A surprising new vehicle for drug delivery?

March 30 2011

(PhysOrg.com) -- Are our bodies vulnerable to some pollutants whose lack of solubility in water, or "hydrophobicity," has always been thought to protect us from them? New Tel Aviv University research has discovered that this is indeed the case.

Studies by Dr. Michael Gozin of Tel Aviv University's School of Chemistry at the Raymond and Beverly Sackler Faculty of Exact Sciences and Dr. Dan Peer of TAU's Laboratory of Nanomedicine in the Department of Cell Research and Immunology have revealed that mucus — the thick substance lining those internal bodily organs that come into contact with the outer environment, such as the respiratory system, the digestive system, and the female reproductive system — may instead

play an active role in the penetration of hydrophobic substances, including toxins and carcinogens, into our cells.

But encouragingly, the researchers believe that their discovery will one day prove useful in enabling non-water-soluble drugs to enter cells and treat diseases such as cancer. Their most recent study was published in the *American Chemical Society's Chemical Research in Toxicology* journal.

When mucus fails

Some of these dangerous substances, such as polycyclic aromatic hydrocarbons, are present in petroleum products and also formed through the partial combustion of fossil fuels that are used to operate power stations, planes, cars, space heaters, and stoves. In the new publication, Drs. Gozin and Peer describe their success in getting certain substances, some of them toxic, to penetrate digestive-system cell cultures and bacterial cells bathed in a mucus solution.

"Until now, mucus has been regarded as a mechanical and chemical protective membrane. We did not expect to find it actually absorbing these toxic hydrocarbons and facilitating their transport into bodily systems," explains Dr. Gozin.

Dr. Gozin, Dr. Peer and their research teams show that petroleum-based toxins can dissolve in water with the aid of mucins, the proteins that constitute the main component of mucus.

A new drug delivery system?

In their laboratory, Drs. Gozin and Peer bathed single-celled organisms in a solution of the hydrocarbon-mucin complex, and observed that the

hydrocarbons penetrated the cells much more rapidly than when no mucins were present. "We do not know what mechanism enables these substances to penetrate the cell membranes. Clearly it is not a simple infiltration. Our assumption is that an endocytosis-like process is at work — substances are being absorbed into the cell through entrapment, with the cell membrane folding in on itself and creating a bubble," Dr. Gozin explains.

In an earlier study, published in 2010 in the nanotechnology journal *Small*, Dr. Gozin's team demonstrated that nanometer-scale substances such as carbon-based and inorganic fullerenes (ball-shaped nanoparticles) as well as carbon nanotubes can also be dispersed in physiological solutions with the aid of mucins.

"It will be possible to employ the mechanism we have discovered to facilitate the penetration of hydrophobic drugs into the body, whether via the respiratory tract — with drugs entering the body through the lungs — or by swallowing a delayed-release drug formulation to be absorbed by the digestive system beyond the stomach," Dr. Gozin notes. The next stage of the research will focus on developing systems for the transport of hydrophobic drugs.

Provided by Tel Aviv University