

Microbicides: New Delivery and Formulation Methods



INTERNATIONAL
PARTNERSHIP for
MICROBICIDES

The feminization of the HIV/AIDS epidemic has made the development and introduction of female-initiated prevention strategies imperative. Microbicides are vaginal products being developed to prevent the transmission of HIV during sexual intercourse. The earliest microbicide candidates to be developed have the potential to be broadly active against HIV and other sexually transmitted infections (STIs) and have been formulated as coitally dependent (used at time of sex) gels and creams. These microbicide candidates are currently in large-scale efficacy trials in Africa and Asia. The next generation of microbicides containing highly active antiretroviral (ARV)-based drugs that specifically target HIV is well into safety studies and progressing towards efficacy trials. Although the next generation will involve single drugs, the development of microbicides containing combinations of drugs with various mechanisms of action will follow.

The delivery vehicle for an active drug(s) is just as critical as the active itself. Gels have typically been the primary formulation for vaginal products. Scientists developing microbicides need to take into consideration the various characteristics of the product that may affect compliant use over prolonged periods, as well as issues such as cost and women's preferences. In addition, one of the most important issues is the avoidance of formulations with time-sensitive application requirements. To address this, microbicide developers are investigating once-a-day gels (applied independent of sex) and other semisolid formulations including creams, lotions and emulsions.

Novel alternatives to semisolids for microbicide delivery are also needed. The long history of vaginal products used for medicinal and other purposes has shown that no single product configuration will be universally accepted. Microbicide developers agree that multiple formats must be investigated, as no one delivery method will be acceptable to all women. Some of the alternative methods currently being explored include intravaginal rings, films, suppositories, sponges and the diaphragm. Like the semisolid products (e.g., gels and creams), these alternatives are also versatile in terms of their ability to deliver combinations of drugs with multiple mechanisms of protective action. Importantly, these alternative delivery vehicles hold the promise of greater dosing versatility and potentially lower costs.

Development of "non-coitally dependent" (independent of sex) microbicides is essential. As the next generation of microbicide products advances, attention needs to be directed towards the development of non-coitally dependent microbicides that can be formulated for use once a day (or even less frequently), and independent of sex. For example, the ARV-based dapivirine (TMC120 gel), an IPM candidate microbicide, is formulated in a once-a-day gel designed to be used independent of sexual activity, and is intended to provide protection for at least 24 hours. IPM is currently conducting safety studies of this product in Africa. Microbicide developers are investigating other delivery vehicles ranging from microbicide-containing vaginal rings with time-release capabilities to solid dosage forms, as well as novel polymers and biologically triggered drug release approaches, all of which could reduce or eliminate the need for application at or around the time of sex.

continued

Headquarters

8401 Colesville Road, Suite 200
Silver Spring, MD 20910 USA
TEL +1-301-608-2221
FAX +1-301-608-2241

IPM Belgium

Rue du Trône, 98, 7th floor
1050 Brussels, Belgium
TEL +32(0)2 507 1224
FAX +32(0)2 507 1222

IPM South Africa

PO Box 3460
Paarl 7620 South Africa
TEL +27-21-860-2300
FAX +27-21-860-2308/9

www.ipm-microbicides.org



Vaginal rings have already been successfully developed for other applications, such as contraceptives and post-menopausal hormone replacement therapy. A microbicide delivered in a vaginal ring may be able to deliver a drug for periods greater than 30 days. Recently, IPM completed two, first-ever clinical safety studies of microbicide-containing, silicone vaginal rings. IPM will be following these initial safety studies on an ARV-containing ring in Europe with an acceptability study early in 2007 in Kenya, Tanzania and South Africa. A new, multi-chambered ring is also under development which could allow for the inclusion of combinations of drugs in the same ring, mirroring the use of drug combinations which has become the standard in HIV/AIDS treatment. While still in the early stages of research and development, this structure could also allow for the inclusion of contraceptive properties, as well as protection against other STIs. The ring could be used discreetly, and may need to be changed as infrequently as every three months. Issues still to be considered in using a vaginal ring include multi-drug compatibility, production limitations, environmental impact and product acceptability.

What do women want? Effectiveness is influenced by acceptability. Even the most efficacious microbicide in the world will not work if it is not used correctly. Feedback from safety studies in many developing countries points to the need for microbicides that do not interfere with sexual intercourse and may be used discreetly. It is crucial that cultural differences surrounding sexual practices are considered in the development of novel delivery methods for microbicides. IPM has already completed one of several consumer studies aimed at determining the preferences and opinions of African women and their male partners regarding different types of gels, and is also planning for an acceptability study for the vaginal ring. Results from these studies and others will enable IPM and other microbicide developers to appropriately address women's preferences for different types of microbicide delivery methods.

October 2006