

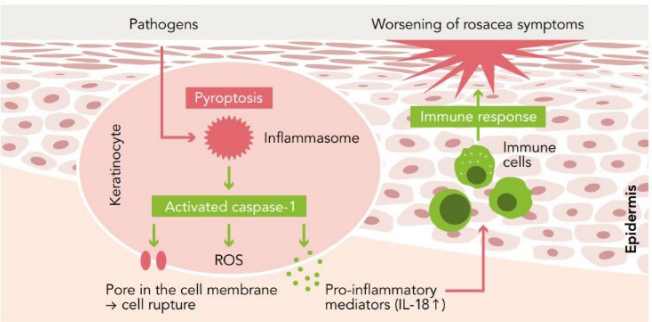


Calm the Flame of Pyroptosis—Soothe Irritated Skin

In the dynamic world of skin care, innovation is the key to meeting the complex needs of consumers. At the forefront of this is AmelioSense™, an innovative new active ingredient developed by Mibelle Biochemistry. Designed to combat skin redness and irritation by targeting pyroptosis, AmelioSense™ combines the power of shepherd's purse with a potent antioxidant complex, offering a comprehensive solution for irritated and flushed skin.

INFLAMED SKIN CONDITIONS REMAIN A CHALLENGE

Rosacea is a chronic inflammatory skin condition that mainly affects the face, particularly the cheeks and chin. It causes redness, visible blood vessels, and sometimes itching and pain. The exact causes are multifactorial, involving genetic and environ-



The pyroptosis scheme

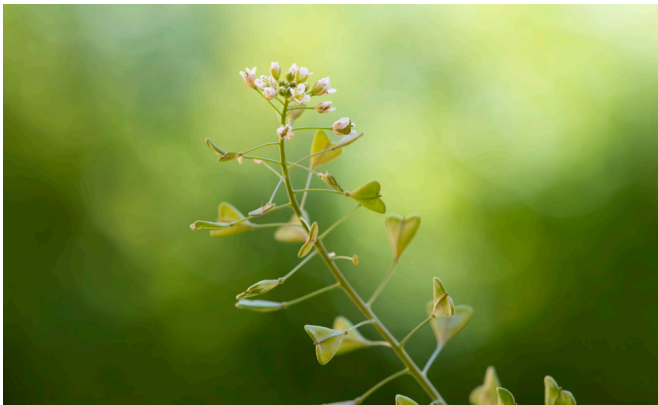


Figure1: Shepherd's purse (*Capsella bursa-pastoris*)

mental factors. Rosacea significantly impacts quality of life and self-esteem. Treatment is challenging and often does not provide lasting relief. Elevated pro-inflammatory mediators make the skin hypersensitive, leading to increased inflammation and blood vessel formation, causing typical facial redness.

PYROPTOSIS, THE SPREADING FIRE

Pyroptosis is a rapid inflammatory response triggered by pathogens, leading to cell death and inflammation. The term, from Greek, means “fiery falling,” describing the explosive release of pro-inflammatory signals from a dying cell. Unlike other cell deaths, pyroptosis causes a quick, intense inflammatory response, crucial for fighting infections and removing infected cells as fast as possible. Pathogens trigger the formation of the inflammasome, a large protein complex that activates caspase-1. This enzyme releases pro-inflammatory mediators like IL-18 and ROS and orchestrates pores in the cell membrane, causing cell rupture. This process summons immune cells but can also harm nearby cells, potentially leading to chronic inflammation and tissue damage.

But what exactly does pyroptosis have to do with rosacea? Recent research links pyroptosis to worsening rosacea symptoms, as the inflammasome activation worsens inflammation in rosacea (1). Thus, targeting pyroptosis is essential for optimizing rosacea care. AmelioSense™ by Mibelle Biochemistry offers a new approach to combat pyroptosis and skin irritation.

DISCOVER THE POWER OF AMELIOSENSE™!

AmelioSense™ combines shepherd's purse (*Capsella bursa-pastoris*) (Figure 1) extract with an advanced liposomal preparation containing three powerful antioxidants, AmelioSense™ ef-

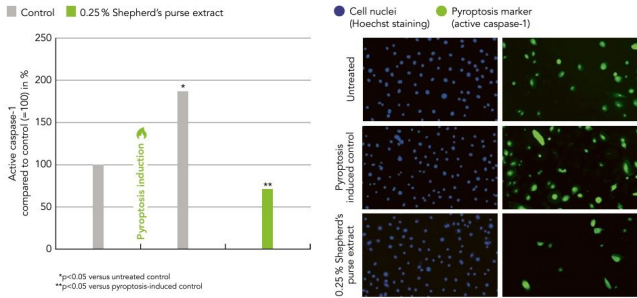


Figure 2: Inhibition of caspase-1 as a key enzyme of pyroptosis

fectively addresses the mechanism of pyroptosis. The antioxidants in the complex include carnosine, a dipeptide, which primarily fights skin glycation and oxidative stress; silymarin, a flavonoid extracted from milk thistle, known for its anti-inflammatory properties; and tocopherol, which protects against oxidative damage. This complex is designed as a liposomal formulation that uses lecithin to improve penetration into the skin. Mibelle Biochemistry has harnessed the calming properties of shepherd's purse and the protective effects of the antioxidant complex, combining them into AmelioSense™, an innovative formulation that offers remarkable benefits for fighting skin redness and irritation.

THE SCIENCE BEHIND THE ACTIVE

In an *in vitro* keratinocyte cell model, AmelioSense™ inhibited active caspase-1 (Figure 2), the key enzyme in pyroptosis. It also inhibited the release of free radicals (ROS) and the gene expression of diverse inflammatory markers known to be crucial in rosacea.

Rosacea-prone skin is characterized by visible redness caused by increased blood flow and the dilation of small blood vessels. Targeting these processes can help alleviate skin flushes and improve appearance. In a double-blind, randomized, placebo-controlled clinical study with volunteers aged between 29 and 70 years exhibiting redness and visible blood vessels on the cheeks, treatment with 2 % AmelioSense™ visibly reduced the appearance of blood vessels and redness in the cheek area after 56 days (Figure 3).

In the same clinical study, skin redness and blood flow were measured with a Laser Doppler instrument. After 28 days of treatment with 2% AmelioSense™, redness was reduced by 10.6%, and by 15.3% after 56 days. Blood flow

was reduced by 29.1% after 28 days and by 46.3% after 56 days. All results were statistically significant compared to the placebo. Lower blood flow results in less severe skin flushes, demonstrating the ability of AmelioSense™ to reduce blood flow and facial redness.

Volunteers self-evaluated AmelioSense™ with a questionnaire at the end of the study. 82% reported reduced flushing effects, and 91% described the product as soothing. In summary, AmelioSense™ effectively improves the visible signs of irritated skin and provides a soothing feeling, enhancing the quality of life for those suffering from facial redness.



Figure 3: Visible reduction of skin redness

A PROMISING NEW ACTIVE INGREDIENT TO TREAT SKIN REDNESS AND FLUSHING

The benefits of AmelioSense™ are numerous. It provides clear, visible effects, making it an attractive ingredient for skincare formulations targeting irritated, red skin. Its unique combination of shepherd's purse extract and an advanced liposomal formulation for better skin penetration makes it special. By targeting pyroptosis, AmelioSense™ acts on a new mechanism underlying skin irritation and rosacea, yielding a scientific and innovative approach to skin soothing. ■

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1. (1Hu et al. Epub 2023. Pyroptosis-related gene signature elicits immune response in rosacea. Experimental dermatology.