

## Microbicides: A Possible Prevention Approach to HIV Transmission among African Women

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### ABSTRACT

*Poverty, cultural belief and refusal to use condoms are some of the factors that contribute to the spread of HIV infection among African communities. There is a dire need to pursue research into the development, provision and the use of microbicides for African women. This review paper provides information and recommendations on the possible use of microbicides to prevent HIV infection among African women.*

## Microbidas: un Enfoque Acerca de la Prevención Posible de la Transmisión del VIH entre las Mujeres Africanas

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### RESUMEN

*La pobreza, las creencias culturales, y el rechazo al uso del condón son algunos de los factores que contribuyen a diseminar la infección por VIH entre las comunidades africanas. Se necesita emprender con urgencia investigaciones encaminadas a desarrollar, suministrar, y usar microbidas entre las mujeres africanas. El presente estudio ofrece información y recomendaciones sobre el posible uso de microbidas a fin de prevenir la infección por VIH entre las mujeres africanas.*

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### INTRODUCTION

Females (young girls and women) are considered to be the most vulnerable group to HIV infection in Africa. This group is not protected by appropriate law on sexual abuse and marriage at a young age and the fact that the majority of them are uneducated and unemployed, leave them with but one choice, a dependence on sex for money in order to survive. There is a lack of cooperation from men to use condoms and because of the problems which may emanate from this (*eg* early pregnancy, sexual infections) there is a dire need to pursue research into the development, provision and the use of microbicides for African women. There is an urgent need to further develop the existing methods of preventive interventions regarding HIV transmission. It is uncertain when a safe and

effective vaccine would be available for use in the prevention of HIV transmission. In the meantime, non-vaccine prevention approaches that can be managed by women to prevent both HIV transmission and other sexually transmitted infections (STIs) are necessary. The use of microbicides is considered to be such a possibility (1).

Microbicides are described as antimicrobial agents that could be topically applied for the prevention of HIV and STIs. Microbicides can also be described as products intended for vaginal or rectal administration that are able to decrease the transmission of HIV and other STIs (2). Development of an effective microbicide would be of great benefit and it would empower women to contribute even more to the fight against HIV infection. The use of microbicides either alone or in combination with other physical barriers can be used by HIV-infected persons. It is believed that the action of microbicides may enhance killing or immobilization of pathogens such as viruses (HIV inclusive). They may block infection by creating a barrier between the pathogen and the cells of the vagina or rectum therefore preventing the infection from manifesting itself following the entrance

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of the pathogen (1). There is a probability that microbicides could reduce the risk of HIV transmission by 40 to 60%. Therefore, microbicides could possibly have a significant influence on preventing the spread of HIV and other STIs in persons who do not use condoms due to cost, religious belief or inaccessibility, particularly women whose partners refuse to use condoms or who have been raped.

Mathematical modelling has shown that if a small proportion of women in low-income countries (such as African countries) use a 60 per cent effective microbicide for half the sexual encounters in which condoms are not used, 2.5 million HIV infections could be averted over a three-year period (2 – 4). Mathematical models are constantly being applied to scientific research as useful tools in providing an estimate of events that could possibly happen. It should also be noted that over time, microbicides are likely to improve incrementally both in effectiveness and in the range of HIV and STIs that they could prevent. Third-generation products could be developed that are up to 85 per cent effective, according to one pharmaco-economic analysis (1, 3, 4). This improvement may be enhanced by the development of combination products, when agents with two or more mechanisms of action are combined.

### **Perceptions about microbicides**

Evidence from studies performed on the use of female condoms (5, 6), emergency contraception (7) and medical abortion (8, 9) have reported the significant influence that healthcare providers' beliefs and attitudes can have on the promotion of these products to potential users in the field of HIV prevention. Emerging products such as microbicides have the potential to impact on public health significantly and the role that healthcare providers play as the patients' primary source of HIV and STI information could be crucial in successfully dispensing, educating and providing access to microbicides once a product becomes available for use (10). Studies in Africa regarding knowledge of microbicides are almost non-existent. Only one detailed study on knowledge and the use of microbicides done in South Africa by Ramjee *et al* (4) is available and some of the outcomes of this study on the perception of healthcare professionals concerning microbicides are discussed.

### **Microbicides as a prevention method and empowering tool for women**

In a study carried out in South Africa (4), it was reported that hospital managers saw potential microbicides as an empowering tool for women, recognizing that a person could make a decision alone without having to involve the partner, particularly when men resist the use of condoms. It was also noted that pharmacists within the health sector were of the opinion that it was an excellent idea to use microbicides, however they could not guarantee their full effect without the simultaneous use of a condom which has an advantage as a contraception whereas microbicides may or may not be indi-

cated for contraception. Most nurses recognized that microbicides could potentially empower women especially in the black communities since most men did not want to use condoms. The researchers noted that fifteen nurses were uncertain of their opinions about potential products while some of them who had prior knowledge about microbicides, were concerned about the acceptability and effectiveness of the product in preventing HIV infection/transmission. It was important that the product not be considered messy by women.

### **Access to microbicides**

Healthcare providers interviewed with the aid of a semi-structured questionnaire thought that microbicides should be dispensed to sexually active people irrespective of their HIV status (4). One of the participants in the study felt that since most people did not disclose their HIV status to their sexual partners, it would be advisable to make microbicides available to everyone. Nurses who will possibly be in the position of dispensing potential microbicides to the public were of the opinion that HIV-positive persons should be given microbicides to prevent re-infection, decrease HIV/STIs transmission to others and also prevent infection by other STIs. For HIV-negative persons, it was thought that prevention of HIV infection should be the primary aim for using microbicides. Some of the participants were of the belief that making microbicides available to HIV-positive persons could lead to an assumption that the use of a microbicide offers a cure for HIV infection which could perpetuate the problem of sexual promiscuity as well as the danger of not using condoms with the belief that they have been cured of the HIV infection. Some participants argued that there should be age restrictions. However others oppose that view since HIV/STI is not restricted to any particular age.

### **Disseminating the message for microbicide usage**

As reported by Ramjee and colleagues (4), about 99% of 149 healthcare providers interviewed reported that they would be willing to recommend the use of potential microbicides to patients if proven to be effective for HIV prevention. All nurses and pharmacists agreed that they would be willing to counsel patients on the use of microbicides for HIV and STI prevention. Most nurses also believe that counselling would encourage clients to make informed decisions.

### **Resources required for distribution**

Nurses and pharmacists believed that their facilities were properly situated for microbicide distribution. Some health-workers suggested that mobile clinics and health-visitors participating in and promoting home visits could help in the distribution and utilization of microbicides. Some health managers were of the opinion that sufficient staff was available to handle the demand of microbicide distribution when the product becomes available while other health-workers suggested that the Department of Health could provide additional staff. Health education and advertising of products

were generally seen as important tools in the distribution of microbicides. Family planning programmes, one-to-one counselling, advertisements on posters in different locations within health institutions and other public locations, life orientation programmes in clinics/health centres, secondary schools, institutions of higher learning could all promote the use of microbicides among African women.

### **Packaging of microbicides**

Healthcare workers were of the opinion that the packaging of microbicides must be appealing to potential users. Different opinions have been expressed as regards the packaging (packaged in boxes and tubes). When packaged, instruction leaflets with clearly written manufacturing and expiry dates must be provided and preferably be of a small size as to fit into a lady's purse as has been suggested by different health professionals.

### **Factors that could enhance acceptance and use of microbicides by African women**

#### **(i) Education**

Education has been and is still playing a significant role in the campaign against HIV transmission (11). Education has provided information about condom use/protected sex and HIV-infection prevention and has helped to reduce the stigma directed towards people infected with HIV. Education would be the appropriate vehicle for effective dissemination of information concerning the role of microbicides as a preventive measure against HIV transmission. African women (including their husbands and boyfriends) need to be informed that microbicides are not directed against them, does not necessarily reduce sexual pleasure and does not contain HIV as some Africans had viewed the condom as a carrier of HIV. Undoubtedly, this negative view has, to a certain degree aided the spread of HIV infection in the African countries. Education can be done amongst others *via* workshops, seminars and community gatherings. Both women and men should be targeted.

#### **(ii) Healthcare system**

Women will be more willing to use microbicides in an environment with a better healthcare system. In other words, accessibility to a healthcare system could encourage women to use microbicides due to the ease to visit healthcare professionals for counselling if they encountered social, biological or any other problem when using microbicides.

#### **(iii) Gender issues**

Observational studies have shown that women are willing and capable to lead the campaign for the use of microbicides and consequently the fight against HIV infection. Therefore, for women to continue to engage meaningfully in the fight against HIV infection and transmission, more attention should be paid to their needs and their social and living conditions should be improved comparatively to their counter-

parts in developed countries. African women should be provided with the necessary communication skills to empower them in negotiating for the use of microbicides. African men must be part of the education process.

#### **(iv) Leaders**

Religious, community, national and international leaders in political and other fields could be involved in communicating the importance of the use of microbicides in the prevention of HIV infection and transmission. National and international leaders need to commit resources for microbicidal research and train personnel who will be involved in disseminating relevant information concerning the proper use of microbicides and thereby changing the views of the people who suffered any stigmatized opinions associated with the use of microbicides. Community leaders still have significant influence over the people at the local level (12) and should be involved in the decision-making process and development of a strategic plan on HIV prevention methods which should include the use of microbicides. One of the setbacks facing the prevention of HIV/AIDS today is religious views on the use of preventable approaches such as condoms. These religious views may directly or indirectly affect the use of microbicides. Religious leaders must be part of the education process to affect behaviour change positively towards HIV prevention methods.

#### **(v) Communication**

Effective communication is important in preventing HIV transmission. Leaders at various levels, mass media and donor-agencies need to meet regularly to discuss the important role microbicides can play in the prevention of HIV infection when they become available. Also, implementation of policies on microbicides, its distribution and proper use need to be properly and effectively communicated to users as well as the general public.

### **Challenges facing the development of microbicides**

#### **(i) Commitment and support**

UNAIDS (2) noted that the development of microbicides requires the active commitment of both private and public entities. As the costs to develop effective microbicides may be too large for governments alone to bear, private industries/individuals will need to play an important role in providing technical and financial assistance in the development of microbicides. However, many research-based pharmaceutical companies have to date not significantly invested in microbicide research and development partly due to the assumption that the production of a microbicide may not have a profitable outcome. Although an effective microbicide is desperately needed in the developing countries with a high incidence of HIV, it is feared that due to poverty the purchasing power of the people of these countries may be limited and thus limit the profitability of such production by pharmaceutical companies.

The time required to develop an effective and acceptable microbicide could be very long. This may be related to limited funding for microbicide research. In 2000, about 65 million US dollars were invested worldwide on microbicide research, development, testing, policy-making and advocacy (3). By 2004, the global investment on microbicide research increased to 142 million United States dollars per year; however this investment is lower than the amount projected by different organizations such as International Partnership for Microbicides, Alliance for Microbicide Development and Global Campaign for Microbicides. These three organizations estimated that the annual global investment on microbicides to ensure the timely development of a safe and effective microbicide should be increased to 280 million US dollars for the next five years and that this amount should be invested annually until satisfactory microbicides have been developed and licensed.

The cost of microbicides at an exorbitant price will further add to the economic burden of poor countries and further lower the standard of living of the population. The pharmaceutical companies should therefore place profit as a secondary issue due to the millions of people that are being infected and die of AIDS yearly. Companies involved in the development of microbicides could also enter into partnership arrangements with the government of these developing countries in order to supply affordable microbicides to users.

Microbicides produced in developed countries might soon become over-the-counter products which carries a lower profit margin than other prescription drugs whereas companies that intend to manufacture microbicides in developing countries may face manufacturing regulatory problems/uncertainties and constraints as well as having the potential for unreasonable liability claims. These factors can affect the cost of production of microbicides in developing countries and companies may therefore be tempted to charge higher price to cover cost of production and probably generate some profits.

In developing countries, where the HIV epidemic is currently concentrated, there is very little female activism to campaign for vaginal microbicides due to the generally low economic status of African women activists. These activists are equally faced with teething problems such as maternal mortality, abortion, education for women and discrimination against women and these problems continue to hinder the ability of such activists to strongly argue their rights for the widespread use of vaginal microbicides. Unfortunately, even in the scientific community, there is a growing and worrying perception that other therapeutic research is financially more rewarding, innovative and attractive than microbicide research.

### (ii) Scientific questions

These questions are not restricted to research, development, access and use of microbicides in the African context but

questions that are globally posed and demand global answers by all the stakeholders in the development of microbicides. For instance, scientists are worried and do not know for example (1) which cells in the mucosa are most susceptible to HIV infection, (2) whether HIV is transmitted as free or as cell-associated viruses or both; (3) whether HIV infectivity or the target cell differ according to subtypes.

### (iii) Conducting clinical trials

Evaluation of the efficacy of a microbicide requires clinical trials on a large population of women at high risk of HIV infection. Cohorts with a high incidence of HIV and STIs are expensive, difficult to recruit and maintain and must be followed up for long periods of time. For efficacy, the cohort studies should preferably be conducted in developing countries such as African countries where the HIV incidence is higher than in developed countries. Strengthening the research capacity of study centres and addressing ethical issues may be some of the challenges associated with conducting studies in developing countries such as the African countries (1, 2).

Finding the right population where clinical trials should be conducted may be another challenge. It is suggested that female sex-workers (FSW) would be more acceptable participants for microbicide research studies however, FSW tend to differ in many significant ways from other women. For instance, FSW have many partners, have other STIs and frequently clean the vagina with either water or chemicals which interfere with the physiological and biological composition of their vaginas (13). Post-natal women, teenage girls, university students in high HIV prevalence countries and homosexual men could also be target populations for microbicide research.

### (iv) Ignorance

HIV infection has been seen as a disease associated with sex-workers and homosexual men. Despite extensive sex-education, ignorance remains a main problem contributing to the spread of the epidemic. It is reported that over 30% of South African women believe that if a man appears healthy, he could not be HIV-positive or be a carrier of the virus (14). A similar view is reported to exist in other parts of Africa. Some young African men and women believe that HIV infection is a disease associated with rape, commercial sex and excessive alcohol consumption. These kinds of beliefs could impact negatively on the use of condoms and other preventive measures such as microbicides in the prevention of HIV infection. Ignorance can however be overcome through using education programmes which should address all fears and misconceptions that young men and women have about HIV/STIs preventive measures.

### Steps to take in developing microbicides

*In vitro*, animal and human study data will all be required for a microbicide to be licensed. Laboratory studies (*in vitro*) on

microbicides should evaluate the following: (1) the activity of a potential product against HIV and other STIs, (2) its spermicidal activity, (3) the impact on embryogenesis and teratogenicity and (4) the interactions with latex and polyurethane condoms. It is suggested that animal studies should: (1) assess the product's safety, (2) predict its dosing regimen, (3) confirm its activity against the transmission of HIV and other STIs and (4) assess the product's carcinogenic potential and reproductive toxicity.

Studies with humans should consist of: (1) small phase I clinical trials to obtain initial information on safety and pharmacokinetics, (2) phase II studies to confirm the product's safety and (3) phase III studies to determine whether the product prevents the sexual transmission of HIV and other STIs. For the assessment of local safety, it is recommended that colposcopy be performed in phase II studies and on a relatively small number of female participants in phase III studies (1, 2).

### Recommendations

Currently, there is a dire need for the renewed and sustained advocacy by activists, public institutions and the private sector to request that microbicide research and development become an integral part of the mainstream HIV agenda. Global advocacy organizations such as UNAIDS should continue to take the responsibility to speak out for and support the voice of the underprivileged and women, in particular, in developing countries concerning microbicide research.

Activists need to call on governments for wider and stronger public sector support for microbicide development. The public needs to be educated and made to understand that having a readily available microbicide is a significant tool which can be used in the prevention of HIV infection, even if a HIV vaccine becomes available since different people could be interested in using different prevention methods.

Microbicide advocates need to present industry with facts that would reverse their biased perception that a microbicide product would be unprofitable especially in developing countries such as in Africa. Microbicide advocates should support the efforts of small companies who are engaged and those planning to engage in microbicide research and development.

Principal HIV researchers should be persuaded of the importance to develop an effective microbicide. These researchers should be encouraged to investigate the sexual transmission of HIV and to develop methods to decrease HIV infection. The findings of such research studies can be presented at scientific conferences/congresses and published in appropriate scientific journals to show that microbicide development can be possible.

There is also a need to conduct clinical trials on the safety of the use of microbicides among women who are already infected with HIV, since microbicides will most likely be used by women who are aware of their HIV status

and/or those using the product to avoid transmitting HIV to their partners.

Globally, more than fifteen thousand HIV-negative women are participating in vaginal microbicide trials. Researchers who conduct these trials face many challenges, including high pregnancy rates (which requires that those participants immediately discontinue using experimental agents), the unreliability of self-reported adherence to protocol and unexpectedly low HIV incidence in trial areas. These controversies need to be addressed and resolved to facilitate further research into microbicides.

In light of the recent cancellation of some clinical trials evaluating oral tenofovir as a potential prophylactic against HIV infection (although others are ongoing), the issue of post-trial care for participants who become infected during a HIV prevention trial raise questions that need to be investigated and resolved. There is also a need for additional investment in microbicide research and development and to train African scientists who could become involved in microbicide research.

### CONCLUSION

From evidence provided by mathematical modelling and as indicated by a study done in South Africa which reported the responses of healthcare providers in favour of the use of a potential microbicide, it is postulated that there could be a significant reduction in the rate of HIV infection and transmission. Production, acceptance and use of microbicides definitely face some challenges. This paper offers some recommendations on how to address these challenges. More needs to be done if microbicides are to be made available to African women as it is realized that HIV/AIDS represents a critical challenge to humanity and the response to it should be based on a vision of social justice, freedom and equality. Government and the private sector have a legal and moral duty to meet all the demands required to halt the epidemic and this also includes the demand from the pharmaceutical industry to invest in microbicide research and development.

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