Nanodiamonds deliver insulin for wound healing

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(PhysOrg.com) -- Bacterial infection is a major health threat to patients with severe burns and other kinds of serious wounds such as traumatic bone fractures. Recent studies have identified an important new weapon for fighting infection and healing wounds: insulin.

Now, using tiny nanodiamonds, researchers at Northwestern University have demonstrated an innovative method for delivering and releasing the curative hormone at a specific location over a period of time. The nanodiamond-insulin clusters hold promise for wound-healing applications and could be integrated into gels, ointments, bandages or suture materials.

Localized release of a therapeutic is a major challenge in biomedicine. The Northwestern method takes advantage of a condition typically found at a wound site -- skin pH levels can reach very basic levels during the repair and healing process. The researchers found that the insulin, bound firmly to the tiny carbon-based nanodiamonds, is released when it encounters basic pH levels, similar to those commonly observed in bacterially infected wounds. These basic pH levels are significantly greater than the physiological pH level of 7.4.

The results of the study were published online July 26 by the journal *Biomaterials.*

"This study introduces the concept of nanodiamond-mediated release of therapeutic proteins," said Dean Ho, assistant professor of biomedical engineering and mechanical engineering at the McCormick School of Engineering and Applied Science. Ho led the research. "It's a tricky problem because proteins, even small ones like insulin, bind so well to the nanodiamonds. But, in this case, the right pH level effectively triggers the release of the insulin."

A substantial amount of insulin can be loaded onto the nanodiamonds, which have a high surface area. The nanodiamond-insulin clusters, by releasing insulin in alkaline wound areas, could accelerate the healing process and decrease the incidence of infection. Ho says this ability to release therapeutics from the nanodiamonds on demand represents an exciting strategy towards enhancing the specificity of wound treatment.

In their studies, Ho and his colleagues showed that the insulin was very tightly bound to the nanodiamonds when in an aqueous solution near the normal physiological pH level. Measurements of insulin function revealed that the protein was virtually inactive when bound to the nanodiamonds -- a beneficial property for preventing excess or unnecessary drug release.

Upon increasing the pH to the basic levels commonly observed in the skin during severe burns, the researchers confirmed the insulin was released from the nanodiamond clusters and retained its function. Exploiting this pH-mediated release mechanism may provide unique advantages for enhanced drug delivery methods.

The researchers also found the insulin slowly and consistently released from the nanodiamond clusters over a period of several days.

Insulin accelerates wound healing by acting as a growth hormone. It encourages skin cells to proliferate and divide, restores blood flow to the wound, suppresses inflammation and fights infection. Earlier investigations have confirmed an increase in alkalinity of wound tissue, due to bacterial colonization, to levels as high as pH 10.5, the pH level that promoted insulin release from the nanodiamonds in the Northwestern study.

Ho's group next will work on integrating the nanodiamond-insulin complexes into a gel and conducting preclinical studies. The researchers also will investigate different areas of medicine in which the nanodiamond-insulin clusters could be used.

Nanodiamonds have many advantages for biomedical applications. The large surface area allows a large amount of therapeutic to be loaded onto the particles. They can be functionalized with nearly any type of therapeutic, including small molecules, proteins and antibodies. They can be suspended easily in water, an important property in biomedicine. The nanodiamonds, each being four to six nanometers in diameter, are minimally invasive to cells, biocompatible and do not cause inflammation, a serious complication. And they are very scalable and can be produced in large quantities in uniform sizes.

By harnessing the unique surface properties of the nanodiamonds, Ho and his colleagues have demonstrated that the nanodiamonds serve as platforms that can successfully bind, deliver and release several classes of therapeutics, which could impact a broad range of medical needs.

Ho's research group also has studied nanodiamonds for applications in cancer therapy. They demonstrated that nanodiamonds are capable of releasing the chemotherapy agent Doxorubicin in a sustained and consistent manner. (Ho is a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.)

In addition to using the nanodiamonds in their particle form, Ho's group has developed devices that harness the slow drug-release capabilities of the nanodiamonds. More recently, his team has shown that nanodiamonds are effective in dispersing insoluble drugs in water, boosting their potential for broader applications in medicine.

More information: The title of the *Biomaterials* paper is "Nanodiamond-Insulin Complexes as pH-Dependent Protein Delivery Vehicles." www.elsevier.com/wps/find/jour … me/30392/description

Source: Northwestern University (news : web)