

Nanoparticles, 'pH phoresis' could improve cancer drug delivery

July 10 2013, by Emil Venere

(Phys.org) —Researchers have developed a concept to potentially improve delivery of drugs for cancer treatment using nanoparticles that concentrate and expand in the presence of higher acidity found in tumor cells.

The concept involves using nanoparticles made of "weak polybases," compounds that expand when transported into environments mimicking [tumor cells](#), which have a higher acidity than surrounding tissues. The researchers used sophisticated modeling to show how the particles would accumulate in regions of higher acidity and remain there long enough to deliver anticancer drugs.

"This phenomenon, which we term pH phoresis, may provide a useful mechanism for improving the delivery of drugs to [cancer cells](#) in solid tumor tissues," said You-Yeon Won, an associate professor of chemical engineering at Purdue University.

Solutions with a pH less than 7 are said to be acidic, and those with a higher pH are basic or alkaline. The pH phoresis concept hinges on using synthetic "polymer micelles," tiny drug-delivery spheres that harbor medications in their inner core and contain an [outer shell](#) made of a material that has been shown to expand dramatically as the pH changes from alkaline to acidic.

A twofold size increase could result in a similar increase in the efficiency of drug delivery to tumors.

"Such an effect would be a game changer by delivering the proper dose of anticancer drugs inside tumor cells," Won said. "This pH phoresis concept also could be combined readily within other established drug-delivery methodologies, making it potentially practical for medical application."

The concept is described in a research paper that will appear in the *Journal of Controlled Release* on July 15, and an unedited version appeared online June 19. The paper was written by Won and doctoral student Hoyoung Lee. Findings showed how the micelles' expansion is optimized in the specific pH in tumor cells.

The researchers demonstrated that the highest degree of micelle swelling in tumors needs to occur when there is a pH of about 7.0, plus or minus 0.5, for optimal delivery of drugs to tumor tissue.

"Solid tumors have a significantly lower extracellular pH, about 6.5-6.9, compared to normal tissue, which has an average pH of 7.4," Won said.

The weak polybases in the micelles contain molecules called amines, which are made of nitrogen and hydrogen atoms. The micelles swell at lower pH due to the increased "protonation," or the addition of protons to nitrogen atoms in the amines. Because the protons are positively charged, the like-charged amines repel each other, causing the nanoparticles to expand.

The positive charge slows the movement of micelles out of tumor tissue, which would cause the nanoparticles to accumulate inside the tumor mass long enough to enter tumor cells and release [anticancer drugs](#).

"This concept is straightforward to understand, yet no one recognized it previously," Won said. "And it took us a while to put this description on a mathematical footing. To do that, we had to modify the famous Fick's

first law diffusion equation."

The law, derived by physician and physiologist Adolf Fick in 1855, describes how molecules diffuse from regions of high concentration to regions of low concentration.

The micelles also are coated with protective varnish so that they might remain intact long enough to reach tumor sites, where they would expand and then biodegrade.

More research is needed to determine how well the approach could enhance drug delivery, but the pH phoresis concept developed by Won and his student represents a step in developing nanomedicine techniques in [drug delivery](#), he said.

More information: pH Phoresis": A New Concept That Can Be Used for Improving Drug Delivery to Tumor Cells,

Abstract

We propose a new concept describing how nanoparticles composed of weak polybases (such as polyamines) would behave when they are exposed to a pH gradient; weak polybase-containing particles will tend to accumulate preferentially in low pH regions under a pH gradient environment. This phenomenon, which we term pH phoresis, may provide a useful mechanism for improving the delivery of drugs to cancer cells in solid tumor tissues.

Provided by Purdue University

Citation: Nanoparticles, 'pH phoresis' could improve cancer drug delivery (2013, July 10) retrieved 20 April 2024 from

<https://phys.org/news/2013-07-nanoparticles-ph-phoresis-cancer-drug.html>

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