INTRODUCTION

1.1 Sexually Transmitted Diseases

Sexually Transmitted Diseases (STDs) or Sexually transmitted infections (STIs) are diseases/infections that can be transferred from one person to another through sexual contact (Figure 1). Some sexually transmitted Infections are also transmitted through birth, intravenous needles or breastfeeding.

Types of Primary STDs/STIs

- Bacterial Vaginosis
- Thrush
- Viral Hepatitis
- Crab Louse
- Trichomoniasis
- Chlamydia (Candidiasis)
- Herpes simplex
- Scabies
- Gonorrhea
- HIV
- Syphilis
- Genital warts
- Molluscum contagiosum

Figure 1

1.2 Microbicides

Microbicides are the group of pharmacologic agents and chemical substances that are capable of killing certain microorganism that commonly cause human infection by bacteria, fungi and viruses like HIV. Some microbicides are also effective as spermicides.
Candidate microbicides in clinical trials include detergents or surfactants such as sodium dodecyl sulphate (SDS) and C31G that act pre-binding and disrupt virion membranes; acid-buffering agents, which are designed to maintain the natural vaginal acidity in the presence of the alkalinizing effects of semen thereby inactivating acid-sensitive pathogens; reverse transcriptase inhibitors such as PMPA; and sulphated or sulphonated polysaccharides (SPs) such as cellulose sulphate, dextran sulphate, polystyrene sulphonate, PRO 2000 and carrageenan, which target gp120 and prevent viral binding and entry. Keller M. J. et al, (2003) have studied some compounds in pre-clinical development, which include small molecule or antibody-based fusion inhibitors and natural antimicrobial peptides.

A fundamental principle in the development of microbicides (alone or in combination) is identifying agents that are non-toxic to the genital mucosa. Using cultured primary human cervical and vaginal epithelial cells, we found the surfactant N-9 to be highly cytotoxic and more cytotoxic for primary cells compared with permanent cell lines. In a recent meta-analysis of nine randomized clinical trials, N-9 was associated with a significantly enhanced risk of genital ulcers. In addition, the analysis revealed a higher risk of HIV infection with N-9 relative to placebo. The recent failure of N-9 as a potential microbicide candidate highlights the importance of the toxicity profile of any potential agent or formulation.

1.3 Role of Cationic Surfactants as Antimicrobials
Various types of detergents, including deoxycholate, sodium dodecyl sulfate, Triton X-100 and cetyltrimethylammonium bromide weakly inactivate the antigenic activity of HBsAg (Hepatitis B surface antigen), a type of sexually transmitted disease. But cationic detergents $N^\alpha$-lauroyl-L-lysine ethyl ester (LLE) and $N^\alpha$-cocoyl-L-arginine amide (CAA) as well as $N^\alpha$-cocoyl-L-arginine ethyl ester (CAE) strongly inactivate HBsAg at relatively low concentrations.

The effectiveness of $N^\alpha$-acyl-L-arginine ethyl ester depends upon the length of the acyl group, with the optimum length for the inactivation of HBsAg being $C_{12}$ to $C_{14}$.

**Types of surfactants**

![Diagram showing Types of surfactants]

- **Cationic surfactants**: Obtained by esterification of the $\alpha$-carboxyl gr.
  - Properties: Highly water soluble, surface active
  - Use: Highly antimicrobial

- **Amphoteric surfactants**: Obtained with free $\alpha$-carboxyl gr.
  - Properties: water insoluble, do not show surface activity
  - Use: Antimicrobial activity absent

**Figure 3**

Cationic surfactants (Figure 3) derived from the condensation of fatty acids and esterified dibasic amino acids, such as from lauric acid and arginine, in particular the Et ester of the lauramide of the arginine monohydrochloride (LAE), may be used for the protection against the growth of the microorganisms. The cationic surfactants of this type are also effective against virus infections. Rocabayera B. et al, (2008), observed that addition of LAE to cultures of Herpes virus type 1 Vaccinia virus and bovine parainfluenzae 3 virus leads to nearly complete redn. of the virus organisms in these cultures, such effects being observed after 5 and 60 min.

Arginine-based surfactants have turned out to be an important class of cationic surface active compounds with antimicrobial activity against a broad spectrum of bacteria biodegradability and low toxicity.
Essential structural factors for their antimicrobial activity include both the length of the fatty residue and the presence of the protonated guanidine function. These features and the use of natural raw materials such as arginine and fatty acids for their synthesis, make them interesting candidates as preservatives and antiseptics in pharmaceutical, food and cosmetic formulations.

One example of amino acid-based surfactants as food preservative is Mirenat-N, a solution of Lauric arginate. This is a novel antimicrobial compound derivative of lauric acid, L-Arginine and Ethanol, all naturally occurring substances. The molecule was first synthesized by the Department of Surfactant Technology, CSIC, in Barcelona in 1984. Then patented and commercialized by Vedeqsa Lamirsa group. Its most notable features are a broad spectrum of antimicrobial efficacy; high partition coefficient (meaning the product concentrates in the water phase of products; where most bacterial action occurs); activity over a wide pH range (3 to 7) and safety. Mirenat-N is hydrolysed in the human body and it has “Generally recognized safe” (GRAS) by the Food and Drug Administration. Thus Mirenat-N is used as Food preservative in deli meats and sausages, which are long worrisome potential sources of contamination.

I am optimistic & would strongly suggest that certain amino acids with and without monolaurin would be effective as a microbicide against HIV and other sexually transmitted diseases as well as having germicidal activity. The synthesis would involve making LAE compounds,

\[
R' = C_{7,8,11,13,15} \text{ carbonatoms} \; ; \; R = \text{Et, Bu}
\]

following the scheme given below,

\[
\text{L-Arginine} \xrightarrow{\text{O}} \text{L-Arginine alkyl ester dihydrochloride}
\]

**Fig. 4 Synthetic scheme for Arginine derivatives**