resolution of 8 mega-pixel (*Canon*). An evaluation and stability test used petri dishes, measuring cups, centrifuge tubes, a *Viscometer* (*Boeco*), a pH meter (*Boeco*), a centrifugator (*Kubota 5100*), a hot chamber and a refrigerator.

The active ingredients for this study were gotu kola leaves liquid extract (7%) from *Crodarom* and green coffee bean powder extract (0.2%) from *Naturex*. Both kinds of extract have undergone *in vitro* assays and been certified.

The oil in water cream formula was made from olive oil (7%) as the oil phase, plus other chemical constituents, including emulsifier (3%), a thickening agent (polyacrilate-13, polyisobutene, polysorbate 20), 1% of emulsifier and stabilizer (polysorbate 80), 1% of preservative (phenoxyethanol, methylparaben, ethylparaben, propylparaben, butylparaben) and water added up to 100%.

This research applied the descriptive-true experimental method. Thirty volunteers used the trial cream without placebo comparison [13] for 84 days continuously. The volunteers should follow the instruction, which are 2 grams of trial cream applied twice a day after bath regularly at the specific area (abdomen and thigh) with light circular motion massage until the cream absorbed. The volunteers were selected based on factors that influence the presence of cellulite (i.e., age, gender, heredity, race and body mass index [4,14-15] as an inclusion criteria. Any weight-reduction diet or hard exercise would be exclusion criteria. Before treatment (T-0), all volunteers were observed to determine the grade of their cellulite and they had first measurement for their abdominal and thigh circumferences. The irritation test and the efficacy test used in this study were approved by the health research ethics committee of *Fakultas Kedokteran Universitas Indonesia RSCM, Jakarta*. The prospective volunteers were advised about the purpose of the research and they all signed an informed-consent form.

A measuring tape was used to measure the circumference of the thighs 5 cm and 10 cm below the gluteal fold and the circumference of the abdomen 5 cm

and 10 cm below the navel [14]. Photographs were taken to determine the difference or the improvement in the cellulite before and after the treatment. In all instances, the distance from the camera to the object was 150 cm, and the photographs were taken using the same location, background, and lighting.

All the measurements and the photographs were compared before (T-0) and after the treatment (T-84). Statistical analysis used the numeric scale paired *t*-test for the before and after comparison of the photographs and the abdominal and thigh circumferences. An alpha level of 5% ($p < 0.05$) was considered significant.

3. Results and Discussion

None of the 30 volunteers showed any signs of irritation in the irritation test except prospective volunteer #18. She expressed a sense of warmth in the area immediately after the first application (30-minute session), which might be due to itchiness she experienced following shrimp consumption. The volunteer stated that she wished to remain in the study when asked if she wished to continue, and she completed all the irritation test sessions.

The statistical evaluation of the photographic data showed no correlation between the before and after treatment (significance value, 0.460; $p > 0.05$). However, the paired *t*-test analysis showed significant differences between the before and after treatment ($p < 0.000$), with more than 75% of the volunteers reporting an improvement in their cellulite [16] (Table 1).

Twenty-three volunteers reported an improvement in their cellulite after 84 days of treatment. Their cellulite were improved at one level, two volunteers (6.67%) moved from grade 3 to grade 2 cellulite [A]), 13 (43.33%) moved from grade 2 to grade 1 [B], and 8 (26.67%) moved from grade 1 to grade 0 [C] (Fig. 1).

The improvement of the cellulite in the volunteers points to the efficacy of the trial cream preparation, although the potential contribution of the massage factor in the application cannot be ruled out. Massage can help reduce the appearance of cellulite because circular motion while massaging at normal force can move the interstitial fluid and expedite lymphatic flow. Although short-term treatment can move the fluid, only long-term treatment can improve the condition under the skin (subcutaneous area) [2].

Table 1. Statistical Analysis of the Photographic Data

Result	Mean	SD	SE	<i>p</i> value	N
Before treatment	3.43	0.73	0.13	0.460	30
After treatment	1.96	1.16	0.21		
Paired t-test	1.46	1.28	0.23	0.000	

Maquart *et al.* showed that the topical application of gotu kola extract could stimulate collagen synthesis in their research with outer human fibroblast monolayer culture-tissue [17]. Bonte *et al.* continued this research with human skin fibroblast type I collagen *in vitro* and proved that asiaticoside could accelerate the secretion of type I collagen [18].

The current study had more than a 75% success rate. It demonstrates that the combination of PLE (7%) and GCBE (0.2%) is effective from descriptive data and photographs in reducing the appearance of cellulite. The stimulation of the development of type I collagen and the viscoelasticity of the skin by gotu kola could, in theory, explain the reduced appearance of "orange peel," the reduction in skin dimpling, and smoother skin [16].

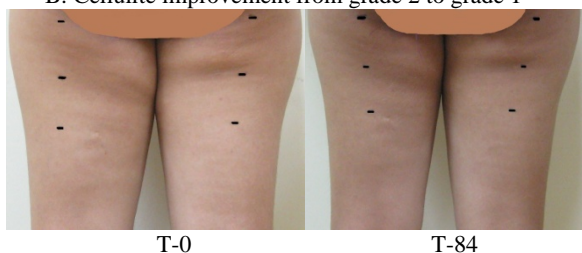
The first sets of measurements (T-0, before the treatment) of the circumference of the abdomen and the thighs and the last sets (T-84, 84 days after the treatment) were compared to determine their statistical significance (Table 2).

The cream can be viewed as a success based on the volunteers' observations of their cellulite and the photographic evidence. However, it is less successful when considered in relation to the reduction in their

A. Cellulite improvement from grade 3 to grade 2



B. Cellulite improvement from grade 2 to grade 1



C. Cellulite improvement from grade 1 to grade 0



Figure 1. Photographs Showing the Improvement in the Cellulite Before (T-0) and After (T-84) the Treatment

Table 2. Statistical Analysis of Circumference of the Abdomen and Thighs

Result	Mean	SD	SE	<i>p</i> value	N
*Abdominal circ.					
Before	86.8	6.92	0.89	0.000	60
After	85.7	6.08	0.78		
Paired <i>t</i> -test	1.14	3.46	0.45	0.013	
*Thigh circ.					
Before	51.1	4.66	0.60	0.000	60
After	50.9	4.56	0.59		
Paired <i>t</i> -test	0.13	1.47	0.19	0.512	

*circ. = circumference

abdominal and thigh circumferences, a factor indicative of an overall improvement in the condition of the cellulite.

Reducing calorie intake was an exclusion criterion for this study. Thus, this research is less bias, but it makes volunteers less obey the standard diet (three time meals a day). Only 15 of the volunteers (50%) showed a reduction in their abdominal circumference without any negative outcome (increased size) [16]. The reduction was established by reported looseness of their clothes or pants. However, in relation to the circumference of the thighs, less than (5) 25% of the volunteers felt these areas were slimmer.

Escudier *et al.* stated that the success of topical slimming product depends on regular dietary habits (without any reduction of calorie intake) [19]. In their study of a slimming cream treatment preparation, they recorded the volunteers' eating habits and advised them how to eat healthily. They reported a reduction in the circumference of the volunteers' thighs and an improvement in the appearance of the cellulite in one month.

4. Conclusions

Based on the photographic evidence and the statistical evaluation, we conclude that the combination of 7% PLE and 0.2% GCBE cream preparation reduced the appearance of the cellulite, with significant differences observed between the before and after treatment.

The results for the secondary outcome, a reduction in the circumference of the abdomen and thighs, were not as good as expected, with the former showing a reduction, but the latter not showing a similar decrease. A total of 50% of the volunteers felt slimmer in the abdominal area, which was established by the looseness of their clothes or their pants, but they did not feel the same with regards to their thighs. This finding can be

explained by the volunteers not adhering to a balanced nutrition program in their diet. This was consistent with the exclusion criterion to ensure the outcomes were not biased by diet or strenuous exercise.

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