Nanoemulsion Potent Against Superbugs That Kill Cystic Fibrosis Patients, Study Suggests
by The News Staff
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ScienceDaily (Feb. 4, 2009) University of Michigan scientists report highly encouraging evidence that a super-fine oil-and-water emulsion, already shown to kill many other microbes, may be able to quell the ravaging, often drug-resistant infections that cause nearly all cystic fibrosis deaths. Cystic fibrosis is an inherited chronic lung disease that affects 30,000 children and adults in the United States. Patients have mucus-clogged lungs that leave them vulnerable to repeated, ever more serious respiratory infections. A key finding in the study is that we have a product that shows very good activity against a variety of bacteria that are very resistant to all known antibiotics. These really are superbugs, says John J. LiPuma, M.D., first and corresponding author of the study in the journal Antimicrobial Agents and Chemotherapy.

The research is a collaboration between LiPuma, professor of pediatrics at the U-M Medical School, and James R. Baker Jr., M.D., director of the Michigan Nanotechnology Institute for Medicine and Biological Sciences at U-M and the study’s senior author. Nanoemulsions developed at Bakers institute consist of soybean oil, water, alcohol and surfactants forced by high-stress mechanical extrusion into droplets less than 400 nanometers in size.

These emulsions have already proved to be non-toxic, potent killers of bacteria such as Streptococcus pneumoniae, H. influenzae and gonorrhea, of viruses such as herpes simplex and influenza A, and of several fungi. Nanoemulsion treatments for cold sores and toenail fungus are in Phase 3 clinical trials. We have a product that looks like it could be safely administered to the lungs of people with cystic fibrosis, LiPuma says. If future trials show that patients can tolerate effective doses of the nanoemulsion, he adds, This could be a major breakthrough in the treatment of cystic fibrosis. The novel physical mode of action -- the nanoemulsion appears to kill bacteria by disrupting their outer membranes makes developing resistance unlikely, LiPuma says. Given that this technology works differently from antibiotic drugs, it provides a potential alternative for treatment in antibiotic-resistant bacteria. Since the material has already shown success in treating skin infections, we believe it has potential to treat antibiotic-resistant lung infections, says Baker. If the technique proves safe and effective, people would inhale the nanoemulsion using a nebulizer and be able to reduce the severity and frequency of infections that spiral out of control due to resistance to current antibiotics.

Context

Increasingly, cystic fibrosis patients are receiving antibiotic treatments they inhale using a nebulizer, rather than taking them systemically. Localizing antibiotics to the lungs allows for higher concentrations, but resistance is still a major stumbling block. Antibiotic resistance is a bigger problem now than it was five or 10 years ago, and there are also more types of bacteria causing cystic fibrosis infections.

Not long ago, few people with cystic fibrosis lived to become adults. But improved treatments in recent decades now allow more people with the disease to survive into their 30s or 40s.

However, doctors have hit a wall in improving those prospects. About 95 percent of cystic fibrosis patients die as a result of uncontrollable infections. Drugs have trouble penetrating two barricades in the lungs: biofilms that bacteria form around them, and thick sputum present in the lungs of patients with cystic fibrosis.

Research details
In cell cultures in the lab, the U-M scientists tested a nanoemulsion against 150 bacterial strains that attack cystic fibrosis patients. The emulsion proved effective at killing all of them, including one-third that are resistant to many antibiotics and 13 percent that resist all antibiotics.

They then tested the nanoemulsion against several bacterial strains grown in biofilms and sputum, to more closely simulate conditions in a patients body. Antibiotics often cant penetrate biofilms and sputum unless given at high doses with unacceptable side effects. We saw, not surprisingly, that greater concentrations of nanoemulsion were required to kill the bacteria, but we saw no strains that were resistant, LiPuma says. Whether humans can tolerate those concentrations well remains to be seen. LiPumas lab, funded by the Cystic Fibrosis Foundation as a national reference lab, has collected more than 30,000 strains of bacteria from the lungs of cystic fibrosis patients. The lab receives samples from around the world for analysis. Whats next The University of Michigan has filed for patent protection on the CF nanoemulsion, and licensed this technology to Ann Arbor-based NanoBio Corporation. Baker is a founder and equity holder of NanoBio. NanoBio and LiPumas lab will cooperate in the next steps toward bringing the treatment to market. LiPuma is optimistic that if animal and human trials go well, a nanoemulsion treatment for cystic fibrosis infections could be available in as little as five years.

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LiPuma is also a professor of epidemiology in the U-M School of Public Health.

Baker is also the Ruth Dow Doan Professor and allergy division chief in the U-M Department of Medicine. He has a significant financial stake in the NanoBio Corporation, which is commercializing this technology.