

Cellulite is THE topic that affects nearly all women, regardless of their age

With NOCTURSHAPE™ *blue ingredient*, Lipotec has developed an effective ingredient that is active at night and should help to reduce fat deposits



NOCTURSHAPE™ blue ingredient target the expression of the circadian protein nocturnin in adipocytes, which peaks at early night. By reducing its levels, it does the lipid accumulation. The stimulation of lipolysis has been significant in vitro at the tested concentration in synchronized cells during the differentiation process. Moreover, fat reduction has showed to be more effective with NOCTURSHAPE™ blue ingredient than with caffeine.

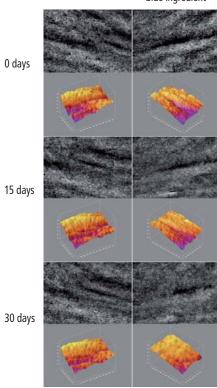
This new active ingredient is an exopolysaccharide which has been obtained through biotechnology from a planktonic microorganism. Its slimming profile is completed with its efficacy in reinforcing the dermal matrix through type I collagen, what contributes to reducing visible fat nodules that characterises cellulite.

Macroscopic benefit

A complete *in vivo* test supports the efficacy of NOCTURSHAPETM *blue ingredient* in reducing centimetres while improving the appearance and quality of the skin.

The reduction in thighs was of almost -1 cm after only 15 days of a nighttime active cream application (4%). The improvement of cellulite appearance was also visible per the increase of skin relief, as show the digital photographs, and the unevenness of subcutaneous fat deposits. This trend was also evident at the end of a 30-day treatment as well as when measuring skin firmness, improved by 23%. A clinical evaluation on the signs and intensity of cellulite complete the efficacy study.

Placebo 4% nocturshape™ blue ingredient



Volunteers applied the active cream on one side (left or right) of the body and a placebo cream on the other side, once daily at night, on hips and thighs, for 30 days. As per the results, NOCTURSHAPE™ blue ingredient can be incorporated into body care formulations claiming global anticellulite, slimming and firming properties with specific nightime application. Within chronobiology, circadian rhythms can give us a clue of which is the most favourable time to apply a specific cosmetic product. With this, more and more, efficient active ingredients can contribute to the saving time concept, a key theme in today's cosmetic market, while benefits can be accommodated to a wider range of lifestyles of modern consumers.

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Circadian rhythms are the most relevant of biological cycles in living organisms and comprise several processes with oscillations every 24 hours. The sleepwakefulness cycle and the changes in body temperature, which decreases at night and rises during the last hours of sleep, are an example. Indeed. An optimal adaptation of the organism to both its external and internal environments is critical to health and well-being. The intracellular biological clock is controlled by a network of feedback loops composed of activators and repressors. The main clock genes are Clock and Bmal1, regulating the expression of hundreds of downstream circadian genes, such as nocturnin.



Elena Cañadas

5 questions on this to Elena Cañadas, Marketing Manager Lipotec

Euro Cosmetics: What exactly does NOCTURSHAPE™ blue ingredient do in its fight against cellulite?

Elena Cañadas: This new biotechnological active ingredient produced by a planktonic microorganism targets nocturnin in adipocytes, a circadian protein involved in adipogenesis and lipid accumulation, reducing its levels specifically at nighttime. NOCTURSHAPETM blue ingredient reduces thigh contour and smoothes skin relief, providing a general improvement of cellulite appearance.

Euro Cosmetics: Why does application in the evening make sense?

Elena Cañadas: Biological processes in living organisms are subjected to a cyclic temporal organization that allows the regulation of various physiological processes. Circadian rhythms are the most relevant of the biological cycles, comprising the oscillations that recur with a period of approximately 24 hours. This circadian organization of biological functions provides an optimal adaptation of the organism to the recurrent

variations in the environment that means synchrony of the organism with external and internal environments is critical to health and well-being.

All the circadian processes in the body are regulated by an internal biological clock that receives external signals and maintains the synchronization with the 24-hour period, being light the major external synchronizing signal. This internal clock consists of an array of clock genes and proteins that oscillates its activity along a 24-hour period, forming a network of regulatory feedback loops.

One of the tissues that exhibit circadian patterns is adipose tissue. Adipocyte differentiation is regulated by clock genes, and some genes that enhance the process increase their expression at night, such as nocturnin gene, promoting the maturation of adipocytes. This is the reason why a formulation containing NOCTURSHAPETM *blue ingredient* should be applied at nighttime, in order to be more effective and provide greater results.

Euro Cosmetics: The gene Nocturnin plays a decisive role in creating the fat deposits that result in unsightly dimples. What have you achieved here?

Elena Cañadas: Nocturnin is a circadian CCG (clock-controlled gene) that controls adipogenesis in adipose tissue. Its levels oscillate daily, with a peak occurring at the start of the dark cycle (evening). Nocturnin protein is upregulated in early adipogenesis and is necessary for the stimulation of their differentiation to mature adipocytes.

In-vitro, NOCTURSHAPETM blue ingredient reduced the levels of the circadian protein nocturnin and increased lipolysis in human subcutaneous adipocytes, previously synchronized to a day-night rhythm during differentiation. Moreover, this new ingredient demonstrated to be more effective than caffeine in reducing lipid accumulation.

At the light of these in-vitro results, NOCTURSHAPE $^{\text{TM}}$ blue ingredient can be considered as one of the best partners to

help reducing the visible fat nodules characteristic of cellulite condition.

Euro Cosmetics: *In which products can this effective ingredient be used?*

Elena Cañadas: NOCTURSHAPETM *blue ingredient* can be incorporated into any formulation developed to offer a definition of the silhouette and smoothening of the skin relief. This novel ingredient is designed to provide the formulations with global anticellulite, slimming and firming benefits, being especially active during the night hours.

Euro Cosmetics: What success bas been achieved with the use of NOCTURSHAPETM blue ingredient?

Elena Cañadas: The in-vivo efficacy of this biotech ingredient was tested at two different concentrations, 2% and 4% in two panels of female volunteers with cellulite grades II and III of Nurnberger-Muller scale. Each volunteer applied the cream with NOCTURSHAPETM *blue ingredient* (either at 2% or 4%) on one side of the body (in the area of the hips and thighs) and the placebo cream on the other side, once a day at night for 30 days.

Impressive results were observed, 4% NOCTURSHAPE™ *blue ingredient* reduced thigh contours up to -1.5 after 15 days and after 30 days, the unevenness of subcutaneous fat deposits were reduced by 39%.

Increasing of skin firmness and smoothing of skin relief were other additional parameters that notably improved after the treatment with NOCTURSHAPE™ *blue ingredient*, providing a great visible improvement of cellulite condition in only 15 days.

Euro Cosmetics: *Thank you for the conversation.*