

Inflammatory skin damage in mice blocked by bleach solution, study finds

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Processes that age and damage skin are impeded by dilute bleach solution, according to a new study by researchers at the Stanford University School of Medicine.

The study was conducted on mice. But if shown to work similarly in humans, the inexpensive, widely available household chemical could provide a new way to treat skin damage caused by <u>radiation therapy</u>, excess sun exposure or aging.

Dilute bleach baths have been used for decades to treat moderate to severe eczema in humans, but it has not been clear until now why they work. "Originally it was thought that bleach may serve an antimicrobial function, killing bacteria and viruses on the skin," said Thomas Leung, MD, PhD, an instructor in dermatology at Stanford and a pediatric dermatologist at Lucile Packard Children's Hospital. "But the concentrations used in clinic are not high enough for this to be the sole reason. So we wondered if there could be something else going on."

Leung is the lead author of the study, which will be published online Nov. 15 in the *Journal of Clinical Investigation*. Seung Kim, MD, PhD, professor of developmental biology and a Howard Hughes Medical Institute investigator, is the study's senior author.

"Dr. Leung relentlessly followed his hunch that an antimicrobial effect of dilute bleach wasn't the whole story," Kim said. "And his work has revealed new mechanisms for targeting inflammatory pathways with this



versatile small molecule. It has also identified new possible clinical applications."

Leung and his colleagues knew that many skin disorders, including eczema and radiation dermatitis, have an inflammatory component. When the skin is damaged, immune cells rush to the site of the injury to protect against infection. Because inflammation itself can be harmful if it spirals out of control, the researchers wondered if the bleach (sodium hypochlorite) solution somehow played a role in blocking this response.

To find out, they homed in on a molecule called nuclear factor kappalight-chain-enhancer of activated B cells, or NF-kB, which is known to play a critical role in inflammation, aging and response to radiation. When activated by signaling molecules, it enters the cell's nucleus and binds to DNA to control gene expression. When inactive, it is sequestered in the cytoplasm, away from the DNA.

Leung wondered if there could be a link between the effect of the dilute bleach solution and NF-kB's role in skin. He exposed human keratinocytes, or skin cells, to 0.005 percent bleach for one hour before treating them with a signaling molecule that normally activates NF-kB function. He found that exposure to the solution blocked the expression of two genes known to be regulated by NF-kB. The effect was reversible, however—waiting 24 hours after the bleach treatment restored NF-kB's ability to activate expression of the target genes.

Further investigation divulged how this happens.

"We found that the bleach solution oxidizes and inhibits an activator necessary for NF-kB to enter the nucleus, essentially blocking NF-kB's effect," Leung said. When the researchers mutated the activator to be oxidation-resistant, NF-kB's gene targeting activity was unhindered.



Next, the researchers turned to potential clinical applications. Radiation dermatitis is a common side effect of radiation therapy for cancer. While radiation therapy is directed at cancer cells inside the body, the normal skin in the radiation therapy field is also affected. Radiation therapy often causes a sunburn-like skin reaction. In some cases, these reactions can be quite painful and can require interrupting the radiation therapy course to allow the skin to heal before resuming treatment. However, prolonged treatment interruptions are undesirable.

"An effective way to prevent and treat radiation dermatitis would be of tremendous benefit to many patients receiving radiation therapy," said Susan Knox, MD, PhD, associate professor of radiation oncology and study co-author.

Leung and his colleagues tested the effect of daily, 30-minute baths in bleach solution on laboratory mice with radiation dermatitis. They found that the animals bathed in the bleach solution experienced less severe skin damage and better healing and hair regrowth than animals bathed in water.

They then turned their attention to old—but healthy—laboratory mice.

"Multiple research studies have linked increased NF-kB activity with aging," Leung said. "We found that if we blocked NF-kB activity in elderly laboratory mice by bathing them in the bleach solution, the animals' skin began to look younger. It went from old and fragile to thicker, with increased cell proliferation." The effect diminished soon after the dilute-bleach baths were stopped, indicating that regular exposure is necessary to maintain skin thickness.

The researchers are now considering clinical trials in humans, and they are also looking at other diseases that could be treated by dilute-bleach baths. "It's possible that, in addition to being beneficial to radiation



dermatitis, it could also aid in healing wounds like diabetic ulcers," Leung said. "This is exciting because there are so few side effects to dilute bleach. We may have identified other ways to use hypochlorite to really help patients. It could be easy, safe and inexpensive."

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