

Cellulite treatment: a comprehensive literature review

Irene Zerini, MD, Andrea Sisti, MD, Roberto Cuomo, MD, Serena Ciappi, MD, Francesco Russo, MD, Cesare Brandi, MD, Carlo D'Aniello, MD, & Giuseppe Nisi, MD

Plastic Surgery Division, General and Specialist Surgery Department, University of Siena, Siena, Italy

Summary

An effective and long-term treatment of cellulite has not been well established. To our knowledge, no review has analyzed the whole range of treatments for this condition. We conducted a review of *in vivo* studies on humans adopting the key words “cellulite” and “treatment.” The studies were included according to eligibility criteria. We performed an analysis to estimate the overall effect of cellulite treatments from clinical studies. Medline library was screened up to December 2014 to identify eligible studies. We included 73 original studies in the present review. All of them were clinical studies, in most of them, only women were recruited. Above the studies searched up, 66 tested the effectiveness of an exclusive treatment performed without the association to other procedures: 11 topical agents, 10 shock-wave therapy, 10 radio frequency, eight laser therapy, five oral therapy, four manual massage therapy, three carbon dioxide therapy, two compressive therapy, two infrared therapy, one dermabrasion, and 11 devices that use an association of multiple treatments. Seven papers tested a combination of two or more treatments. The mean difference of clinical morphologic features and ultrastructural changes between the treated group and the controlled showed significant heterogeneity between studies. It is still difficult to indicate an exclusive and effective single treatment for this condition. Our analysis purposed to obtain a complete overview of the available treatments in cellulite reduction.

Keywords: cellulite, fatty tissue, elasticity

Introduction

Cellulite (also called “gynoid lipodystrophy,” “edematous fibrosclerotic panniculopathy,” or “local lipodystrophy”) is defined as a localized metabolic disorder of subcutaneous tissue that alters the local body shape leading to a unesthetic appearance of the skin called “orange peel” or “cottage cheese-like.”^{1,2}

Important to know, cellulite is to be distinguished from cellulitis, which is an inflammation of the adipose tissue. Cellulite affects 80–90% of all females.³ It is not considered as a pathological condition but as estheti-

cally disturbing dimpling of the skin seen most commonly on the thighs and buttocks.⁴ Macroscopically, cellulite is characterized by dimpling, visible either spontaneously or after provoking maneuvers.

The cause of cellulite is still a matter of debate. It is considered an endocrine-metabolic microcirculatory disorder that causes interstitial matrix alterations and structural changes in subcutaneous adipose tissue. However, its pathogenesis is not completely understood. Cellulite is a physiological phenomenon or at least, it has a physiological origin, which is characteristic of women, and multicausal, with the coexistence of a number of factors that trigger, perpetuate, or exacerbate it. The outstanding factors include, among others, connective tissue architecture, estrogen action, microvascular alterations, and certain genetic and hormonal characteristics.⁵ As regards the pathophysiological

Correspondence: Andrea Sisti, MD, Plastic Surgery Division, General and Specialist Surgery Department, University of Siena, Siena, Italy. E-mail: asisti6@gmail.com

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genesis of cellulite, it is considered that cellulite represents a condition in which fibrosis arises with the proliferation of fibroblasts around adipose cells in association with progressing peripheral circulatory failure and metabolic failure in normal tissue, thereby leading to progressively enhancing metabolic failure in adipose tissue and eventually to adipose tissue degeneration and advanced fibrosis in the surrounding tissues.⁶ A number of different classification systems have been used to categorize cellulite according to its clinical and histopathologic changes.^{7,8} Current classification system sorts the changes on a scale of four grades.⁹ There is a wide range of products and professional approaches (surgical or not) to treat cellulite.¹⁰ A variety of treatment options have evolved ranging from topical retinol to interstitial laser.^{1,2,11–22} Little scientific evidence exists to support any of the many advertised treatments for it. An efficacy testing of this variety of procedures is still missing, and there has been no large-scale study demonstrating their effectiveness.^{2,23,24}

To our knowledge, no systematic review and meta-analyses have been performed to examine the whole range of the treatments disposable.²⁵

The aim of this study was to evaluate and summarize the efficacy of all the treatments in cellulite reduction from published data in human studies using a systematic approach.^{6,7}

Materials and methods

A systematic literature review of the PubMed database was performed using the following key words: “cellulite,” “treatment.” Additional articles were selected reviewing the references of the papers identified using this algorithm. Inclusion criteria among these papers were as follows:

- Paper is a case study, case report, clinical trial, open-label prospective study, case series, retrospective study.
 - Cellulite was the primary aim of treatment.
 - Studies are *in vivo* on humans.
- Exclusion criteria were as follows:
- Paper is a review of literature.
 - The treatment is not specified, and it is impossible to deduce it from the text.
 - Articles have not specific outcome measures.

The entire PubMed database was considered, until December 2014. Both English and not-English language papers were included. No studies were excluded *a priori* because of weakness of design of data quality. Each article was tabulated as follows: authors, year of

the study, number of patients, age of patients (years), study design, type of treatment, duration and frequency of treatment, outcomes measures, post-treatment follow-up, outcomes, and adverse events. Disagreements of judgment were resolved by discussion between the review team members. All kinds of cellulite treatment were considered, including studies that used personal techniques. The publications were screened manually and reviewed to identify reports for cellulite treatment. Three investigators independently reviewed and extracted data from the papers according to the predetermined criteria.

Results

We found 233 references in PubMed. One hundred and sixty articles were excluded (Fig. 1). We finally collected 73 articles (Table 1), which satisfied our inclusion criteria: 70 were prospective studies, and 3 were retrospective studies. All of them were clinical studies.

The first study was published in 1997,²⁶ and most of the articles were published in the 2010–2013 period. Most of the studies recruited women only. The smallest trial²⁷ enrolled 1 patient, and the biggest one enrolled 272 541 subjects.²⁸ Most of the controlled trials included a placebo group or a control group. Most of the studies that reported information on age at

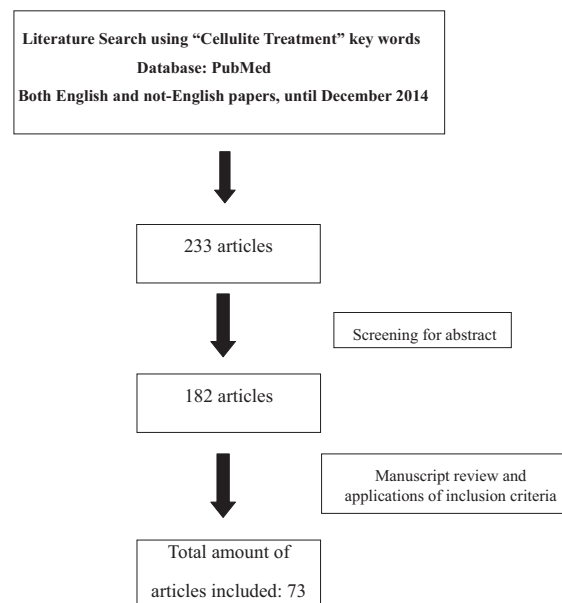


Figure 1 Flow diagram of study selection.

Table 1 Overview of studies on cellulite treatment

Author, year	Demographic data	Study design	Type of treatment	Duration and frequency of treatment	Outcome measures	Follow-up (post-treatment)	Outcomes (pt = patient, ps = patients)	Adverse events (pt = patient, ps = patients)
Epstein, 1997 ²⁶	11 women	Randomized study	Topical lipolytic agent	8 weeks	Photographs, weight, body measures	None	This study failed to support the efficacy of topically applied lipolytic creams in eliminating unwanted fat manifesting as a localized bulge or cellulite presenting as a dimpling of the skin	None
McDaniel, 1998 ²⁵	Three patients (36, 40 and 39 years)	Prospective pilot study	Roller massage therapy	16 treatments twice weekly (30 min each)	Photographs, high-resolution evaluation, infrared interferometry, body measures, objective blinded grading	3 months	Moderate softening of the skin and cellulite. Cellulite had improved in appearance (combined average improvement was found to be 57%)	Occasional small transient 1–2 cm blisters
Collis, 1999 ⁴⁶	52 women	Prospective randomized, controlled trial	Aminophylline cream and Endermologie	Twice-daily application of aminophylline cream and weekly treatment with Endermologie	Clinical examination Photographic assessment Ultrasound	None	The authors do not believe that either of these two treatments is superior to the other in the appearance of cellulite	None
Us-Balchin, 1999 ⁷	11 women	Placebo-controlled clinical study	Topical agent Containing Ginkgo biloba, sweet clover, seaweed, grape seed oil, lecithin and primrose oil	2 months	Body circumference measurements	None	Only three of the women in the treatment group thought that their cellulite had slightly improved against two women in the control group	None
Péard-Franchimont, 2000 ⁴⁸ Esot, 2000 ⁴⁹	15 women (26–44 years) 232 women (18–52 years)	Randomized study Retrospective study	Topical retinol agent Suction technique	6 months One stage	Biinstrumental evaluations Clinical assessment	None Up to more than 2 years	Seven of 11 treated women gained weight, as did 8 in the placebo-controlled group. The weight gain in both groups was apparent after the first 2 weeks Favorable results (78.87% of patients were satisfied)	None
Brandi, 2001 ⁷	48 female patients (24–51 years) mean age: 34 years	Prospective study	Carbon Dioxide Therapy	Two weekly subcutaneous applications of CO ₂ for three consecutive weeks (total of six sessions)	Circumference of the abdomen, thighs, and knees Laser Doppler examination Subcutaneous biopsies	3 months	The data regarding measurements of the maximum circumference of the thigh, knee, and abdomen, taken before and at the end of treatment, showed a significant reduction in all the sites. The dermis presented a thicker appearance than before treatment, with the collagenous fibers distributed more diffusely	Pain, bruise and hemoridrosis (almost all pts) Erythema (3% of patients) Crackling sensation beneath the skin, which was limited to the first hour of treatment (all pts) Slight hematomas which eventually disappeared, without leaving any scars (30% of patients) Pain at the site of injection (70% of pts), never so intense that gas administration had to be interrupted
Lairenta, 2001 ⁴⁰	25 women mean age 36.5 years Group 1: n = 6, 25–35 years Mean age group 2: 29.02 ± 7.11	Prospective nonrandomized two group study (EUAL external ultrasound assisted lipolysis+ endermologie), group 2 (only EUAL)	Endermologie	10 days for 20 weeks	Photographs, circumference measurements, and patient questionnaire	9 months	92% improvement in body contouring in group 1 and a mean 87% improvement in group 2	No significant complications
Bimbaun, 2001 ⁵¹	60 women (26–57 years) average age 40 years	Prospective randomized study	Herbal anticellulite pill	60 days	Skin appearance, digital photographs	None	Overall improvement in about 50% of patients	None
Bertin, 2001 ⁵²	46 women	Double-blind, randomized, placebo-controlled study	Topical agent contains retinol, caffeine, and ruscogénine	Twice a day for 3 months	Macro-relief of the skin, structure of the dermis and lipodermis, mechanical characteristics of the skin, firmometry of the skin periorum	None	Significantly active of the orange peel of the skin Significant improvement of the parameters	None

(continued)

Table 1 (Continued)

Author, year	Demographic data	Study design	Type of treatment	Duration and frequency of treatment	Outcome measures	Follow-up (post-treatment)	Outcomes (pt = patient, pts = patients)	Adverse events (pt = patient, pts = patients)
Brandl, 2004 ¹⁸	42 patients	Prospective comparative study	Group A: liposuction Group B: liposuction+CO ₂ therapy Group C: CO ₂ therapy alone	Group A: 1 stage Group B-C: Twice weekly for 10 weeks	Measurement of elasticity and circumference	3 months	The effect of CO ₂ therapy on skin elasticity was verified by treating group C with CO ₂ therapy alone and groups with both CO ₂ therapy and liposuction. The results show a statistically significant improvement with regard to skin elasticity in group C, confirming the positive effect of treatment with CO ₂ alone on skin elasticity. In the other two groups, the results showed no effect. A standard cellulite grading scale was used. The best outcome, in terms of skin elasticity, has been obtained by combining liposuction and CO ₂ therapy	Only minimal side effects were observed, and all were quickly resolved. Cradling sensation beneath the treatment area was reported in group C. Treatment and 25% of the patients had slight ecchymosis which disappeared without causing any esthetic damage (all pts). Pain at the area of injection, although frequently observed (50%), was of low pain intensity that gas administration had to be interrupted
Sadick, 2004 ¹³	35 women	Prospective two-center study	VealSmooth	From 8 to 16 treatments twice weekly	Circumference measures	4 weeks	100% of pts had some level of improvement in skin smoothing. The mean improvement was 2.3%, who showed "excellent" or "very good," 35% who showed "good," and 42% who showed "mild" improvement. Overall, 90% of the patients would recommend the treatment to their friends. Pre- and post-treatment photographs were analyzed by a blinded dermatologist who applied a standard cellulite grading score to the photographs and the unblinded analysis revealed an average 40% improvement in the cellulite score	Minimal discomfort and temporary swelling (small number of pts) were reported, which resolved within 72 h (two pts)
Rao, 2004 ¹⁴	20 women	Double-blinded, randomized trial	An anticellulite cream was applied to the affected sites on a nightly basis. Each subject was randomized to receive liposuction or no liposuction and to receive neoprene garment on either the right or left leg, with the contralateral side serving as a control with no occlusion	4 weeks	High-quality digital photography was taken before treatment and after 4 weeks at various angles, with tangential full-spectrum lighting. Four blinded, independent dermatologist photographs for improvement. Subjects completed questionnaire forms to assess tolerability and efficacy	None	Of the 17 subjects who completed the study, 76% noticed an overall improvement in their cellulite, with 54% reporting greater improvement in the thigh that average measured decrease in circumference of 1.3 cm reduction with occlusion and a 1.1 cm reduction without occlusion. Upon review of the pre- and poststudy photographs, the dermatologist evaluators found an improvement in the thigh circumference with occlusion and 59% of treated legs without occlusion. Further, the evaluators found the occluded thighs to show greater improvement than the nonoccluded thighs in 65% of subjects	None
Alter, 2005 ⁵⁴	20 women (25–57 years) mean age 48.1 years	Prospective study	Combination radiofrequency, infrared light, and mechanical suction-based massage device	Eight 30-min treatment sessions	Standardized digital photographs (two masked medical assessors and patients' evaluation); circumferential thigh measurements, body weight	6 months	All 20 pts noticed overall improvement in cellulite in the treated thigh/buttock regions based on subjective questionnaires. Slight diminution of clinical effect was noted at the three-and six-month follow-up evaluations. The average cellulite scores measured as Young modulus stiffness index increased significantly by SWT	Transient erythema in most patients (average duration <1 h). Pruning (two pts)
Siems, 2005 ⁹	26 women	Retrospective study	Shock-wave therapy (SWT)	2 weeks period with six sessions of shock-wave application each for 8 min	Oxidative stress parameters of blood serum, biomechanics of skin properties, expression of factors stimulating angiogenesis	None	None	None
Rao, 2005 ⁵⁶	40 women (26–74 years) mean age 49	Two-center, double-blinded, randomized trial	Anticellulite cream with biostratin-coated neoprene garment	4 weeks	Digital photographs	None	62% of pts noticed an overall improvement of cellulite	Uncomfortable wearing sensation of the shorts (some pts)

(continued)

Table 1 (Continued)

Author, year	Demographic data	Study design	Type of treatment	Duration and frequency of treatment	Outcome measures	Follow-up (post-treatment)	Outcomes (pt = patient, pts = patients)	Adverse events (pt = patient, pts = patients)
Distante, 2006 ⁵⁷	37 female mean age 37 ± 13 years	Prospective, longitudinal, double-blind designed study	A plant complex based on seed extracts of grape, Ginkgo biloba, Asiatic centella, ginseng, fish oil and boape oil administered orally	Two capsules per day for total of 47 days (only two capsules for the last day)	Videocapillaroscopy with digital image processing, ectography, photoplethysmography	None	Clinical–conographic assessment showed symptom improvement (i.e. edema and pain) in 71% of patients who had received the active treatment. Conographic assessment showed a decrease of all signs related to tissue edema in 70% of patients who had received the active treatment. The results show a considerably predictable and statistically significant improvement in the number of capillary loops, with a negative effect in the placebo cases	None
Noocheti, 2006 ⁵²	127 patients, (18–45 years) Average age 31.6 years	Prospective, longitudinal, double-blind designed study	Three products: group A consisted of bioisoprenols, polyphenols, fatty acids, Vitamin E, Ginkgo biloba, Ruscus, Melilotus, Centella, group B consisted of inert substances and group C consisted of bioflavonoids expressed as polyphenols, Resipracel, Ginkgo biloba, Ruscus, Melilotus, Centella and Fucus VelaSmooth system vs. TriActive system	Twice a week for 6 weeks	Photographs, circumference measurements	None	Although there was improvement in the reduction of cellulite for each device individually, there was no significant difference between VelaSmooth or TriActive devices in terms of reduction of high circumference, photographic evaluation, and perceived change in before and after photographic grading. There was a statistically significant increase in the incidence of post-treatment erythema with VelaSmooth compared to TriActive (68% of pts) Both groups showed an improvement in the smoothness of the affected area	Bruising (55% of pts) Bruising with VelaSmooth (seven pts) Bruising with TriActive (one pt)
Emilia del Pino, 2006 ⁵⁸ Finck, 2006 ¹¹	26 women (18–50 years) 20 women (23–56 years)	Prospective study Prospective pilot study	Unipolar radiofrequency Intense pulsed light and a retinyl-based cream	Two treatment session (15 days apart) 9–12 sessions (once weekly), 20–30 min. 12 treated with intense pulsed light and cream, eight treated only with cream Twice a week for 6 weeks	Skin architecture, photographs, and ultrasound Skin ultrasounds, photographs, clinical evaluation	15 days 8 months	Volumetric contraction effect in VelaSmooth compared to TriActive 68% of pts Most subjects reported an improvement of the skin treated	Small blisters (two pts) Ectchymosis (three pts) Minor hypopigmentation (resolved at end of study)
Angheem, 2007 ⁵⁹	21 female (20–60 years)	Prospective study	Low-energy defocused extracorporeal shock-wave therapy	Twice a week for 6 weeks	High-resolution ultrasound of the skin	6 months	Most subjects reported an improvement of the skin treated Five subjects reported a re-occurrence of cellulite	A few subjects reported that treatment was unacceptable because it caused some pain
Sadick, 2007 ⁶⁰	16 women	Prospective study	VelaSmooth system	Twice a week for 6 weeks	Circumferential measurements; independent evaluator grade Visual improvement	8 weeks	The overall high circumference decreased in 71.87% of the treated patients. The average was 0.44 cm of the lower thigh and 0.53 cm of the upper thigh. There was significant visual improvement in cellulite and skin texture. At the final follow-up visit, 50% of subjects had greater than 25% improvement	Redness (six pts) Transient discomfort (seven pts) Bruising (five pts)

(continued)

Table 1 (Continued)

Author, year	Demographic data	Study design	Type of treatment	Duration and frequency of treatment	Outcome measures	Follow-up (post-treatment)	Outcomes (pt = patient, pts = patients)	Adverse events (pt = patient, pts = patients)
Goldman, 2008 ³³	52 female (18–47 years) Average age 24.2 years	Prospective study (case study of an unique instance)	Neodymium-doped yttrium aluminum garnet (Nd: YAG) laser combined with subcision for skin tightening and transplantation	One stage	Histological analysis of tissue samples Patient's assessment	12–30 months	Skin biopsies obtained after the treatment showed disruption of adipocytes (focal lipolysis), collagen coagulation of the fibrous septa, and blood vessel coagulation, and degenerative alterations of the septal connective tissue layer. Majority of patients (84.6%) rated the results of treatment as either good or excellent.	Echymosis (eight pts, 15.3%) Edema (39 pts, 75%) Hemorrhoids (one pt, 1.9%) Decrease in sensibility (37 pts, 71.1%)
Kulth, 2008 ²⁷	50 years old woman	Prospective design study (case study of an unique instance)	Extracorporeal shock-wave therapy (ESWT)	Four therapy Sessions in 21 days	Liquid crystal contact thermography (LCCT) measures High frequency ultrasound	None	Improvement visible by LCCT at the site of ESW treatment, starting from immediately thereafter and lasting days. Comparing high frequency, high-resolution ultrasound measurements of medium-energy, high-frequency ESWT applied on untreated skin areas, we could see some improvement in the epidermis and the extracellular matrix of the dermis.	None
Alexiades-Armada, 2008 ¹	10 women (32–57 years)	Bilateral paired blinded comparative study	Unipolar radiofrequency	Six treatments	Photographs	3 months	All participants responded to treatment (mean of 4.22 and range of one to six treatments). The overall improvement of photographs using the cellulite grading scale demonstrated the following mean grading scores for the treated leg vs. the control leg: dimple density of 2.73 vs. 3.18 (11.25% mean improvement), wrinkle density of 0.32 vs. 0.32 (0% mean improvement), dimple depth 1.47 vs. 1.54 (2.5% mean improvement). Clinical improvement Dermal fibrosis	Erythema which resolved within 1–3 h
Goldberg, 2008 ²²	30 women (<30 years)	Prospective study	Unipolar radiofrequency device	Every week for six sessions	Photographs, circumference measurements, bopses, MRI, and blood lipid evaluation	6 months	16 months after dermalization, the cosmetic result was considered good.	Erythema
Emsen, 2008 ^{6a}	Two women (35 and 38 years)	Retrospective case series	Dermaabrasion	Dermaabrasion was performed in one stage	Clinical observation	16 months and 20 months	16 months after dermalization, the cosmetic result was considered good.	None
Christ, 2008 ^{6a}	59 women	Two group: group 1 15 patients, group 2 44 patients	Extracorporeal shock-wave therapy	Group 1 (six sessions within 3 weeks), group 2 (eight sessions within 4 weeks)	Connective tissue, skin elasticity measurements, and photographs	3 months	Improvement in skin elasticity (long lasting, up to 6 months)	Minor pain Slight skin reddening
Kaplan, 2009 ⁶⁵	12 patients	Prospective study	Tripolar Technology (radiofrequency)	An average of 7 weekly treatments (range 4–11)	Photographs, histopathology assessment score	None	Immediate abdominal skin tightening observed.	Transient erythema
Gülç, 2009 ⁶⁶	33 women (26–62 years)	Prospective study	Endermologie	35–40 min, twice weekly for a total of 15 sessions	Digital photographs, circumferential thickness measurements	None	Significant cellulite appearance improvement in only five women (15%).	Muscle ache lasting approximately 1 or 2 days after the session Mild ecchymosis (three pts)
Van Der Lugt, 2009 ¹	55 women (24–58 years) average age 36 years	Prospective study	Bipolar radiofrequency device	One treatment per week for 12 sessions	Histological evaluation, digital photography, 3D optical skin assessment	2 months	Very good and good results were achieved (overall efficacy 66% evaluated by the clinicians)	Erythema
Bousquet-Rouland, 2009 ²⁷	12 pts	Prospective study	1064 nm Nd: YAG Laser	Three treatments at intervals of 3–4 weeks	Photographs and ultrasound images	3 months	Tightening of the skin and improvement in cellulite. 11/12 pts were satisfied with the procedure	None

(continued)

Table 1 (Continued)

Author, year	Demographic data	Study design	Type of treatment	Duration and frequency of treatment	Outcome measures	Follow-up (post-treatment)	Outcomes (pt = patient, ps = patients)	Adverse events (pt = patient, ps = patients)
Manuskajati, 2009 ⁴	39 women (23–60 years)	Prospective study	Trifollar radiofrequency	Once a week for 8 weeks	Circumference measurements, weight, body mass index, and skin elasticity measurement	4 weeks	Thirty-seven patients (95%) completed the treatment protocol. There was significant circumference reduction at the abdomen and thigh regions, respectively. At 4 weeks after the last treatment, the average circumferential reductions of the abdomen and thighs were 8.2 and 6.2 cm, respectively. Circumferential reductions of the buttocks and arms at the last treatment visit compared to baseline were demonstrated. Quartile grading score correlating to approximately 50% improvement in appearance were noted	Of a total of 656 treatment sessions performed, 100 adverse effects of cellulite treatment were observed including: erythematous papules, popular urticaria, primary degree burns, blisters, and bruising were observed
Winter, 2009 ⁶⁹	20 postpartum women	Prospective self-controlled study	VeloShape system	Five weekly treatments	Circumference measurements, digital photography, and physician's and patient's evaluation	4 weeks	Significant improvement in skin laxity and tightening was noted by both the physician and patients	Purpura (one pt) Mild burn (one pt)
Kulick, 2010 ⁷⁰	17 women (28–37 years) average age	Prospective study	SmoothShapes device	Patients received two treatments per week for 4 weeks	Weight, body mass index, percent body fat, digital photographs, VECTRA three-dimensional images, and patient questionnaire	5 months	Using the untextured VECTRA images, 82 percent of patients were noted 1 month (14 of 17), 76 percent were improved at 3 months (13 of 17), and 76 percent were improved at 6 months (13 of 17)	None
Aditto, 2010 ⁷¹	25 women (27–63 years)	Randomized study	D-ACTOR 200 system (acoustic wave therapy, manual lymphatic pulse activation technology) Radiofrequency using Trifollar technology	Six sessions over the course of 4 weeks	3D skin texture measurements (DermalOF system), elasticity measurements (Dermalab system)	3 months	Improvement with regard to depression, elevations, roughness, and elasticity	Immediate redness
Boisnic, 2010 ⁷²	24 women	Prospective study	Radiofrequency	None	Circumference measures, skin tightening	2 months	Almost all pts noted an improvement of cellulite and body silhouette at the final session, which slightly decreased at the 2-month assessment. Improved skin appearance was objectively detected	None
Elhan, 2010 ⁷³	23 pts	Prospective study	Radiofrequency	Six treatments (four weekly treatments and two additional treatments at 2-week intervals, total)	Standardized photography and circumference measurements	None	Evidence of a significant improvement in body contour with skin tightening and circumference reduction	Transient erythema (23 pts)
Lee, 2010 ⁷⁴	101 women and 10 men (20–50 years)	Prospective study	Carbon Dioxide Therapy	Multiple of 5 CO ₂ therapy sessions at 1- to 2-week intervals	Ultrasound measurements and circumference measurements	2 weeks	Ultrasound evidence of decreased subdermal thickness after five sessions of carboxytherapy. Younger women (20–29 years) appear to derive less objective benefit of CO ₂ therapy	Pain at the injection site Minor aches Needle-entry bruising
Bayrakci, May, 2010 ⁷⁵	60 women (>30 years)	Randomized study	Group I: mechanical massage, group II: manual lymphatic drainage, group III: connective tissue manipulation techniques Acoustic wave	5 weeks	Visual assessment	None	All groups had an improvement in thinning of the subcutaneous fat	None
Knobloch, 2010 ⁷⁶	272,541 females	Randomized controlled trial	Intervention group: six sessions of extracorporeal shock wave therapy (1–2 weeks), plus waves plus daily home-based gluteal strength exercise Control group: six sessions of sham extracorporeal shock wave therapy (1–2 weeks), plus waves plus daily gluteal strength exercise	Intervention group: six sessions of extracorporeal shock wave therapy (1–2 weeks), plus waves plus daily home-based gluteal strength exercise Control group: six sessions of sham extracorporeal shock wave therapy (1–2 weeks), plus waves plus daily gluteal strength exercise	Digital photographs, circumference measurements, blood flow, tissue oxygen saturation, and post capillary venous blood flow	None	The combination of extracorporeal shock wave therapy with a daily gluteal strength program alone in cellulite	None

(continued)

Table 1 (Continued)

Author, year	Demographic data	Study design	Type of treatment	Duration and frequency of treatment	Outcome measures	Follow-up (post-treatment)	Outcomes (p1 = patient, p2 = patients)	Adverse events (p1 = patient, p2 = patients)
Gold, 2011 ³²	83 women mean age 39.7 years	Open-label, multicenter study	Dual-wavelength, low-level laser energy and massage	Twice weekly for 4 weeks, for a total of eight treatments	Circumferences of the upper, middle, and lower thighs (treated and untreated) were measured	3 months	Reduction in thigh circumference of the treated areas exceeded those of the control areas for the upper, middle, and lower thigh in most	Erythema Swelling Increased urination
Hexsel, 2011 ³⁶	11 female (19–45 years)	Prospective study	Bipolar, radiofrequency, infrared, vacuum and mechanical massage device	12 sessions for a total of 6 weeks	Cellulite severity scale grading, BMI and thigh and hips circumferences Self-assessment and satisfaction questionnaires	4 weeks	Cellulite grade has improved specifically on both on buttocks and no changes were observed on the thighs Most of the subjects reported they were satisfied Cellulite score after 4 weeks when compared with the base value, but this reduction was significantly greater and earlier on the treated side than on the untreated side. Furthermore, skin tensity, a major cellulite-related parameter, also significantly improved on the treated side after only 2 weeks All the points reported that they liked the results, and in the analysis of the photographs, both examiners were in agreement that the cellulite improved for 13 of the 14 points	None
Escudé, 2011 ²⁹	50 women (18–45 years) mean age 32 years	Randomized right/left comparison study	Cream containing 5% caffeine and a flavonoid-rich Nelumbonucifera extract in conjunction with a balanced but not low-calorie diet	Twice daily for 4 weeks	Cellulite Clinical Score DermalTannermeter Circumference measurement Reconstructed volume with 3D Fringe projection and 3D reconstruction images	None	Cellulite Clinical Score improved the cellulite score after 4 weeks when compared with the base value, but this reduction was significantly greater and earlier on the treated side than on the untreated side. Furthermore, skin tensity, a major cellulite-related parameter, also significantly improved on the treated side after only 2 weeks	None
De Gooijer, 2011 ⁷⁷	14 women (19–36 years)	Randomized and controlled study	Manual and mechanical lymph drainage and cervical stimulation using the Gooijer and Gooijer technique	1.5 h per day for 10 sessions over 2 weeks	Photographs, perimetry measures	None	All the points reported that they liked the results, and in the analysis of the photographs, both examiners were in agreement that the cellulite improved for 13 of the 14 points	None
Roore, 2011 ⁷⁸	78 women	Double-blind randomized placebo-controlled study	Topical agent: tetrahydroxypropylthierylenedisulfonate, caffeine, carnitine, forskolin and retinol	Twice daily for 12 weeks	Photographs, circumferences measurements	None	The "orange peel" aspect and "stubborn cellulite" were both significantly improved on all body areas after 4 weeks of applying the anticellulite product and the skin tensity significantly enhanced (vs. baseline on all sites except thigh). After 12 weeks of application, an average of 79% (ranging from 64.5% to 96%) of the subjects presented improvements in their skin elasticity	None
Díbernardo, 2011 ³⁹	10 women Mean age 47 years	Prospective study	1440 nm Nd:Yag laser	Single treatment	Mean skin thickness and elasticity	1 year	Increase in skin thickness and elasticity	Minimal adverse effects (discomfort, bruising, swelling and numbness), ranged 0.0.3 on a scale from 0 to 3
Conrado, 2011 ³⁹	42 women (20–60 years)	Prospective study	Compressive therapy	8 h daily for 30 days	Body circumference measurements	None	The experimental data showed reduction in body measurements	None
Vogelzang, 2011 ³⁹	50 women (21–29 years)	Randomized double-blind study	Sulfo-carbamioisotopic agent	Twice a day for 8 weeks	Thigh volume, circumference measurements	None	Thigh volume was also significantly reduced after sulfo-carbamioisotopic treatment The appearance of cellulite assessed by clinical evaluation was also significantly reduced within 28 days	None
Adatto, 2011 ⁴¹	14 women	Randomized and controlled study	Acoustic wave therapy	1 weekly for 4 weeks	Fat thickness measured by the ultrasound system Thigh circumference measurements Digital picture of the treated areas Patient satisfaction (questionnaire)	12 weeks	Patent satisfaction was very good to excellent (mean 4.5/5) pts. Measurements with the ultrasound system clearly demonstrate a significant diminution in the subcutaneous fat layer thickness and a reduction of the averaged circumference of thighs There is also an additional benefit observed in the improvement of cellulite appearance and improving the skin firmness Instrumental and clinical evaluation showed efficacy of the active formulation in counteracting the signs and symptoms of cellulite	Minor pain Skin reddening and minor bruising (two pts)
Sparavigna, 2011 ³	23 females (30–55 years)	Randomized controlled study	Topical product (venadine + ginkgobloba + escn)	Twice daily for 4 weeks	Thermography, morphometric measures of thigh circumference and microcirculation evaluation, clinical evaluation	None	Instrumental and clinical evaluation showed efficacy of the active formulation in counteracting the signs and symptoms of cellulite	None

(continued)

Table 1 (Continued)

Author, year	Demographic data	Study design	Type of treatment	Duration and frequency of treatment	Outcome measures	Follow-up (post-treatment)	Outcomes (pt = patient, pts = patients)	Adverse events (pt = patient, pts = patients)
Paolino, 2011 ⁸³	20 women (25–55 years)	Prospective controlled study	Infrared-LED illumination applied during high-intensity training	45 min twice a week over 3 months	Photographs and thermography	None	Reduction of saddlebag and thigh circumference	None
Godby, 2012 ⁸⁴	10 women (25–59 years)	Prospective study	Mechanical lymph drainage and cervical stimulation by the Godby & Godby technique	10 sessions (40 h)	Reduction of thighs and gluteal parameters	None	Significant reductions were observed for all the measurement points	None
Truitt, 2012 ⁸⁵	22 women	Randomized prospective study	1064-nm Nd: YAG laser treatment	Three treatments at 4 weeks interval	Digital photographs	6 months	Blinded evaluators noted mild improvement in three of seven subjects in high-energy group and moderate improvement in two of nine subjects in low-energy group	Erythema (22 pts) Pain during treatment
A-Bader, 2012 ⁸⁵	35 women (35–65 years)	Prospective study	Topical cosmetic agents: Furcellularimbricals, Fucus vesiculosus, retinol, conjugated linoleic acid, and a glycolic acid wave	Once a day for 12 weeks	Ultrasound imaging and clinical evaluation	12 weeks	Significant improvement in cellulite grading and significant decrease in fat thickness showed by ultrasound imaging	None
Ferraro, 2012 ⁸⁶	50 patients (37 women, 13 men, 21–62 years)	Prospective study	Cryolipolysis and shock wave	20–60 min for session. One session every 15 days (mean total of 3.73 sessions)	Photographs and histological features	12 months	High patients' satisfaction and a modification of the cutaneous aspect with an attenuation of the "orange peel" skin effect was observed	Erythema
Mosk, 2012 ⁸⁶	28 women (17 in placebo group)	Prospective study	Radiofrequency	Eight treatments at intervals of 7–8 days	Classical and high frequency ultrasound	4 weeks	Decrease in the epidermis and dermis Decrease in subcutaneous tissue and dermis	None
Löberbauer-Pürer, 2012 ⁸⁴	86 female (25–55 years)	Randomized and controlled study	Four groups: 1: control group 2: diet only 3: diet plus exercise and body pressure 4: exercise and lower body pressure	Depending on treatment	Multivariate analysis	12 weeks	Subjects of all three intervention groups rated the severity of cellulite, as well as the general condition of their skin on their own as significantly lower or better than in the pretest	None
Knobloch, 2013 ⁸⁷	25 women (18–65 years)	Double-blinded, randomized, controlled study	Extracorporeal shock-wave therapy	Six sessions (every 1–2 weeks) for 12 weeks	Digital photographs, number of depressions, cellulite severity scale (CSS)	None	The change of the CSS in the intervention group vs. the control group was significantly different The change of the number of depressions in the intervention vs. the control group was significantly different	None
Savoia, 2013 ⁸⁵	33 patients (nine men, 24 women, age 18–64 years)	Prospective study	Low-level laser therapy and vibration therapy	Two sessions per week for a total of 4 weeks	The evaluation parameters were: photographic evaluation, perimetric evaluation, blood tests, histological evaluation, and subjective and objective tests	None	Effective treatment in all patients	None
Valentin da Silva, 2013 ⁸⁸	Eight women (25–40 years)	Randomized study	Low-temperature radiofrequency	10 biweekly session	Ultrasound	None	Pre- and post-treatment mean collagen fiber thickness showed a 24.66% reduction from 1.01 to 0.67 mm	None
Katiz, 2013 ⁸¹	15 women (20–55 years)	Randomized study	Nd: YAG 1440 nm Laser	Single treatment	2D and 3D imaging	6 months	66.6% showed improvement in overall skin contour at 6 months follow-up. Patient and physician satisfaction scores were high	Echymosis and edema
Sasaki, 2013 ⁸³	24 women (27–67 years)	Randomized study	Minimal invasive 1440-nm Pulsed Nd:YAG Laser and side-firing fiber	6 months	Standardized high-resolution photography, skin elasticity measurements, ultrasound scanning for dermal thickness, body weight, investigator global assessment scores	2 years	Increase over the baseline mean skin elasticity (34%) and mean dermal thickness (11%), as well as an increase in the average percentage of dermal thickening	Pain (3 pts) Erythema and swelling (five pts) Exudative collections (three pts) Numbness (six pts)
Bagatini, 2013 ⁸⁹	30 women (25–40 years)	Randomized study	Infrared therapy	None	Photographs and ultrasound images	None	The overall appearance of cellulite in the thighs improved on the side exposed to infrared therapy	None

(continued)

Table 1 (Continued)

Author, year	Demographic data	Study design	Type of treatment	Duration and frequency of treatment	Outcome measures	Follow-up (post-treatment)	Outcomes (p = patient, pts = patients)	Adverse events (p = patient, pts = patients)
Ruse-Willingseder, 2013 ^{3d}	17 patients	Controlled double-blinded	Acoustic wave therapy	Once a week for 7 weeks	Standardized photography (3D imaging system) and patient's questionnaire	12 weeks	Most of the treated patients in the verum group saw an improvement in the number and depth of dimples (8 of 11) and in the skin firmness (9 of 11) and texture (10 of 11). The improvement achieved after the LPG treatment was found to be statistically significant when compared to the initial cellulite grade. The questionnaire indicated patient satisfaction (81 patients, 69%). At 6 months post-treatment, blinded evaluators rated at least a 1-point improvement in the appearance of cellulite in 96% of treated sites. Blinded evaluators were also able to correctly identify lipedema in 95% of cases. At least 90% of post-treatment photographs of points and physicians reported satisfaction with the results of treatment throughout 6 months.	None
Kutubov, 2013 ³¹	118 women Mean age 34.59	Randomized study	Endermologie	Twice weekly for 15 sessions	Body circumference measurements, patient satisfaction questionnaire	None	The improvement achieved after the LPG treatment was found to be statistically significant when compared to the initial cellulite grade. The questionnaire indicated patient satisfaction (81 patients, 69%). At 6 months post-treatment, blinded evaluators rated at least a 1-point improvement in the appearance of cellulite in 96% of treated sites. Blinded evaluators were also able to correctly identify lipedema in 95% of cases. At least 90% of post-treatment photographs of points and physicians reported satisfaction with the results of treatment throughout 6 months.	None
Dibbernado, 2013 ^{3b}	57 patients (21–55 years) mean age 43.3	Multicenter study	440-nm Nd:YAG laser with a side-firing fiber and temperature-sensing cannula	Single 3 step	Photonic scale	None	Nineteen subjects in the LLT group achieved a decrease of one or more points on the Muller grading scale (55.88%) vs. sham-treated group. Pronounced reduction in body measurements.	Swelling (two pts) Purpura (four pts) Itching (four pts)
Jackson, 2013 ^{3b}	19 women	Double-blind study randomized	Low-Level Laser Therapy device (LLT)	None	Skin appearance	None	Nineteen subjects in the LLT group achieved a decrease of one or more points on the Muller grading scale (55.88%) vs. sham-treated group. Pronounced reduction in body measurements.	None
Conrado, 2013 ^{3c}	32 women (20–60 years)	Prospective study	Compressive therapy: garment containing ceramic nanoparticles	8 h daily for 120 days	Anthropometric measures	4 months	Reduction of edema. Reduction of dermal and subcutaneous tissue. Decrease in body weight was observed in 16/29 women.	Diarrhea, melitry, constipation (13.8% of subjects)
Saikhin K, 2014 ³³	29 women (25–48 years)	Randomized study	Dietary intervention rich in polyphenols, flavonoids and phenolic acids	100 mL/day for 90 days of organic chokeberry juice	Photography and ultrasound measurements; questionnaire	None	Reduction of body fat in 20/29 women. Reduction in the abdominal circumference in 18/29 women. Reduction in thigh circumference in 18/29 women. 41.4% of subjects observed visual improvement in the condition of cellulite.	None
Sawkin, 2014 ³³	29 women (25–48 years)	Prospective study	Organic chokeberry juice (ironia melanocarpa: rich source of polyphenols, flavonoids and phenolic acids)	All subjects consumed 100 mL of CJ/day, during 90 days	BMI, percent of fat, the circumference, thigh, knee, hip circumference, blood tests, anthropometric measurements of the skin	None	A marked reduction in the subcutaneous tissue thickness was observed in all subjects. There was a marked visual improvement in the condition of cellulite.	None
Schonwetter, 2014 ³⁴	15 women (22–38 years) mean age of 30 ± 4 years	Prospective study	Manual lymphatic drainage	Fourteen sessions of manual lymphatic drainage once a week on lower limbs and buttocks	Subjective assessment; digital photographs body measurements; measure of edema by ultrasonography; high-resolution ultrasonography questionnaire (Dermatology Life Quality Index)	None	Only 33% of points showed improvement in the grade of cellulite.	None
Schlaudraff, 2014 ³⁵	14 female (23–7 years) mean age 42.4	Prospective, single-center, randomized, open-label phase II study	Extracorporeal shock-wave therapy	Patients were treated unilaterally with 2 weekly treatments for 4 weeks on a randomly selected side (left or right) and on the selected side	Photographs, contact dermatography, clinical inspection of the skin, patient satisfaction questionnaires	4 weeks	The mean cellulite grade improved from 2.5 ± 0.09 at baseline to 1.57 ± 0.18 after the last treatment and 1.68 ± 0.16 at follow-up.	None

baseline included women below 45 years old, and the mean age was generally between 20 and 48 years. The efficacy of the treatment was mainly assessed using instrumental evaluations (such as thigh circumference, ultrasound analysis, and photography) and clinical observations.

Among the studies searched up, 63 tested the effectiveness of an exclusive treatment performed without the association to other procedures: 11 topical agents, 10 extracorporeal shock-wave therapy, 10 radio frequency, eight laser therapy, five oral therapy (three pill-based therapy and two juice therapy), four manual massage therapy, three carbon dioxide therapy, two compressive therapy, two infrared therapy, one dermabrasion, and 11 devices that use a association of multiple treatments (massaging, rolling, sucking, infrared, and radiofrequency). The combined treatments were the following: intense pulsed light and retinyl-based cream, Nd: YAG laser combined with autologous fat transplantation, dual-wave length laser and massage, topical agents in conjunction with a low-calorie diet, exercise and lower body pressure intervention, laser therapy and vibration therapy, cryolipolysis, and shock-wave therapy.^{29–35}

The metrics used for evaluation of the results of the treatments were heterogeneous. The gradation scales used were varied and often proposed by individual authors. Only in some cases, there has been the use of internationally standardized rating scales. The most used was cellulite severity scale (CSS).⁷

Also with regard to the questionnaires proposed to patients, there is no uniqueness among studies. The more standardized among these questionnaires was the Dermatology Life Quality Index (DLQI).³⁶ Age of patients was not specified in 22/73 papers (30.1%). Follow-up ranged from 0 to 30 months. Post-treatment follow-up totally missed in 45.2% of the studies (33/73).

The postoperative outcome was satisfactory, with almost all the performed treatments. In general, almost all of the patients were satisfied with the improvement in their skin appearance.

Pooling the data, side effects were observed in a small percent of patients. They were only minor adverse events, all localized on the treated areas: bruising, edema, erythema, decrease in sensibility, numbness, and itching. No major complication was observed. All the side effects resolved in a short time after treatment.

About the outcomes, we did not observe a significant difference between the studies that took into consideration single treatments and those that considered the tested combined treatments.

Laser therapy, appears to be the one that provides the best results in terms of long-term persistence, although it is not free from side effects post-treatment.^{37–44} Neodymium-doped yttrium aluminum garnet (Nd: YAG) laser was the type of laser used in each of the 8 studies that we found from the literature review.

Post-treatment erythema, edema, ecchymosis, dysesthesia, and pain were observed in a significant percent of patients, but disappeared in 3 months, at the latest.

Discussion

Treatment options for cellulite are varied and numerous.¹⁰ The final objective of these treatments is to improve the appearance of cellulite and maintaining its response over a period of time. While many treatments claim to be able to improve the appearance of cellulite, this condition remains elusive to treatment.⁹⁶ In fact, no treatment is completely successful as none is more than mildly and temporarily effective. Despite the lack of evidence to support efficacy, treatment options continue to proliferate.⁹⁷

The first noninvasive device for the treatment of cellulite is known as Endermologie. It is a cellulite treatment that combines very firm massaging, rolling, and sucking at the skin's surface. The skin is pulled into a mechanical massaging device and kneaded between its rollers to promote lymphatic drainage and alter the skin's architectural framework. Poor outcomes of this treatment were observed.^{46,66}

Further suction, mechanical massage, and light-based devices are the VelaSmooth and its next-generation device, the VelaShape. VelaSmooth and VelaShape use infrared light, along with radiofrequency energy, to improve the appearance of cellulite. VelaShape combines the VelaSmooth treatment head with a smaller treatment head, known as the VelaContour. These devices demonstrated to provide medium-high improvement of cellulite appearance, even if there was not a long follow-up time.^{53,60,69}

One of the first combination devices featuring suction, massage, and low-level diode laser light sources, as well as contact cooling was the TriActive. Noo-theti⁴² compared VelaSmooth system vs. TriActive system in a randomized controlled trial. Although there was improvement in the reduction of cellulite for each device individually, there was no significant difference between VelaSmooth or TriActive devices in the following categories: reduction of thigh circumference, photographic evaluation, and perceived change in before and after photographic grading. There was a statisti-

cally significant increase in the incidence of post-treatment bruising with the VelaSmooth compared to Tri-Active.

Regarding carboxytherapy, prospective studies^{17,18,74} have shown a decrease in the subepidermal thickness and clinical improvement consisting in increasing the elasticity of the skin and reducing the circumference of the treated areas. Crackling sensation beneath the skin was the most frequent side effect. Adverse effects were always meager and resolved spontaneously within a short time after completion of therapy.

Other energy-based modalities have also been shown to be effective for the treatment of cellulite. Radiofrequency (RF) technology has become a standard treatment in esthetic medicine with many indications due to its versatility, efficacy, and safety.^{98,99} Radiofrequency currents are commonly used in dermatology to treat cutaneous and subcutaneous tissues by heating.¹⁰⁰ RF differs from lasers in that it uses an electric current rather than a light source.¹⁰¹ It is used worldwide for cellulite reduction, acne scar revision, treatment of hypertrophic scars and keloids, rosacea, and inflammatory acne in all skin types.¹⁰² However, the most common indication for RF technology is the nonablative tightening of tissue to improve skin laxity and reduce wrinkles. Radiofrequency energy can be applied to body skin to create tightening without surgical incisions and recovery time.¹⁰³ Immediate abdominal skin tightening and fat reduction were clinically observed in several studies,^{58,61,62,65,67,68,72,73,86,88} with a high satisfaction rate. The benefit of RF in terms of reduction of abdomen and cellulite appearance is today well established.¹⁰⁴ Additional modalities include fractional RF, subablative RF, phase-controlled RF, and combination RF therapies that apply light, massage, or pulsed electromagnetic fields. In contrast to first-generation monopolar/bipolar and "X-polar," RF systems which use one RF generator connected to one or more skin electrodes, multisource radiofrequency devices use six independent RF generators allowing efficient dermal heating to 52–55 °C, with no pain or risk of other side effects.¹⁰⁵

Extracorporeal shock-wave therapy^{27,28,55,59,64,71,81,87,90,95} (ESWT) demonstrated to provide a significant diminution in the subcutaneous fat layer thickness and a reduction of the averaged circumference of thighs. There is also an additional benefit for patients in reducing the cellulite appearance and improving the skin firmness. Adverse effects of this treatment are pain, redness, and minor bruising, localized in the treated area. Important to remember, pregnancy is considered a contraindication for extracorporeal shock-wave treat-

ment.¹⁰⁶ Siems⁵⁵ found increased concentrations of serum malondialdehyde and plasma protein carbonyls in cellulite patients with edematous and lipid-enriched dermis resulting from oxidative stress. Concentrations of both these substances decreased after application of ESWT. Also lipid peroxidation products were released demonstrating the sclerosis-preventing effect of ESWT (smoothing of dermis and hypodermis). Expression of factors stimulating angiogenesis and lymphangiogenesis was not induced by ESWT.⁵⁹

The first study that we found in literature regarding the use of laser in the treatment of cellulite dates back to 2008. Goldman³³ reported the biggest number of adverse effects, using a combination treatment with Nd: YAG laser and autologous fat transplantation: edema (75%), decrease in sensibility (71.1%), ecchymosis (15.3%), and hemosiderosis (1.9%). Nevertheless, the majority of patients (84.6%) rated the results of treatment as either good or excellent. The follow-up time ranged from 12 to 30 months.

DiBernardo,³⁸ in 2013, tested 1440-nm Nd: YAG laser with a side-firing fiber and temperature-sensing cannula, in a multicenter study on 57 patients. At 6 months post-treatment, blinded evaluators rated at least a 1-point improvement in the appearance of cellulite in 96% of treated sites. Blinded evaluators were also able to correctly identify baseline vs. post-treatment photos in 95% of cases. At least 90% of patients and physicians reported satisfaction with the results of treatment throughout 6 months. Sasaki,⁴³ in 2013, evaluated the safety and efficacy of the 1440-nm laser and the duration of the clinical benefits during 2 years. Of the 24 subjects who underwent treatment, only 20 were available for the 6-month follow-up assessment. Objective measurements at 2 years demonstrated an increase over the baseline mean skin elasticity (34%) and mean dermal thickness (11%), as well as an increase in the average percentage of dermal thickening determined by ultrasound imaging. Independent investigator global assessments were rated higher for grade II subjects than for grade III subjects throughout the 2-year follow-up period.

Topical treatments showed good results at the end of treatment time. Post-treatment follow-up was not considered in any of the studies dealing with topical agents. Over the years, new products have been developed that can produce results on skin thickness and elasticity of the skin affected by cellulite.

Al-Bader⁸⁵ revealed a potent cocktail of ingredients that when combined together can act *in vitro* to markedly improve lipolysis mechanisms and by way of stimulating procollagen I can also have an effect on the

surrounding extracellular matrix. The *in vitro* actions of the ingredients were translated *in vivo*, where a clinical improvement of cellulite condition was observed.

Roure⁷⁸ evaluated the efficacy of a topical cosmetic slimming product combining tetrahydroxypropylethylenediamine, caffeine, carnitine, forskolin, and retinol. The “orange peel” aspect and “stubborn cellulite” were both significantly improved on all body areas after 4 weeks of applying the anticellulite product and continued to improve throughout the test. Starting from week 8, tonicity was significantly enhanced vs. baseline on all sites except thigh. After 12 weeks of application, an average of 79% (ranging from 64.5% to 96%) of the subjects presented improvements in their skin condition. As for a cosmetic purpose, caffeine is used as an active compound in anticellulite products because it prevents excessive accumulation of fat in cells. This alkaloid stimulates the degradation of fats during lipolysis through inhibition of the phosphodiesterase activity. Caffeine has potent antioxidant properties. It helps protect cells against the UV radiation and slows down the process of photoaging of the skin. Caffeine contained in cosmetics increases the microcirculation of blood in the skin and also stimulates the growth of hair through inhibition of the 5- α -reductase activity.¹⁰⁷ Furthermore, bioceramic-coated neoprene garment occlusion seems to potentiate the effect of topical agents in cellulite reduction.¹⁴

Unique and bold attempt for the treatment of cellulite was the use of the subcision technique,⁴⁹ usually performed for the treatment of postacne scars. The results of 282 patients were encouraging, at the cost of a high percentage of immediate side effects (pain, bruises, and hemosiderosis).

The main limits of this analysis were the high heterogeneity of the study populations. Selection bias and lack of common outcome measures were some of the problems that prevented a proper meta-analysis. Although this review is not a meta-analysis, we critically assessed the literature and tried to identify high-quality studies. Moreover, many of the technique papers showing favorable results are biased from authors promoting their preferred treatment.

Conclusions

Recent advances in technology have drastically improved esthetic treatment for skin. Even if there is a high number of treatments for cellulite reduction available on the market, there is not a treatment that may be defined as the final and definitive therapy for this condition. Cellulite is a multifactor disease that requires

a multidisciplinary approach for the treatment. This is the reason why it is still difficult to indicate an exclusive and effective single treatment for this condition. Available studies in literature showed a better success of the combined treatments, than the single treatment.^{29–35} Follow-up observation is essential, as the maintenance of long-term results is one of the main targets of anticellulite treatments.

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