Oral Session VI

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Development of a Guinea Pig Model for Determining the Pharmacokinetics of Antiviral Agents.

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Guinea Pigs inoculated with herpes simplex virus are the animals of choice for determining antiviral efficacy against genital and cutaneous herpes. To determine systemic absorption of a topical antiviral agent, we surgically implanted indwelling catheters into the jugular vein and collected blood at 1,2,4,6,8, 10,12,24,32, and 48h. Animals were housed in metabolic cages and urine and feces collected. Radiolabeled 2-fluoro-iodo-arabinosyl-uracil (2-^{14}C-FIAU) at a final concentration of 1%, 5%, or 10%, was applied to the genital skin of 3-5 guinea pigs. The pharmacokinetic parameters for FIAU and its metabolite FAU were as follows:

Parameter (mean ± SD)		1% FIAU	5% FIAU	10% FIAU
Cmax	µg/ml	0.07 ± 0.04	0.10 ± 0.03	0.18 ± 0.06
Tmax	hr	5.3 ± 2.3	8.0 ± 0.0	6.5 ± 3.8
$T_{\frac{1}{2}}$	hr	12.3 ± 3.8	11.2 ± 4.4	12.3 ± 7.4
AUC	µg/hr/ml	1.07 ± 0.51	2.39 ± 0.50	3.97 ± 2.34
UR	%	20.7 ± 2.0	13.7 ± 4.5	11.8 ± 4.4
CLR	L/hr/kg	0.63 ± 0.25	0.81 ± 0.19	1.1 ± 0.8

The amount of systemic absorption of combined FIAU-FAU based on urinary excretion was about 21%, 14%, and 12% for 1%, 5%, and 10% FIAU respectively. These data indicate that guinea pigs provide an excellent model for topical drug administration in which efficacy and pharmacokinetics can be correlated. Additionally, the amount of drug absorption can be determined allowing some degree of predictability for potential systemic toxicity.