Could engineered fatty particles help prevent AIDS?

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Could engineered fatty particles help prevent AIDS? Liposomes block HIV infection in early tests; could be a cost-effective preventive for developing countries

HIV vaccines are in their infancy, and effective microbicides to prevent sexual transmission of HIV still don't exist. Protection is especially needed for women, who make up nearly half of all global cases. Researchers at Children's Hospital Boston envision a new way for women to protect themselves before sex: an applicator filled with specially formulated fatty particles called liposomes.

In tests led by Daniel Kohane, MD, PhD, director of the Laboratory for Biomaterials and Drug Delivery at Children's Hospital Boston, liposomes inhibited HIV infection in cell culture and appeared safe in female mice when injected intravaginally. The findings are reported in the November issue of the journal *Biomaterials*, published online September 19.

Liposomes are spherical particles with a double outer layer of lipids (fats) and hollow centers. They are relatively easy and cheap to engineer, and thus present a viable option for developing countries, where the cost of anti-HIV drugs bars access for most people.

Liposomes can be filled with drugs or other compounds, but in this case, Kohane and colleagues found, to their surprise, that the liposomes alone were effective in blocking infection.

"We had been planning do much more complex things, like putting ligands on the surface to increase binding to HIV," says Kohane. "It was a surprise that liposomes alone worked so well. Simplicity is always better – if liposomes work by themselves, we may not need anything else, and it would be cheaper and potentially much safer."

Kohane and colleagues hope to conduct further tests to better understand how the liposomes are blocking infection. They bind to HIV, perhaps interfering with the virus's ability to fuse with cell membranes, the first step in infection.

"The idea, simplistically, is that liposomes look like cell membranes," says Kohane, "so maybe we could use them as decoys to prevent HIV infection."

Kohane and colleagues formulated a range of liposomes using various naturally occurring and synthetic lipids and screened them systematically in cell cultures. Several formulations showed a good therapeutic profile, protecting the cells from HIV infection without being toxic. Especially effective were liposomes containing cardiolipin, a fat that was first found in animal hearts; performance was further improved by adding a synthetic phospholipid.

Tested in female mice, these formulations caused little or no inflammation, which can compromise the vaginal lining and increase the risk of HIV transmission. Imaging confirmed that the liposomes remained in place or left the body, but did not travel beyond the vagina.

"This research makes an important contribution towards creating a safe and effective form of HIV prevention for women," says Nikita Malavia, PhD, the study's first author, who worked in Kohane's lab and in the lab of Robert Langer, ScD, of MIT. "Women in areas such as sub-Saharan Africa often cannot control their male partners' use of condoms, making

them three times more likely to be HIV-positive than men. This technology could enable women to take control in their own hands."

Though some intravaginal compounds are in the pipeline, none are available yet. The advantage of using liposomes is that they are inexpensive, easy to formulate into ointments or gels, and stable for long periods of time, making them a particularly good option in resource-poor settings.

Provided by Children's Hospital Boston