Sensory-tested drug-delivery vehicle could limit spread of HIV, AIDS

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A unique method for delivering compounds that could positively impact the global battle against HIV and AIDS may be possible, thanks to researchers in Penn State's College of Agricultural Sciences.

A semi-soft vaginal suppository made from the seaweed-derived food ingredient carrageenan and loaded with the antiviral drug Tenofovir provides a woman-initiated, drug-delivery vehicle that can protect against the spread of sexually transmitted infections during unprotected heterosexual intercourse, the researchers said.

With more than 34 million people worldwide living with HIV, microbicides—compounds that can be applied vaginally or rectally—offer a way to slow the spread of the virus, noted lead researcher Toral Zaveri, postdoctoral scholar in food science. Containing agents known to prevent transmission of HIV and other viruses, microbicides can be inserted into the vagina prior to intercourse as a gel, cream, foam, sponge, suppository or film.

Zaveri pointed out that carrageenan was selected over gelatin—which traditionally has been used for semi-soft suppositories—because it offers a number of important advantages. Because carrageenan is plant based, it is acceptable to vegetarians, there is no risk of animal-acquired infections and it avoids religious objections. Also, it is more stable than gelatin at higher ambient temperatures common in tropical regions of the world.

The suppositories developed by the Penn State researchers hold particular promise for places such as regions of Africa, where HIV is widespread and women often are not in control of sexual situations, according to Zaveri. 1"Condoms have been successful in preventing transmission of HIV and other sexually transmitted infections. However, effectiveness depends on correct and consistent use by the male partner," she said. "Due to socioeconomic and gender inequities, women in some countries and cultures are not always in a position to negotiate regular condom use, so a drug-dispersing suppository can protect against transmission of HIV and other sexually transmitted infections during heterosexual intercourse with a partner whose infection status may or may not be known to the woman."

As part of the research, Zaveri, who earned her doctorate in biomedical engineering at the University of Florida, conducted extensive sensory-perception testing to assess acceptability of the suppositories among women. Women participating in the study at the Sensory Evaluation Center in Penn State's Department of Food Science were presented with suppositories—without the drug—in a variety of sizes, shapes and textures. They indicated their preferences and rated the suppositories for willingness to try and imagined ease of insertion.

The initial evaluations all were done only in the hand as part of this preclinical development effort. Many factors go into making choices, Zaveri explained, such as vaginal products women may have used previously, as well as their sexual and cultural practices. Understanding women's perception of the suppository and reasons behind their choices is a critical step in the development of the suppository as a vaginal drug-delivery system.

Zaveri also studied the release of Tenofovir from the suppositories in a simulated vaginal environment to ensure that the drug will be released once inserted in the body, even in the presence of semen.

"Many people work on drug delivery and use different methods to create drug-delivery products, but not many focus on the end-user aspect of this," she said. "Obviously, the product can be effective only if it is acceptable to women and they use it. We have gone a step farther with this study to validate the acceptability of our suppositories among women—and that's critical. We are not just trying to make our product better, we also are trying to understand the reasoning behind the choices women make regarding vaginal drug delivery in general."

Zaveri noted that some may be surprised that biomedical research is done in the Department of Food Science. But she said it seemed natural given her collaboration on the study with Penn State faculty members Gregory Ziegler—with recognized expertise in biopolymers such as carrageenan—and John Hayes, who is known for his proficiency in sensory-perception research on bitterness, oral burn and consumer acceptability.

"The biomedical use of a food additive—a material widely used in the food industry for its gelling, thickening and stabilizing properties—as a medium for a drug-delivery system is a novel idea, but we were playing to all of our strengths on the team," she said.

Previous microbicides were generally solids or liquids.

"We exploited the intermediate design space of viscoelastic materials known as gels," said Ziegler, "thus avoiding some of the drawbacks of these other dosage forms."

The real beauty of the concept, Zaveri suggested, is its potential for relatively quick commercialization because the material used to formulate the suppositories, carrageenan, is already approved, and safety studies have been done in previous microbicide clinical trials.

"Currently the suppositories are prepared in the lab by simple molding," she said. "However, the research team is investigating methods for large-scale production and packaging—key factors to be considered for product commercialization. Considering the safety, efficacy and user-acceptability tests that we are doing, it easily is possible for a company to take this product and run with it."

More information: The work was described in a series of papers in *PLOS ONE*, *Antiviral Research* and, most recently, the July and September issues of *Pharmaceutics*.

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