

Intra-oculaire penetratie antivirale therapie

In deze bijlage wordt weergegeven welke spiegels er intra-oculair bereikt kunnen worden met verschillende antivirale middelen en de verschillende toedieningswijzen. De spiegel in de voorste oogkamer wordt als maat genomen voor de effectiviteit omdat er geen bruikbare gegevens bekend zijn van de humane cornea.

Spiegel in de VOK boven de gemiddelde IC50 van HSV-1

Spiegel in de VOK onder de gemiddelde IC50 van HSV-1

Spiegel in de VOK intermediate ten opzichte van de gemiddelde IC50 van HSV-1

Ocular tissue penetration (measured indirectly by the aqueous humor concentration)						
Formulation	Dosage	Epithelial defect	Aqueous concentration		Model	IC50 HSV-1
			Epithelium intact	Times higher than mean ID50 HSV-1		
Aciclovir ointment 3% topical (Castela,1994)	4 times daily	308 ng/ml SD 146	na		Rabbit aqueous humor	120-240 ng/ml
Aciclovir ointment 3% topical (Poirier,1982)	4-6 doses every 4-6 h prior to surgery	na	1700 ng/ml	9,40	Human aqueous humor	120-240 ng/ml
Aciclovir 400 mg oral (Hung,1984)	5 doses every 4-6 hours prior to surgery	na	3,26 µM	3,80	Human aqueous humor	0,1-1,6 µM
Aciclovir 800 mg oral (Harding,1998)	6 doses every 4 hours prior to surgery	na	5,37 µM	6,30	Human aqueous humor	0,1-1,6 µM
Valaciclovir 100 mg oral (Harding,1998)	3 doses every 8 hours prior to surgery	na	9,63 µM	11,32	Human aqueous humor	0,1-1,6 µM
Valaciclovir 1000 mg oral (Huynh, 2008)	3 doses every 8 hours prior to surgery; one dose in the morning prior to surgery	na	1030 ng/ml	5,70	Human vitreous	120-240 ng/ml
Famciclovir=penciclovir 500 mg oral (Chong, 2009)	3 doses every 8 hours prior to surgery	na	1210 ng/ml	24,20	Human vitreous	40-60 ng/ml
Ganciclovir 0.05% eye gel (Castela,1994)	4 times daily for 10 days	18ng/ml SD 0,25	na		Rabbit aqueous humor	200-320 ng/ml
Ganciclovir 0,2 % eye gel (Castela,1994)	4 times daily for 10 days	394 ng/ml SD 419	na		Rabbit aqueous humor	200-320 ng/ml
Ganciclovir 0.15% eye gel (Spectrum Théa Pharmaceuticals; 2003)	1 time	na	1700 ng/mg		Rabbit corneal stroma	200-320 ng/ml
Ganciclovir 0.15% eye gel (Spectrum Théa Pharmaceuticals; 2003)	1 time	na	1000 ng/ml		Rabbit aqueous humor	200-320 ng/ml

Ganciclovir 0.15% eye gel (Spectrum Théa Pharmaceuticals; 2003)	1 time	na	16000 ng/ml		Rabbit conjunctiva	200-320 ng/ml
Ganciclovir 0.15% eye gel (Spectrum Théa Pharmaceuticals; 2003)	1 time	na	4000 ng/ml		Rabbit iris/ ciliary body	200-320 ng/ml
Ganciclovir 3% salt in ointment (Schulman,1986)	6 doses every hour prior to surgery	na	4,73 µM 2h after administration		Rabbit aqueous humor	0,2-0,5 µM
Ganciclovir 3% salt in ointment (Schulman,1986)	6 doses every hour prior to surgery	na	1,84 µM 3h after administration		Rabbit aqueous humor	0,2-0,5 µM
Ganciclovir 0.5% eye drops (Okumura,2019)	1 dose 1 h prior to surgery	na	2800ng/ml 1h after administration		Rabbit endothelium	200-320 ng/ml
Ganciclovir 0.15% eye gel (Koizumi,2011)	6 times daily	na	162+202ng/ml		Human aqueous humor	200-320 ng/ml
Ganciclovir 0.15% eye gel (Waduthantri,2018)	5 Times daily	na	17.4 ± 30.6 ng/ml		Human aqueous humor	200-320 ng/ml
Ganciclovir 0.15% eye gel (Waduthantri,2018)	5 Times daily	na	20420.9 ± 33120.8 ng/ml		Human tears	200-320 ng/ml
TFT 1 % solution eye drops (Pavan-Langston, 1979)	4 doses every 10 minutes before surgery	6,4-43,9 µM	6,4-43,9 µM		Human aqueous humor	0,75-45 µM
TFT 1 % solution eye drops (Poirier,1982)	5 doses every 30 minutes before surgery	na	Not detected		Human aqueous humor	0,75-45 µM
TFT 1 % solution eye drops (Sugar,1973)	4 doses every 5 minutes	37 µg/ml	6 µg/ml		Rabbit aqueous humor	200-1700 ng/ml
Foscarnet 1.2% eye drops	na	na	na	na	na	

Castela, N., et al., *Ganciclovir ophthalmic gel in herpes simplex virus rabbit keratitis: intraocular penetration and efficacy*. J Ocul Pharmacol, 1994. **10**(2): p. 439-51

Chong, D.Y., et al., *Vitreous penetration of orally administered famciclovir*. Am J Ophthalmol, 2009. **148**(1): p. 38-42.e1.

Harding, S., *Superior intraocular penetration of aciclovir after valaciclovir in comparison with oral aciclovir* Abstracts of Interscience conference on antimicrobial agents ; session 69 A paper A-45, 1998

Hung, S.O., A. Patterson, and P.J. Rees, *Pharmacokinetics of oral acyclovir (Zovirax) in the eye*. Br J Ophthalmol, 1984. **68**(3): p. 192-5.

Huynh, T.H., et al., *Vitreous penetration of orally administered valacyclovir*. Am J Ophthalmol, 2008. **145**(4): p. 682-6.

Koizumi, N., et al., *The effect of topical application of 0.15% ganciclovir gel on cytomegalovirus corneal endotheliitis*. Br J Ophthalmol, 2017. **101**(2): p. 114-119.

Okumura, N., et al., *Stability, safety, and pharmacokinetics of ganciclovir eye drops prepared from ganciclovir for intravenous infusion*. Jpn J Ophthalmol, 2019. **63**(3): p. 289-296.

Pavan-Langston, D. and D.J. Nelson, *Intraocular penetration of trifluridine*. Am J Ophthalmol, 1979. **87**(6): p. 814-8.

Poirier, R.H., et al., *Intraocular antiviral penetration*. Arch Ophthalmol, 1982. **100**(12): p. 1964-7.

Schulman, J., et al., *Intraocular penetration of new antiviral agent, hydroxyacyclovir (BW-B759U)*. Jpn J Ophthalmol, 1986. **30**(1): p. 116-24

Sugar, J., et al., *Trifluorothymidine treatment of herpetic iritis in rabbits and ocular penetration*. Invest Ophthalmol, 1973. **12**(7): p. 532-4

Spectrum Théa Pharmaceuticals; *Virgan® summary of product characteristics*. . Macclesfield: Spectrum Théa Pharmaceuticals;2003.

Waduthantri, S., L. Zhou, and S.P. Chee, *Intra-cameral level of ganciclovir gel, 0.15% following topical application for cytomegalovirus anterior segment infection: A pilot study*. PLoS One, 2018. **13**(1): p. e0191850.