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Cellulite – Actiology and Treatment

Will Detergents Disappear? Alternative Wash Technologies A. Oborska*

The Cellulite – Aetiology and Treatment

Cellulite and its Aetiology

Despite its high prevalence, the aetiology of cellulite is still not well known. There have been just a few reviewed articles devoted to this subject in the medical literature over the past years (4). As it has been observed, the appearance of cellulite is usually connected with significant changes in the skin structure, problems with microcirculation or inflammation (Fig. 1).

Changes in the structure of skin

Many hypothesis quoted in the literature maintain that the appearance of cellulite is determined by fatty protrusions through the dermal-hypodermal interface (5). This process can be connected with the collagen breakdown that can be caused by the hormone estrogen – it has been proven that this hormon stimulates collagenase production in fibroblasts (6). Weakening of the collagen fibres enables the fat to bulge upward. The fat gains more space to expand – the adipocytes enlarge their size and stimulate preadipocytes to form adipocytes (7). Then the subcutaneous fat projection into the upper dermis can be observed.

It has been also proven that estrogens are able to increase production of hyaluronic acid and chondroitin sulphate. From one hand, the alterations in the structure of glycosaminoglycans and increase in their hydrophilicity can cause water retention which results in oedema, from the other hand it results in increased viscosity what can cause vessel compression. Also significant changes in the structure of proteoglycans have been observed (8).

Inflammatory factors

Another important aspect of the generation of cellulite involves the inflammatory processes taking place in the changed



tissue. The inflammatory response results in activation of proteinases, such as col-

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in activation of proteinases, such as collagenase and elastase what finally weakens the structure of such as important proteins as collagen and elastin (9).

Introduction

ellulite is a problem of complex nature, manifesting by irregular skin contours and reflecting a variety of conditions introduced in the scientific literature as adiposis edematosa or gynoid lipodystrophy (1,2). According to the scientific literature the range of symptoms characterising cellulite includes disturbed fat metabolism, fluid accumulation, microcirculatory breakdown as well as alteration in the structure of dermal collagen and elastic fibres (3). All factors mentioned above results in the condition which is popularly known as »orange-peel skin«.

So, what the cellulite really is – is it only an aesthetic problem? What happens in the tissue giving such an effect?

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Dysfunctions in adipocyte metabolism The fatty tissue includes two layers separated by superficial fascia and composes of adipocytes - cells that store triglycerides and other substances. The processes concerning synthesis and degradation of fats called respectively lipogenesis and lypolysis are controlled by several factors. As it has been proven, lypolysis is strictly dependent on the presence of cAMP that influences activity of key enzymes in this processes - lipases. The synthesis of cAMP requires presence of adenyl cyclase. The degradation of cAMP occurs in the presence of phosphodiesterase. Hence, some substances acting through the activation of adenyl cyclase (e.g. catecholamines) or inhibition of phosphodiesterase (e.g. methylxanthines) can stimulate lipolysis (6) (Fig. 2).

Microcirculatory disturbances

Another important aspect concerns the disturbance in the microcirculatory system. Many authors have reported limitation of fluid movement and lack of lymphatic drainage as well as the lack of balance between arterial capillary filtering and venous capillary absorption (10). It may occur due to an increase in capillary pressure or decrease of the lymphatic flux and finally results in intercellular oedema (11).

Functional defects in lymphatic drainage can lead to the fluid accumulation, slow down the circulation what finally increases the rate of lipogenesis. The relationship between the deposition of fat and lymphatic system has been proven (12). The researchers have observed that the rate of blood flow and lymph flow through adipose tissue is inversely related to its growth.

The very significant role in oedema creation plays also capillary permeability. It has been proven that high concentration of prostaglandins in blood brings about an increase of capillary permeability what is strictly connected with oedema. The blood circulation system and lymphatic drainage are regulated by several factors, e.g. humoral factors such as catecholamines, prostaglandin, acetylcholine, histamine, serotonin, amino acids or for instance by many pharmacological factors such as phosphodiesterase inhibitors or alpha and beta blockers.



The neuro-vegetative unit

Lipolysis and lipogenesis are processes partially mediated by nervous system through the action of beta and alpha2 adrenergic receptors situated on the fatcell surface. It has been documented. that factors activating *B*-adrenergic receptor encourage lipolysis. From the other hand, it has been observed that factors that activate the α2-adrenergic receptor discourage lipolysis. So, agents promoting lipolysis should act as β-adrenergic stimulators or/and α2-adrenergic inhibitors (6). Their activity on the alpha and beta receptors provokes a response through the adenyl cyclase system and modifies the level of cAMP, which is necessary to the trigliceryde hydrolysis. Popular β-adrenergic stimulators are theobromine, theophylline, caffeine, epinephrine and aminophylline. Substances acting as α 2-adrenergic inhibitors includes among others yohimbine and piperoxan.

Materials of Plant Origin – Treatment of Cellulite

The complex nature of cellulite forces the cosmetic industry to employ still new active substances that would be able to overcame this problem. The very common ingredients of anti-cellulite products became various plant extracts, mixtures including substances that are expected to influence the rate of lipolysis, improve microcirculation, decrease the permeability of microvessels, facilitate lymphatic drainage, influence collagen synthesis or act as β -adrenergic stimulators or α 2-adrenergic inhibitors (13). The most common plant extracts employed in the anti-cellulite products are ivy, algae, butcher's-broom, ginkgo biloba, arnica, horse-chestnut, green tea, sweet clover, grapes, evening primerose (oil).

Ivy (Hedera helix)

One of the most common plant that has found a broad application in the cellulite treatment is ivy which displays anti-inflammatory and bacteriostatic activity, influences microcirculation and prevents oedema. Ivy is a plant rich in triterpenoid saponins - contains high level of hederagenin glycosides, hederacoside C and Bhederin as well as oleanolic acid glycosides. Other active components of ivy are flavonoids, caffeic and chlorogenic acids. Saponins contained in ivy are compound responsible for blood vessel protection and permeability decrease. Flavonoids present in ivy display anti-radical and anti-inflammatory activity, decrease the permeability of microvessels and influence the activity of many important for the cellulite enzymes (collagenase, elastase) (14). According to these features ivy has found broad application in anticellulite products.

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Butcher's broom (Ruscus aculeatus) Other plant widely used in cellulite treatment is butcher's broom. In the medicine butcher's broom has found application in improving disorders involving the venous system, including venous fragility or varicose veins. The experiments have proven that butcher's broom displays positive effect on microcirculation, what plays a significant role in the cellulite treatment (15). Butcher's broom contains saponin compounds such as ruscogenin (0.12%), neoruscogenin, as well as flavonoids, sterols (sitosterol, campesterol, and stigmasterol), fatty acids (tetracosanoic acid) (16). The activity of compounds mentioned above makes Butcher's broom useful in the treatment of venous insufficiency and lymphedema as well as in the treatment of disturbances in the microcirculatory system accompanying cellulite.

Ginkgo biloba (Ginkgo biloba)

Other plant strongly influencing microcirculatory system is Ginkgo biloba – plant of Asian origin, containing high level of flavonoids as well as characteristic diterpenes ginkgolides.

According to the presence of compounds mentioned above Ginkgo biloba has found an application as a capillary fragility preventing agent as well as plant that decreases blood pressure. It is to be noted, that the Ginkgo extract contains quercetin and kaempferol what secures high antioxidant activity (17).

Other components characteristic for ginkgo biloba are ginkgetin and isoginkgetin. Ginkgetin, called also amentoflavone 7,4'- dimethyl ether, turned out to be a compound based on the linkage of two flavone nuclei that created a biflavonoid molecule, composed of two dimethyl ethers of apigenin. Isoginkgetin is known also as amentoflavone 4', 4'''- dimethyl ether. High level of flavonoids, ginkgolides and other compounds make ginkgo biloba useful in the treatment of disturbances in the field of microcirculatory system, as it take place also during cellulite.

Green Tea (*Camellia sinensis*) Tea is a beverage widely cultivated around the whole world. Black tea, green tea and

Oolong tea are known as three major kinds of manufactured teas and the green tea appears as the richest in flavonoid compounds (18).

Generally, fresh green tea leaves can contain about 20-35% of polyphenols in a dry weight and the composition of this plant varies with the age of leaves, season and climate. The major components of green tea extract are catechins - compounds displaying anti-radical and antiinflammatory activity (19). Except for these compounds the tea contains interesting from the cellulite point of view caffeine. Caffeine is a methylxanthine which stimulates lipolysis by acting through phosphodiesterase inhibition, what leads to the increase in the concentration of necessary to proper triglyceride hydrolysis cAMP (20). Apart from it, the tea contains beta-adrenergic stimulators - theobromine and theophylline, which are methylxanthines. These properties make green tea extract useful raw material in the cellulite treatment.

Arnica (Arnica montana)

Due to the high level of flavonoids such as quercetin, isoquercetin, kaempferol, rutin and apigenin –7–0-glucoside Arnica montana has found wide application in cosmetic industry including products dedicated to the skin with microvascular problems as well as in cosmetics appropriated for swollen legs and cellulite.

Guarana (Paullinia cupana)

The very exotic plant that can be found in anti-cellulite products is guarana (*Paullinia cupana*) – a creeping shrub native to the Amazon. It contains alkaloids, flavonoids, terpenes, tannins, saponins and other substances. The components that could be especially important for the cellulite reduction are caffeine, theobromine, and theophylline (23).

Other materials of plant origin

The wide market of anti-cellulite products employs many kinds of plant materials. That could be including high amount of iodine seaweed or protecting blood vessels grape seed extract. The researchers have documented that anthocyanins and proanthocyanidins of grape origin display wide spectrum of biochemical properties including influence on the microvascular system – they can be helpful in the capillary fragility and varicose vein treatment (21). Proanthocyanidins are known to inhibit elastase, collagenase and hyaluronidase activity what makes them important in the treatment of cellulite.

Other plant present in these kind of cosmetics is sweet-clover (*Melilotus officinalis*) – the herb containing among others flavonoids, coumarins, tannins, monoterpenes, playing anti-oedemic and venotonic activity (22). Anti-oedemic and vasoprotective activity displays also escin contained in horse-chestnut (*Aesculus hippocastanum*).

The other interesting plant is Asiatic centella (Centella asiatica) that contains triterpenic derivatives being able to stimulate collagen synthesis (*in vitro* study).

To summarise, plant materials that found application in the cellulite treatment usually influence microcirculatory system, preventing oedema and decreasing the permeability and fragility of microvessels. According to some constituents such as flavonoids, introduced extracts can play anti-inflammatory role and by modification of activity of such an enzymes as collagenase and elastase influence the skin structure.

Other plant extracts contain compounds acting as β -adrenergic stimulators such as theobromine, theophylline and caffeine, or α_2 -adrenergic inhibitors as well as substances that inhibit phosphodiesterase or stimulate adenyl cyclase.

Diminishing Cellulite – Scientific Proves

Coming to the final conclusions one question appears – do all of these compounds act as they supposed to do in the cosmetics available on the market? What are scientific proves that they influence cellulite? How many publications concerning skin penetration ability of these active compounds from particular products can we find in the literature? The main problem in cosmetic applica-

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tion of active compounds is their skin penetration ability. It has been documented, that activity of the substance depends strictly on its skin penetration ability (24). To be effective, the compound must overcome the skin barrier, which is *stratum corneum* and reach the proper skin layer.

The experiments carried out by Heard and Johnson have proven that caffeine, theobromine, theophylline and catechin from applied in anti-cellulite cosmetics guarana extract can penetrate the skin (25). Transdermal delivery across full thickness pig ear skin was investigated in vitro using Frantz-type diffusion cells with the reverse-phase HPLC being used for the quantification of the permeation of substances mentioned above. It has been also proven that applied vehicle and concentration of substance play very important role in the penetration rate of all studied compounds.

In vitro transdermal delivery of caffeine and the major catechins from extract of Camellia sinensis was the subject of other study (26). Transdermal delivery was determinated across full thickness pig ear skin from saturated solutions of green tea extract in pH 5.5 citrate –phosphate buffer. It has been proven that all examined substances penetrated the skin under *in vitro* conditions (Frantz-type diffusion cells).

Analysing the reports concerning evaluation of the activity of an anti-cellulite products the very different results of studies can be observed. Although there are numerous topical treatments that are available at pharmacies, spas and via the Internet there are no large-scale studies demonstrating the effectiveness of these therapies. French scientists carried out the evaluation of the activity of an anti-cellulite product containing caffeine, ruscogenine and retinol (27). The study was conducted with 46 female volunteers and parameters such as skin macrorelief, the dermal and hypodermal structures and the cutaneous flowmetry were evaluated. The authors have noticed improved skin macrorelief and an increased cutaneous microcirculation after skin application of studied anti-cellulite product.

One of the other substances present in plant extracts applied in anti-cellulite



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products which were evaluated was aminophylline. However, in this case the result of research was negative – evaluating the effectiveness of emulsion containing aminophylline Collis and coworkers concluded that therapy was not effective. It has been observed that only 3 of 35 persons showed improvement (28).

Similar effectiveness was observed in the case of other anti-cellulite product containing gingko biloba, sea-weed, grape seed oil, evening primrose oil and sweet clover. A parallel placebo – controlled clinical study comparing the effectiveness of the product failed to reveal significant changes after a 2-month therapy (29).

Cellulite – Facts and Fiction

The rules of competitive market are a powerful agent. Being aware of the factthat so many women suffer from the cellulite one can easily guess that anti-cellulite products make a very important part of the cosmetic market. Analysing the labels of these products we can find following claims:

- eliminates cellulite
- minimizes orange peel
- restores skin firmness
- reduction in thigh measurement
- many other promising declarations

»Eliminates cellulite« means that the cellulite problem should disappear after the therapy! »Minimizes orange peel« forces us to strange considerations - when the orange peel becomes minimal? We should be also aware, that some other ingredients contained in the product can be responsible for skin firmness and smooth restoration. Moisturizing factors present in the formulation can increase the water content in the skin what can give an effect of smoother skin surface. To sum up - all of these claims should be confirmed by research carried out in laboratory. Despite of the significance of the problem the literature concerning the influence of plant materials applied in anti-cellulite formulations available on the market is very narrow - a very small study purports significant medical claims.

Conclusion

Cellulite is a problem of complex nature, manifesting by irregular skin contours and reflecting a variety of conditions introduced in the scientific literature as adiposis edematosa or gynoid lipodystrophy. The appearance of cellulite is usually connected with significant changes in the skin structure, problems with microcirculation or inflammation.

The large scale of the problem forces the cosmetic industry to look for solutions that would be able to overcame it. One of the very common raw materials applied in anti-cellulite products are plant extracts containing compounds that are recognized as agents influencing the rate of lipolysis, improving microcirculation, influencing collagen synthesis, facilitating lymphatic drainage as well as acting as β -adrenergic stimulators or α 2-adrenergic inhibitors. The very common plant materials are ivy, algae, butcher's-broom, ginkgo biloba, arnica, green tea, sweet clover, horse-chestnut, grapes, evening primerose and many others.

Unfortunately, despite the high prevalence of this problem the scientific literature confirming activity of these extracts is still very narrow. The number of publications concerning the activity of particular active substances contained in plant extracts applied in anti-cellulite formulations is still limited and the problem has received very little attention as yet. This creates a broad field for scientists, researchers and producers - the significance of anti-cellulite products on the market should find a reflection in broad studies concerning the activity of applied substances and their skin penetration ability.

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