



BOTOPICAL[®]

BOTOX[®]-LIKE ACTIVE INGREDIENT FOR A SKIN RELAXING EFFECT

Spontaneous and regular face movements show our emotions throughout the day and mark the skin with lines of varying depth: expression lines.

Starting around 30 years of age, a number of changes occur in the course of a process called intrinsic aging because the support tissues have lost their 'intrinsic' mechanical properties resulting in deterioration's that involve expression wrinkles that are reversible, through relaxation of the muscles, and wrinkles due to the effects of gravity that inexorably increase with time.

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Cosmetic medicine now offers injections of botulinum toxin which acts directly on the contractility of the facial muscles. This technique carries risks and inconveniences; for this reason, Ingredients To Die For is offering BOTOPICAL[®], a BOTOX[®]-like cosmetic solution to reduce tension in subcutaneous muscles and lessen the effects of time without setting the features.

In order to avoid the unpleasantness and risks related to botulinum toxin injections, To Die For proposes BOTOPICAL[®] a non-aggressive alternative to reduce expression wrinkles. Rich in organic compounds from rye, BOTOPICAL[®] favors the relaxation of subcutaneous muscles, thus correcting wrinkles caused by facial movements.

Cosmetic science has an alternative **solution** to this recurring issue ...
BOTOPICAL[®]

BOTOPICAL[®] rich in arabinoxylans is purified from rye seeds. These arabinoxylans serve plants as structural agents while offering fungal defense through their high level of Ferulic, and other phenolic, Acids. In skin care they offer a long lasting tensor effect by stimulating the mechanical cell functions involved in the modulation of skin tension forces and reducing the phenomena of microtensing to visibly smooth expression lines.

Recommended in all anti-wrinkle formula, BOTOPICAL[®] relaxes the features while at the same time conserving the natural mobility of the face.

BOTOPICAL[®] stimulates the formation of the mechano-receptors. Tested at 0.25%, on normal human fibroblasts, **BOTOPICAL[®]** stimulates the synthesis of integrin $\alpha 2\beta 1$ by 20%, and boosts the synthesis of vinculin, a marker of focal adhesions, by 28%.

BOTOPICAL[®] increases the mechanical resistance of the skin. Tested at 0.50% on normal human fibroblasts, **BOTOPICAL[®]** lead to a 62% increase in the synthesis of α SMA fibers, responsible for the retractile forces of fibroblasts. Moreover, the in vivo tests have shown the anti-wrinkle properties of **BOTOPICAL[®]** at 4% after 56 days of treatment on the level of the crow's foot and the nasolabial fold in 72% and 78% of volunteers, respectively.

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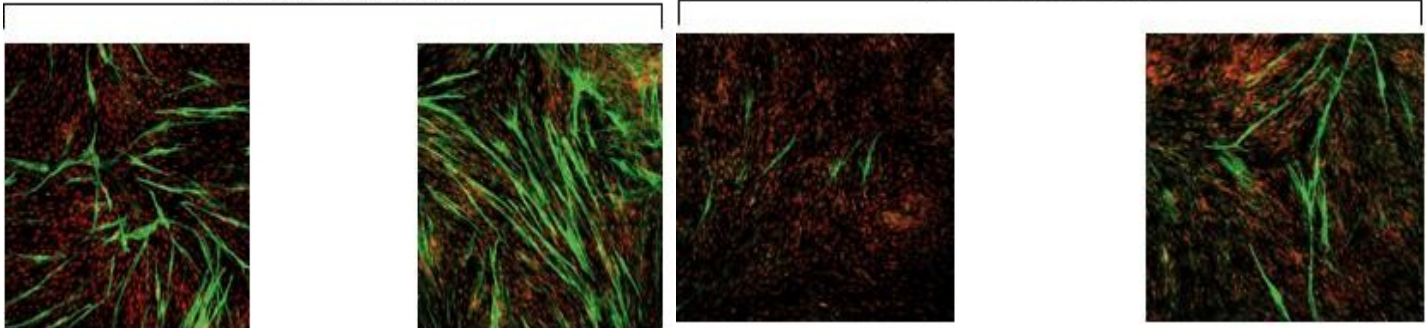
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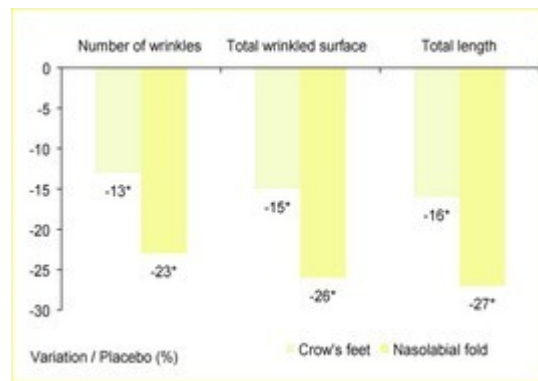
0.10% **BOTOPICAL®**

Normal human fibroblasts

Aged human fibroblasts



Visualization by immunocytology of the effect of **BOTOPICAL®** on the expression of α -SMA



Acting as an inside skin tensor, **BOTOPICAL®** is recommended for a long lasting anti-gravity and lifting effect.

BOTOPICAL® increases the mechanical resistance of the skin. Tested at 0.50% on normal human fibroblasts, **BOTOPICAL®** lead to a 62% increase in the synthesis of α -SMA fibers, responsible for the retractile forces of fibroblasts. Moreover, the in vivo tests have shown the anti-wrinkle properties of **BOTOPICAL®** at 4% after 56 days of treatment on the level of the crow's foot and the nasolabial fold in 72% and 78% of volunteers, respectively.

BOTOPICAL® An **Alternative** to **BOTOX®**... **Against** Expression **Wrinkles**

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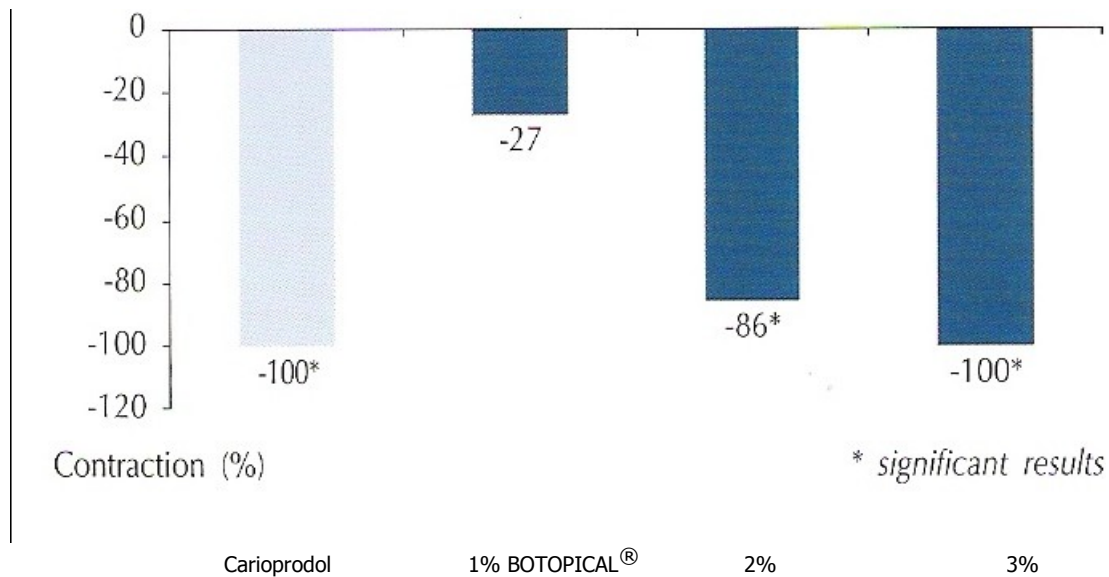
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BOTOPICAL® limits micro-contractions, acts effectively on the three target zones of expression wrinkles and significantly reduces the total wrinkled surface:

- Frown line (glabella) wrinkles (-20%)
- Crow's feet wrinkles (-40%)
- Nasolabial fold wrinkles (-22%)

Figure 1 Cosmetic Efficacy



Muscle Relaxing Properties:

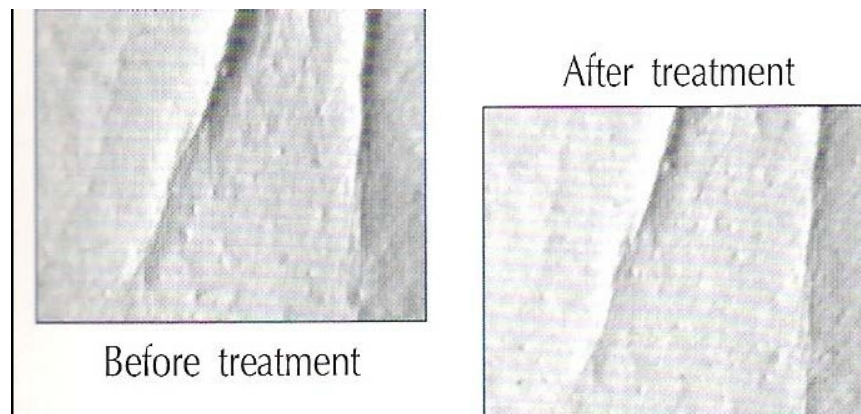
Effect on the contraction of muscle cells A nerve-muscle co-culture model was used to determine the effect of BOTOPICAL® on the frequency of muscle contractions. After localizing a zone with regular contractions under the microscope, the number of contractions was counted before and after 20 minutes of treatment. Tested at 3% BOTOPICAL® inhibits contractions of muscle cells by 100%.

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Anti- Wrinkle Properties:

BOTOPICAL® reduces contractions of the dermis and thus favors the reduction of wrinkles. Using a profilometer equipped with an image analyzer, the observation of the replicas of the 3 zones primarily involved by the appearance of expression wrinkles enabled the following parameters to be obtained: total wrinkled surface, total length of wrinkles, number of wrinkles, thereby measuring the anti-wrinkle efficacy of BOTOPICAL® formulated in 4% in an emulsion.

Figure 2 Crow's Feet wrinkles

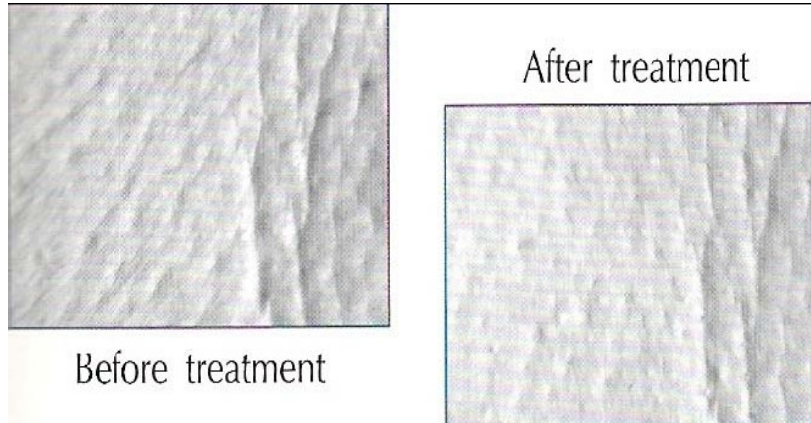


After 28 days of twice daily application and in comparison to the placebo, BOTOPICAL® significantly decreased the Crow's feet wrinkles:

Total wrinkled surface (-40%, P=0.020)
Total length of wrinkles (-34%, P=0.004)
Number of wrinkles (-13%, P=0.028)

The study of distribution of the results shows that the wrinkles on the crow's feet area decreased in 87% of the volunteers .

Figure 3 Frown lines (glabella) wrinkles

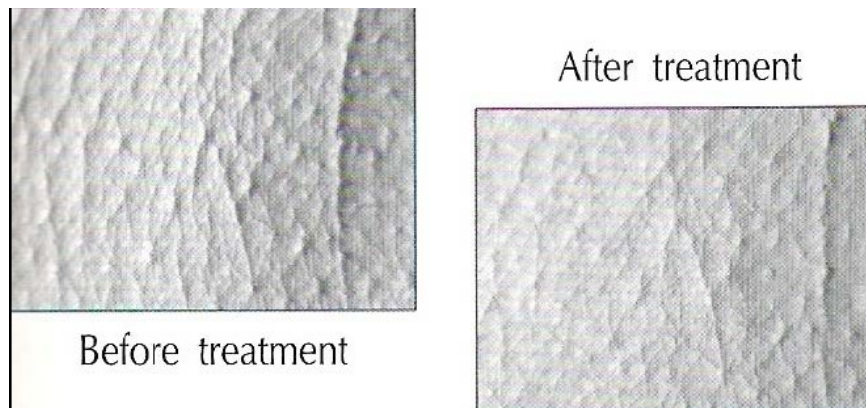


After 28 days of twice daily application on the glabella (frown line) and in comparison to the placebo, BOTOPICAL® significantly reduced the:

Total wrinkled surface (by 20%, $P=0.025$)
Total length of wrinkles (by 21%, $P=0.025$)
Number of wrinkles (by 18%, $P=0.042$)

The study of distribution of the results shows that the wrinkles on the frown line area decreased in 59% of the volunteers .

Figure 4 Nasolabial fold wrinkles



After 28 days of twice daily application and in comparison to the placebo, BOTOPICAL® significantly decreased the Nasolabial Fold wrinkles:

Total wrinkled surface (-22%, P=0.0013)
Total length of wrinkles (-20%, P=0.0039)
Number of wrinkles (-17%, P=0.0206)

The study of distribution of the results shows that the wrinkles on the frown line area decreased in 59% of the volunteers.

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A BOTOX®-LIKE ACTIVE INGREDIENT FOR A SKIN RELAXING EFFECT

See the attached Technical Data Sheet for more information.



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Technical Data Sheet

Trade Name: BOTOPICAL®
INCI name: Water & *Secale Cereale* (Rye) Seed Extract .
Form: Amber Colored Aqueous solution, characteristic odor.
Usage Rate: 4-10%
Dry matter: 40-60 g/L
Total Protein: 12-20 g/L (Lowry method)
Mineral ashes: 11-18 g/L
pH: 4.5 - 5.5
Preservative: Phenoxyethanol

Bacteriology: Sterile product, no yeast or mold present, no pathogenic germs present.

Storage: Store preferably at +20°C (in a dark place).

Use: Fully soluble in aqueous medium, solubility in ethanol: soluble up to 40/60 ethanol/water (v/v)

Innocuousness: Cutaneous irritation tests in vivo on human volunteers: non irritating.
No mutagenicity, no phototoxicity, no cytotoxicity. Evaluation of sensitizing capacity in vivo on human volunteers: non irritating.

The data submitted in this publication are based on our current knowledge and experience. They do not constitute a guarantee in the legal sense of the term and, in view of the manifold factors that may affect processing and application, do not relieve those to whom we supply our products from the responsibility of carrying out their own tests and experiments. Any relevant patent rights and existing legislation and regulations must be observed.