The reconstruction of psoriatic skin

Joint leaders of a groundbreaking study looking into the treatment of conditions like psoriasis, Professors Roxane Pouliot and Michèle Auger explain how their skin model stands to make a radical impact on the non-invasive approach offered by the transdermal drug industry.
Skin conditions like psoriasis are so complex and unpredictable that assessing treatment has so far been problematic. Now, a pioneering research project based at Université Laval, Canada, is developing replica diseased skin that could pave the way for safer and more effective testing.

PSORIASIS IS A skin condition for which there is no cure that affects an estimated 80 million people worldwide. Its severity varies greatly, depending on the individual. Presenting itself through red and flaky patches, some people experience it as nothing more than a minor irritation, but for others it has a major impact on their quality of life.

THE STORY SO FAR

Up until now, testing the treatment for skin conditions like psoriasis has come across significant barriers. Traditionally, in vitro and in vivo experiments have been the primary methods adopted for investigating these conditions, but they may be limited either by prohibitive cost, or by the differentiation between the characteristics when studied in isolation, from actual diseased skin.

By using new techniques, a team led by Professors Roxane Pouliot and Michèle Auger from Université Laval in Canada have been working on the reconstruction and characterisation of psoriatic skin. They claim it will revolutionise the understanding of psoriasis, which is still very limited because of its complex and unpredictable nature: “To date, many studies demonstrate that psoriasis is undoubtedly an immune-mediated disease,” Pouliot explains. “However, the knowledge of the exact role of the major cell types involved remains very fragmentary. Our in vitro model will be invaluable in understanding the respective role of soluble factors and direct cell-to-cell contact. The study will also help us to understand the disease and to discover new pharmacologic targets.”

THE METHOD

Before transdermal products reach the market, they must be thoroughly analysed. One method, the ‘Franz Diffusion Cell’ system, is known to be particularly effective. First popularised by Dr Thomas Franz, it has been applied to a number of skin permeation studies, including topical and transdermal drug delivery formulations, as well as ophthalmics, cosmetics, skin care products and pesticides. The vertical diffusion cell system is an ideal tool for quality control of topical preparations.

Despite this method being a widely recognised tool for performing in vitro studies on transdermal drugs, the use of artificial membranes, animal or healthy human skin poses a myriad of problems. Healthy human skin does not possess the same skin characteristics of people that will receive these treatments. Artificial membranes are even less likely to be close enough to human skin for testing to be effective. Furthermore, aside from potential ethical issues, no animal model accurately and suitably develops psoriasis and getting hold of psoriatic skin in vivo is both difficult and expensive. “The need for innovative and effective tools to evaluate new dermopharmaceutical formulations is therefore essential,” Pouliot points out. “The objective of this project is the development and characterisation of reconstructed psoriatic skin.”

THE NATURE OF SKIN

The cells that make up the skin have a life cycle. The body produces new cells in the deepest skin level and these skin cells gradually move up until they reach the outermost layer. Subsequently they die and flake off and the entire process normally takes around 21-28 days. When someone suffers from psoriasis,
The objective of this work is to probe, using infrared and Raman spectroscopies, the lipid phase transitions and chain order, the protein secondary structure as well as the hydration of healthy and psoriatic skin substitutes. In addition, these techniques are used to investigate the skin substitutes at different depths and to investigate the spatial distribution of drugs in the substitutes.

**OBJECTIVES**

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**INFRARED AND RAMAN MICROSCROPE**

Raman microscrope, named after Sir C V Raman, are used to study vibrational and rotational modes in a system. It relies on a Raman scattering of monochromatic light, usually from a laser in the visible, near infrared, or near ultraviolet range. The laser light interacts with molecular vibrations, resulting in the energy of the laser photons being shifted up or down. This shift in energy gives information about the vibrational modes in the system. Infrared spectroscopy yields similar but complementary information.

Encouragingly, Auger also points out that for the first time, using such techniques, it will be possible to test transdermal drugs directly on pathological, reconstructed skin. Moreover, these pathological samples will be more efficient because of their reproducibility and their accessibility. The results from the proposed research will also lead to the development of new formulations conceived and appropriate for particular skin healing treatments.

**OVERCOMING CHALLENGES**

Despite its successes, the project has not come without its fair share of hurdles along the way: “One of the big challenges is the preparation of the skin substitutes as it is so time-consuming. The self-assembly approach takes about two months to perform,” notes Pouliot. “Several substitutes can be prepared simultaneously; however, the fact that for most experiments, the substitutes have to be analysed within a few days after their preparation, also makes it difficult.”

The interdisciplinary nature of Pouliot and Auger’s collaboration was also the source of another barrier. The wider group of students and postdoctoral fellows involved had to be specially trained in cell culture, tissue engineering and advanced spectroscopic techniques that had never before been applied in their laboratories to study skin substitutes. That said, Auger reveals that such sharing of expertise soon became a key part of the success of their work, even to the point of making the most of local natural materials: “Roxane is also involved in the establishment of the possible utilisation of polyphenolic extracts from barks of Canadian wood species in psoriasis treatment, and the study of their antioxidant capacity and toxicological properties”.

The future for this partnership looks promising. Certainly, amongst psoriasis sufferers, one in five of whom may have to endure frequent hospital admissions, there will no doubt be many who welcome the efforts of Pouliot and Auger in driving treatment advances forward.