BODY FIRMING GEL incorporates a **plant extract complex. Each plant was selected on the basis of its specific action** on the connective tissue of the dermis, so as to influence all the **factors involved in the loss of elasticity.**

Contains:

- ✓ **Alchemilla vulgaris**
- ✓ **Equisetum arvense**
- ✓ **Glycine max**
- ✓ **Medicago sativa**
- ✓ **Raphanus sativus**
- ✓ **Silybum marianum**
- ✓ **Triticum vulgare**

Alchemilla Lady's thistle Horsetail Germinated seeds

Introduction

Skin elasticity is a mechanical property of the skin due to its elastin content. Elastin is a dermal protein which, together with collagen and glycosaminoglycans, constitutes the connective tissue. All these elements are produced from fibroblasts.

Elastin is composed of a lineal polypeptide called tropoelastin – the basic structural unit – whose main amino acids are alanine, valine and glycine. The arrangement of amino acids in this polypeptide determines two different types of zones that alternate along the chain: hydrophobic zones (α-helix) – where the most abundant amino acids are proline, valine and glycine – are probably responsible for the elastic properties of the molecule; the other type

of zone, with alanine and lysine as the most abundant amino acids, contains the bonds with other tropoelastin polypeptides.

The elastin polypeptides form fibrous networks based on the covalent bonds between desmosine and its isomer isodesmosine residues, formed from the lateral chains of the lysine residues in tropoelastin. These bonds, which occur in the extracellular space, originate elastic fibers. These fibers are rather thin, 1 to 3 µm in diameter; they are thicker in the lower dermis, where they are arranged parallel to the skin surface, and become thinner as they approach the epidermis. These fibers contain 15% microfibers and 85% elastin.

Collagen is a protein composed of fibers, which vary largely in diameter (2-15 µm). Collagen accounts for 70% of the skin connective tissue; it is synthesized as three α-polypeptide chains (procollagen) that convert into collagen in the extracellular space. The most abundant amino acids are: glycine, proline, hydroxyproline and alanine, which form the helicoidal and triple-helix structures. Seven types of collagen have been described according to their composition and antigenic properties: type I is the most abundant one in the dermis, although type III (reticular fibers) can also be found. Collagen fibers are assumed to be responsible for the consistency of the connective tissue.

Glycosaminoglycans or acid mucopolysaccharides in the dermal connective tissue fill the extracellular spaces among fibers and cells. Covalent bonds are established between them and the peptide chains; the so-formed high molecular weight complexes are called proteoglycans. About 95% of proteoglycan weight consists of carbohydrates; their structure corresponds to non-ramified lineal chains. Differently from proteins, mucopolysaccharides do not fold into globular structures or rigid helicoidal structures, but are arranged at random in a rather rigid but expanded way, thus filling a huge volume in relation to their mass.

Because of their numerous hydroxyl and acid groups, they form hydrated gels, even at very low concentrations. Their high negative charge density attracts osmotic active cations, which results in better water retention. All the elements in the skin connective tissue are related to each other and together determine the functions of this tissue. Water is an essential factor in this scenario, because the water content determines the behavior of connective tissue constituents, especially elastin, due to the high hydrophobicity of this molecule.

FACTORS THAT MODIFY THE SKIN

Even when the **metabolism of proteins in the connective tissue is relatively slow**, as compared with that of other proteins in the body, the elements that constitute this tissue are continuously being degraded and synthesized during the early stages of development.
As this tissue reaches maturity, protein turnover becomes much slower. In general, such slowdown becomes evident from the age of forty. Besides the age-related slowdown, it is necessary to take into account a number of processes affecting the skin connective tissue such as the action of elastin- and collagen-degrading enzymes as well as internal/external factors that modulate the skin processes (UV radiation, lipid deposits, calcification, and lifestyle).

Cellulite is one of the processes that modify the connective tissue. This condition is defined as an edematous-adipose state of the skin, which starts in the hypodermis and is associated to other phenomena that also affect the skin structure. Cellulite dramatically reduces the elasticity of the skin; first because of the presence of edema fluids and later on, because of the formation of sclerotic nodules in the dermis and the epidermis, which stretch the tissues in a continued and disproportionate way. After an effective anti-cellulite treatment, the consequent tissue flaccidity is revealed.

Skin aging is also one of the most relevant processes that modify the connective tissue. Aging is a physiological process that produces morphological changes in the skin, observable in the epidermis, the dermis and the skin appendages. Aging-inducing factors include intrinsic factors, such as the passage of time, and extrinsic factors, such as environmental agents, the main one being sunlight.

Physiological aging reduces the amount of peripheral microfibers, which eventually disappear, leaving the elastic fibers surface irregular and granular; the microfibers in the elastin matrix become thicker and the amount of glycosaminoglycans decreases as well as the number of fibroblasts and their ability to synthesize connective tissue components.

In aging processes induced by external agents, especially by sunlight, amorphous elastic fibers and larger amounts of glycosaminoglycans are observed, as well as excessive formation of bonds between elastin and collagen; the fibers become thicker and their functionality decreases. Additionally, abnormal elastin deposits in the higher skin layers may substitute collagen, and calcification, lipid deposits and increased amounts of enzymes (elastases) may contribute to the general effects of aging. The activity of elastases accelerates the degradation of the connective tissue.

Because of its histological characteristics, the breast is prone to premature aging, observable as reduced firmness and tone. The breast is particularly sensitive to pregnancy, fast weight-loss and some sports. Progressive firmness loss eventually results in drooping breasts, called ptosis. Several changes take place in the skin connective tissue that surrounds and supports the mammary gland. Therefore, any factor modifying the constituents of the connective tissue may result in breast drooping.

Obesity is another process that modifies the connective tissue. It is defined as an excessive fat accumulation in the body or else, as general a hypertrophy of the adipose tissue. Fast weight-loss and weight fluctuations produce connective tissue modifications that affect the elasticity.
In summary, the factors that modify the connective tissue and reduce elasticity are:

- Cellulite
- Physiological aging and related processes
- Environmental aging-producing agents: UV radiation
- Body weight fluctuations
- Possible consequences of connective tissue modifications include:
- Ptosis or drooping breasts
- Atrophic stretch marks
- General skin flaccidity

PREVENTION

To prevent the loss of tissue elasticity it is necessary to take into account all the factors that produce modifications to the connective tissue. Thus, it is necessary to prevent the effects of physiological and environmental aging, the onset of cellulite, and the fast weight fluctuations. During weight loss processes, the dermal connective tissue should be allowed to restructure, thus preventing the occurrence of stretch marks and ptosis.

To maintain a healthy turnover of connective tissue components frequently used products include: products that stimulate fibroblastic protein synthesis, elastase inhibitors to prevent elastin proteolysis and the consequent firmness loss and mineral-rich, especially silicon-rich, products because of their ability to stabilize glycosaminoglycans in the connective tissue, particularly in the collagen fibers.

UV sunlight largely accelerates intrinsic aging as well as aging induced by external factors. The use of free radical scavenger substances prevents the oxidation of unsaturated membrane fatty acids and the consequent lipoperoxidation – a process that normally accelerates aging and reduces skin firmness.

Cellulite also reduces tissue firmness and should therefore be prevented by using adequate anti-cellulite treatments followed by firming treatments aimed at restructuring the affected area.

Fast weight loss also reduces skin firmness, in general or in local areas, such as the breasts. Furthermore, fast weight loss breaks the skin fibrous network, which results in stretch marks. Therefore, weight loss should be progressive, without affecting the connective tissue structure, using products that stimulate fibroblastic protein synthesis and substances that help restructuring this tissue.

BOTANY AND CHEMISTRY

The extracts contained in the BODY FIRMING GEL are: Lady's thistle, Alchemille, Equisetum and Germinated seeds.

Plant	Elements of the connective tissue
Lady's thistle	Collagen-Elastin
Alchemille	Elastin
Equisetum	Glycosaminoglycans
Germinated seeds	Fibroblasts

- **Lady's thistle** (Silybum marianum Gaertn.): **Free radical scavenger action and remarkable anti-elastase action.**

- **Alchemille (Alchemilla vulgaris L.):** The leaves are the used part of the plant, because of their **6-8% tannin content, mainly oligomeric gallotannins and flavonoids; these components have anti-elastase activity.**

- **Equisetum (Equisetum arvense L.)**: Abundant mineral components, especially **silicon, and flavone compounds**. Its high silicon content helps **stabilize the glycosaminoglycans in the connective tissue.**

- **diverse Germinated seeds (Glycine soja Siebold y Zucc.; Triticum vulgare Villars; Medicago sativa L.; Raphanus sativus L.)**: are produced by inducing embryo development under specific temperature and humidity conditions. **The resulting amino acid and vitamin rich product have stimulating action on fibroblastic protein synthesis.**

CLINICAL EFFICACY STUDIES

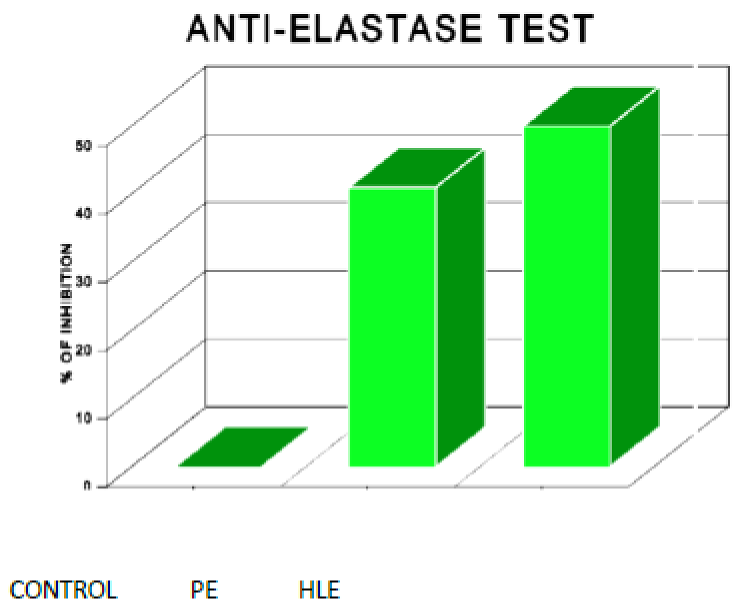
IN VITRO: ANTI-ELASTASE ACTIVITY

Elastases affect the elasticity of the skin connective tissue by breaking down elastin molecules. In order to assess the anti-elastase activity of PRONALEN FIRMING, two enzymatic tests were carried out: one using Pancreatic Elastase (PE) and another using Human Leukocyte Elastase (HLE). PE is a serine-protease, whose inactive form is stored in the pancreas and activated by trypsin in the intestines. HLE has been isolated from neutrophils and macrophages; it is one of the most powerful enzymes, which can break elastic fibers and other proteins in the connective tissue at neutral pH values;

this enzyme participates in inflammatory conditions and processes involving skin tissue degradation.

The concentration of PRONALEN FIRMING was 0.0036%.

Results demonstrated non-competitive inhibition by PRONALEN FIRMING on PE (41.0%) and HLE (50.0%) thus supporting the use of this product in cosmetic formulations aimed at improving the firmness of the skin tissue.



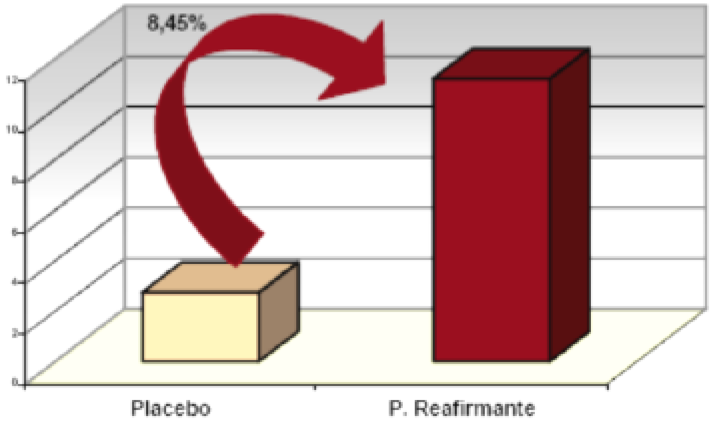
These results were presented during the 1st MEDITERRANEAN CONGRESS OF COSMETOLOGY-La Grande Motte (Montpellier-France, March 1996), organized by the Spanish, French and Italian Societies of Cosmetic Chemists, as part of the following articles:

- ✓ **Actividad anti-elastasa de un complejo vegetal.Benaiges, A., Betés, C., Armengol, R.**
- ✓ **Estudio de actividad y estabilidad de la sibilina.o Betés, C., Benaiges, A.**

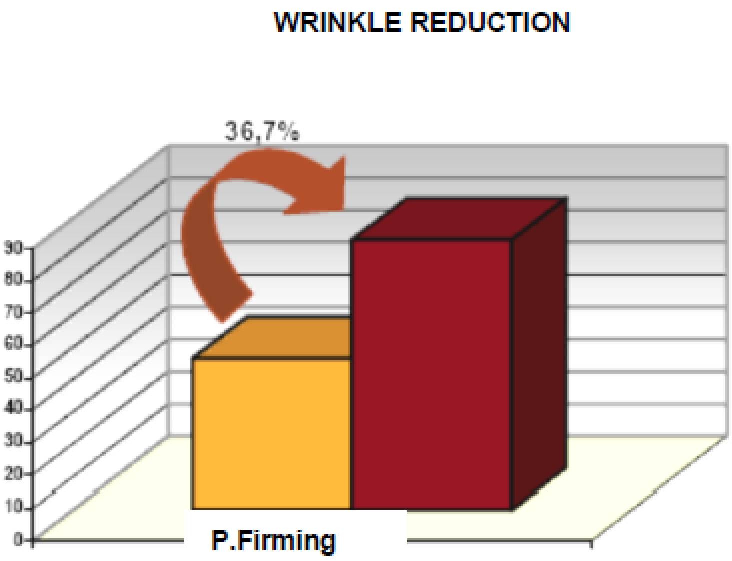
IN VIVO: EFFECT ON THE MECHANICAL PROPERTIES OF THE SKIN (ELASTICITY)

The in vivo efficacy of a cosmetic formulation containing PRONALEN FIRMING was evaluated by evaluating – before and after the treatment – its effects on skin mechanical properties (elasticity) and by image analysis of the skin surface, particularly the wrinkles.

Skin elasticity can be evaluated by measuring the degree of skin recovery after applying suction with a Cutometer (SEM 474 Courage & Khazaka). In this study, 350 mbar constant pressure were applied and the recovery was measured three consecutive times. On the basis of these measurements, an elasticity curve was built, where the parameters R0, R1 and R9 could be calculated.



R0 is the height of the curve, obtained when the suction pressure is applied; R1 is the width of the curve, corresponding to the skin capacity to recover its initial state after pressure has been applied; R9 is an experimental elasticity value calculated from R0 and R1.



This test was carried out on a group of six women aged 45-55 (average age = 50); the treated area was the eye contour; the treatment consisted in two daily applications of the mentioned cosmetic formulation for a 30 days period. Results revealed significant improvement of skin elasticity, which supports the use of this product in cosmetic formulations.

Results showed 8.45% increase of skin elasticity after 30 days of treatment.

Image analysis of skin surface duplicates was carried out before and after the treatment. This analysis allows for evaluation of the skin relief and its evolution after a certain treatment. In this study, the depth of wrinkles was measured before the treatment and 45 days after the treatment.

Results demonstrated that PRONALEN FIRMING reduced the wrinkles by 36.7% thus indicating that it has anti-aging properties.

References:

1.- Activités inhibitrices vis-à-vis de l'elastase, de la trypsine et de l'I-chymotrypsine in vitro,

2.- Activités angioprotectrices comparées in vivo. J. Pharmacol., 17, 1986, nº1, 21-27.

Benaiges, A., Betés, C., Armengol, R. "Actividad anti-elastasa de un complejo vegetal". 1º Congreso Mediterráneo de Cosmetología, La Grande Motte (Montpellier-France) Marzo, 1996.

Betés, C., Benaiges, A. "Estudio de Actividad Y Estabilidad de la Silibina". 1º Congreso Mediterráneo de Cosmetología, La Grande Motte (Montpellier-France) Marzo, 1996.

Bieth, J., Spiess, B., Wermuth, C.G. "The synthesis and analytical use of a highly sensitive and convenient substrates of Elastase". Biochemical medicine 11, 1974, p. 350-357.

Bombardelli, E., Spelta, M., Loggia, R.D., Tubaro, S.S.A. "Agin skin: protective effect of silymarin-Phytosome". Fitoterapia, 1991, volume LXII, nº2, p. 115-122.

Carnat, A., Petitjean-Freytet, C., Muller, D., Lamaison, J.L. "Teneurs en principaux constituants de la Prêle, Equisetum arvense, L.". Plantes médicinales et phytothérapie, 1991, Tome XXV, nº 1, p. 32-38.

Cillard, J., Cillard, P. "Composés phénoliques et radicaux libres" S.T.P. Pharma, 1988, 4 (7), p. 592-596.

Fiebrich, F., Koch, H."Silymarin, an inhibitor of lipoxygenase". Experientia 35, 1979, Birkhäuser Verlag, Bassel (Schwiez).

Fornieri, C., Quaglino, D., Lungarella, G., Cavarra, E., Tiozzo, R., Giro, M.G., Canciani, M., Davidson, J.M., Pasquali-Ronchetti, I. "Elastin production and degradation in cutis laxa acquisita". The Journal of Investigative Dermatology, 1994, vol. 103, Iss 4, p. 583-588.

Homsy, R., Pelletier-Lebon, P., Tixier, J.M., Codeau, G., Robert, L., Hornebeck, W. "Characterization of human skin fibroblasts elastase activity". The Journal of Investigative,Dermatology, november 1988, Vol. 91, No 5, p. 472-477.

Jonadet, M., Meunier, M.T., Villie, F., Bastide, J.P., Lamaison, J.L. "Flavonoides extraits de Ribes nigrum L. et d'Alchemilla vulgaris L.:

Koch, H.P., Löffler, E. "Influence of Silymarin and some flavonoids on lipid peroxidation in human platelets". Meth.and Find.Exptl. Clin. Pharmacolo., 1985, 7(1): p. 13-18.

Lamaison J.L., Carnat, A., Petitjean-Freytet, C. "Teneur en tannins et activité inhibitrice de l'elastase chez les Rosaceae". Ann. pharmaceutiques françaises, 1990, 48, nº 6, p. 335- 340.

Lassus, A. "Colloidal silicic acid for oral and topical treatment of aged skin, fragile hair and brittle nails in females". The Journal of International Medical Research, 1993, 21, p. 209-215.

Oikarinen, A. "Aging of the skin connective tissue: how to measure the biochemical and mechanical properties of aging dermis". Photodermatol. Photoimmunol. Photomed., 1994,10, p. 47-52.

Saint-Paul, A. "La composition élémentaire de quelques Equisetum médicinaux". Plantes médicinales et phytothérapie, 1980, tome XIV, nº2, p. 73-82.

Sincholle, D. "Etude de l'effet anti-radicalaire in vivo d'un extrait de graines de Chardon-Marie". Plantes médicinales et phytothérapie, 1988, tome XXII, nº2, p. 119-123.