hydrolysis of the corresponding *cyclo*Sal-phosphatetriesters. The nucleosides and the triesters were subjected to antiviral evaluation.

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Cyclopentenylcytosine (CPE-C) Inhibits Adenovirus Replication in the Ad5/NZW Rabbit Ocular Model

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Purpose: Presently, there is no FDA approved antiviral therapy for the treatment of adenovirus (Ad) ocular infections. The goal of the current study was to determine the antiviral efficacy of topical cyclopentenylcytosine (CPE-C), a nucleoside analog of cytosine, on acute Ad replication in the Ad5/NZW rabbit ocular model.
Method: 40 NZW rabbits were topically inoculated in both eyes, following corneal scarification, with 1.5×0^6 pfu/eye of Ad5. On day 1, the rabbits were divided into 4 topical treatment groups ($n = 10$/group): (I) 3% CPE-C, QID × 7 days; (II) 3% CPE-C, BID × 7 days; (III) 0.5% Cidofovir (CDV), BID × 7 days; (IV) Control (saline), QID × 7 days. Both eyes of the rabbits were similarly treated. All eyes were cultured for virus on days 0, 1, 3, 4, 5, 7, 9, 11, and 14.
Results:

Group	+ Cultures/total (days 1–14)	Duration of shedding (D)	Mean titer (days 1–5)	Mean titer (days 7–14)
CPE-C (QID)	24/160 (15%)*	1.3 ± 1.6*	$3.5 \pm 18.1 \times 10^{1}$*	$3.6 \pm 25.2 \times 10^{0}$*
CPE-C (BID)	31/160 (19%)*	2.5 ± 2.3*	$1.6 \pm 4.8 \times 10^{1}$*	$1.0 \pm 4.4 \times 10^{0}$*
CDV	27/160 (17%)*	2.0 ± 1.8*	$6.7 \pm 12.7 \times 10^{0}$*	$0.3 \pm 2.2 \times 10^{0}$*
Control	97/160 (61%)	8.1 ± 3.5	$1.0 \pm 3.0 \times 10^{2}$	$2.2 \pm 9.2 \times 10^{1}$

* $p \leq 0.011$ compared to the Control.

Topical 3% CPE-C QID and BID and 0.5% Cidofovir BID were significantly more effective than the control in reducing positive cultures/total (days 1–14), duration of shedding, mean titer (days 1–5), and mean titer (days 7–14) in the Ad5/NZW rabbit ocular model. There were no significant differences between the two topical regimens of 3% CPE-C and both were as effective as the positive antiviral control, 0.5% Cidofovir.
Conclusions: CPE-C demonstrated potent anti-adenoviral activity in the Ad5/NZW rabbit ocular model. Additional studies are warranted to establish the clinical potential of CPE-C as a topical antiviral treatment for adenovirus ocular infections.

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Synthesis and Properties of Glycosyl-functionalised *Cyclo*Sal–Pronucleotides

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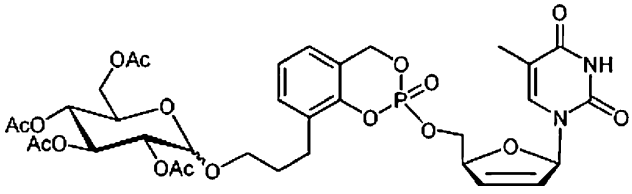
Nucleoside analogues are widely used in antiviral and cancer chemotherapy. The antiviral activity of nucleoside analogues like 2′,3′-dideoxy-2′,3′-didehydrothymidine (d4T) depends on their conversion to the ultimately bioactive 5′-*O*-triphosphates. The intracellular phosphorylation via mono- and diphosphates is catalysed by host cell enzymes and is often the metabolism-limiting step. The use of nucleotides as therapeutic agents is impossible because they are inable to penetrate the cellular membrane due to high polarity. In addition they are catabolised in blood by unspecific nucleotidases. The *cyclo*Sal-pronucleotide approach circumvents these hurdles. These lipophilic prodrugs penetrate the cell membrane and the nucleotide is released by a pH-driven chemical hydrolysis. Due to passive diffusion this could occur inside or outside the cellular membrane possibly leading to a decreased amount of nucleotide in the cytoplasm. Improvement of intracellular delivery might be achieved by using cellular transporters and/or recognition mechanisms, e.g. glucose transporter. In a first attempt, *cyclo*Sal–nucleotide–sugar conjugates (Fig. 1) were synthesized and their biological properties were investigated concerning pH-stability, cell extract stability, cytotoxicity and antiviral activity in CEM/0 and TK-deficient CEM cells.



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