Safety and Anti-HIV Activity of Over-the-Counter Lubricant Gels

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Overview

- Rationale for investigating lubricants.
- What we know about lubricants; safety and anti-HIV activity.
- Our testing approach and results.
Lubricant history

- Personal lubricants were created from surgical lubricants.
- US FDA deemed them medical devices 1976.
- Lubricants have been used as “placebos” for microbicide clinical trials.
- Lubricant use is common in developed countries.
Safety and anti-HIV activity

- Lubricants impede sperm mobility

- Lubricants were shown to be toxic to vaginal tracts of mice and enhance susceptibility to HSV

- Hyperosmolar lubricants increased irritation and damage in a slug mucosal irritation assay
  - Adriaens and Remon, STD 35:512, 2008

- Lubricant excipients, glycerin and polyquaternium-32, showed anti-HIV activity; however, no cellular toxicity determined
IRMA survey

- International Rectal Microbicide Advocates [www.rectalmicrobicides.org]
- 29-week web-based survey (6 languages) on lubricants used during anal sex
- Which lubricants were used the most for anal sex

<table>
<thead>
<tr>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astroglide*</td>
</tr>
<tr>
<td>Durex*</td>
</tr>
<tr>
<td>Elbow Grease</td>
</tr>
<tr>
<td>Gun Oil</td>
</tr>
<tr>
<td>ID*</td>
</tr>
<tr>
<td>KY*</td>
</tr>
<tr>
<td>Liquid Silk</td>
</tr>
<tr>
<td>Pjur Eros</td>
</tr>
<tr>
<td>spit</td>
</tr>
<tr>
<td>Swiss Navy</td>
</tr>
<tr>
<td>Vaseline</td>
</tr>
<tr>
<td>Wet*</td>
</tr>
</tbody>
</table>


*Multiple formulations of this brand
Our approach

Formulation Testing
- Osmolality, pH, viscosity, in vitro release

Product

In vitro Testing
- Dose Range
- Cell line: Lactobacillus
- HIV efficacy
  ± mucosal secretions

Ex vivo Testing
- Cervical/colorectal tissue
- Absorption, permeability, and safety
- HIV efficacy
  ± mucosal secretions

This is the same approach the MTN uses to evaluate topical microbicides
# Formulation characteristics

<table>
<thead>
<tr>
<th>Lubricant</th>
<th>Osmolality (mmol/kg)</th>
<th>pH</th>
<th>Viscosity (cps, 10 rpm @ 25°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Semen</td>
<td>321</td>
<td>8.1</td>
<td>4</td>
</tr>
<tr>
<td>PRÉ</td>
<td>502</td>
<td>7.3</td>
<td>1683</td>
</tr>
<tr>
<td>KY Jelly</td>
<td>2510</td>
<td>4.5</td>
<td>5913</td>
</tr>
<tr>
<td>ID Glide</td>
<td>3150</td>
<td>5.2</td>
<td>751</td>
</tr>
<tr>
<td>Elbow Grease</td>
<td>3865</td>
<td>5.7</td>
<td>3159</td>
</tr>
<tr>
<td>Astroglide</td>
<td>6113</td>
<td>4.0</td>
<td>207</td>
</tr>
<tr>
<td>Gynol II (N9)</td>
<td>1245</td>
<td>4.7</td>
<td>1248</td>
</tr>
<tr>
<td>Wet Platinum</td>
<td>NA</td>
<td>NA</td>
<td>145</td>
</tr>
</tbody>
</table>
Toxicity testing – vaginal flora

*KY Jelly contains chlorhexidine which is bactericidal to gram-positive and gram-negative bacteria
Toxicity testing – epithelial cells

Caco-2

HEC-1-A

TZM-bl

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4 experiments; mean ± SD
Toxicity testing – epithelial cells

Wet Platinum

6 experiments; mean ± SD
Toxicity testing – explant tissue

Lubricant

MTT assay
(mitochondrial activity)

Histology
Explant viability – MTT assay

Colorectal explant viability

Ectocervical explant viability

% Viability of Control

- Astroglide
- Elbow Grease
- ID Glide
- KY Jelly
- Wet Platinum
- PRE
- N9
Explant viability – Histology

Colorectal tissue

Control
N9
PRÉ
Wet Platinum
Astroglide
Elbow Grease
ID Glide
KY Jelly
Explant viability – Histology

Ectocervical tissue

Control
N9
PRE
Wet Platinum
Astroglide
Elbow Grease
ID Glide
KY Jelly
Anti-HIV activity – TZM-bl assay

Efficacy

Toxicity

Astroglide

Elbow Grease

ID Glide

KY Jelly

PRÉ

N9

% Inhibition/% Viability

Dilution
Therapeutic index (TI)

- TI is the lethal dose of a drug for 50% of the population (LD50) divided by the minimum effective dose for 50% of the population (ED50)
- The higher the number, the more likely you will see efficacy without toxicity – should exceed 100

<table>
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<tr>
<th>Lubricant</th>
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<th>Elbow Grease</th>
<th>ID Glide</th>
<th>KY Jelly</th>
<th>PRÉ</th>
<th>N9</th>
</tr>
</thead>
<tbody>
<tr>
<td>TI</td>
<td>1.5</td>
<td>10</td>
<td>5</td>
<td>2</td>
<td>15</td>
<td>4</td>
</tr>
</tbody>
</table>
Summary

- KY Jelly is toxic to lactobacilli
- Elbow Grease, ID Glide, and KY Jelly have similar toxicity profiles for cells, cell lines, and tissues
- Astroglide is the most toxic
- PRÉ and Wet Platinum appear safest
- None of the lubricants have anti-HIV activity
Conclusion

- The in vitro toxicity of the hyperosmolar lubricants suggests that they may cause damage to mucosal surfaces in people.
- This may lead to increased susceptibility to HIV.
- So...choose your lube carefully!
  - Make it isosmolar and condom friendly!
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