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Pharmacokinetics of 1-(ß-D-arabinofuranosyl)-5(*E*)-(2-[^{125}I]-iodovinyl)uracil, ([^{125}I] IVaraU), following intravenous and subconjunctival injection in New Zealand White (NZW), rabbits.

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1-(ß-D-Arabinofuranosyl)-5(*E*)-(2-halogenovinyl)uracils have significant antiviral activity against both herpes simplex virus type 1 (HSV-1) and varicella zoster virus (VZV). Radiohalogenated derivatives also have a potential role in the development of noninvasive diagnostic techniques. In order to further explore the potential for intraocular penetration of these compounds, no-carrier-added (NCA)-[^{125}I] IVaraU was studied in NZW rabbits following either intravenous administration of 2.6 X 10^8 cpm per kg or subconjunctival administration of 1.3 x 10^8 cpm per eye. Serial concentrations (0.5, 1.0, 2.0, 4.0 h) in plasma, aqueous and vitreous humors were then determined by γ-counting and confirmed as [^{125}I] IVaraU by HPLC.

Compartment	Route of Administration			
	Intravenous		Subconjunctival	
	Time (h)	(cpm per mL)	Time (h)	(cpm per mL)
Plasma	0.5	2.4×10^5	1	3.3×10^4
Aqueous Humor	2	5.7×10^4	0.5	5.1×10^5
Vitreous Humor	2	1.3×10^4	1	2.3×10^4

Subconjuctival injections resulted in 9-fold higher levels of IVaraU in aqueous humor, and 7-fold lower levels in plasma, compared with intravenous injections. Although higher levels were obtained in the vitreous humor following subconjunctival injection, they were not significantly different from intravenous injections. The half life of intraveneously injected IVaraU was 5.1 hours in plasma, similar to the half life of 1-(ß-D-arabinofuranosyl)-5(*E*)-(2-bromovinyl)uracil (BVaraU) in humans. Subconjuctival injections may minimize any potential for systemic toxicity while enhancing anterior section penetration of IVaraU. Further investigations to determine the importance of anterior section antiviral penetration are underway. Efficacy studies of IVaraU and/or BVaraU for the systemic and/or subconjunctival treatment of HSV and/or VZV keratoconjuctivitis appear warranted.

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New non-invasive diagnostic method for herpes simplex virus encephalitis (HSVE) by chemiluminescent study

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[Purpose] This study was to detect herpes simplex virus (HSV) antigen in cerebrospinal fluid (CSF) using measurment of chemiluminescence.

[Materials and methods] The materials consisted of 10 CSF samples of 6 patients with HSVE and 10 of non-HSVE. Method (1): Chemiluminescence of normal granulocytes were doubly measured in two assay systems: one including CSF (assay A) and the other including CSF and anti-HSV antibody (assay B). Alteration in chemiluminescence with the two assays was evaluated as a ratio of value in B assay to value in A assay (B/A ratio) in each sample. Method(2): Infected fibroblasts by HSV type 1 were diluted in negative CSF sample to a concentration of 10^n (n=0,···5) infectious units (pfu/ml). Chemiluminescence values of these diluted and negative CSF samples as well as 10 samples including 10^1 to 10^3 infectious units were measured in assay B.

[Results] (1) B/A ratios were higher than 1.4 in all CSF samples taken from 5th to 38th day of HSVE. (2) B/A ratios ranged between 0.9 and 1.0 in all non-HSVE patients. (3) The difference in frequency of B/A ratio above 1.3 between HSVE and non-HSVE was statistically significant ($p<0.01$). (4) Values of samples including 10^0 to 10^5 infectious units showed marked increase compared with negative CSF sample. (5)The correlation between infectious units of samples including 10^1 to 10^3 infectious units and chemiluminescence values was linear increase ($p<0.01$).

[Conclusion] This method could be a valuable quantitative, diagnostic tool for intrathecal HSV antigen in HSVE.