Topical treatment for fighting skin cancer yields positive results in tests

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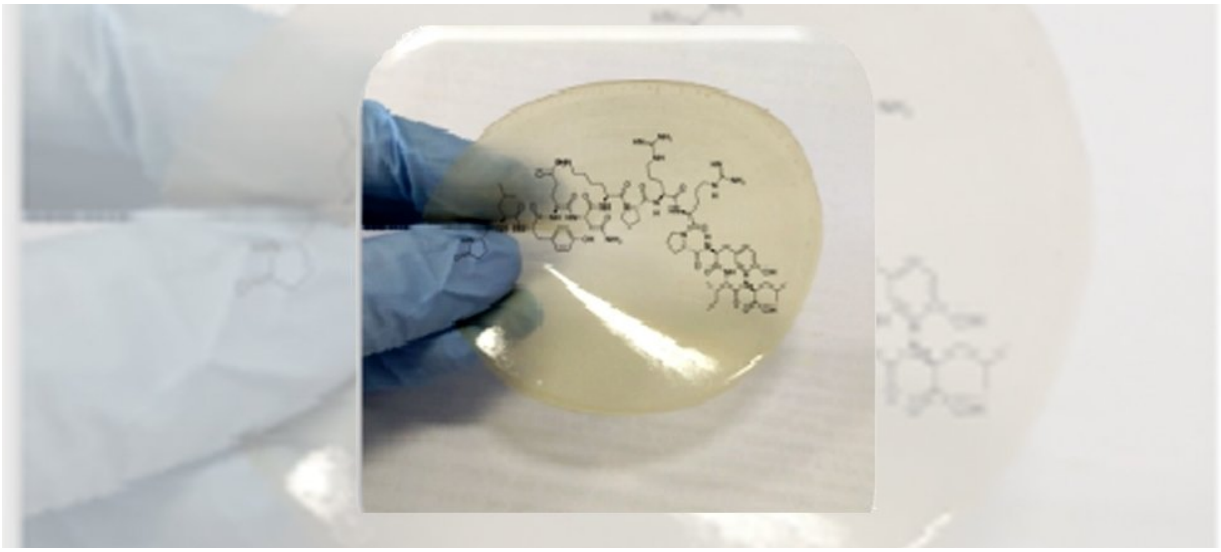

Methodology developed in Brazil combines low-intensity electric current with a formulation containing nanoencapsulated chemotherapy. Credit: FAPESP

Researchers at the University of São Paulo (USP), in Brazil, are testing a technique in mice that combines low-intensity electric current with a formulation containing nanoencapsulated chemotherapy to treat skin cancer.

Applying a low-intensity unidirectional current is one of the ways to ensure that chemical substances penetrate the skin, pushed into the bloodstream through the electric field using a technique known as

iontophoresis. According to preliminary results of the study, cancer-induced mice which received the formulation combined with iontophoresis presented a significantly greater reduction in tumour size than those that received it through injection.

"One of the challenges involved in this type of topical treatment is ensuring that the drug penetrates the stratum corneum—the outermost layer of the epidermis, composed mainly of dead cells. It is an important tissue barrier against the entry of microorganisms, but it also makes it more difficult for medicines to penetrate," explained Renata Fonseca Vianna Lopez, the project supervisor.

In the case of skin cancer, however, the intent is that the drug becomes concentrated in the area below the stratum corneum that requires treatment. This is the reason why, in the study led by Lopez, she chose to place the chemotherapeutic agent inside nanoparticles.

Using mice, the researchers induced the formation of a tumor associated with one of the most common types of skin cancer—squamous cell carcinoma—through a subcutaneous injection of human tumor cells that overexpress the epidermal growth factor receptor (EGFR). Lopez explained that the presence of this protein causes the tumor to become more aggressive. The topical formulation contains chemotherapy agent 5-fluorouracil encapsulated in a nanoparticle (liposome) that functions as an anti-EGFR antibody. The malignant cells are able to capture a larger quantity of the drug encapsulated in these liposomes.

One group of rodents received the treatment formulation through subcutaneous injections and another group received it through topical application combined with iontophoresis. Lopez compared both methods and says, "In addition to reducing the size of the tumor, the topical treatment left the tumor less aggressive. We believe that this method combined with iontophoresis allows the drug to be dispersed over the

entire area of the tumor, whereas the subcutaneous application causes it to be concentrated in a single location," Lopez noted.

In another study, Lopez' group used a stiffer type of polymeric nanoparticle, one containing the anti-inflammatory dexamethasone associated with iontophoresis for the treatment of uveitis—an inflammation of the eye tissue. The results, published in 2015 in the *Journal of Controlled Release*, is the outcome of the doctoral thesis of Joel Gonçalves Souza, winner of the 2015 Capes Thesis Award in Pharmacy.

"When we apply the medicine directly to the eye, it is quickly eliminated through the defense mechanisms, such as tears. Increased penetration and better results are obtained by using the application method combined with iontophoresis," Lopez said.

Currently, in dissertation research by Camila Lemos, the group plans to test a method that uses iontophoresis in the treatment of chronic wounds such as those that develop in patients with diabetes.

"In this case, we are not dealing with the stratum corneum barrier. We use iontophoresis to assess its influence on release of the substance of interest in a formulation, and to investigate its effect on the growth of microorganisms," Lopez explained. The strategy consists of placing a peptide with anti-inflammatory properties on a film made of fibers extracted from the cocoon of a silkworm (fibroin). The film is placed on the wound as a dressing, to which an electric current is then applied.

"When we placed the peptide directly on the wound, it degraded very quickly. When placed on the film, however, release occurs in a slower and more sustained way. Iontophoresis allows a larger amount of the peptide to be released from the film at the start of treatment to accelerate healing," the researcher explained.

Lopez went on to say that preliminary results suggest that iontophoresis also stops the proliferation of some types of microorganisms (particularly gram-positive bacteria) that could aggravate wounds.

More information: Joel G. Souza et al. Transcorneal iontophoresis of dendrimers: PAMAM corneal penetration and dexamethasone delivery, *Journal of Controlled Release* (2015). DOI: 10.1016/j.jconrel.2014.12.037

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