with a sequence of HSV-1 UL5 helicase that contains most resistance mutations to herpes simplex virus (HSV) helicase-primase inhibitors, several of which are in (pre)clinical testing. The finding that these bicyclic sulfones act as HHV-6 helicase inhibitors opens new perspectives for the development of HHV-6 specific antiviral compounds.

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133

Antiviral Effect of Oxoglaucine in Combination with Some Enterovirus Replication Inhibitors

Lubomira Nikolaeva-Glomb*, Adelina Stoyanova, Anna Metodieva, Angel S. Galabov

The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences, Sofia, Bulgaria

Despite the fact that enteroviruses are ubiquitous human pathogens, up to date there is no specific antienteroviral drug available. A clear need exists for the development of effective inhibitors of enterovirus replication, as well as for different approaches to enhance the effect of the existing ones. Recently in our laboratory the antienteroviral effect of oxoglaucine *in vitro* was described. In the present study an attempt is made to enhance the activity of oxoglaucine by combining it in dual concomitant combinations with other inhibitors of enterovirus replication, i.e. disoxaril, 2-(alpha-hydroxybenzyl)benzimidazole (HBB), guanidine-hydrochloride, 2-(3,4-dichlorophenoxy)-5-nitrobenzonitrile (DNB) and ribiavirin. The effect of the dual combinations was studied as regards the *in vitro* replication of poliovirus 1, strain LSc-2ab) and coxsackievirus B1. The combined effect character was analyzed by the three-dimensional model for evaluating drug interactions proposed by Prichard and Shipman. The combinations of oxoglaucine were additive or synergistic ones with the exception of those with ribaviin. The latter were mildly antagonistic. The highest volume of synergy was observed when oxoglaucine was combined with DNB. The same antiviral effect was achieved with doses much lesser than the necessary ones if drugs were applied alone. The synergy contributed to the higher selectivity of the combination. Greater synergy was usually observed against the replication of poliovirus 1 in comparison to coxsackievirus B1. In conclusion, combining oxoglaucine with other enterovirus inhibitors expectedly lead to enhanced reduction of virus replication and decrease of toxicity. The most promising synergistic combination in this respect was the dual combination of oxogaucine and DNB.

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134

Antiadenoviral Assay, Based on the Quantitative Detection of Infected Cells Containing Virus-induced Intranuclear Inclusion Bodies

Lidiya N. Nosach*

Institute of Microbiology and Virology NASU, Kyiv, Ukraine

Activity of compounds against adenoviruses (AdV) usually is determined using indirect tests of AdV replication: the cytopathic effect (CPE), plaque formation or the viability of infected cells. All these assays are based on the development of degenerative changes in infected cells in the multiple cycle of AdV reproduction. CPE is induce penton and it may take place at incomplete AdV reproduction when structural AdV proteins are synthesis abundant but the formation of infectious virus to is absent. Development of CPE at complete reproduction cycle is accompanied by the accumulation of viral DNA, proteins and virions in the nucleus and the formation DNA-containing intranuclear inclusion bodies. In order to the accurate estimation of antiadenoviral activity we recommend to use method based on the quantitative detection of number infective cells containing AdV-induced intranuclear inclusion bodies. The inclusions were revealed by luminescent microscopy using the acridine orange. Previously optimal conditions of infection must been determined. The virus control must have nearly 80% cells with inclusions at 48 h p.i. We determined the efficacy of some antiviral compounds against AdV type 1 by with method in a comparison with imunofluorescence assay to reveal the number of cells producing the hexon antigen. Both test showed dose-dependent antiviral effect of ribavirin, 6-azacytidine and 6-azauridine and the correlation of received values. However, the reveal of infected cells with intranuclear virus-induced inclusion bodies is easy to perform, rapid and eliminate the need labeled reagents. EC_{50} was calculated as a concentration decreasing the percentage of inclusion-positive or hexon-positive cells on 50% in comparison to control. Ribavirin had EC_{50} nearly 32 μM. EC_{50} of 6-azacytidine and 6-azauridine ranged between 4 and 8 μM. This method may by used to determine more precisely antiadenoviral activity of compounds witch were showed effect in indirect test of AdV replication.

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135

Triterpenoids from *Platycodon grandiflorum* Inhibit Hepatitis C Virus Replication

Sang Jin Park[1,*], Jong Hwan Lim[1], Jae Won Yang[1], Jung Cheul Shin[1], Eun-Joo Kim[4], Joo Won Suh[2], Soon B. Hwang[3], Jong Woo Kim[1,2]

[1] *Laboratory of Infectious Disease, B&C Biopharm Co. Ltd., Suwon, Republic of Korea*
[2] *Division of Bioscience and Bioinformatics, Myongji University, Yongin, Republic of Korea*
[3] *Ilsong Institute of Life Science, Hallym University, Anyang, Republic of Korea*
[4] *Department of Pharmacology, Korea Institute of Toxicology, Korea Research Institute of Chemical Technology, Daejeon, Republic of Korea*

Hepatitis C virus (HCV) afflicts approximately 200 million people worldwide. Currently there are no directly acting antiviral agents available to cure HCV patients. In this study, while searching for new anti-HCV agents from natural products, we found a potent inhibitor from extracts of *Platycodon grandiflorum* (PG) that inhibited HCV RNA replication. PG has been known to possess anti-allergic, neuro-protective, anti-obesity, immune regulative and anti-inflammatory activities. However, whether PG has an anti-HCV therapeutic activity has not yet been investigated. We found that PG-extracts efficiently inhibited RNA replication in Huh7 cells harboring HCV replicon. Furthermore, six triterpenoids (PD, PD_2, PD_3, DPD, DPD_2, and PA) were identified as active components involved in anti-HCV activity. Each of these components directly inhibited RNA-dependent RNA polymerase activity of HCV NS5B protein. Our computational molecular modeling data showed that these triterpenoids bound near the active site of HCV polymerase. Importantly, these triterpenoids exerted synergistic antiviral activity in combination either with IFN-α or NS5A inhibitor (BMS 790052), or with HCV protease inhibitor (Danoprevir: ITMN-191). Moreover, we also found that triterpenoids of PG provided good