IIT Delhi team develops a new antibacterial drug-delivery system

The nanoconjugates will be useful for cancer patients suffering from bacterial infections

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A new antibiotic drug-delivery system that improves the efficacy of drugs thereby reducing the dosage used for treating bacterial infections has been tested in a lab by researchers at the Indian Institute of Technology (IIT) Delhi. A peptide, which has not been approved for clinical use, bound to gold nanoparticles was able to kill *E. coli* and *Salmonella typhi* more efficiently at lower dosages.

"Drug delivery becomes better and the bioavailability improves when the drug is conjugated [bound] to gold nanoparticles. So reduced dosage is sufficient to kill the bacteria. Reducing the dosage of antibiotics used is one of the strategies to reduce the possibility of drug resistance setting in," says Dr. Neetu Singh from the Centre for Biomedical Engineering, IIT Delhi, and one of the corresponding authors of the paper published in the journal *Scientific Reports*.

More effective: The nanoparticles were able to kill 50% of bacteria at much lower concentration than free peptides, say Smita Patil (left) and Rohini Singh. ▪SPECIAL ARRANGEMENT

Bioavailability

The peptide in a free form may not be bioavailable as it gets degraded relatively fast. In a free form, the peptide is also not able to effectively kill the bacteria by engaging with the bacterial membrane and disrupting it, while the nanoconjugate fares better on these counts.

The challenge was to arrive at an optimum number of peptides that are bound to nanoparticles to get the best results. When there are too few or too many peptides bound to the nanoparticles the antibacterial activity gets compromised. "There is significant antibacterial activity when about 1000 peptides are bound to a nanoparticle," says Dr. Singh.

The peptide called sushi-peptide bound to nanoparticles was able to kill 50% of bacteria at much lower concentration (400 nM) while the free peptide's antibacterial activity was not significant at the same concentration, says Smita Patil from the Centre for Biomedical Engineering, IIT Delhi and one of the first authors of the paper.

Besides normal cells infected with bacteria, the peptide bound to nanoparticles will be particularly useful in the case of cancer patients suffering from bacterial infections. "Rapid metabolism at the cancer site sucks al nutrients and leads to nutritional deficit in the body. When chemotherapy is given even the bacteria already present in the body but kept under check become disease-causing," says Dr. Pankaj Chaturvedi, cancer specialist at the Tata Memorial Hospital, Mumbai.

After chemotherapy the immunological response gets damaged as cells responsible for protecting against bacteria are reduced in number. So the person becomes vulnerable to infection. "Antibiotics by itself cannot kill all the bacteria. The inherent immunological response should be able to challenge the bacteria once antibiotic treatment is completed. Since this does not happen, the bacteria develop drug resistance," says Dr. Chaturvedi.

Folate receptors

Specific receptors called folate receptors are present in large numbers on the surface of cancer cells. Folic acid added to the nanoconjugates is recognised by these receptors and help in the binding process. "Once the nanoconjugates enter the cancer cells they interact with the bacteria and kill them by disrupting the cell membrane. The nanoconjugates have 40% better antibacterial activity compared with free peptides," says Rohini Singh from the Department of Chemical Engineering, IIT Delhi, and one of the first authors of the paper.

The nanoconjugate is not toxic to cancer cells and targets only the bacteria.

"We would next like to study if our nanoconjugates can be used on antibiotic-resistant strains and also understand the fate of gold nanoparticles used for making the nanoconjugates," says Dr. Neetu Singh. Instead of gold nanoparticle, biodegradable polymers can be used. The only condition is that the peptide should be able to interact with the bacterial membrane. A few more studies have to be carried out before the nanoconjugate can be tested on animals.