BODY REDUCING GEL: Synergistic combination of plant actives with lipolytic, Anti-edema and capillar permeability regulation properties

BODY REDUCING GEL

Incorporates a **synergistic combination of plant ingredients** intended to treat areas with localized adiposity as they bring:

- ✓ **Lipolytic properties,**
- ✓ **Anti-edema**
- ✓ **Capillary permeability regulators**

BODY REDUCING GEL includes:

- **Seaweed**
- **Guaraná**
- **Lemon**
- **Abrupt**
- **Imidazole derivatives**
- **Caffeine**
- **Naringin**
- **Hesperidin**
- **Neohesperidine**
- **Ruscogenin**

Introduction

Cellulite is the name identifying the **painful nodules that may appear in the connective tissue of the skin**. An aesthetic problem affecting 80-95% of women, cellulite generally

appears after puberty. It affects both obese and thin women and must not be confused with localised adiposity, which usually appears alongside.

The formation of cutaneous nodules has been quoted bibliographically since 1816 and many theories have been written on why it occurs, including gynaecological causes, hypophysarial malfunctions, hyerparathyroidal disorders, endocrine dystrophies, etc. Today we can say that there are various causes that enhance the appearance of cellulite, such as hereditary and constitutional factors, hormonal dysfunctions, circulatory problems, premature aging and psychological factors.

To understand the mechanism of its formation, we must remember that the skin is a heterogeneous organ constituted by three superimposed layers:

1. **the epidermis,**
2. **the epithelial covering;**
3. **the dermis, a vascularised area containing the elements of the connective tissue;**
4. **and the hypodermis, which mainly contains the adipose tissue.**

The dermis is made up of cells, fibers and the matrix of glycosaminoglicans. All of the components give the skin strength, resistance and elasticity. On a more internal level, the adipose tissue is made up of adipocytes, which store fat and whose main function is as a source of energy.

The fat deposited in the adipocytes is obtained from the diet, from the triglycerides synthesised in the liver and carried by the blood, and from the triglycerides synthesised in the adipocyte itself from glucose. The speed of the deposition and the use of the fats in the adipose tissue is determined to a very large extent by the ingest of the diet and energy expense, however, some hormones and the sympathetic nervous system contribute notably in the fatty metabolism of the adipocytes.

The skin is abundantly irrigated by a complex vascular system with two parallel plexus, one in the area separating the epidermis from the dermis and the other in the upper part of the hypodermis, and there are vertical branches connecting them. This irrigation system has a

dual function: it supplies the components needed for the metabolism and is simultaneously responsible for regulating the body temperature.

An important aspect of this system is the regulation of the blood flow and capillary permeability by the prostaglandins. These products are the fruit of a metabolic way that sets out from linoleic acid and passes through arachidonic acid. A greater concentration of prostaglandins in the blood causes an increase in the capillary permeability.

The blood flow system and lymphatic drainage are subject to a number of factors that regulate the way they work. On a hormonal level, there is a balance between progesterone and estrogens, which cause the elimination and retention of liquids respectively. It is obvious that an imbalance in these hormones may cause significant changes in the interstitial fluid.

The phenomenon of cellulite begins with a failure in the micro-circulation, as has been shown by a number of authors. The result of this abnormal capillary function is the initial formation of oedema, which may be started by four causes:

1. by an **increase in the capillary pressure** causing fluids to be accumulated in the interstitial spaces.
2. by a **decrease in the plasmatic proteins** with the result that the capillary pressure will try to compensate and enhance the release of fluid from the capillaries into the tissue spaces.
3. by a **lymphatic obstruction**, which will cause fluids to accumulate in the interstitial spaces.
4. by an **increase in the permeability of the capillary membranes**, enormously enhancing the flow of fluids to the tissue space.

This failure in the micro-circulation also affects the normal function of the adipocytes, which synthesise larger amounts of triglycerides, accumulated in the cell causing an increase in size. All this accelerates the exchange of the cellular phosphates with the consequent

release of linoleic acid, which causes the formation of prostaglandins and brings about an increase in the permeability of the capillaries.

These processes of fluid retention in the interstitial spaces and the accumulation of lipids in the adipocytes create a vicious cycle that is difficult to break. The fluids retained put pressure on the circulatory and lymphatic system, causing dysfunctions in the adipocytes, which, in turn, produce more prostaglandins, leading to an increase in capillary permeability.

The adipocytes grow because of their increasing triglyceride content. They are trapped and gathered, gradually failing to carry out their function of transforming lipids and other energy nutrients (glucose). In this way, nodules or capsules are formed which stand out on the surface of the skin, as the fibres of the dermis are also compressed. The appearance of these nodules further compresses the blood and lymphatic vessels and prevents them from carrying out their function of eliminating the fluids accumulating in the interstitial space. This vicious circle accelerates the progressive worsening of the situation. Finally, as a side effect of the obstruction of the blood flow, the temperature of the tissue drops and the metabolism slows.

All of this process is reflected externally by oedema, a painful feeling and roughness known as orange peel. An effective cellulite cosmetic treatment must have the following actions:

1. **Action on the blood flow**
2. **Action on the metabolism of the fatty acids**
3. **Action on capillary permeability**

ACTION ON THE BLOOD FLOW

Active principles must be included that are capable of allowing the oedema to be reabsorbed in order to reduce and finally eliminate the liquids in the interstitial spaces. This is the case of the saponosides, complex molecules that are found in many vegetables and which are made up of a glucidic fraction and another that is non-glucidic, generically known as sapogenin. Depending on the structure of the sapogenin fraction, the saponosides may be triterpenic (ginsenosides, 18-β-Glycyrrhetic acid, escin, asiaticoside) and steroidal (ruscogenin, saponaria saponins).

Ruscus is a powerful venous vasoconstrictor, which provides an anti-oedema effect, an action caused by the presence of two genines, ruscogenin and neoruscogenin.

The improvement and activation of the blood flow is another of the effects we hope to achieve with cellulite treatment, and the plants containing purine bases are active in this field. The active principles responsible for this action are xanthine alkaloids the most important of which are caffeine, theophylline and theobromine, all found in cocoa, tea, coffee, cola nut, guarana and mate.

ACTION ON THE METABOLISM OF FATTY ACIDS

In cellulite treatments, it is necessary to activate the metabolism of the fats, firstly by increasing the cAMP, thus increasing the levels of lipase, which enhances the hydrolysis of the glycerides, and secondly, by inhibiting phosphodiesterase, which will bring about an increase in the lypolitic processes. All of this will lead to a regularisation of the size of the adipocytes.
Marine plant extracts are used because of their ability to activate lipase and also because they inhibit phosphodiesterase, thus reducing the accumulation of triglycerides in the adipocytes. Similarly, the xanthic bases specifically inhibit the phosphodiesterase responsible for inactivating the cAMP, acting as a powerful activator of lipolysis.

ACTION ON CAPILLARY PERMEABILITY

In order to reduce capillary permeability to normal levels and at the same time reinforce the resistance of the capillaries, use is made of the flavonoids. These actives inhibit various enzymatic systems of the prostaglandin-forming metabolic route (lipoxygenase, cyclooxygenase...), and when the circulating levels fall, the permeability is regulated and capillary resistance increases. The flavonoids are widespread in nature, especially hesperidin, neohesperidin, naringin, derivatives of quercetin, apigenin and rutin.

The creation of complexes that include active ingredients belonging to each of the described groups is an excellent solution for the cosmetic treatment of cellulite.

BODY REDUCING GEL contains the following extracts:

PLANT	BOTANICAL NAME	ACTIVES	ACTIONS
SEAWEED	Laminaria digitata Lamx	Imidazol derivatives	Fatty acid metabolism
GUARANA	Paullinia cupana Mill.	Caffein	Fatty acid metabolism Blood flow
LEMON	Citrus limonum Risso	Naringin, Hesperidin, Neohesperidin	Capillary permeability
BUTCHER BROOM	Ruscus aculeatus L.	Ruscogenin	Blood flow

BODY REDUCING GEL COMPOSITION

- **LAMINARIA**

Laminaria in dry form contains 12% water, 15% mineral salts (chlorines, sulphates and iodines). The dried seaweed contains less than 1% lipids, some 5% proteins and about 65% of its content is represented by sugars, represented by the following:

Mannitol (12-15%)

Soluble condensed glucides (15-40%) and particularly **fucoidine and laminaran.** Laminaran is a glucane which exists in two forms, one insoluble in cold form and the other soluble. The two forms are made up of D-glucose (1-3), but there are also proportions of 1-6 links and residues of mannitol. Their content varies depending on the time of year when they are collected, and represents as much as 35% of the dry weight.

Algin: 15-40% of the dry weight.

For centuries, algae have been included in the human diet and used as fertilizers. For more than a century, algae have also been a source of colloids, successfully used in a wide range of applications such as thickeners, gelling agents and stabilizers for the food industry.

Only for the last 30 years approximately, marine algae have been recognized as a potential source of substances with pharmacological properties.

"Laminaria digitata L." Scientifically these plants belong to the family of brown algae.

Its content in **mineral salts and especially iodine stimulate** the **general metabolism** and cause an **increase in the osmotic exchanges** thus bringing about elimination of the excess fluids.

- **GUARANÁ**

Xanthine bases: Caffeine (3-5%), traces of theobromine (0.02-0.03%) and theophylline (0.25%).

Catechin-tannins: Up to 12%. 6% (+)-catechin, 3% (-) epicatechin and proanthocyanidins.

Essential oil: Traces. Compounds identified include: 2 methylbencenes, 2-methoxyphenyl-propenes, 2 alkyl-phenol derivatives, 2 cyclic sesquiterpenes and 1 cyclic monoterpene.

Minerals: Calcium (0.1%), phosphorus (0.3%), potassium (0.3%), magnesium (0.8%) and iron (4.3 mg).

Other active principles: Guaranine (3.5%), a crystallizable substance, chemically similar to caffeine. Saponins, choline, resin, mucilage, flavonoids (catechol and epicatechol) and starch (8%).

The guaraná name was conferred by the knowledge of the Guarani Indians who used the seeds to make a tonic-stimulating drink called " long life elixir." it was also used by the indigenous of the Orinoco and Maués, who considered it a sacred plant.

In the popular medicine, guarana is used as a cardiotonic, febrifuge, diuretic, relief for headache and diarrhea, treatment for dysentery, general stimulant and aphrodisiac. For cosmetic purposes, it is orally administered as an adjuvant for obesity treatments and locally applied as a treatment for cellulite.

- **LEMON**

- **Vessel-protection and venotonic activities**

Lemon flavonoids are vein-active and vessel-protective agents because they reduce the permeability and increase the resistance of blood capillaries.

Flavonoids are used in the treatment of blood vessel disorders such as varices, chronic venous insufficiency (CVI), low capillary resistance, etc. Their protective effect is due to their high affinity for proline-rich proteins, such as collagen and elastin. These proteins are structural components of the veins. Their degradation weakens the blood vessels, inducing oedema and swelling of the lower limbs. Oral administration of flavonoids has been observed to effectively improve the capillary resistance in animal models.

The RELIEF study ("Reflexus asessment and quality of life improvement with micronized flavonoids in chronic venous insufficiency") is a controlled multi-centre study carried out between March 1997 and December 1998, in 23 countries around the world, in which more than 10,000 patients suffering CVI participated. These patients were treated with a purified flavonoid fraction for six months. The results of this study showed that the flavonoid treatment significantly improved the cases of pain, tired legs, swelling, cramps and oedema (when it was present) (Spignoli, G., 2000).

Thus, Lemon is of great use to formulate cosmetic products aimed at improving general blood circulation.

- **Collagen synthesis stimulating activity**

This activity is due to the **vitamin C content of lemon.**

Vitamin C, or L-ascorbic acid, also acts as a co-factor in the collagen synthesis. Vitamin C is essential for proline hydroxylation to occur. Consequently, it is essential to produce and maintain the integrity of collagen. Different studies have demonstrated that it can directly stimulate the collagen synthesis by activating the transcription of the pro-collagen mRNA and stabilizing it. Additionally, vitamin C reduces the production of metalloproteinase enzymes in the extracellular matrix (metalloproteinases stimulate collagen degradation in the dermis). In a study carried out with human volunteers, vitamin C 5% was applied on one of their forearms and placebo on the other, during a 6 months treatment. Skin biopsies of the forearms treated with vitamin C showed increased mRNA synthesis for collagen I, collagen III and the extracellular-matrix metalloproteinase 1 inhibitor. Interestingly, the best results were observed in those subjects who followed the poorest vitamin C diets (Chiu, A. & Kimball, A.B., 2003).

The collagen synthesis stimulating activity gives vitamin C wound-healing properties useful to treat injuries from traumatisms, skin burn or surgery. It is also beneficial for new tissue formation.

- **RUSCUS ACULEATUS**

Phlebotonic and anti-inflammatory properties. Mainly due to its phenolic acids and flavonoids content.

Ruscogenin potent vein-constrictor that exerts anti-oedema actions.

Mircetol, quercetol and kaemferol (phenolic acids) are inhibitors of different mediators at inflammatory process.

Rutin and Hesperidin Methyl-chalcone (Flavonoids) improves venous insufficiency.

Anti-inflammatory and **anti-edema** properties, due mainly to the presence of **triterpenic saponins** (10%), and particularly to that of **escin.**

Escin works on the connective tissue and the cell membranes.

CLINICAL EFFICACY STUDY

To check the efficacy of PRONALEN, we proceeded to carry out a biometrological test on human volunteers for 28 days with posterior evaluation against a control.

1. AIM OF THE STUDY

To evaluate the efficacy of PRONALEN against a control by measuring the density in terms of the fat infiltrated in the dermis, thigh's perimeter before and after treatment and the subjective evaluation of the cosmetic product. The study was designed as a simple blind.

2. TECHNIQUE

To evaluate PRONALEN, ecography was used as a non-invasive biophysical technique (2D DermaScan CR), measurement of thigh perimeter and objective evaluation.
2D DermaScan CR uses ultrasounds to measure the thickness of the cutaneous layers.

This method allows the two dimensional visualisation of the skin on the epidermis and dermis. The thickness and density of these layers can also be measured, and the cellulite nodules in the hypodermis may be studied. The images obtained with this system enable us to calculate the density of the dermis and see the percentage of fat infiltrated. The accuracy of the method is estimated at 2%. The equipment used, 2DDermaScan CR, is fitted with a 20 MHz transducer and the probe is applied directly to the skin.

Once treatment ended, a subjective evaluation was made of the product by the panellists filling out an evaluation questionnaire of slimming products.

3. PROTOCOL OF THE TEST

The study was made on 15 female volunteers of between 35 and 55 years of age. The selection of volunteers was carried out along the criteria of the laboratory responsible for the study and in compliance with the Helsinki/Tokyo/Venice declaration, on ethical and safety procedures on the practice of clinical trials on humans.

Treatment was carried out by applying a O/W type gel-cream (Gel B) containing 7.5% PRONALEN on one of the thighs, while the other was treated with the O/W type gel-cream control (Gel A). Application was made twice a day with a circular massage to enhance absorption.

The study was designed as simple blind, randomised, so the patient could not differentiate between the active and the control gel. The subject is his own control, as he applied the two products on himself.

5. RESULTS

Perimeter measurement

The results obtained show a significant decrease in the perimeter of the thighs after 28 days treatment. This decrease was observed in 87% of the volunteers and oscillated between 0.1 and 1.4 cm as compared with the control treatment (-0.4±0.1cm, p=0.01).

2DDermaScan CR

The results obtained establish that the treatment with the gel-cream containing PRONALEN causes a significant decrease of 10.4% in the amount of fat infiltrated in the dermis, as compared with the control (10.4±0.9%, p=0.01).

Subjective evaluation

78.5% of the volunteers said that they had felt a positive global effect after treatment with PRONALEN as compared with the control.

5. CONCLUSION

The use of a gel-cream containing 7.5% of PRONALEN as compared with a control in a slimming treatment for 28 days causes a significant decrease in thigh perimeter of between 0.1 and 1.4 cm and in fat infiltrated in the dermis of 10.4 %.

References

Alcaraz, J.; Ferrándiz, M. J. Ethnopharmacol. (1987), 21 (3), 209-229.

Armengol, R. et al. 17th IFSCC Internat. Congress, Yokohama, (1992), 3, 1218-1240.

Arturson, S.; Jonsson, K. Prostaglandins, (1975), 10, 941-948.

Baltassat, F ; Darbour, N ; Ferry, S. Plant Med. et Phytoth. (1985), 19 (2), 68-74.

Belitz, H.D. & Grosch, W. Química de los alimentos. Zaragoza: ed. Acribia, 1997; p: 237-39; 444 (ref. 613 BEL).

Bousquet V. et al. Bulletin d'esth. Dermatol et de Cosmétol., (1990), 64, 37-50.

Curri, S.B. Cosm. Toil. (1993), 108 (4), 51-58.

Das, L.; Ratty, K. Progress in Clin. Biol. Res. (1986), 213, 243-247.

Di Salvo, R.M. Cosm. Toil. (1995), 110 (7), 50-56.

Fain, J. N.; Malbon, C. Mol. Cell. Biochem. (1979), 25, 143-169.

Freile Pelegrín, Y. Algas en la "botica". Avance y Prespectiva. vol.20: 283-292.

González, J et col. Int. J. Biochem. (1989), 21 (8), 883-888.

Greenway, F.L. et al. Clinical Therapeutics (1987), 9 (6), 663-669.

Kale, P.N. & Adsule, P.G. Citrus In Handbook of Fruit Science and Technology. Production, Composition, Storage, and Processing. New York: Marcel Dekker, Inc., 1995; 39-65 (ref. 641* SAL).

Kashiwagi, A.; Hueckstead, T.; Foley, J. J. Biol. Chem. (1983), 258, 13685-13692.

Lucassen, G.W.; van der Sluys, W.L.N.; van Herk, J.J.; Nuijs, A.M.; Wierenga, P.E.; Barel, A.O.;

Lambrecht, R. Skin Research and Technology (1997), 3, 154-160.

Marcelon, G.; Verbeuren, T.J.; Lauressergues, H.; Vanhoutte, P. M. Gen. Pharmacol. (1983), 14,103-106.