PEPITEM sequence shows effects in psoriasis, comparable to steroid cream

A sequence of just three amino acids from the PEPITEM molecule may reduce the severity of psoriasis, when applied topically in an emollient cream.

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> “There is a clear need for new psoriasis therapies that can be used continuously, and without the risk of excessive side effects, to prevent psoriasis flares.”
>
> *Professor Ed Rainger, University of Birmingham, U.K.*

Scientists from the University of Birmingham, U.K., have shown that a sequence of just three amino acids may reduce the severity of psoriasis, when applied topically in an emollient cream.

The researchers, whose study is published in Pharmacological Research, identified the smallest part of a peptide (small protein) called PEPITEM, which occurs naturally in the body and regulates inflammation.

The study also showed that both PEPITEM and the three amino acid (tripeptide) sequence delivered a significant reduction in the severity of psoriasis, that is comparable to a steroid cream.

Psoriasis is a long-term disease with no cure, where the skin cells multiply too quickly, resulting in raised scaly patches of dry skin that can be itchy, painful, interfere with sleep, or make it hard to concentrate, and may crack, bleed, or ooze. It is caused by an over-active immune system, and tends to go through cycles, becoming more intense during ‘flares’, which may last weeks or months.

It is usually treated in the first instance with emollients, or creams containing vitamin D analogues (such as calcipotriol), vitamin A (retinoids) or corticosteroids.

These therapies can only be used for short periods due to side effects that occur with continuous use, but as a natural molecule, PEPITEM, and the tripeptide sequence that is derived from it are less likely to show these ‘off target’ effects.

In its native state, PEPITEM consists of a chain of 14 amino acids, but in this most recent study, researchers led by Professor Ed Rainger from the University of Birmingham and Professor Francesco Maione from the University of Naples Federico II, looked for, and identified the

smallest parts of the PEPITEM molecule that influence immune cells and inflammation in psoriasis.

Work by the Birmingham scientists identified two sequences of three amino acids that showed biological activity comparable to the full-length PEPITEM molecule.

The scientists then optimised these tripeptides to improve their stability in the body, and tested their ability to reduce immune cell activation and migration, which are hallmarks of inflammatory disease. Their findings showed these two sequences had at least the same activity as the original PEPITEM molecule.

They then selected the sequence with the greatest biological activity and researchers from the University of Naples Federico II trialled its effectiveness in psoriasis, using an animal model of disease.

They found that topical application directly to the skin every day for seven days in an emollient cream resulted in a clear reduction in disease compared to untreated animals, and their findings were confirmed using PASI (Psoriasis Area and Severity Index) scoring, which is used in clinical practice to measure the extent and severity of psoriasis.

Importantly, the study also showed that both PEPITEM and the tripeptide sequence reduced the PASI score by 50%, making it comparable to the steroid cream Clobetasol Proprionate 0.05%.

Professor Ed Rainger said: “While there are a number of therapies for psoriasis, there is a clear need for new therapeutic agents that can be used continuously, and without the risk of excessive side effects, to prevent psoriasis flares. Our findings raise the possibility of using PEPITEM derived peptides for the treatment of psoriasis.”

“This study also raises the interesting possibility that PEPITEM derived peptides could be used in combination with other psoriasis therapies, allowing lower dosing for longer durations, for example, a ‘steroid sparing’ approach, to reduce the side effects associated with prolonged use of such agents.”

Further investigation showed both the whole PEPITEM molecule and the tripeptide sequences are powerful regulators for the synthesis of signalling molecules that promote inflammation, leading to the recruitment of immune cells and proliferation of other cell types in skin tissue involved in disease, with some tripeptide sequences showing an order of magnitude increase in efficacy compared to the parent PEPITEM sequence.

Professor Rainger added: “We have identified the parts of the PEPITEM molecule that are responsible for its biological action, and delivered peptides that mimic PEPITEM, and dramatically influence the skin’s inflammatory processes. Their significantly smaller size, and higher efficacy should result in substantial advantages in synthesis, formulation, and use in

therapeutics.”

The study is part of a wider research programme on PEPITEM and its potential use in therapies for diseases such as rheumatoid arthritis (RA), diabetes, lupus, and psoriasis, and many others, which feature chronic inflammation as an underlying causative factor.

University of Birmingham Enterprise has filed several patent families related to PEPITEM and the components of the PEPITEM molecule responsible for maintaining a normal immune response. The research team is now seeking investment, licensing, partnering and/or collaborative research opportunities. For commercial inquiries contact University of Birmingham Enterprise.

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