A Scientific Solution to UNSIGHTLY CELLULITE

Cellulite affects nearly every woman as she gets older. The skin dimpling and bumps typically seen on the thighs, hips, and buttocks is a condition that women have endured for centuries.

While purported “cures” for cellulite abound, the billions of dollars spent on specialized creams, diets, and massage therapies have not overcome the problem. The reason why these methods have failed is because they have approached cellulite as purely a cosmetic problem and neglected to address its underlying causes.

Fortunately, major scientific discoveries have uncovered the factors that cause cellulite.

Dermatology experts have taken these new data to develop powerful topical agents that target cellulite by correcting the underlying abnormalities involved in its formation. These active botanicals have been shown to help restore smooth and youthful body contours to the hips and thighs.
How Females Develop Cellulite

Why are women prone to cellulite as soon as they begin menstruation, whereas men are spared? Many experts believe that the primary culprits are hormonal influences on fat deposits over the buttocks, thighs, and hips, as well as anatomical differences in how this fat is stored.\(^1\)

Although there are three layers of fat under the skin, only the top layer is involved in cellulite. Imagine that the skin in this top layer is like a down quilt. The stitches in the quilt represent columns of collagen fibers that give the skin its structure. Adding feathers into the compartments between the stitches is analogous to how fat globules accumulate between the skin's collagen columns. As more fat globules are added, the compartments fill up, causing fat to bulge out from the compartments resulting in the characteristic dimpled appearance of cellulite.

Scientists have discovered how changes in the connective tissue structure in this top fat layer trigger the formation of cellulite. Magnetic resonance imaging studies have shown that women with cellulite have pillar-like columns separating the fat chambers, which are larger and deeper than those in men.\(^3\)

What makes women more vulnerable to cellulite is that these large vertical chambers can store an abundance of fat. Collagen supporting tissue of men, on the other hand, is more like a criss-cross net that is organized into small diagonal chambers, which hold only small amounts of fat.\(^4\)

These longer supportive columns in women are more easily weakened by hormonal, structural, and vascular changes that affect the skin's support structure, allowing fat to protrude deeply into the dermis (the layer of skin beneath the outermost layer), which gives rise to the characteristic lumpy appearance of cellulite.\(^1\)

Pregnancy and other hormonal changes in women affect the formation of cellulite, as do genetics and aging. These factors adversely affect adipose tissue and the supporting connective tissue.\(^1\) Hormones secreted in response to stress, particularly cortisol, also encourage fat deposition in problem areas.\(^5\)

"The adipose tissue in the thighs and buttocks [in women] is special in that it is reserved for nutrition of a fetus in bad times," Peter T. Pugliese, MD, founder of Circadia Skin Care Institute in Reading, PA, tells Life Extension. "So this fat does not move with normal dietary restriction or with exercise."

These differences highlight the fact that cellulite is not purely a cosmetic problem, but involves a number of physiological factors. "Cellulite is multifactorial but mostly related to the underlying structure or framework and relationship of adipose tissue to connective tissue in women," Adam M. Rotunda, MD, a clinical instructor of dermatology at the David Geffen School of Medicine, UCLA, tells Life Extension.

Connective Tissue Structure Abnormalities in Cellulite

Connective tissue structure in women increases vulnerability to cellulite, with the result that female skin becomes loose and more wrinkled with age. "Cellulite-affected skin demonstrates biomechanical properties of increased laxity in contrast to skin without cellulite," Gordon H. Sasaki, MD, FACS, a surgeon at the Sasaki Advanced Aesthetic Medical Center in Pasadena, CA, says.

Other factors compromise the underlying connective tissue such as the enzyme collagenase that is released before a woman's menstrual cycle. This enzyme breaks down collagen, which is a key structural protein within connective tissues.\(^6\) Fibrous tissue, similar to that seen with scarring, may fill in the gaps caused by degraded collagen. This results in the
formation of fibrotic stiff bands that can worsen the appearance of cellulite.

"Cellulite is a disease of the connective tissue initiated by cyclic hormones of the menstrual cycle," Dr. Pugliese says. "The characteristic undulating surface one sees with cellulite is the product of extensive connective tissue destruction."

Poor Circulation Aggravates Cellulite

As well as connective tissue abnormalities, poor circulation and lymph drainage can also aggravate cellulite. Fat, or adipose tissue, is relatively rich in blood vessels. Decreased blood flow, swelling from fluid accumulation (edema), and local inflammation can aggravate the female propensity to skin looseness and hasten the development of cellulite through a domino effect.

When small blood vessels become fragile, they leak excess fluid that accumulates in the compartments between the fat chambers. This effect increases pressure within the tissues, resulting in poor lymphatic drainage. As excess fluid is retained in dermal tissues, fat globules cluster together and inhibit venous return. This vascular damage results in decreased collagen synthesis and an inability to repair tissue damage, which weakens the dermis. Over time, clumps of hardened collagen contribute to the formation of fibrotic collagen bands, which become deposited around fat globules beneath the skin. The tightening of these bands causes a vicious cycle that worsens cellulite and impairs blood flow even more. These changes have been seen in ultrasound imaging of skin affected by cellulite, which reveals thinning of the dermis with fat pushing upward.

As a result of compromised circulation and lymphatic drainage, cellulite may appear and worsen in predisposed areas. "One of the major factors inducing cellulite is venous insufficiency and congestion," Carl R. Thornfeldt, MD, FAAD, founder and CEO of Episciences, Inc., tells Life Extension. "Non-prescription and/or herbal therapies have rarely been studied in this condition. Several are reported to be effective in the literature, but only horse chestnut [Aesculus hippocastanum] and gotu kola [Centella asiatica] have documented efficacy in reversing venous insufficiency." Leslie Baumann, MD, professor of dermatology at the University of Miami, agrees that, "Horse chestnut and gotu kola seem to improve circulation."

"Increasing circulation may help by increasing lymph flow," Dr. Baumann tells Life Extension. "Lymph builds up and makes cellulite appear worse. By increasing circulation this may increase lymph flow and help the appearance of cellulite."
Zeroing in on Anti-Cellulite Compounds

Ideally, an herbal cream to combat cellulite should target the three main causes of cellulite that have been identified. These are excess fat deposition, weakened connective tissue support structure, and poor circulation. Life Extension has identified seven compounds that may be especially promising as a multi-modal approach to correct the underlying causes of cellulite. Glycyrrhetinic acid, for example, is a compound derived from licorice root that targets fat storage in response to stress. Horse chestnut and gotu kola improve circulation, while also supporting connective tissue integrity. All three compounds have additional benefits that may improve the appearance of cellulite-prone skin, including antioxidant and anti-inflammatory activity. For readers interested in technical descriptions of these anti-cellulite nutrients, please see the information outlined in the boxes throughout this article.

While the combination of glycyrrhetinic acid, horse chestnut, and gotu kola has demonstrated favorable anti-cellulite effects, scientists have discovered four additional nutrients that have demonstrated profound fat-reducing benefits. As you will read, these anti-fat ingredients provide a key missing link to resolving cellulite.

Enzymatic Breakdown of Body Fat

Fat storage and breakdown are controlled by two sets of special receptors called alpha and beta receptors on the surface of each fat cell, or adipocyte. Regulated by the hormone epinephrine, beta-adrenergic receptors promote fat breakdown (lipolysis), whereas alpha-adrenergic receptors prevent fat breakdown and promote fat storage. In the case of cellulite fat, the alpha receptors outnumber the beta receptors, Dr. Pugliese says. Women also tend to have more fat-storage alpha receptors than fat-breakdown beta receptors in the hips and thighs so that storage exceeds breakdown in these areas, causing swelling of the stored fat within cells.

Stimulation of these receptors also leads to changes in a crucial lipolytic (fat-breakdown) enzyme called hormone-sensitive lipase. This enzyme is located directly in the fat cell and is activated when beta receptors are stimulated, breaking down triglycerides in fat to release free fatty acids and glycerol into the bloodstream. Conversely, alpha-receptor stimulation inhibits this enzyme and promotes fat storage.

Aerobic exercise improves the ability to mobilize and break apart triglycerides for energy use, whereas obesity makes the fat-breakdown enzyme hormone-sensitive lipase less sensitive to epinephrine. This
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...may help explain why, to some degree, exercise, which is associated with epinephrine release by the sympathetic nervous system, is helpful in improving the appearance of cellulite, whereas obesity aggravates its appearance.

Another enzyme called lipoprotein lipase that is found in large amounts in adipose tissue and in the liver acts on triglycerides within lipoproteins, breaking them down into free fatty acid molecules to be either burned for energy or stored as fat. Lipoprotein lipase is also responsible for the uptake of fat into the adipocytes. Women tend to have higher concentrations and activity of this enzyme in the hips and thighs, favoring fat storage in this region particularly if they are not physically active.9

To overcome these adverse enzymatic changes that make women vulnerable to cellulite formation, scientists have identified two unique marine extracts known as Phycoboreane™ and Rhodysterol™ that are showing promise for their effects in promoting lipolysis and liberating fat.

These compounds appear to stimulate an enzyme called protein kinase A, which in turn activates hormone-sensitive lipase to break down fat, releasing fatty acids and glycerol. These compounds also contain sulfated polysaccharides, which can bind to fatty acids and facilitate their elimination. Studies in all types of cellulite are underway to determine the effects of Phycoboreane™ and Rhodysterol™ on edema, fibrosis, skin suppleness, and tonicity.

The Two Most Exciting Fat-Reducing Ingredients

Scientists in Europe have developed two new breakthrough formulations called ADIPOSLIM™ and ADIPOLESS™. Both of these compounds work in synergy to help reduce stubborn cellulite and prevent its formation.12 ADIPOSLIM™ shrinks adipocytes by activating the fat-burning beta receptors while simultaneously turning off alpha receptors that inhibit fat burning.12 It also boosts fat oxidation, ensuring fat is burned as cellular energy, and inhibits the enzyme lipoprotein lipase to prevent fat storage.12

A clinical trial in adults using ADIPOSLIM™ on the thigh area showed 12% cellulite reduction after only one month, compared with only 6% for a control group, as well as visual cellulite improvement in 71% of treated subjects.12

ADIPOLESS™, meanwhile, blocks the formation of blood vessels needed to transform pre-adipocytes into fully formed fat cells, thereby inhibiting the formation of new fat.12

Doctors interviewed by Life Extension emphasized the importance of reducing fat storage in the regions of the body prone to cellulite. According to Dr. Rotunda, once an anti-cellulite cream is discontinued, it is conceivable any regional benefit at the site of application would be lost unless fat cells are destroyed or removed.

With the advent of these four new topical fat-altering compounds (ADIPOSLIM™, ADIPOLESS™, Phycoboreane™, and Rhodysterol™), a sustainable anti-cellulite program is now a reality.

Practical Treatment Strategies

A healthy lifestyle is very effective in promoting cardiovascular health, but diet and exercise alone may not be enough to adequately tackle cellulite. Dr. Rotunda believes that, “Diet and exercise cannot alter the histologic structure of the perpendicular bands connecting the skin to the underlying fascia and so cannot eliminate cellulite entirely,” he says. “However, lifestyle modifications may assist to reduce the appearance of cellulite by decreasing adipocyte volume, thus placing less tension on surrounding connective tissue, resulting in decreased puckering, but this has not been well documented.”

Dr. Wollina suggests that wearing neoprene compression shorts, as was done in some trials of cellulite cream, may affect absorption or penetration of active anti-cellulite compounds. “[Wearing support hose] will reduce some of the strain on the connective tissues and help prevent more destruction of damaged collagen, but second, it will place a force on the thighs and buttocks that is perpendicular to the long axis of the body to counteract gravitational stress,” Dr. Pugliese says. “In addition, this force is able to directionally stimulate the fibroblasts to produce collagen... through directionally sensitive cell receptors called integrins.”
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Cortisol secreted in response to stress leads to fat storage beneath the skin, thereby aggravating cellulite. Glycyrrhetinic acid, a compound derived from licorice, fights this response \(^1,13-15\) making it a promising candidate for cellulite therapy.

"The mechanism of action of glycyrrhetinic acid is to reduce fat. Cortisol is involved in the distribution and deposition of fat, which is regulated by an enzyme called 11-beta-hydroxysteroid dehydrogenase," Decio Armanini, MD, professor of endocrinology at the University of Padua in Italy, tells Life Extension. "Glycyrrhetinic acid, the active principal of licorice root, blocks 11-beta-hydroxysteroid dehydrogenase type 1, thus reducing the availability of cortisol at the level of adipocytes."

A groundbreaking study by Dr. Armanini’s group \(^15\) showed a promising effect of topical application of a cream containing 2.5% glycyrrhetinic acid in reducing the thickness of thigh fat, as measured by ultrasound. Eighteen healthy young women, 20 to 33 years old and of normal weight, were randomly assigned to apply a cream containing glycyrrhetinic acid cream or placebo to one thigh.

After one month of treatment with glycyrrhetinic acid cream, both the circumference and the thickness of the superficial fat layer were reduced compared with the opposite, untreated thigh, and also compared with the placebo group. Both comparisons were statistically significant (P <0.005). In women treated with glycyrrhetinic acid cream, the thickness of the superficial fat layer decreased by more than 10%, from 16.8 to 14.7 mm. \(^15\)

"Orally ingested licorice and its active principal glycyrrhetinic acid can produce retention of sodium and water and decreased serum potassium and hypertension," Dr. Armanini says. "[In this study using topical glycyrrhetinic acid], no changes were observed in serum potassium, blood pressure, plasma renin activity, plasma aldosterone, or cortisol."

"The effect of glycyrrhetinic acid is at the level of fat cells. It could be effectively and safely used in the reduction of unwanted local fat accumulation," Dr. Armanini says. "We recommend the application of this cream to our patients with cellulite [related to] excessive topical fat accumulation (two applications per day). Its use is recommended [over] a limited skin surface (where cellulite is more evident as demonstrated in our study)."

Other research by Dr. Armanini’s group suggests that topical application of cream containing glycyrrhetinic acid could be helpful for acne and hirsutism (excessive facial or body hair in women), perhaps because of its antibacterial activity and its ability to counteract the effects of male hormones. \(^16-18\)

As well as its effects on fat deposition, glycyrrhetinic acid also has known anti-inflammatory effects, \(^19,20\) according to Dr. Thornfeldt. Fighting inflammation could, in theory, help break the vicious cycle of edema that aggravates cellulite. In fact, an extract of licorice root has been shown to reduce inflammation and swelling in the ear of laboratory mice, and even protect against skin tumors caused by toxic compounds. \(^21\)

The anti-inflammatory activity of licorice root could theoretically protect the connective tissue in skin by reducing the expression of proinflammatory cytokines and suppressing enzymes that degrade collagen \(^22\) and other structural support proteins of the skin.

"[Glycyrrhetinic acid’s] apparent benefit in treating signs of skin photoaging with topical formulations suggests it will help diminish visible cellulite by reversing the atrophic skin and connective tissue component of this condition," Dr. Thornfeldt says. "Formulating this ingredient with horse chestnut for topical application would seem to be promising as a cellulite therapy."
How Gotu Kola Stimulates Collagen Synthesis

The herb gotu kola (Centella asiatica) has a long history of use in Ayurvedic medicine and is widely believed to help retard the aging process.

Like horse chestnut, gotu kola is rich in triterpene saponins with effects that are beneficial in reducing cellulite. It functions by stimulating collagen production to strengthen the support structure, reducing inflammation, and improving blood vessel tone and circulation, thereby reducing capillary leakage.35

In the laboratory, asiaticoside, a major active component of gotu kola, has been shown to stimulate synthesis of human collagen type I,36 a deficiency of which appears to be primarily related to skin aging.

In a study described by Dr. Pavicic, gotu kola extract given orally at a dose of 60 mg for 90 days was effective in the treatment of cellulite.37 Amazingly, gotu kola not only caused shrinkage of fat cells over the buttocks and thighs, but also reduced unsightly fibrous tissue between fat cells.

“In this study there was a significant reduction in the diameter of adipocytes, especially in the gluteofemoral region and a decrease in inter-adipocyte fibrosis,” Dr. Pavicic says. “Another study showed that a cream containing gotu kola formulated with other natural plant complexes significantly improved the biomechanical properties (extensibility and firmness) of the skin. The effects of gotu kola are attributed to triterpenoids that favor lymphatic drainage and stimulate synthesis of the extracellular matrix.”38

According to Dr. Sasaki, “Gotu kola has been used to treat cellulite topically because of its purported effects in strengthening tissues surrounding fat-storage cells, to veins, and to reduce the storage of subdermal moisture in the legs.”

Gotu kola’s ability to improve circulation in small blood vessels is also well demonstrated by a clinical, randomized study of the herb in diabetic patients with microangiopathy, a condition marked by reduced blood flow through the microcirculation.39 Thirty patients were treated for six months with the total triterpenic fraction of gotu kola asiatica, 60 mg twice daily. After six months of treatment, these patients showed significant improvements in microcirculatory values measured with Doppler ultrasound and decreased leakage from capillaries, whereas control patients had no changes.

“Gotu kola has been used as a medicinal herb for thousands of years in India, China, and Indonesia to heal wounds, improve mental clarity, and treat skin disorders such as leprosy and psoriasis,” Dr. Sasaki says. “Today American and Europeans use gotu kola for disorders that cause connective tissue swelling, such as scleroderma and psoriatic arthritis, for depression, and to improve memory and concentration.

Gotu kola is rich in flavonoids with good antioxidant activity needed for healthy skin. The anti-inflammatory properties of gotu kola suggest that it might also be helpful for atopic dermatitis in conditions of cold and dry weather.40

A Multi-Pronged Approach

Effective cellulite therapy may ultimately require a multi-pronged approach: mobilizing and reducing fat, preventing breakdown of support structures within the skin by promoting collagen synthesis, and preventing capillary leakage, while inhibiting inflammation and edema.

Glycyrrhetinic acid, horse chestnut, gotu kola, Phycoboreane™, Rhodysterol™, ADIPOSLIM™, and ADIPOLESS™ are well poised to facilitate this strategy, ideally in combination with healthy lifestyle changes and use of adjunctive measures.

“Since cellulite is the visible manifestation of multiple pathologic processes, one cannot reasonably expect a single agent to effectively treat this disease,” Dr. Thornfeldt concludes.
How Horse Chestnut Reduces Swelling, Improves Circulation

Similarly to licorice root, compounds contained in horse chestnut (*Aesculus hippocastanum*) appear to reduce swelling (edema), combat inflammation, and improve sluggish circulation. The primary active ingredient in horse chestnut is escin, a member of the chemical class known as triterpene saponins, which decrease fluid leakage from small blood vessels, quiet inflammation, and block the action of thrombin, a compound that promotes blood clotting. All of these effects could be of benefit in fighting cellulite.

"Escin purportedly is able to promote increased blood circulation through the veins by increasing the tone in venous walls, thereby enabling blood to flow unrestricted," Dr. Sasaki says. "This effect has made horse chestnut a popular topical and oral treatment for both chronic venous insufficiency and varicose veins."

A rigorous analysis of studies performed by the prestigious UK Cochrane review group showed that horse chestnut extract taken orally improves chronic venous insufficiency. Although the mechanism of action is not fully understood, it may involve blocking the activity of white blood cells involved in producing an inflammatory response.

A randomized trial in patients with chronic venous insufficiency showed that horse chestnut seed extract improves contractibility of blood vessel walls, thereby improving circulation, reducing leakage through capillaries, and preventing edema compared with a control group. In another randomized trial, treatment with oral horse chestnut seed extract in a dosage equivalent to 50 mg escin twice daily was equivalent to compression stocking therapy, which is a standard treatment for chronic venous insufficiency. Horse chestnut is widely used in Europe for chronic venous insufficiency. "It is considered by the Council of Europe to be anti-edematous and is approved by German Commission E for venous congestion," Dr. Thornfeldt says.

In addition to escin, horse chestnut contains an arsenal of other compounds that may help ward off cellulite, in part due to their highly potent antioxidant activity.

Horse chestnut contains compounds that have been used for years in the cosmetic industry to treat varicose veins and spider veins. Its primary active ingredient, escin, blocks the enzyme hyaluronidase that breaks down proteoglycans in the supporting structure surrounding small blood vessels, as well as in the endothelium lining blood vessels, thus helping prevent vascular leakage.

Additional benefits of escin include blocking inflammatory mediators such as 5-hydroxytryptamine and histamine and decreasing the breakdown of mucopoly-saccharides that help support capillary walls.

A recent exciting study has also revealed encouraging benefits of horse chestnut extract on reversing signs of facial aging. This Japanese study has shown that a horse chestnut extract significantly reduces wrinkles around the eyes, prompting the researchers to refer to it as "a potent anti-aging ingredient." In this study, 40 healthy women applied a gel containing 3% horse chestnut extract to the skin around their eyes three times daily for nine weeks, and researchers rated wrinkle severity according to serial photos.

After only six weeks, women who applied horse chestnut extract had significant decreases in the wrinkle scores at the corners of the eyes or in the lower eyelid skin compared with controls. These improvements were maintained at nine weeks.

Researchers are now asking if there is a possible interaction between cellulite and premature skin aging. If so, would horse chestnut extract benefit both conditions? The scientists suggest that compounds in the horse chestnut extract stimulate fibroblasts, which are connective tissue cells involved in shaping tissue structures within the skin, wound healing, and blood vessel contraction. Although fibroblasts are not muscle cells, horse chestnut extract causes them to contract, effectively toning the support structures in skin.

"The results suggest that an extract of horse chestnut can generate contraction forces in fibroblasts," Dr. Pavicic says. "This could be a very useful effect in the treatment of cellulite."

Because it has an anticoagulant effect, horse chestnut should not be taken orally in patients who have bleeding disorders or who take anticoagulant drugs, such as Coumadin®, non-steroidal anti-inflammatory drugs, or aspirin. In a few cases, topically applied horse chestnut has been associated with allergic skin reactions.

In Europe, gels or creams containing 2% escin, applied three to four times daily, are popular for treating hemorrhoids, skin ulcers, varicose veins, and bruises. A randomized trial showed that this therapy is effective in reducing tenderness associated with bruising. For chronic venous insufficiency, the suggested oral dosage of horse chestnut extract is about 500-1,000 mg a day (supplying 100-200 mg of the primary active ingredient escin).

"It is unknown what would be the optimal dose in cellulite but it seems wise to start with a comparable dosage," Dr. Wollina says. "There is evidence for anti-inflammatory activity, increased capillary filtration rate, and anti-edematous activity. Insofar, horse chestnut extracts are candidates for anti-cellulite treatment."

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