

WOUND HEALING: Inspiration from the Intestine and a New Postbiotic Active Ingredient

THE BUZZ ON THE MICROBIOME

Since the early 2000's, extensive research on the microbiome has led to many new scientific discoveries especially within the fields of dermatology. It also brought awareness to bacteria, both inside and outside the body and how it can affect processes such as wound healing. Most of the bacterial species of the human microbiome can be derived from the intestine, and recent studies have shown a link between the intestinal microbiota and its ability to constantly heal and regenerate its epithelium.¹

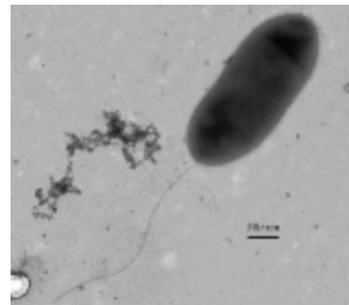
On average, skin is renewed about every twenty-one days, but the intestinal lining has the ability to renew itself every four to five days.¹ The ability of the intestine and its quick regeneration process has inspired researchers to further study this phenomenon.

INTESTINAL INSPIRATION

Further research conducted on the intestine has proved that its epithelial cells and the bacterial flora are able to communicate with each other via Pattern Recognition Receptors (PRR) which are represented by Toll-Like Receptors (TLR).¹ These TLRs are not enhanced by the bacteria itself, but by metabolites of the bacteria such as proteins, enzymes, and peptides. It was found that one of these receptors called the TLR-5 is enhanced by a bacterial protein, flagellin.¹ Upon enhancement by the flagellin, growth factors are activated that multiply on the surface of epithelial stem cells. This means skin regeneration process and healing process are initiated and activated. Ultimately, flagellin has shown to enhance the regeneration of these cells, thus increasing the epithelial renewal process.

DISCOVERY OF A UNIQUE, FLAGELLATED GRAM-NEGATIVE BACTERIUM

Upon research about flagellin, bacteria, and the role on skin renewal, it was only a matter of time until a new active ingredient would be created with inspiration drawn from the microbiome. A unique, flagellated gram-negative bacterium found exclusively in the thermal spring waters of the Cevennes Mountains in Avène, France was discovered. It's a flagellated gram-negative bacterium, meaning it is highly composed of flagella, which are small tail like structures that enable bacterial mobility. Flagella are completely composed of the protein flagellin.¹



Due to extensive laboratory research, scientists have developed extracts from the bacteria via centrifugation that are utilized to target specific skin conditions. It was noted that when this flagellated gram-negative bacterium underwent centrifugation one time, it produced an extract low in flagellin. This extract was found to be very effective for the treatment of itching. When the same bacterium was centrifuged more than once, the extracts contained high amounts of flagellin which ultimately lead to an extract with a high concentration of protein. This highly concentrated flagellin protein extract was instrumental in the reformulation of the repair cream, since it was found that this protein could enhance the skin repair process.¹

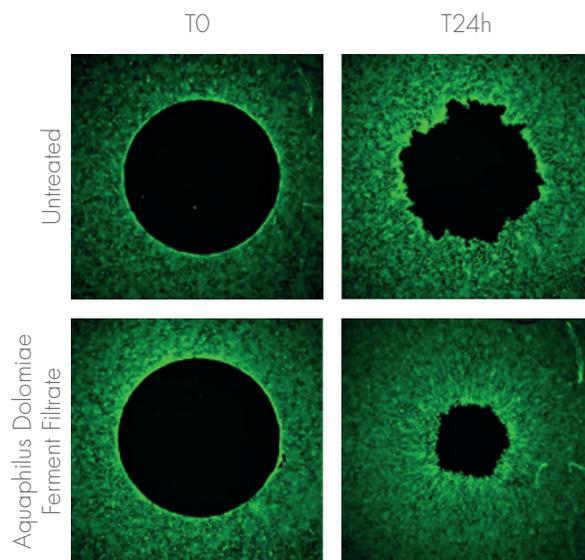
THE NEW POSTBIOTIC BIOTECHNOLOGICAL ACTIVE INGREDIENT

Researchers named this extract, **Aquaphilus Dolomiae Ferment Filtrate**, a new postbiotic biotechnological active ingredient that is derived from a bacterium.¹ Postbiotics are the non-living component derived or secreted from the living bacterium or released after bacterial lysis.^{2,3} Examples of these could be an organic acid or protein that were originally derived from a bacterium. Efficacy of postbiotics vary based on their microbial metabolite composition.⁴ Benefits include but are not limited to, reducing inflammation, accelerating the growth of new cells, and restoring gut dysbiosis.^{2,4} In this case, the protein flagellin, when formulated in the topical repair cream, has been found to enhance skin regeneration and accelerate wound healing by communication with the skin's microbiome.¹

STUDY 1: SIGNIFICANT EFFICACY ON CELL MIGRATION

Aquaphilus Dolomiae Ferment Filtrate has shown promising results even within initial studies. To assess the efficacy of keratinocyte migration, an important step in epidermal healing, an in vitro study was performed. Human keratinocytes were incubated in two environments with one being exposed to Aquaphilus Dolomiae Ferment Filtrate and the other left untreated.¹

RESULTS



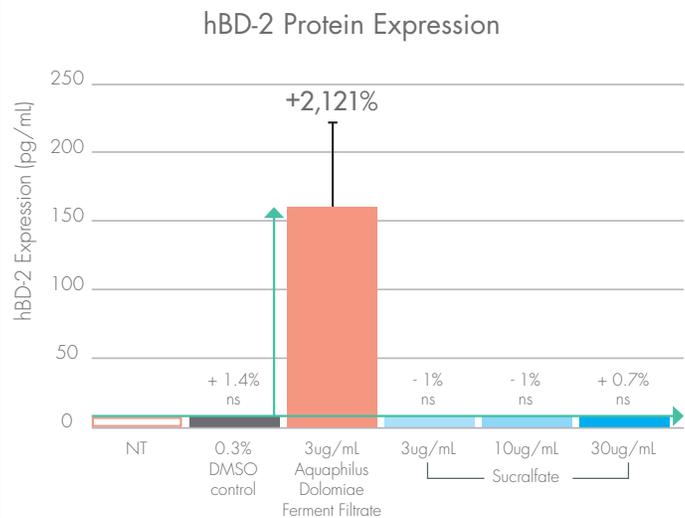
CONCLUSION

In just twenty-four hours, the use of **Aquaphilus Dolomiae Ferment Filtrate** significantly enhanced keratinocyte migration and skin repair process was 2.5 times faster than if it was untreated.

STUDY 2: SIGNIFICANTLY ACTIVATES THE SKIN'S NATURAL DEFENSES

In vitro study was performed to measure the expression of the antimicrobial peptide hBD-2 (human beta-defensin 2) in the presence of Aquaphilus Dolomiae Ferment Filtrate versus untreated, DMSO control and sucralfate, a well-known benchmark for mechanical wound healing.

RESULTS



When skin was exposed to 3ug/mL of Aquaphilus Dolomiae Ferment Filtrate, the synthesis of hBD-2 increased by 2,121.3% while untreated skin, DMSO control and skin exposed to sucralfate showed no significant expression of antimicrobial peptides.¹

CONCLUSION

Aquaphilus Dolomiae Ferment Filtrate significantly enhances the synthesis of antimicrobial peptides, which helps decrease the risk of infection in the wound.¹

REFERENCES

¹Data on file at Pierre Fabre Research Institute, 2019. ²Aguilar-Toalaa et al. Trends in Food Science & Technology 75 (2018) 105-114. ³Gao J et al. Frontiers in Microbiology, 2019. ⁴Wegh et al. Int J Mol Sci. 2019 Oct; 20(19): 4673.