Dental plaque is no match for catalytic nanoparticles

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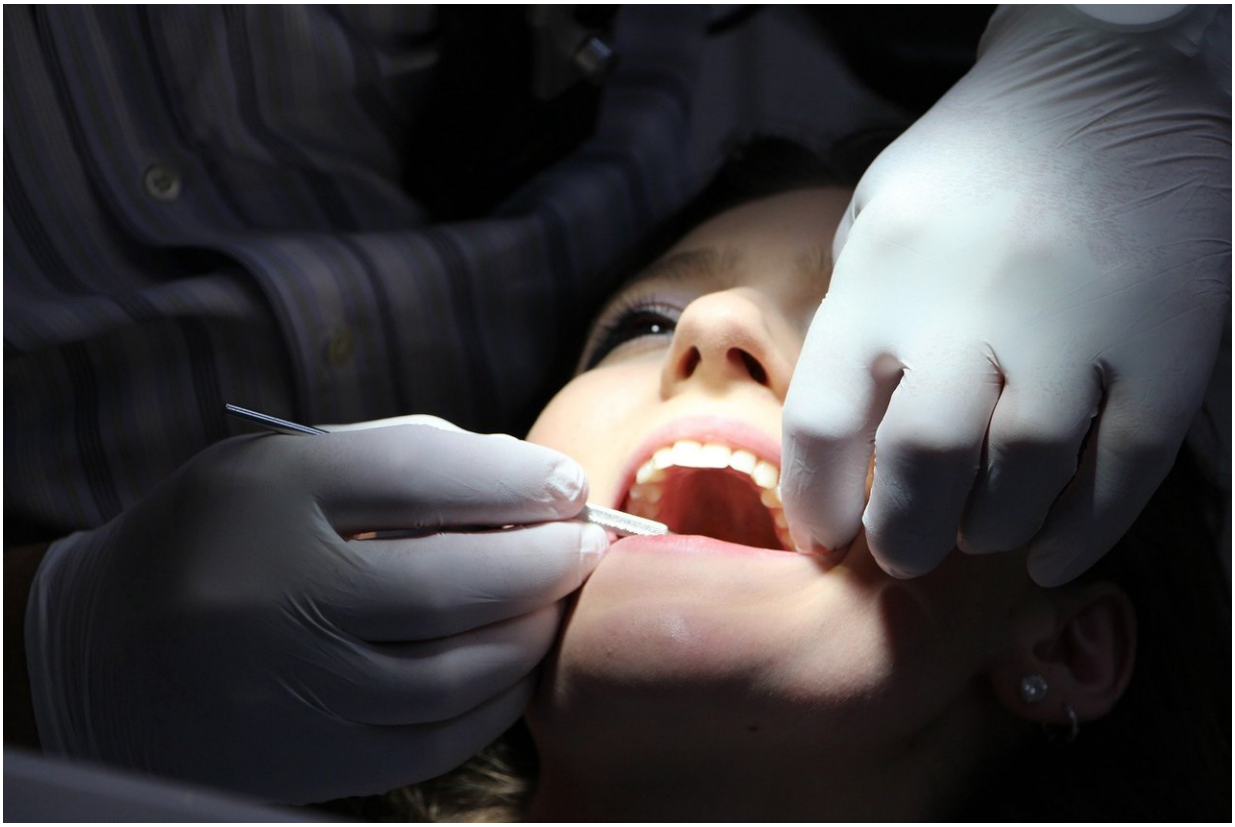

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Combine a diet high in sugar with poor oral hygiene habits and dental cavities, or caries, will likely result. The sugar triggers the formation of an acidic biofilm, known as plaque, on the teeth, eroding the surface.

Early childhood caries is a severe form of tooth decay that affects one in every four children in the United States and hundreds of millions more globally. It's a particularly severe problem in underprivileged populations.

In a study published in *Nature Communications* this week, researchers led by Hyun (Michel) Koo of the University of Pennsylvania School of Dental Medicine in collaboration with David Cormode of Penn's Perelman School of Medicine and School of Engineering and Applied Science used FDA-approved nanoparticles to effectively disrupt biofilms and prevent tooth decay in both an experimental human-plaque-like biofilm and in an animal model that mimics early-childhood caries.

The nanoparticles break apart dental plaque through a unique pH-activated antibiofilm mechanism.

"It displays an intriguing enzyme-like property whereby the catalytic activity is dramatically enhanced at acidic pH but is 'switched off' at neutral pH conditions," says Koo, professor in Penn Dental Medicine's Department of Orthodontics and in the divisions of Pediatric Dentistry and Community Oral Health. "The nanoparticles act as a peroxidase, activating hydrogen peroxide, a commonly used antiseptic, to generate free radicals that potently dismantle and kill biofilms in pathological acidic conditions but not at physiological pH, thus providing a targeted effect."

Because the caries-causing plaque is highly acidic, the new therapy is able to precisely target areas of the teeth harboring pathogenic biofilms without harming the surrounding oral tissues or microbiota.

The particular iron-containing nanoparticle used in the experiments, ferumoxytol, is already FDA-approved to treat iron-deficiency, a promising indication that a topical application of the same nanoparticle,

used at several-hundred-fold lower concentration, would also be safe for human use.

Though some scientists have questioned whether coatings used on ferumoxytol and other nanoparticles used for medical applications would render them catalytically inert, Koo, Liu, and Cormode demonstrated that they maintained peroxidase-like activity, activating hydrogen peroxide.

After testing the ferumoxytol-hydrogen peroxide combination on a tooth-enamel-like material, the team moved on to an experimental set-up that more closely replicated the conditions of the human mouth.

"We used plaque samples from caries-active subjects to reconstruct these highly pathogenic biofilms on real human tooth enamel," says Koo. "This simulation showed that our treatment not only disrupts the biofilm but also prevents mineral destruction of the tooth's surface. That offered very strong evidence that this could work in vivo."

Further studies in a rodent model that closely mirrors the stages of caries development in humans showed that twice-a-day rinses of ferumoxytol and hydrogen peroxide greatly reduced the severity of caries on all of the surfaces of the teeth and also completely blocked the formation of cavities in the enamel.

As further evidence of the treatment's targeted effect, the researchers found no significant change in the diversity of microbes in the mouth after therapy and found no signs of tissue damage.

"This therapy isn't killing microorganisms indiscriminately," Koo says, "but rather it is acting only where the pathological biofilm develops. Such a precise therapeutic approach can target the diseased sites without disrupting the ecological balance of the oral microbiota, which is critical

for a healthy mouth, while also avoiding infection by opportunistic pathogens."

Incorporating nanoparticles in a mouth rinse or toothpaste could be a cost-effective way to significantly improve their effectiveness, says Koo. Many of these products already contain hydrogen peroxide and would only require the addition of a small amount of relatively inexpensive nanoparticles. With evidence backing this approach in both an animal model and a human-like model of tooth decay, the research team is actively working to test its clinical efficacy.

More information: Yuan Liu et al, Topical ferumoxytol nanoparticles disrupt biofilms and prevent tooth decay in vivo via intrinsic catalytic activity, *Nature Communications* (2018). DOI: 10.1038/s41467-018-05342-x

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