

# Combination Microbicidal Mixtures Inactivate Herpes Simplex Virus (HSV)

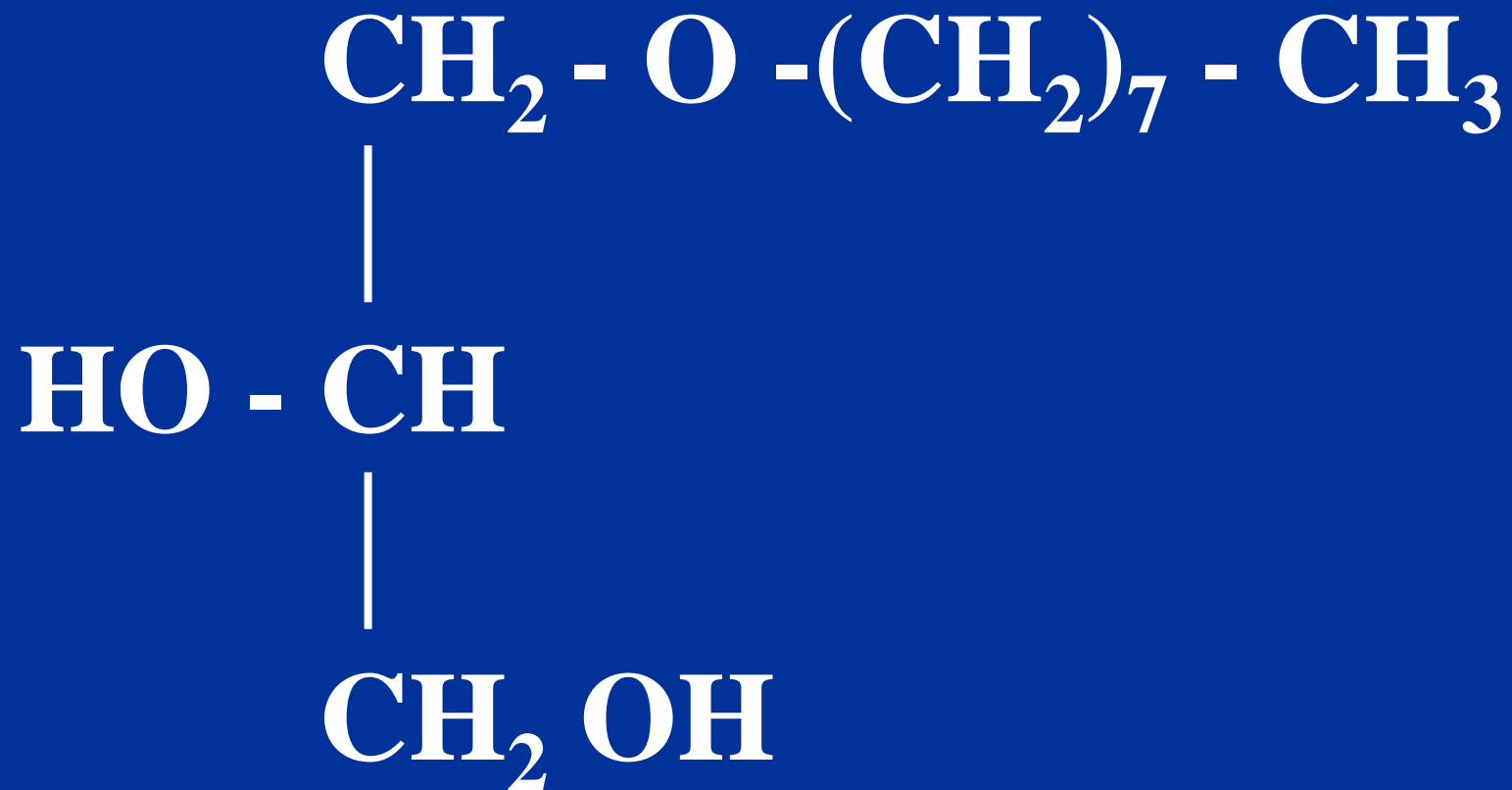


New York State

**Institute for Basic Research**

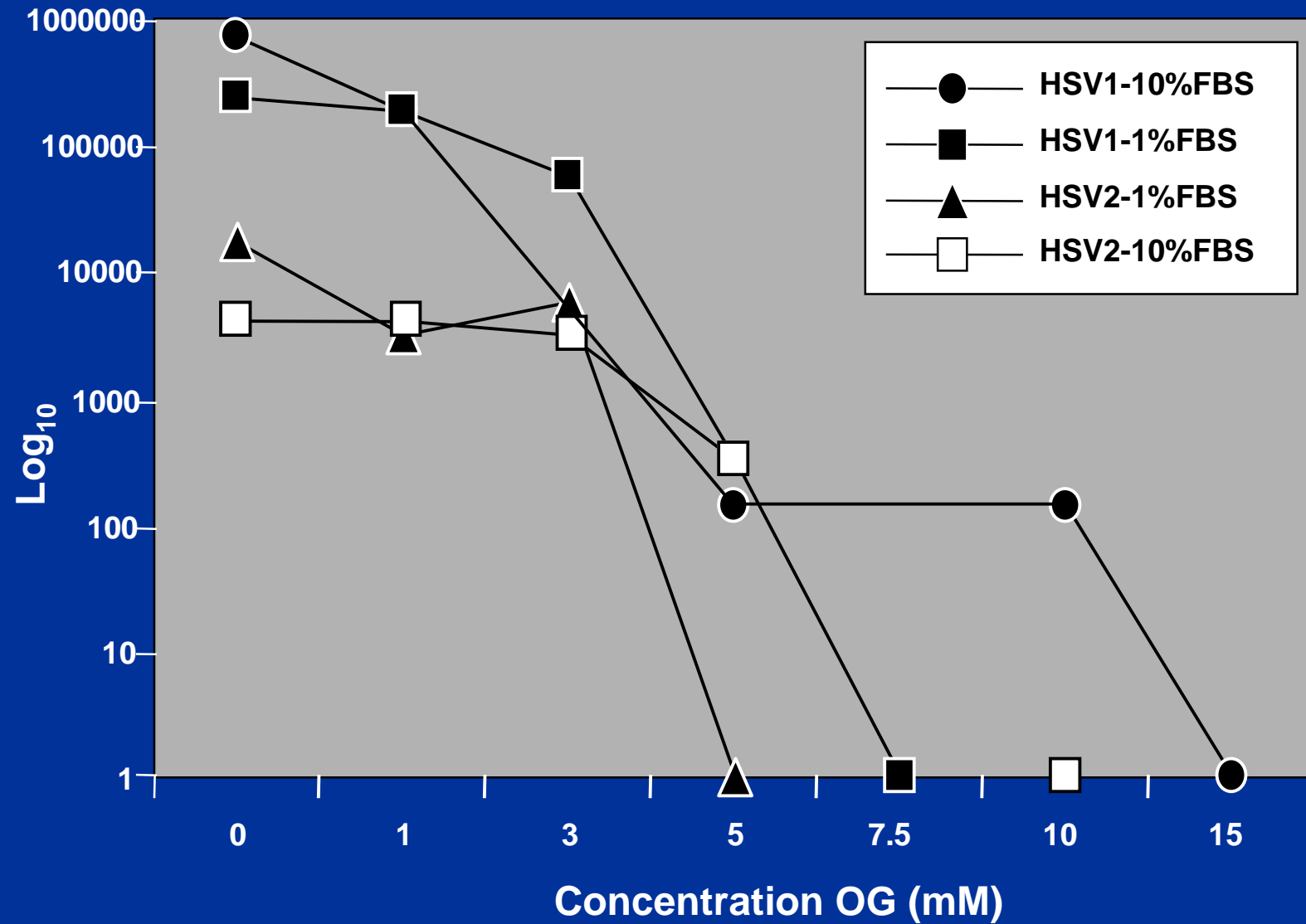
In Developmental Disabilities

- Topical microbicides must provide protection against a broad array of STDs
- Combining **multiple protective factors** as occurs naturally at mucosal surfaces will provide a wider range of protection

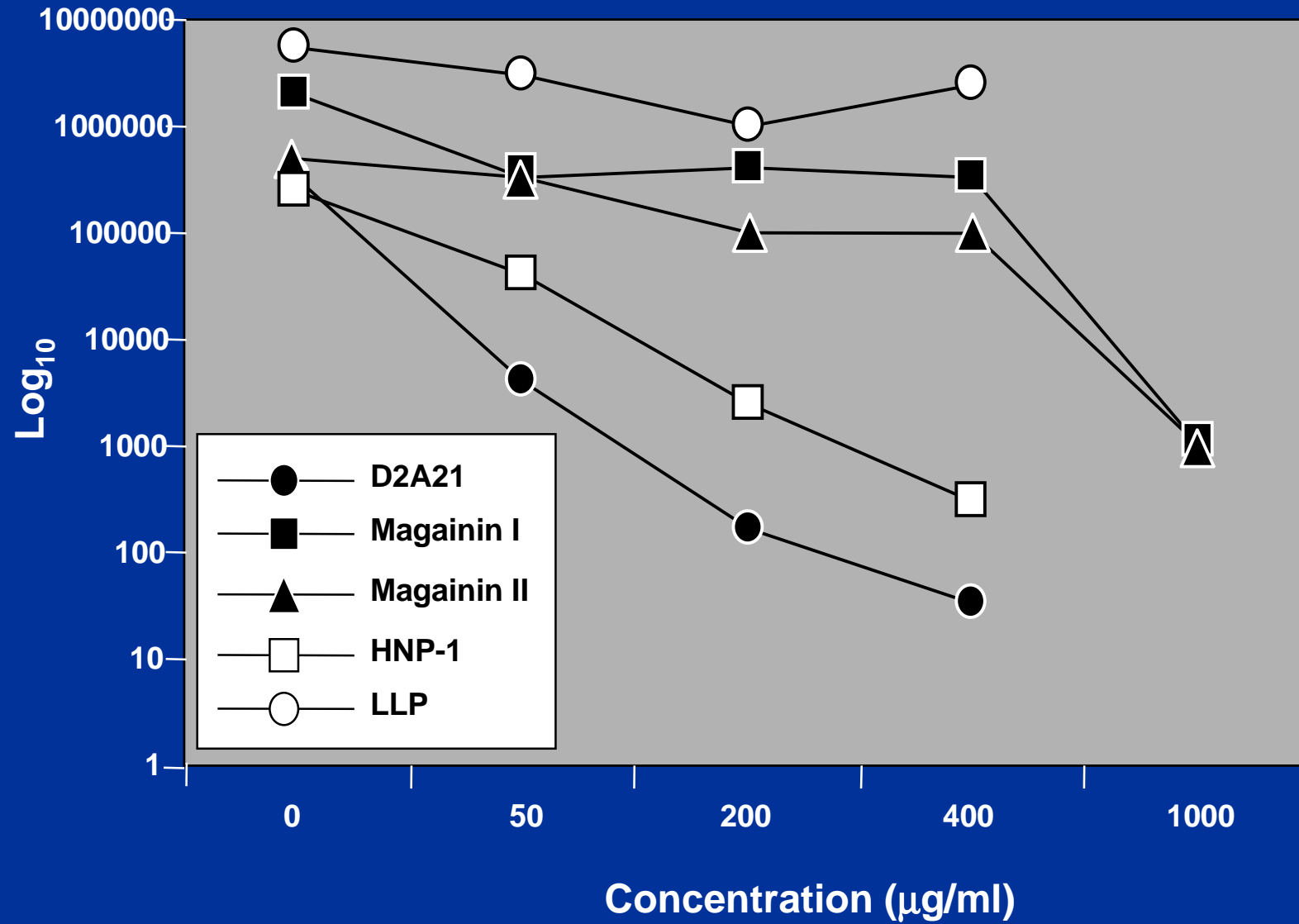


**1-*O*-octyl-*sn*-glycerol**

## 1-O-Octyl-sn-glycerol Inactivates HSV-1 and HSV-2



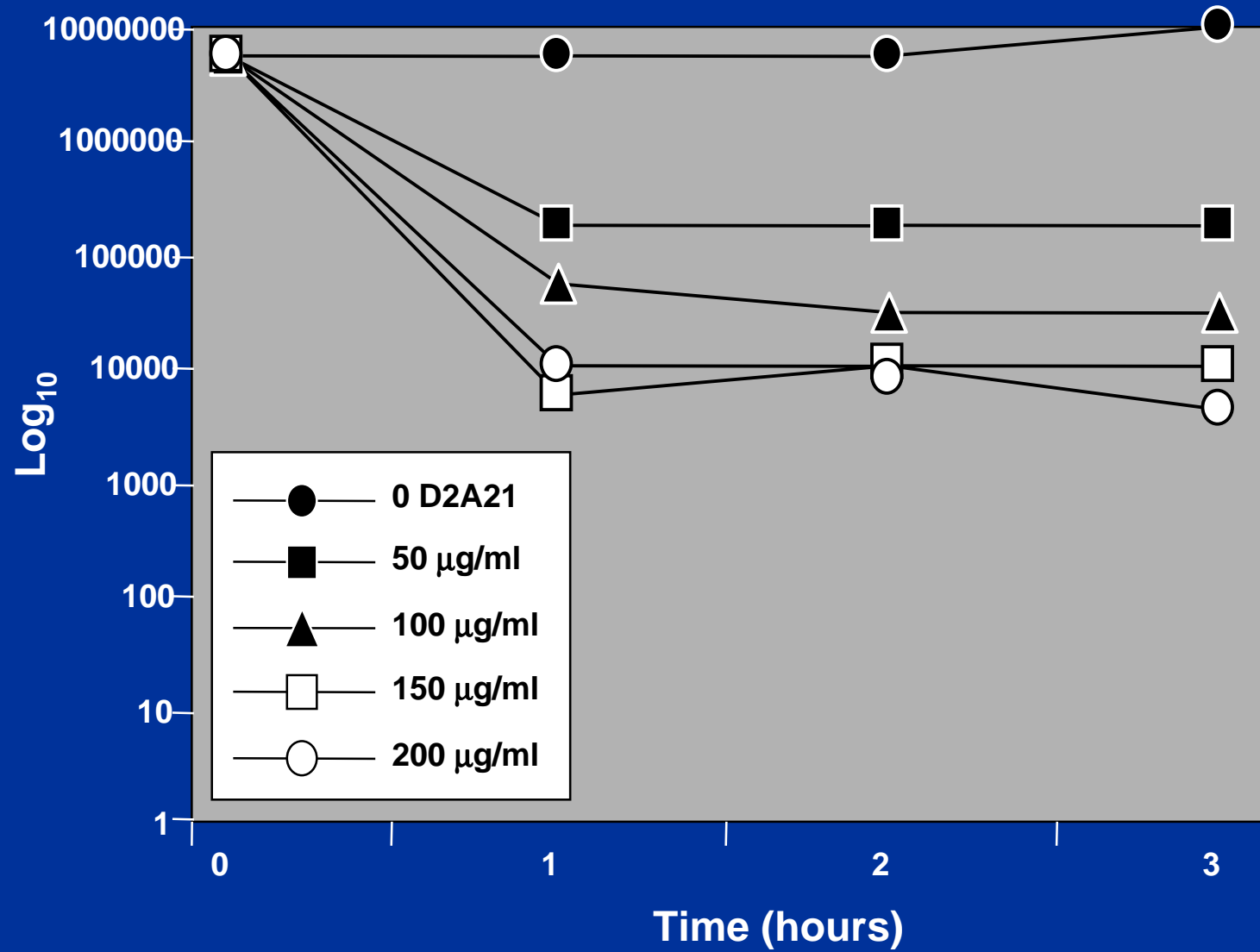
## Inactivation of HSV-1 by Antimicrobial Peptides



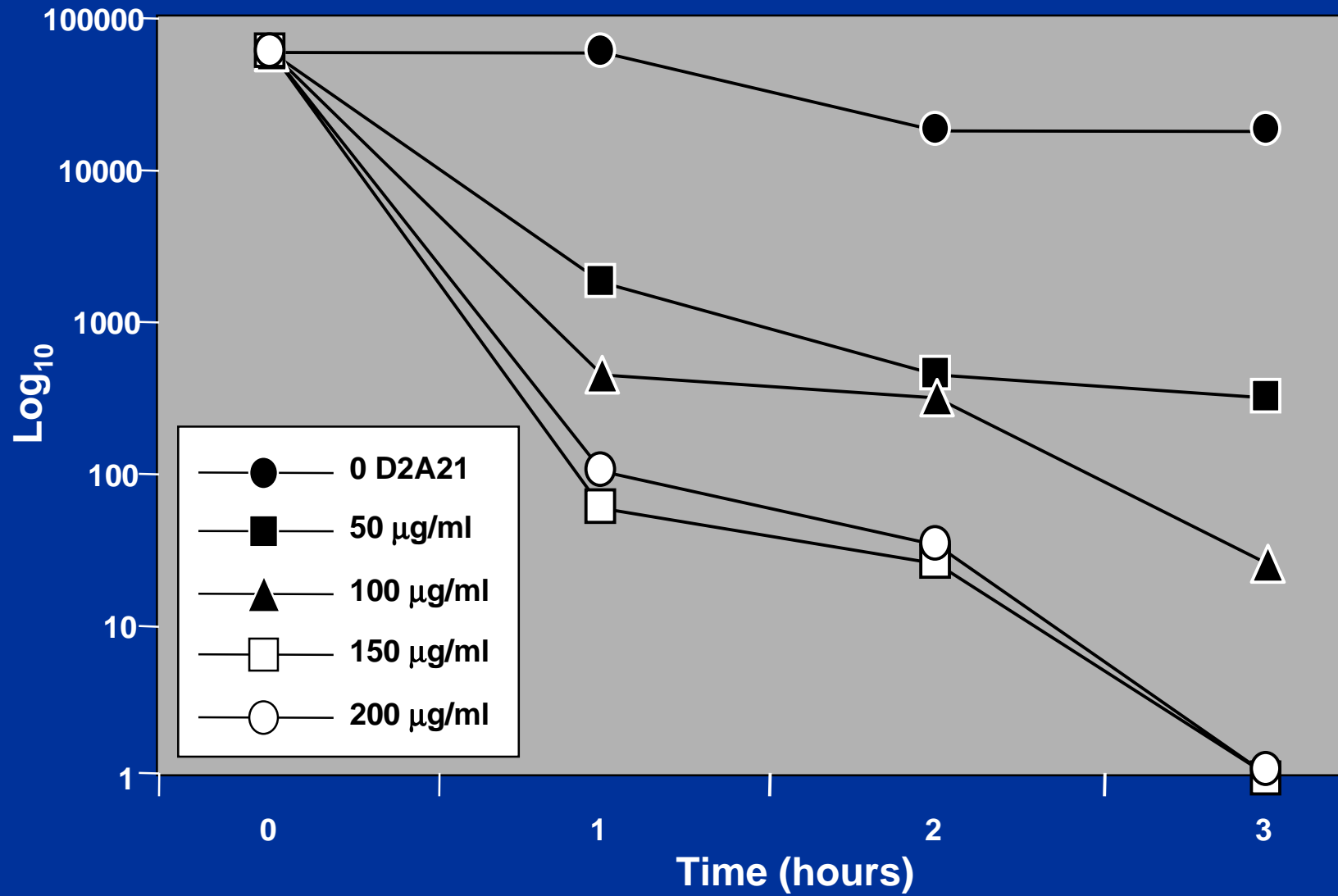
phe-ala-lys-lys-phe-ala-lys-lys-phe-  
lys-lys-phe-ala-lys-lys-phe-ala-lys-  
phe-ala-phe-ala-phe

D2A21 Demegen

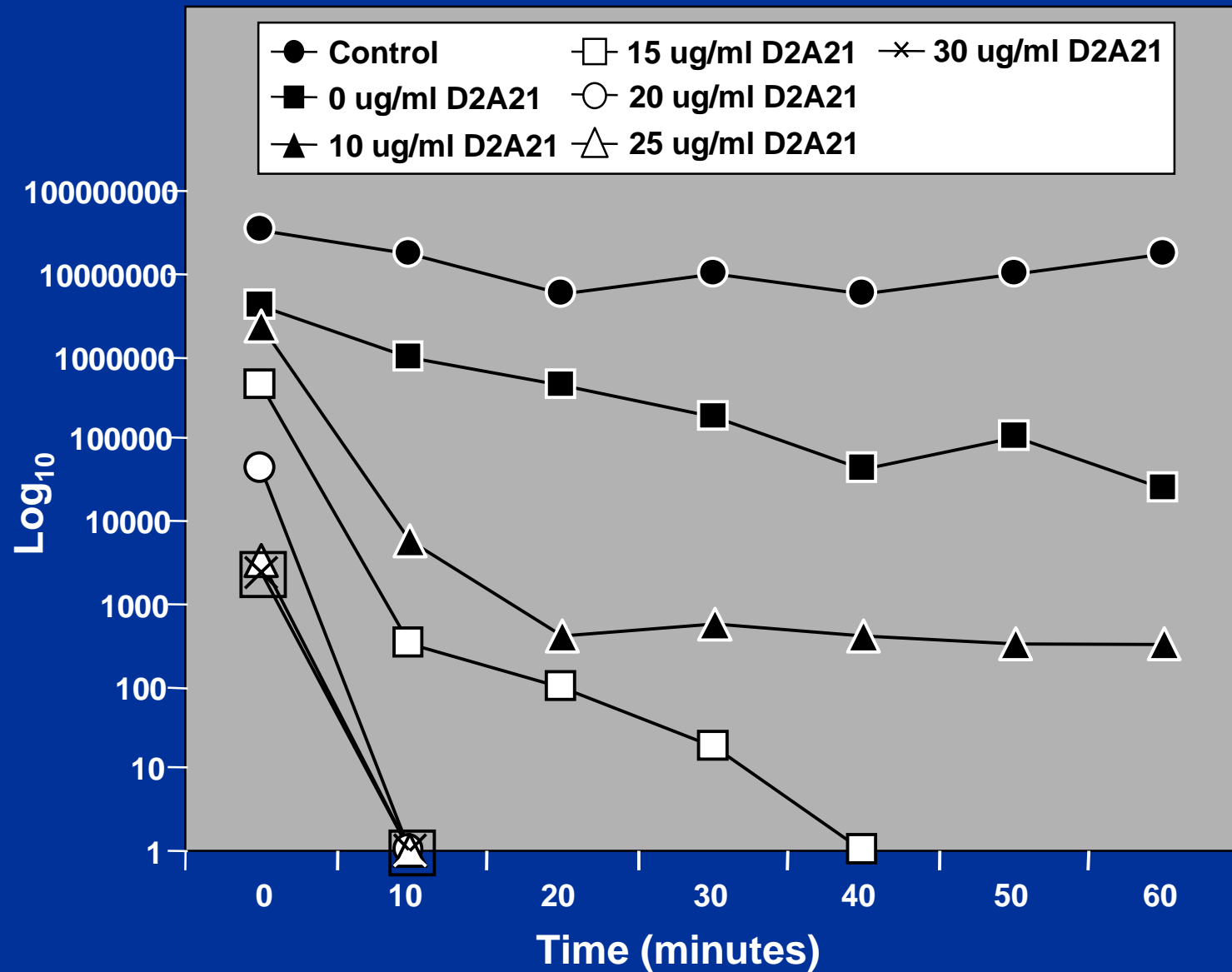
## Reduction of HSV-1 Infectivity by D2A21



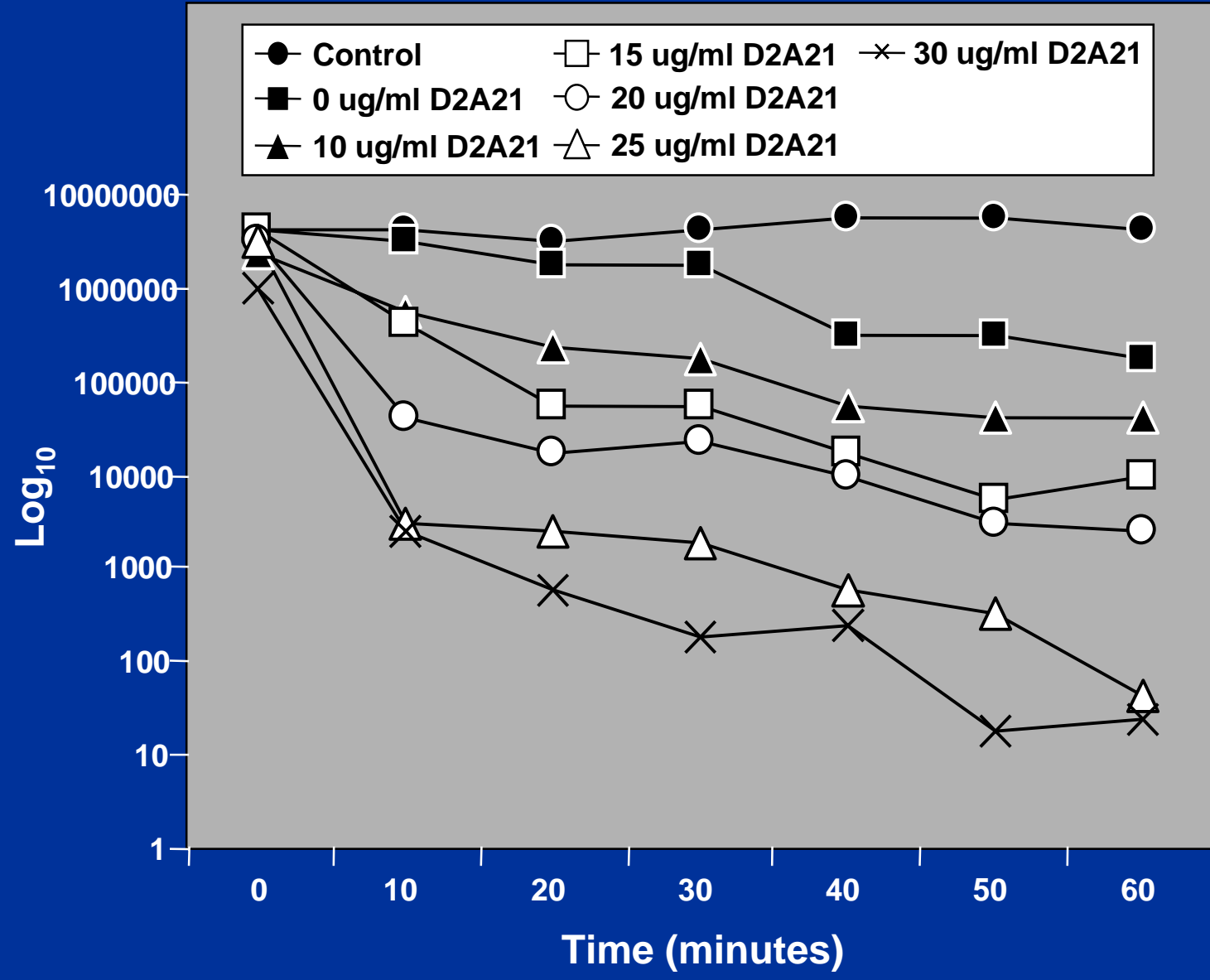
## Reduction of HSV-2 Infectivity by D2A21



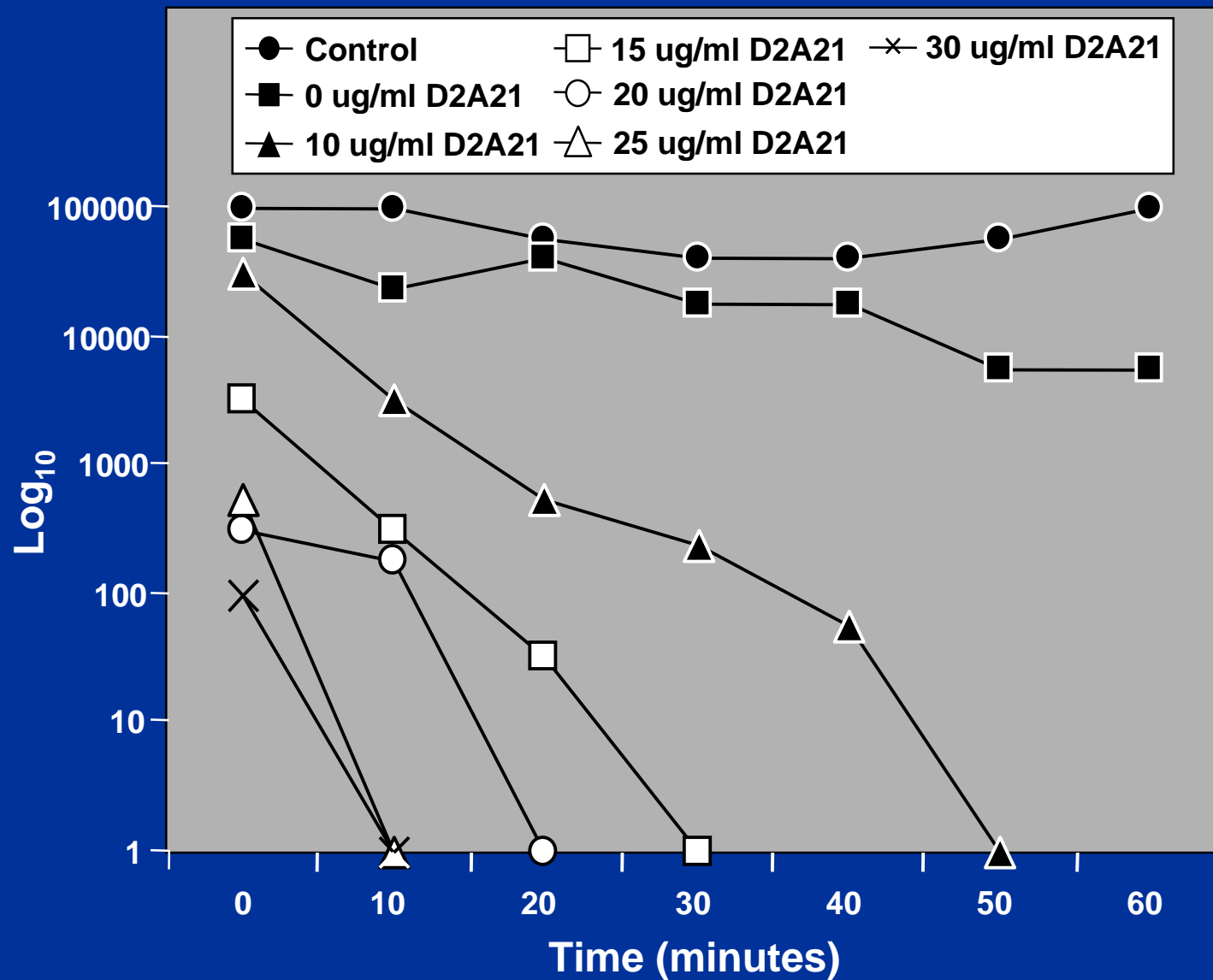
## Time course of Lipid (4 mM)-Peptide Inactivation of HSV-1 (1% FBS)



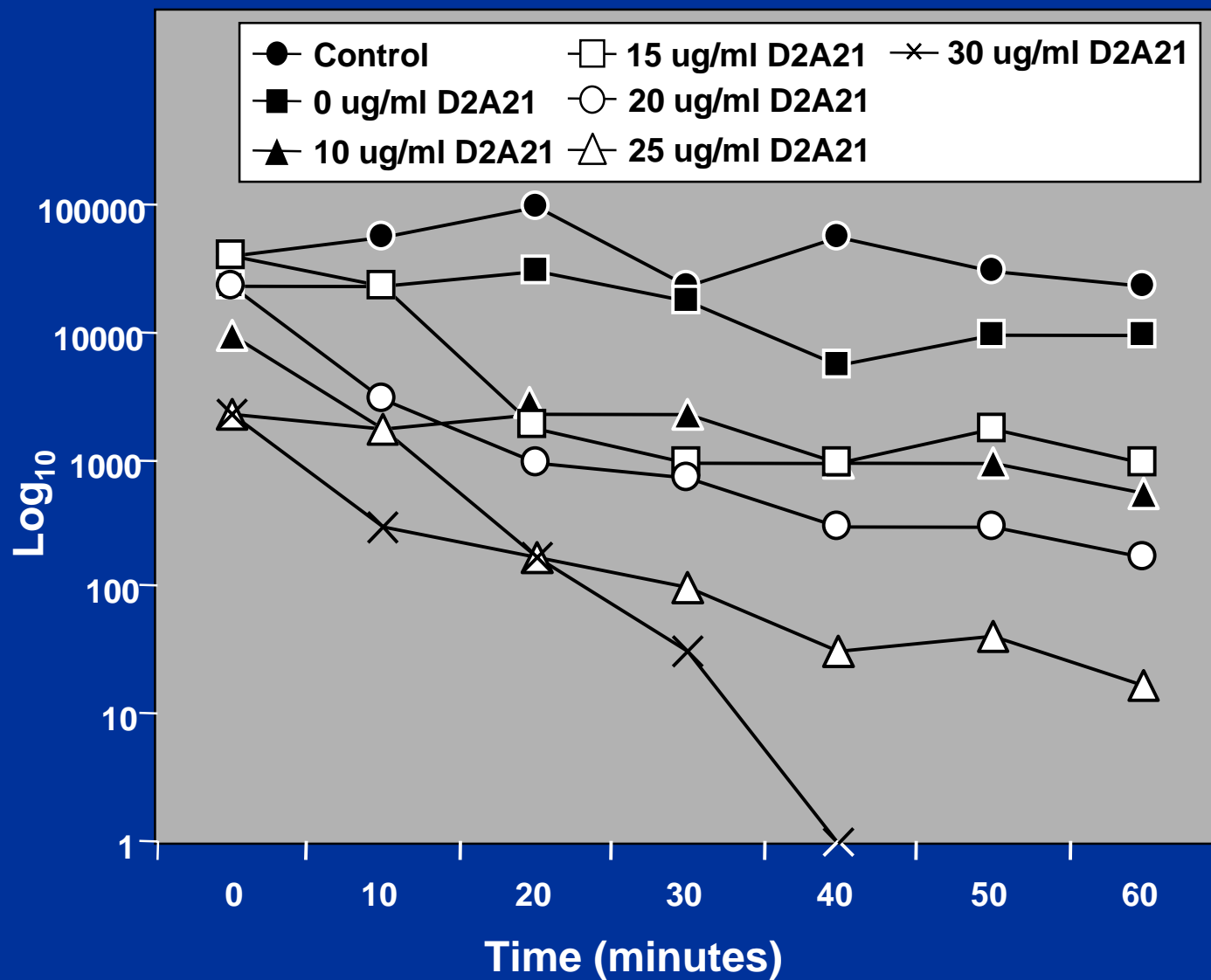
## Time Course of Lipid (4 mM)-Peptide Inactivation of HSV-1 (10% FBS)



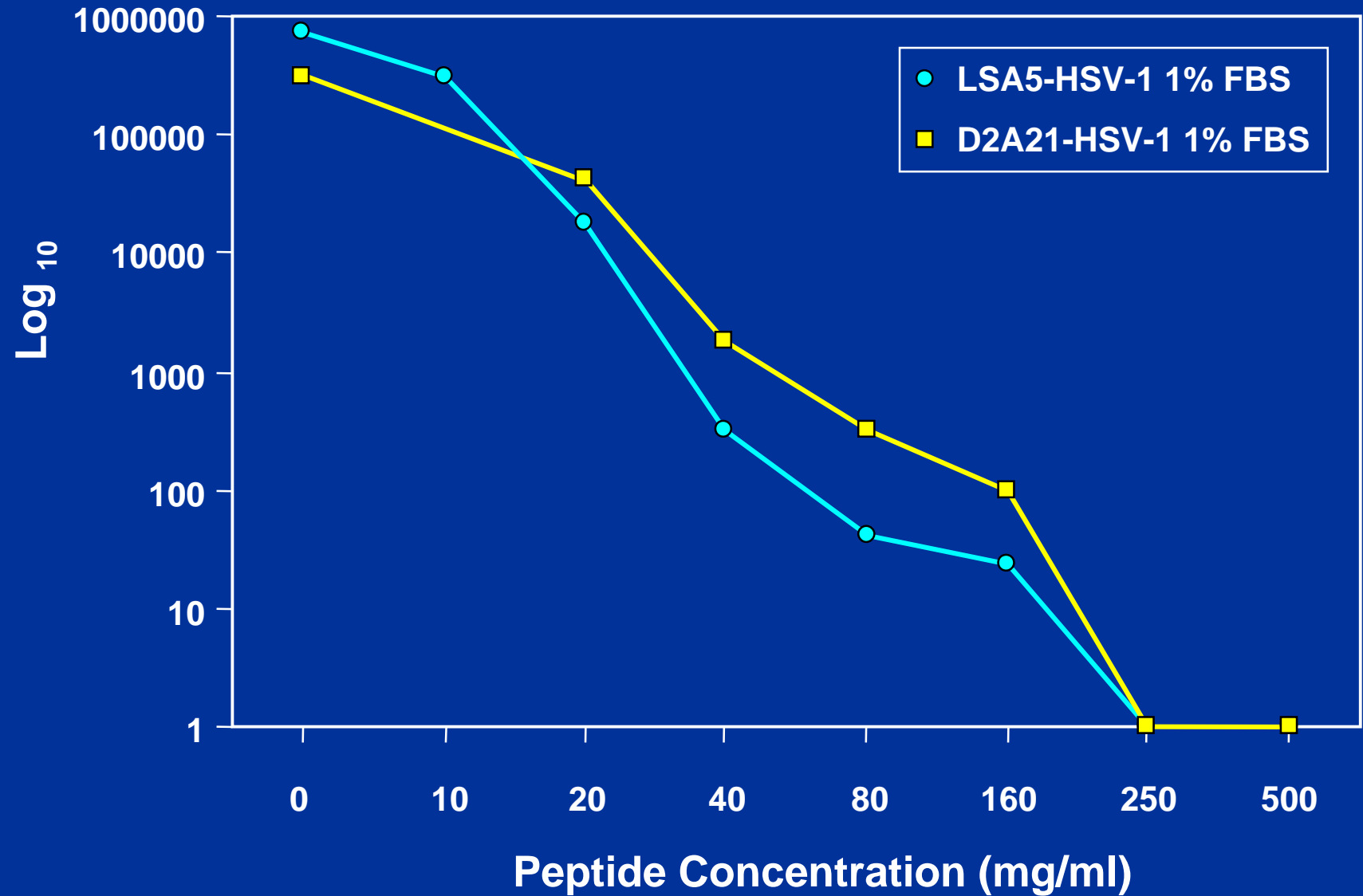
## Time Course of Lipid (4 mM)-Peptide Inactivation of HSV-2 (1% FBS)



## Time Course of Lipid (4 mM)-Peptide Inactivation of HSV-2 (10% FBS)



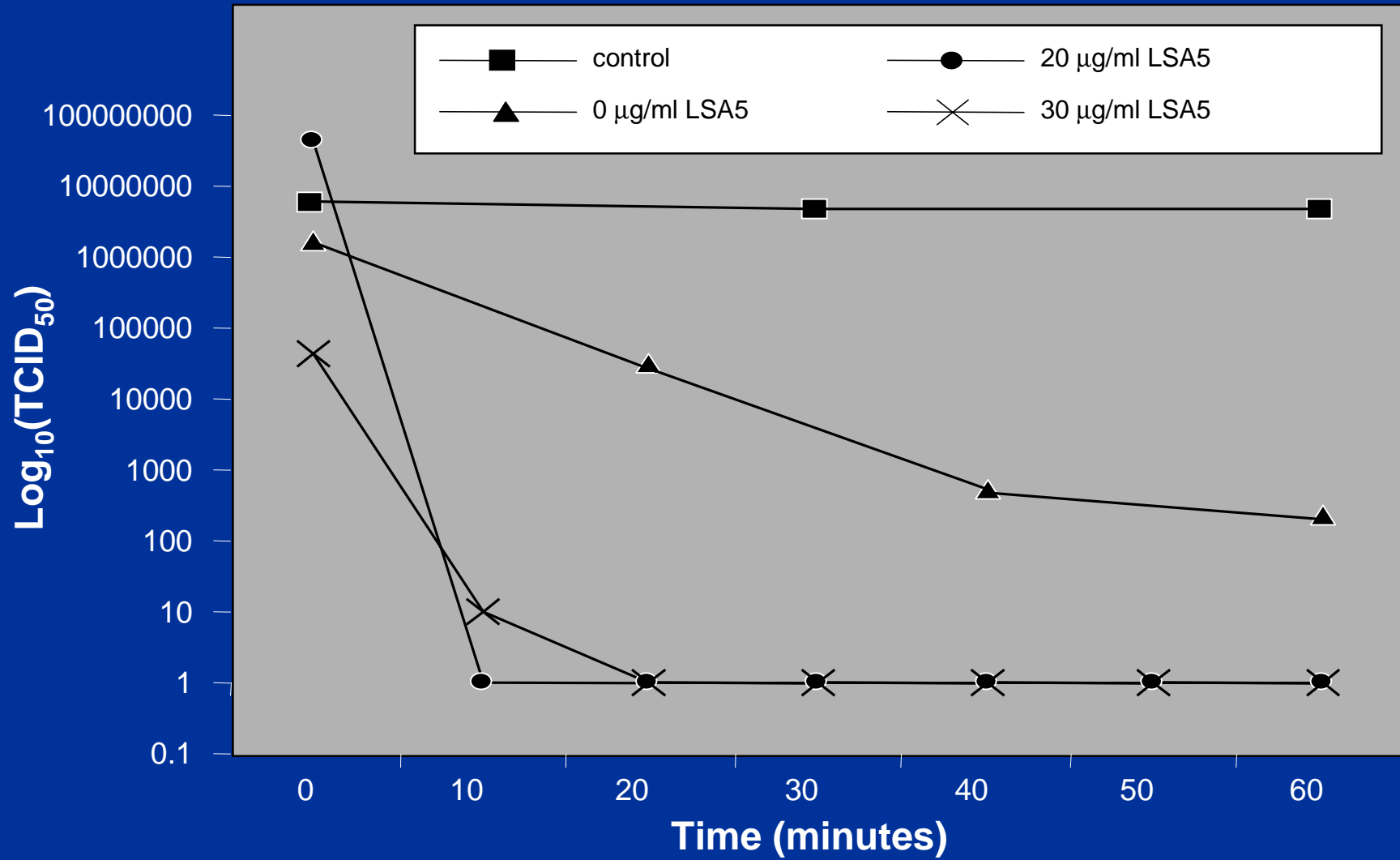
## Inactivation of HSV-1 Comparison of LSA5 and D2A21



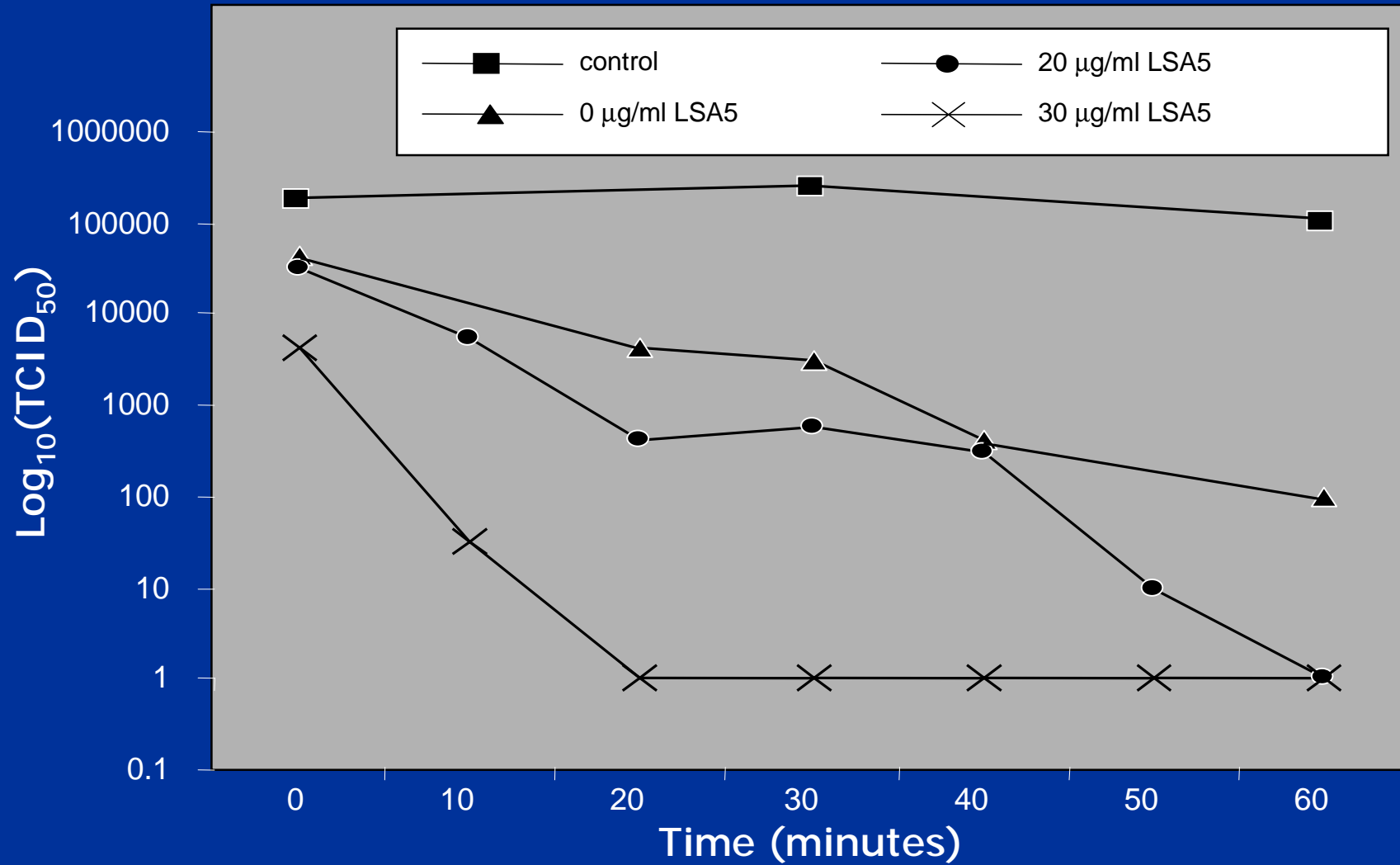
arg-val-ile-arg-val-val-gln-arg-ala-cys-  
arg-ala-ile-arg-his-ile-val-arg-arg-ile-  
arg-gln-gly-leu-arg-arg-ile-leu-arg-val-  
val

LSA5 (From Dr Tim Mietzner)

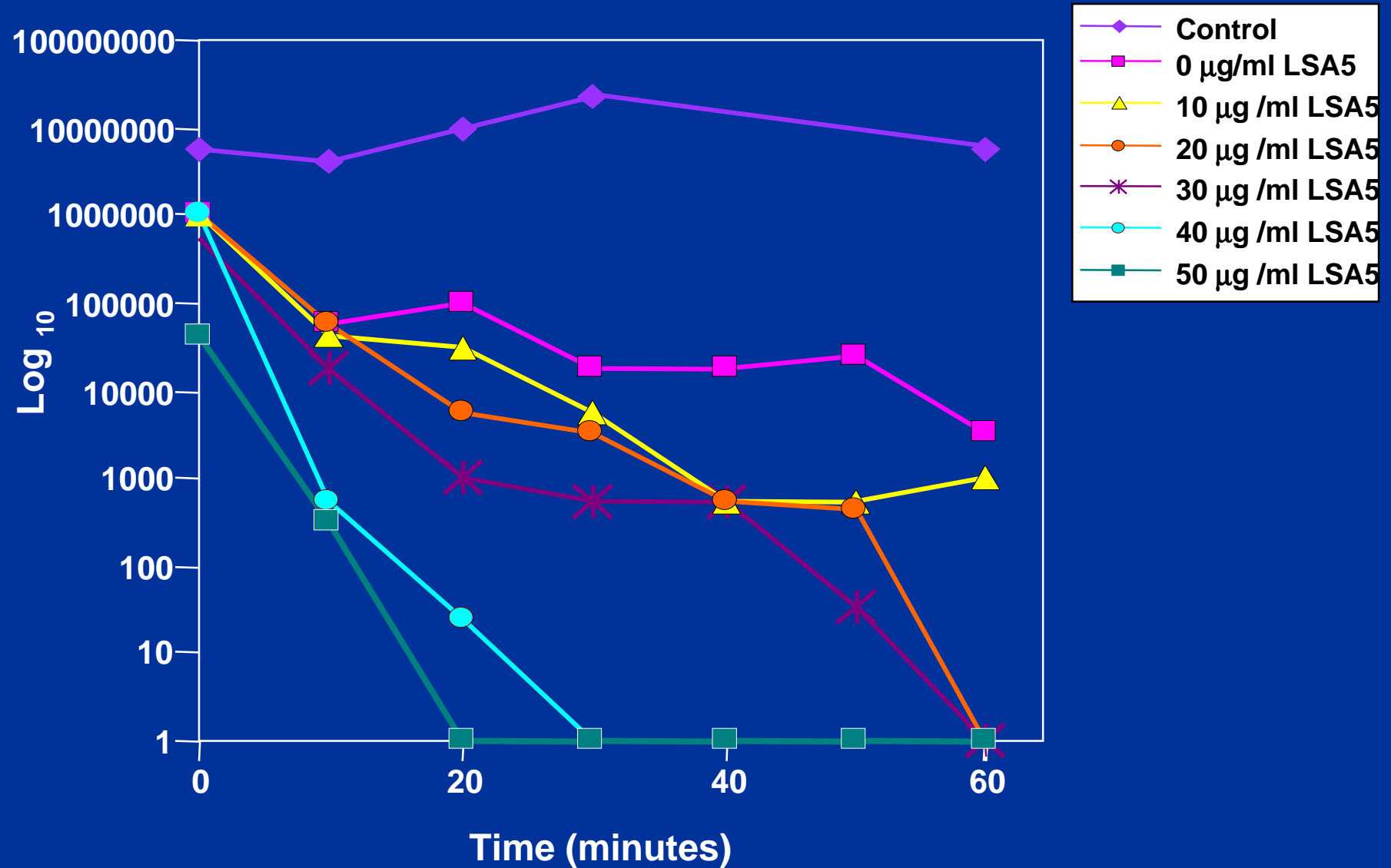
## Time course of Lipid(4mm) -Peptide Inactivation of HSV-1 (1% FBS)



## Time course of Lipid(4mm) -Peptide Inactivation of HSV-2 (1% FBS)



# Time course of Lipid (4 mM) Peptide Inactivation of HSV - 1 (10% FBS)



## Conclusions

1. In a combination microbicide containing the antimicrobial lipid octylglycerol, concentrations of the antimicrobial peptides D2A21 and LSA5 can be reduced by at least 90% of that required when the peptides are used by themselves.
2. HSV-1 and HSV-2 inactivation by a microbicide is strongly influenced by the binding of antimicrobial compounds to macromolecules in serum and potentially to those normally present at mucosal surfaces.

## Conclusions (cont.)

3. HSV titers can be reduced by  $> 1,000$  fold in less than 10 minutes by a combination of LSA5 or D2A21 with octyl glycerol.
4. Shortening the time required to inactivate HSV would decrease the opportunity for successful viral transmission and should be a major focus of microbicide development.

# Acknowledgements

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NIAID  
NYSOMRDD



# FUTURE PLANS

## Mixtures of 1-O-octyl-sn-glycerol and D2A21 Inactivate HSV-1 and HSV-2

