Evaluation of cytotoxic and anti-viral effect of novel B220 compounds against HSV-1

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Background

The Biosynthetic cornea is one of the latest interventions in recent years of regenerative medicine as a remedy to corneal blindness. To date, the biosynthetic corneas can not be used in patients with corneal infections such as herpes simplex type 1 (HSV-1). As HSV-1 is the leading cause of corneal blindness worldwide, search for antiviral compounds that nullify the effects of these microbial pathogens is important. The discovery of new antiviral compounds like B-220 is necessary for future treatment of patients with corneal viral infections..

Aim

To investigate the cytotoxic properties and characterize the antiviral activity of derivatives of B220 compounds against herpes simplex virus type-1.

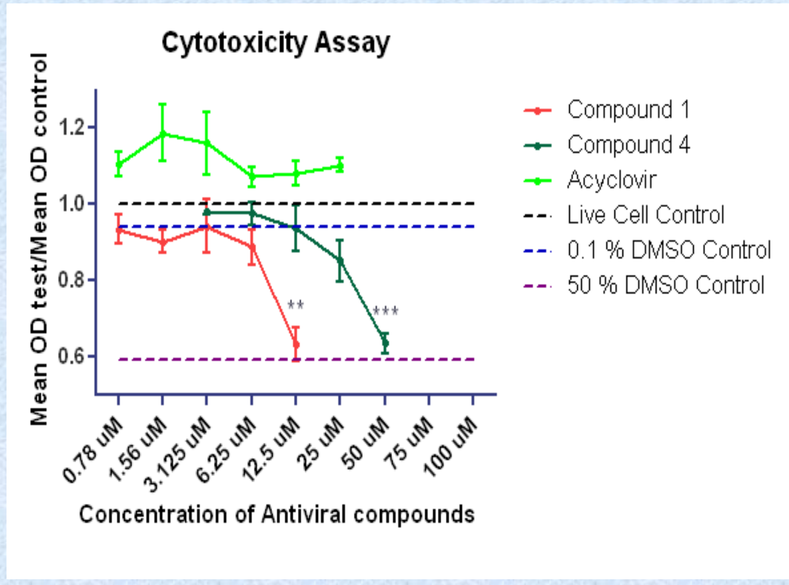
To elucidate the usefulness of B220 compounds as antiviral agents in biosynthetic corneas for patients with HSV-1 infections.

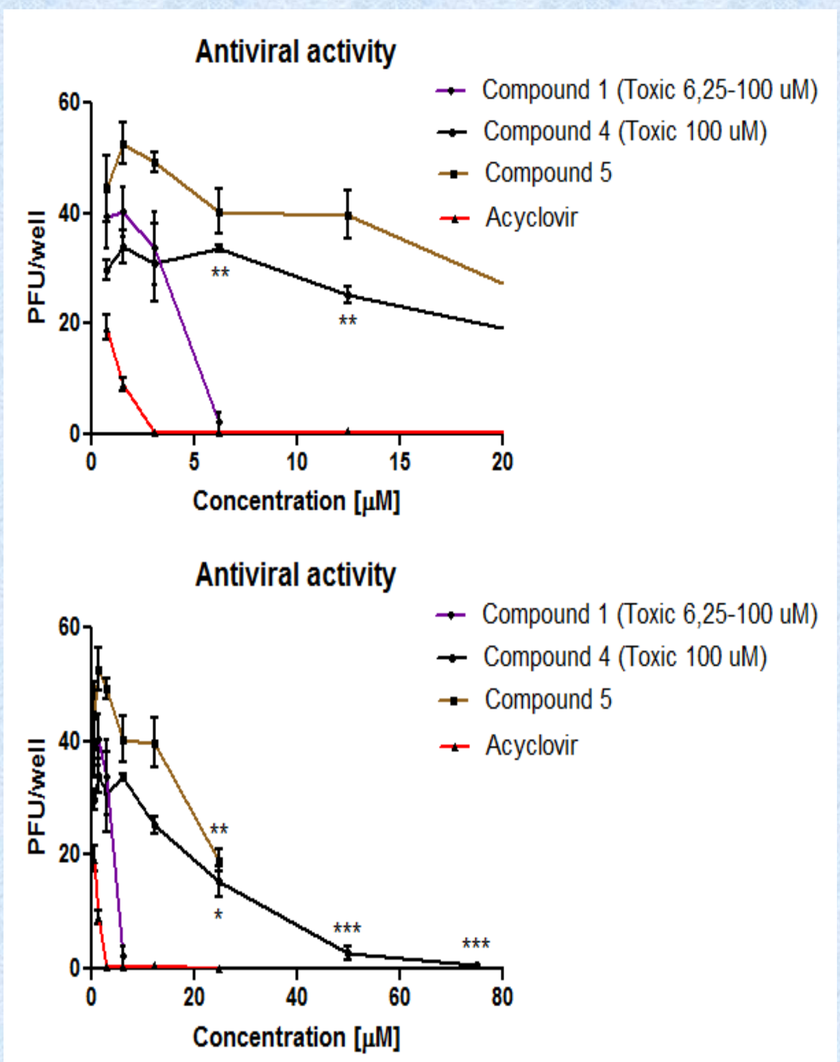
Methods

- Cytotoxicity test by MTS assay
- Direct Plaque Assay

Results

The cytotoxicity of anti-viral compounds (B-220 and its derivatives) from 1 through 7 and 12 through 14 was evaluated by MTS assay using human Stromal cells of Corneal Limbus (hSCLs). Compounds 1 and 4 showed significant level of toxicity at 12.5µM and 50µM respectively by one way analysis of variance followed by Dunnet's test(Graph to the right). Compound 2, 3, 5, 6, 7, 12, 13 and 14 did not show any significant toxicity. The well established antiviral drug acyclovir was used as a reference drug and did not show any significant toxicity.





The anti viral property of B220 compounds from 1 through 7 and 12 through 14 was studied by direct plaque assay on Green Monkey Kidney (GMK) cells.

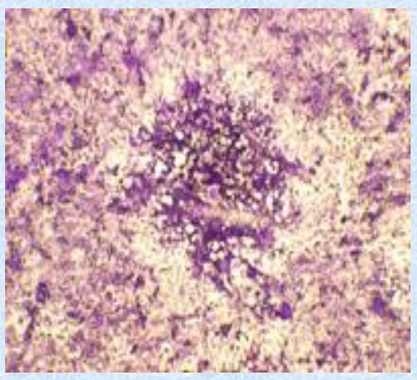


Image showing an HSV-1 plaque

Following statistical analysis (1-way ANOVA followed by Dunnet's test), compounds 1, 4 and 5 were found to show significant level of anti viral activity (graphs above).

Conclusion

The tested anti viral compounds showed more significant anti viral activity but also exhibited cytotoxicity. The study should be continued to find an anti-viral compound with non toxic and high virucidal effect.

The future perspective of this HSV-1 antiviral study is also to release these compounds by micro encapsulation into biosynthetic corneas to see the effect. The mechanism of action of these compounds could be studied and it would be interesting to selectively target trigeminal nerve by coupling the drug to a molecule suitable for cellular transport. Patients with chronic HSV keratitis and recurrent graft rejection due to this infection could then have another treatment option for their disease.

Acknowledgement

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