

A two-center, double-blinded, randomized trial testing the tolerability and efficacy of a novel therapeutic agent for cellulite reduction

Jaggi Rao,¹ Michael H Gold² & Mitchel P Goldman¹

¹Dermatology/Cosmetic Laser Associates of La Jolla, Inc., La Jolla, California

²Gold Skin Care Center, Nashville, Tennessee

Summary

Introduction Cellulite is the unsightly dimpling and nodularity found on the thighs and buttocks of many postadolescent women. Unfortunately, poor understanding of its pathophysiology coupled with very few scientifically based studies have left us with limited treatment options that are tolerable and effective.

Purpose To review current concepts of the etiology and nature of cellulite and summarize available treatment options. To evaluate a novel, pathophysiologically based, topical agent for treatment.

Materials and methods A total of 40 women with a moderate degree of cellulite (20 from each of the two research centers) entered a double-blinded, randomized trial where an anticellulite cream was applied on a nightly basis to the affected sites for four continuous weeks. Each subject was randomized to receive active cream on either the right or left leg, with the contralateral side serving as placebo control. Bioceramic-coated neoprene shorts were worn overnight to enhance penetration of the topical agents by occlusion. High-quality digital photography was taken before treatment and after 4 weeks, with tangential full-spectrum lighting. Five blinded, independent physician reviewers assessed the photographs for improvement. Subject questionnaires were completed to assess tolerability and efficacy.

Results Of the 34 subjects who completed the study, 62% (21/34) noticed an overall improvement in their cellulite, with 62% (13/21) reporting greater improvement in the thigh that received active product. All 34 subjects found the shorts and creams easy and pleasant to use. Overall, the average measured decrease in thigh circumference was 1.9 cm (range: 0.1–4.5) with active product, and 1.3 cm (range: 0.1–3.0) with placebo. Upon review of the pre- and poststudy photographs, dermatologist evaluators found thighs treated with active product showed greater improvement than thighs treated with placebo in 68% of subjects.

Conclusions The active topical agent used in this study was found to be effective in reducing the appearance of cellulite. All subjects tolerated the formulation well with no adverse effects. The success of this research validates the pathophysiologic concepts used to formulate the topical compound. This study both increases our understanding of the nature of cellulite and establishes a tolerable, effective product to treat it.

Keywords: cellulite, topical agent

Correspondence: Mitchel P. Goldman, MD, Dermatology/Cosmetic Laser Associates of La Jolla, Inc. 7630 Fay Avenue, La Jolla, California, 92037.
E-mail: mgoldman@spamd.com

Accepted for publication April 29, 2005

Introduction

Historically a sign of beauty and wealth, the presence of cellulite is now considered aesthetically objectionable. Cellulite is the unsightly skin dimpling frequently seen on the thighs and buttocks of women, regardless of body shape and size. It is estimated that 85% of women over age 20 have some degree of cellulite.¹⁻³ Tremendous resources and effort are continually being directed to develop topical agents, internal supplements, exercise and diet programs, massage, and even surgery to cure this problem. The degree to which any of these remedies is effective in cellulite clearance or reduction remains questionable.

The pathophysiology of cellulite is poorly understood, and a literature review demonstrates a paucity of studies to scientifically validate currently popular treatments.

This article describes the evaluation of a novel topical agent specifically designed to reduce cellulite. As well, a thorough review of the literature is presented, summarizing current concepts of the origin and nature of cellulite and available therapeutic options.

Materials and methods

Twenty healthy adult women with moderate to severe cellulite (cellulite score of at least II out of IV) were selected for enrolment at each of the two sites after assessment by a physician investigator. This was performed against a solid black background and tangential full spectrum lighting delivered from the Verilux Happy Lite™ system (Verilux Inc, Stamford, Connecticut) without additional ambient lighting. The tangential lighting system was always positioned 2 feet from the subject, parallel to the backdrop at the level of the subject's knees.

Exclusion criteria included:

- treatment for cellulite of the thighs within 1 month of the study period;
- history of deep vein thrombosis within the past 2 years;
- history of congestive heart failure;
- occlusive arterial disease of the legs;
- pregnant or lactating women;
- history of topical medication usage (especially corticosteroids) within 2 weeks of the study period;
- history of allergic contact dermatitis to any component of the bioceramic-coated neoprene garment.

Upon enrollment, consent forms, bill of rights for medical subjects, photography release forms, and the Health Insurance Portability and Accountability Act (HIPAA) were reviewed and signed. High-quality color digital photographs were then taken of the posterior and lateral thighs by an investigator trained to use the Fuji S1 Twinflash™

Camera system (Canfield Inc, Fairmont, New Jersey). All photos were taken in the same room and utilizing the same methodology as described during the physician assessment. Three photos were taken at the following angles:

- | | |
|----------------------|---------------------|
| (a) 90° right thigh | (e) 90° left thigh |
| (b) 45° right thigh | (f) 45° left thigh |
| (c) 180° right thigh | (g) 180° left thigh |
| (d) 90° both thighs | |

Thigh circumference measurements were then taken of both legs at 18 cm and 26 cm from the superior pole of the patella for the lower and upper thigh, respectively, using a flexible measuring ruler.

After all data were collected, the subject was fitted with appropriately sized bioceramic-coated neoprene shorts. Subjects were previously randomized to have either the right leg or the left leg treated by the active agent, a specifically designed anticellulite cream (Spa MD Anti-Cellulite Cream™, La Jolla, California) and placebo cream for the contralateral leg. Subjects were blinded as to which cream, either active or placebo, they received, as containers were stripped of all labels and marked randomly as either "A" or "B". The quantities of creams dispensed to each subject were two 60-g tubes of anticellulite cream and two 60-g tubes of placebo. Patients were instructed to apply the appropriate cream to the posterior and lateral aspects of the corresponding thighs from the level of the knee to the buttock on a daily basis. The bioceramic neoprene shorts were to be worn immediately after application of the creams for at least 6 h (ideally while the subject slept). Figure 1 illustrates an example of how the garment appears when worn correctly. Treatment duration was 4 weeks. All unused active product and placebo creams were returned at the follow-up visit to ensure subject compliance.

At the 4-week follow-up, inclusion and exclusion criteria were reviewed to ensure continued enrollment. Each subject was then asked to complete a self-evaluation survey and give feedback regarding their experiences with the creams and shorts. Subjects were also asked to comment on the ease of use and tolerability of the creams and shorts. High-quality digital photography and thigh circumference measurements were taken using the same protocol as the baseline photography and measurements (see Figures 2 and 3).

All photographs were compiled and reviewed by five blinded, independent board-certified dermatologists. The evaluators were shown two pairs of photos for each subject: (1) pre- and post-treatment photographs of a subject's right thigh, and (2) pre- and post-treatment photographs of the same subject's left thigh, blinded to which side received active vs. placebo cream. After close



Figure 1 The bioceramic-coated neoprene shorts, worn after topical application to the posterior and lateral thighs to provide greater penetration into the skin by occlusion.

inspection, the evaluators then determined which thigh, the left or the right, showed greater improvement in cellulite.

All results were tabulated and analyzed.

Results

Thirty-four of the 40 enrolled subjects completed the 4-week study, and were compliant with the study methodology. Subjects ranged in age from 26 to 74 years (mean 49 years). At the La Jolla site, one patient withdrew from the study because of an unrelated yeast infection, and one was lost to follow-up. At the Nashville site, four patients were lost to follow-up. Table 1 summarizes the results of subject questionnaires. Of the subjects who completed the study, 62% (21 out of 34) noticed an overall improvement in cellulite. Of the 21 subjects that noticed an improvement in cellulite, 62% (13 out of 21) reported a greater improvement on the leg that received active product. The remaining 38% (8 out of 21) reported an equal degree of improvement in both legs.

All 34 subjects who completed the study found the shorts and creams easy to use. These subjects all reported having enjoyed using both the placebo and anticellulite cream. Many found both to have a softening and smoothening effect and appealing fragrance. In general, subjects were unable to determine the difference between active product and placebo based on the characteristics of the agents themselves. Some subjects reported the bioceramic-coated neoprene shorts to have generated warmth. Most enjoyed this warm sensation, while the others found it somewhat uncomfortable. At the conclusion of the study, many subjects elected to continue to use the anticellulite cream and occlusive shorts on a regular basis.

Thigh circumference measurements and analyses are presented in Table 2. Of subjects who completed the study, thigh circumference measurements decreased in 74% (25 out of 34) treated with active product, and in 56% (19 out of 34) who received placebo. The average decrease in circumference of the lower thigh treated with



Figure 2 Photographs taken (a) immediately before and (b) 4 weeks after daily use of the anticellulite cream with occlusion by a bioceramic-coated neoprene garment.

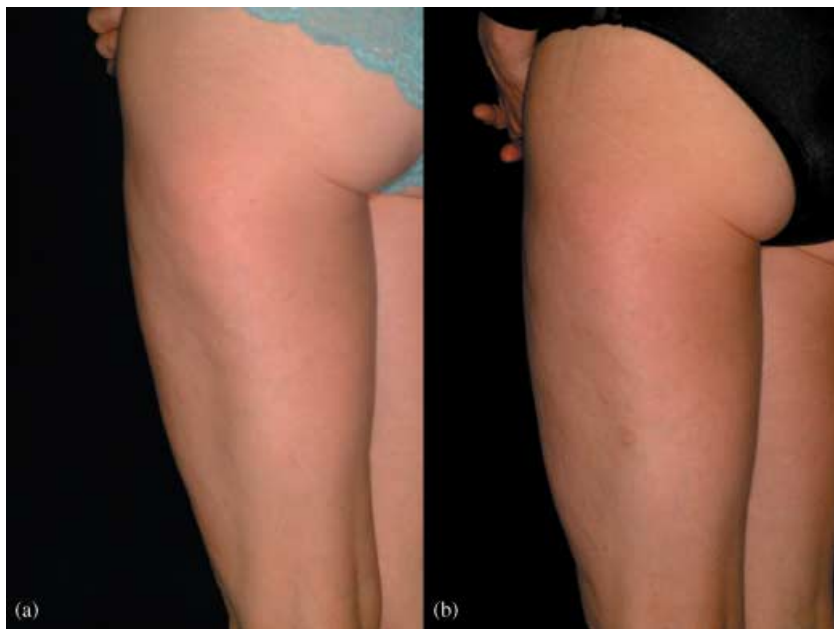


Figure 3 Photographs taken (a) immediately before and (b) 4 weeks after daily use of the anticellulite cream with occlusion by a bioceramic-coated neoprene garment.

active product was 2.08 cm (range: 0.1–3.5), and 1.04 cm (range: 0.1–2.5) treated with placebo. The average decrease in circumference of the upper thigh treated with active product was 1.78 cm (range: 0.1–4.5), and 1.50 cm (range: 0.3–3.0) treated with placebo. Overall, the average measured decrease in thigh circumference was 1.93 cm (range: 0.1–4.5) with active product and 1.27 cm (range: 0.1–3.0) with placebo.

Table 3 summarizes the results of the pre- and post-study photographic evaluations by five blinded, independent board-certified dermatologists. Overall, improvement in cellulite was seen in legs treated with active product in 68% of subjects. Standard deviation in scoring between evaluators was 0.89 at the La Jolla site and 1.14 at the Nashville site, indicating close correlation of scores.

Discussion

Definition and nature of cellulite

The term “cellulite” is used in modern times to describe the dimpled or puckered skin of the posterior and lateral thighs and buttocks seen in many trim and overweight women. The appearance is often described to resemble the surface of an orange peel or that of cottage cheese. The condition is best described by Goldman as a normal physiologic state in postadolescent women, which maximizes adipose retention to ensure adequate caloric availability for pregnancy and lactation.⁴ Adipose tissue is also essential for nutrition, energy, support, protec-

tion, and thermal insulation.⁵ At the histological level, cellulite is the result of localized adipose deposits and edema within the subcutaneous tissue. In women, longitudinal fibers of connective tissue fascia segregate fat into channels resembling a *down quilt*. As the fat layer expands, the perpendicular connective tissue remains fixed, creating a superficial puckered appearance of the skin.^{5–8} This skin dimpling is rarely found in men as the connective tissue in males is arranged in a criss-crossing pattern that is gender-typical for the skin of the thighs and buttocks.^{5,7}

Predisposing factors

There are many predisposing factors that contribute to cellulite development. These include:

- gender: because of the underlying structure of fat and connective tissue described previously, women are more likely to develop cellulite;
- heredity: empirically, it has been found that the degree and presence of cellulite, as with body habitus, is often similar between females within the same family;
- race: Caucasian women are more likely to develop cellulite than Asian or African American women;⁹
- increased subcutaneous fat: because of the unique histology of skin with cellulite, it is evident that greater adipose tissue in the subcutaneous layer enhances the appearance of cellulite on the skin surface;¹⁰
- age: women begin to develop cellulite after puberty as part of normal anatomical and physiological development.

Table 1 Study results based on subject questionnaires.

A) La Jolla site

-
- 72% (13 out of 18) of patients noticed an overall improvement in cellulite
 - 62% (8 out of 13) of patients who noticed an improvement in cellulite reported a greater improvement on the leg that received active product
 - 38% (5 out of 13) of patients noticed the same amount of improvement in the leg treated with active product compared with the placebo-treated leg
 - 100% (18 out of 18) of patients reported to have enjoyed using the anticellulite cream
-

B) Nashville site

-
- 50% (8 out of 16) of patients noticed an overall improvement in cellulite
 - 62% (5 out of 8) of patients who noticed an improvement in cellulite reported a greater improvement on the leg that received active product
 - 38% (3 out of 8) of patients noticed the same amount of improvement in the leg treated with active product compared with the placebo-treated leg
 - 100% (16 out of 16) of patients reported to have enjoyed using the anticellulite cream
-

C) Combined data

-
- 62% (21 out of 34) of patients noticed an overall improvement in cellulite
 - 62% (13 out of 21) of patients who noticed an improvement in cellulite reported a greater improvement on the leg that received active product
 - 38% (8 out of 21) of patients noticed the same amount of improvement in the leg treated with active product compared with the placebo-treated leg
 - 100% (34 out of 34) of patients reported to have enjoyed using the anticellulite cream
-

Unfortunately, these predisposing factors are difficult if not impossible to alter, thus cellulite prevention is currently not attainable. However, based on our understanding of the etiology and nature of this condition, several treatment modalities have been developed.

Pathophysiology of cellulite

Hormones, specifically estrogens and androgens, are thought to influence the formation of cellulite. Estrogen is known to stimulate lipogenesis and inhibit lipolysis, resulting in adipocyte hypertrophy.⁹ This may explain the onset of cellulite at puberty, the condition being more prevalent in females, and the exacerbation of cellulite with

pregnancy, nursing, menstruation, and estrogen therapy (oral contraceptive use and hormone replacement).⁹ The opposite seems true for men. From the limited number of studies involving men, it is hypothesized that the combination of gender-specific soft tissue histology at the cellulite-prone anatomic sites, with a relatively lower circulating estrogen level, may be responsible for the lower incidence of cellulite in males.^{10,11} It may be that circulating androgens have an inhibitory effect on cellulite development by contributing to a different pattern of adipose tissue storage (that is, more truncal than on the buttocks and thighs). As such, regulation of hormone levels may help to minimize the appearance of cellulite. Unfortunately, this treatment option may result in adverse physiological and anatomical sequelae, and has therefore not been widely employed.

Adipose tissue is very vascular, leading to the theory that cellulite may develop in predisposed areas when circulation and lymphatic drainage have been decreased, possibly caused by local injury or inflammation. It is known that in response to impairment of microvascular circulation, there is increased microedema within the subcutaneous fat layer, causing further stress on surrounding connective tissue fibers and accentuation of skin irregularities.^{2,4} Many of the currently accepted cellulite therapies target deficiencies in lymphatic drainage and microvascular circulation.

Evaluation of cellulite

There is a broad spectrum of tools available to evaluate cellulite, ranging from simple observation to tissue biopsy. Such methods include:

- **observation:** this involves direct or photographic visualization of skin irregularities such as puckering, dimpling, and nodularities. Observation is best performed in a dark room with tangential lighting to create shadows that represent even subtle surface elevations and depressions. Gently squeezing the skin under these lighting conditions may accentuate less apparent tethering of the skin.
- **weight or body mass index (BMI; weight in kilograms divided by height in meters, squared):** this is a generalized estimate of body composition used to assess obesity based on a population average.⁹ BMI is not an effective evaluative tool for cellulite as it does not correlate to either cellulite content or distribution.
- **thigh circumference:** the measure of thigh circumference at set points with a flexible ruler can give an indirect measurement of localized fat and possibly cellulite related to this. Unfortunately, changes in thigh circumference may be as a result of a host of other factors, including edema from congestive heart disease, trauma

Table 2 Changes in thigh circumference following a continuous 4-week application of a specifically designed anticellulite cream vs. placebo.*
A) La Jolla site

Subject	With active cream		With placebo	
	Lower thigh (cm)	Upper thigh (cm)	Lower thigh (cm)	Upper thigh (cm)
1	None†	None	None	None
2	-3.3	-1.3	-0.4	-0.3
3	-3.5	-1.5	-0.1	-1.0
4	Patients did not complete study			
5	None	None	None	None
6	None	None	None	None
7	-0.1	-0.4	None	None
8	-0.5	-0.1	None	None
9	-1.8	-2.4	-0.5	-0.8
10	None	None	None	None
11	Patient did not complete study			
12	None	None	None	None
13	-3.0	-4.5	-1.5	-1.0
14	-1.6	-3.5	-0.5	-3.0
15	-2.4	-1.8	-0.2	-0.4
16	None	None	None	None
17	-1.2	-0.9	None	None
18	-2.8	-1.8	-0.5	-0.9
19	-2.5	-3.3	-1.2	-1.5
20	-0.3	-2.7	None	None
Average	-1.92	-2.02	-0.61	-1.11

*Recordings were taken at 18 cm and 26 cm above the superior pole of the patella for lower and upper thigh measurements, respectively. All creams were administered under occlusion.

†No reduction in thigh circumference was noted.

B) Nashville site

Subject	With active cream		With placebo	
	Lower thigh (cm)	Upper thigh (cm)	Lower thigh (cm)	Upper thigh (cm)
1	Patient did not complete study			
2	-1.9	-2.5	-1.3	None†
3	-3.8	-1.9	None	None
4	-1.9	-1.3	-1.3	None
5	-1.9	-2.5	None	None
6	Patient did not complete study			
7	-0.6	None	-0.6	None
8	-2.5	-0.6	-1.3	-2.5
9	-2.5	-1.3	-2.5	-2.5
10	-3.2	-1.9	None	-1.3
11	-1.9	None	-2.5	None
12	-1.3	None	-1.3	None
13	None	None	-1.9	-1.9
14	Patient did not complete study			
15	Patient did not complete study			
16	None	None	-1.3	-2.5
17	None	-0.6	None	-1.3
18	-3.2	None	None	None
19	None	-1.3	-0.6	-1.3
20	None	None	None	None
Average	-2.24	-1.54	-1.46	-1.90

*Recordings were taken at 18 cm and 26 cm above the superior pole of the patella for lower and upper thigh measurements, respectively. All creams were administered under occlusion.

†No reduction in thigh circumference was noted.

Table 2 Continued.

C) Combined data

	With active cream		With placebo	
	Lower thigh (cm)	Upper thigh (cm)	Lower thigh (cm)	Upper thigh (cm)
La Jolla site	-1.92	-2.02	-0.61	-1.11
Nashville site	-2.24	-1.54	-1.46	-1.90
Average	-2.08	-1.78	-1.04	-1.50
Overall average	-1.93		-1.27	

Table 3 Visual improvement of cellulite after 4 weeks of active product vs. placebo, as observed by blinded, independent dermatologist evaluators.

A) La Jolla site

Evaluator	Number of subjects showing greater improvement with active product
1	13/18 (72%)
2	14/18 (78%)
3	13/18 (72%)
4	15/18 (83%)
5	13/18 (72%)
Average	13.6/18 (76%), STD = 0.89

B) Nashville site

Evaluator	Number of subjects showing greater improvement with active product
1	8/16 (50%)
2	10/16 (62%)
3	11/16 (69%)
4	9/16 (56%)
5	9/16 (56%)
Average	9.4/16 (59%), STD = 1.14

C) Combined data

Site	Number of subjects showing greater improvement with active product
La Jolla	13.6/18 (76%)
Nashville	19.4/16 (59%)
Overall	23/34 (68%)

Table 4 Cellulite classification.

Grade I	No or minimal cellulite based on observation when standing, the pinch test, or gluteal muscle contraction.
Grade II	Irregular skin topography upon observation. Cellulite is enhanced by pinching or gluteal contraction. Subjects may have skin pallor or decreased temperature and sensation.
Grade III	Skin exhibits the classic orange peel dimpling, "peau d'orange," at rest. Small subcutaneous nodularities may be palpated.
Grade IV	In addition to the characteristics described above there is more severe puckering and palpable nodules.

or lymphatic impairment, and inflammation from various conditions and external sources. Also, thigh circumference may vary rapidly with activity and exercise, resulting in varying measurements between evaluation sessions.

- skin elasticity: measurement of skin tension with a suction elastometer can give an estimate of the resilience of the dermis, a function of connective tissue helping to gauge the amount of cellulite present. In theory, this tool may be plausible, but to date, clinically useful results remain to be seen;
- electrical conductivity: this is used to measure tissue resistance to electron flow and determine specific percentages of body composition (lean mass, fat mass, water).⁹ Whether cellulite content affects these measurements also remains to be seen;
- tissue analysis from a deep skin biopsy of affected areas: this method is the most specific modality to determine the presence of cellulite histologically. However, even though tested tissue may have the microscopic characteristics of cellulite, the clinical appearance may not correlate with this. Conversely, clinically present cellulite may reveal the histology of normal skin.

Of all these methods to examine cellulite, observation with tangential lighting, and anthropometric measurements are the most common because of their fair reproducibility, relative accuracy, ease, and cost effectiveness.

Classification

To accentuate cellulite dimpling in an effort to classify the degree of severity, it is best to gently pinch an area of

tissue between the fingers and the thumb. For larger areas, the skin of the thigh can be compressed between two hands. This is referred to as the *mattress phenomenon* as the dimpled pinched skin resembles a bed mattress. Cellulite may be graded for severity on a scale of I to IV (see Table 4).^{4,9,12}

Management

There is currently no cure or gold standard for treatment of cellulite. This is due in part to the minimal understanding of cellulite pathophysiology and poor therapeutic effectiveness of most treatment modalities. Therapeutic options to manage cellulite can be characterized as conservative measures, topical treatment, systemic agents, and physical modalities.

Conservative management includes the adoption of a healthy lifestyle. Unfortunately, there is little evidence to support dramatic cellulite reduction with the combination of diet and regular exercise. Diet and exercise cannot alter the histological structure of the perpendicular bands connecting the skin to the underlying fascia and thus cannot eliminate cellulite in its entirety. However, these lifestyle modifications may assist in reducing the appearance of cellulite by decreasing adipocyte volume, thus placing less tension on surrounding connective tissue, resulting in decreased skin puckering.

Topical management consists of gels, ointments, foams, creams, and lotions, all aimed to deliver active product to the skin to reduce the appearance of cellulite. Most active ingredients, including antioxidants and vasodilators, are included to increase microvascular flow and lymphatic drainage, which is thought to play a role in cellulite pathogenesis. Other agents may promote lipolysis, with the goal of reducing the size and volume of adipocytes, thereby decreasing tension on surrounding connective tissue and decreasing the clinical appearance of puckering. Some topical ingredients, such as vitamin C, may help by stabilizing collagen and/or stimulating collagen deposition.^{3,4,9} Topical retinoic acid and related vitamin A derivatives have been used to stimulate circulation, decrease the size of adipocytes, and increase collagen deposition in the dermis.^{9,13} In reality, however, vitamin A derivatives have not provided an ultimate solution to reduce the unshapely appearance of cellulite.

Systemic therapy in the form of hormonal manipulation is not a popular treatment option because of its many potential adverse effects. This may include the avoidance of oral contraceptives and hormone replacement in females and the maintenance of proper androgen levels in males. The opposite situation has been shown to be associated with the presence of relatively more cellulite.^{10,11} An even more aggressive systemic treatment option is the direct injection

of pharmacologic agents into the venous circulation, or local infiltration into the dermal-subcutaneous junction of the skin. This is referred to as *intradermotherapy* or *mesotherapy*, and reduces cellulite through lipolysis of fat or size reduction of adipocytes.⁹ Studies to demonstrate the safety and efficacy of this therapeutic modality have yet to be published.

Physical therapies vary widely from noninvasive modalities such as Endermologie® (LPG Systems, Valence, France) to surgical procedures including deep subcision and liposculpture. Endermologie® is a French-designed form of deep-tissue massage that the United States Food and Drug Administration (FDA) has approved to diminish the appearance of cellulite. During the massage, suction is used to pull the skin into a handheld machine where the skin is compressed and rolled to increase blood and lymphatic flow and to modify the underlying connective tissue.² This therapy is performed in a series of 30–45-min sessions over a period of months. The cellulite-minimizing effect of all forms of deep-tissue massage is temporary and therapy must be continued to maintain results.

A new laser device recently approved by the FDA combines variable rhythmic suction with superficial cooling and a low intensity 808-nm diode laser pulsation to treat cellulite. This technology, labeled Triactive™ (Cynosure, Chelmsford, Massachusetts) was designed to increase lymphatic drainage, tighten the skin by stimulating underlying muscles and fascia, and increase superficial blood flow, thereby reducing the appearance of cellulite. Treatment regimen mimics that of Endermologie®, with greater emphasis directed toward the proposed microcirculation impairment theory of cellulite formation. Although Triactive™ has been proven safe and easy to use, its efficacy in treating cellulite remains to be seen, as research is ongoing.

Subcision is a simple surgical procedure that has been noted to improve moderate to severe cellulite.¹² With the use of local anesthesia, this technique is performed by inserting a notched catheter (such as a Nokor™ needle) into the subcutaneous layer of the skin. The catheter is then manually moved in a repetitive motion parallel to the surface to physically break the connective tissue adhesions that tether the dermis to muscular fascia. Upon rupture of these adhesions, the tethering effect is diminished and cellulite improved. Although reported successful, it is unclear if these beneficial results are long-term, and if not, how long remission time lasts.

Liposculpture involves the removal of local adipose tissue deposits to achieve a greater aesthetic body contour. Performed under general or local tumescent anesthesia, this surgery uses a small tip suction cannula to remove fat from unwanted areas, without altering other skin tissues. Adipose tissue is most commonly extracted from the thighs, buttocks, abdomen, back, face, neck, and arms. Liposculpture

may decrease the appearance of cellulite by reducing local fat volume and by disrupting the fibrous bands that cause the dimpling appearance of the skin surface. The procedure will not, however, permanently eliminate cellulite. It is possible that a combination of liposculpture with other modalities such as Triactive™ may work in synergy to prolong the effects of cellulite reduction. Studies are currently being conducted to verify this hypothesis.

The present study

With the paucity of research that currently exists to aid our understanding of cellulite and its treatment, this study evaluates a novel topical agent specifically designed to remedy the most correctable pathophysiologic mechanism of the condition.

Based on the concept of microcirculatory and lymphatic impairment outlined in this review, an anticellulite cream was formulated. Table 5 lists the active ingredients of this formulation according to their proposed mechanism of action. In contrast, the placebo cream contained vehicle only, and notably lacked these active ingredients. It is likely that the active agents act through vasodilation of capillaries and microlymphatics. Caffeine may work through a variety of mechanisms including the improvement of vascular and lymphatic flow through vasodilation, as well as by lipolysis. The combination of mechanisms of caffeine may be responsible for noted decreases in thigh circumference.¹⁴ The bioceramic-coated neoprene garments were designed to offer maximal occlusion against the skin even during motion. Warmth and external pressure from wearing the garment likely improves absorption, which allows the anticellulite cream to penetrate the dermis, thereby improving efficacy. A tangential lighting system was employed using full-spectrum white lights to accentuate cellulite-related elevations and dimples on the skin surface, without color distortion. Standardization of photography was employed to maximize reproducibility

Table 5 Proposed active ingredients of the anticellulite cream used in this study.

Stimulation of lymphatic and microvascular flow

- *Piper nigrum* (black pepper) seed extract
- *Citrus aurantium dulcis* (sweet orange) peel
- *Zingiber officinale* (ginger) root extract
- *Camellia sinesis* (green tea) extract
- *Cinnamomum cassia* (cinnamon) bark extract
- *Capsicum annum* resin
- Caffeine

Lipolysis of adipose tissue

- Caffeine
-

of picture brightness and clarity, as well as anatomic positioning of the subject.

The results demonstrate that the anticellulite cream is indeed effective and tolerable, both subjectively and objectively (see Tables 1–3). This study was designed to have each subject serve as her own internal control. If daily weight or fluid changes occurred, it would likely affect the active cream group and the placebo cream group equally. Possible sources of error in this study include inter- and intrauser variability in thigh measurements to establish pre- and post-treatment thigh circumference. In addition, daily fluctuations in subcutaneous fluid may occur, contributing to a perceived change in thigh circumference, rather than by cellulite reduction. This study relies heavily upon subject compliance, both in terms of application of appropriate amount of cream to designated anatomic sites, as well as the judicious use of the occlusive garment as outlined in the study protocol. Any deviation or lack of consistency on the part of the subject in this regard may have affected study results. Other contributory factors to error are possible fluctuation of subject weight caused by changes in diet and exercise during the 4-week study. Also, each site utilized a different team of researchers to obtain thigh measurements. However, the same five dermatologists assessed all photographs. The use of photography, although of high quality, is not a perfect substitute for direct physical examination, a point that may contribute to variable scores between evaluators.

This study demonstrates that a topical agent based on current mechanistic knowledge of cellulite formation can be used to treat this unwanted condition. A study of longer duration and more subjects would be useful in establishing the long-term efficacy of this therapy. Perhaps an in-depth analysis of individual components of the cream may reveal that ingredients previously thought to be active are in fact not contributory to the anticellulite effect of the cream as a whole. Conversely, it is possible that the addition of new ingredients to the formulation may enhance the effect of the cream. Of note, the fact that improvement was subjectively and objectively demonstrated with placebo indicates that the occlusive garments not only assisted in drug delivery, but also independently served as a topical treatment for cellulite reduction.

Conclusion

With the proven tolerability and efficacy of this topical agent in improving cellulite, several implications are manifested. First, this formulation offers a valuable treatment option for a condition that has few effective therapeutic choices. Second, with this treatment based on the theory that

microcirculatory and lymphatic impairment is contributory to cellulite development, the success of this regimen validates the plausibility of this concept. As such, this study has helped strengthen our understanding of cellulite formation and maintenance, which remains one of the most common aesthetic concerns of women worldwide. Based on this and on future research, it is certain that improved treatment modalities will continue to evolve.

References

- 1 Draelos ZD, Marenus KD. Cellulite – etiology and purported treatment. *Dermatol Surg* 1997; **23**: 1177–81.
- 2 Cellulite meltdown. *Harvard Women's Health Watch* 1998; **5**: 7.
- 3 Sainio EL, Rantanen T, Kanerva L. Ingredients and safety of cellulite creams. *Europ J Derm* 2000; **10**: 596–603.
- 4 Goldman MP. Cellulite: a review of current treatments. *Cosmet Derm* 2002; **15**: 17–20.
- 5 Querleux B, Cornillon C, Jolivet O, Bittoun J. Anatomy and physiology of subcutaneous adipose tissue by in vivo magnetic resonance imaging and spectroscopy: relationships with sex and presence of cellulite. *Skin Res Technol* 2002; **8**: 118–24.
- 6 Another cellulite remedy. *Harvard Women's Health Watch* 1999; **6**: 7.
- 7 Piérard GE, Nizet JL, Piérard-Franchimont C. Cellulite: from standing fat herniation to hypodermal stretch marks. *Am J Dermatopathol* 2000; **22**: 34–47.
- 8 Pellicier F, Andre P, Schnebert S. The adipocyte in the history of slimming agents. *Pathol Biol* 2003; **51**: 244–7.
- 9 Rossi ABR, Vergnanini AL. Cellulite: a review. *J Eur Acad Dermatol Venereal* 2000; **14**: 251–62.
- 10 Nurnberger F, Muller G. So-called cellulite: an invented disease. *J Dermatol Surg Oncol* 1978; **4**: 221–9.
- 11 Rosenbaum M, Prieto V, Hellmer J *et al*. An exploratory investigation of the morphology and biochemistry of cellulite. *Plast Reconstr Surg* 1998; **101**: 1934–9.
- 12 Hexsel DM, Mazzuco R. Subcision: a treatment for cellulite. *Int J Derm* 2000; **39**: 539–44.
- 13 Kligman AM, Pagnoni A, Stoudemayer T. Topical retinol improves cellulite. *J Dermatol Treat* 1999; **10**: 119–25.
- 14 *Stedman's Medical Dictionary*, 26th edn. Baltimore: Williams & Wilkins; 1995: pp. 307.