lagin SI values of 1048 and 97.6, respectively, being registered). The combination effect of ellagitannins with ACV was studied through the three-dimensional analytical approach of Prichard and Shipman for evaluation of the impact of drug–drug interactions. A markedly synergistic character of the ellagitannins–ACV combinations effects was registered on the replication of both HSV-1 and HSV-2 ACV-sensitive strain. Testing of combinations ellagitannins plus ACV against HSV-1 and HSV-2 strains resistant to ACV demonstrated also marked synergistic effects. The synergism was more pronouncedly expressed towards HSV-1 as compared to HSV-2 strain. Data obtained showed that ACV as a partner in the combinations with ellagitannins against ACV-resistant HSV strains could be applied in comparatively lower concentrations. The data we collected demonstrate the high potential of *C*-glucosidic ellagitannins as antiherpetic agents. Obviously, one of these substances, castalagin, applied alone or in combination with ACV, could be considered as a perspective for further anti-herpesvirus chemotherapeutic studies.

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In Vitro Combination Therapy with Tegobuvir (GS-9190) is Highly Efficient in Curing Cells from HCV Replicon and in Delaying/Preventing the Development of Antiviral Resistance

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Tegobuvir (GS-9190) is a novel non-nucleoside inhibitor of HCV RNA replication with proven activity in HCV infected patients. When combined with either the protease inhibitor VX-950, the nucleoside polymerase inhibitor 2′-*C*-methylcytidine or various non-nucleoside polymerase inhibitors in short-term assays, an overall additive antiviral activity was calculated. A slight synergistic effect was observed when low concentrations of GS-9190 were combined with low concentrations of either a benzimidazole or benzofuran non-nucleoside polymerase inhibitors. It was next studied whether prolonged culturing of replicon-containing cells in the presence of combinations of GS-9190 with other DAA delayed or prevented resistance development against either compound. When GS-9190 (at concentrations of 6, 30 or 150 nM) was added to replicon-containing cells that were cultured in the presence of suboptimal concentrations of VX-950 or the various polymerase inhibitors, resistance development against these compounds was either markedly delayed or completely prevented. Next, the potential of various combinations to clear cells of HCV replicons was evaluated. GS-9190, at the concentration of 150 nM, was able to cure replicon-containing cells after a single passage when combined with VX-950. The triple combination of GS-9190 (11 nM), VX-950 and 2′-*C*-methylcytidine resulted in clearance of replicon RNA after two passages. In contrast, the inhibitors when used alone at 3-fold higher concentrations were not able to cure the cells from the replicon after 6 passages. In conclusion GS-9190 resulted in an additive to slightly synergistic antiviral effect when combined in short term antiviral assays with other DAA in vitro. Antiviral combinations containing low concentrations of GS-9190 are highly effective in curing cells from their replicon and in delaying or preventing the development of resistance against other DAA.

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Human Papillomavirus Genotype Distribution in Women in Montenegro

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Infection with high-risk genotypes of human papillomaviruses (HPV) is the main etiological agent of cervical cancer, the second most common form of cancer in women worldwide. Despite the existence of screening programs, the disease is still responsible for more than 10,000 deaths registered annually in the European Union. Information on distribution of HPV genotypes in women in a certain country is important for the selection of the appropriate screening test for detection of HPV infection in a given country. Therefore, the purpose of this study was to determine the range and frequency of HPV genotypes in women in Montenegro. HPV genotypes were determined using the method of enzyme restriction of PCR products amplified with group-specific primers MY09/MY11 and restricted with seven different restriction endonucleases. In all 189 women cervical smears were taken during a routine gynecological examination at the Clinical Center in Podgorica.

Out of the total number of women HPV infection was found in 1/5 of participants (20%, 38/189). Genotyping performed in 38 HPV DNA positive women shows that the HPV genotype 16 is dominant in Montenegro (36.8%, 14/38). The second most frequent HPV infection is with HPV genotype 58 and it is found in 10.5% of participants. HPV 31 and HPV 6 infections are present in 7.9% of women, while infections with other genotypes were demonstrated individually by 2.6%. Mixed infection was demonstrated in 18.4%.

Also, in our group of participants it was found that mixed HPV infection, with more than one HPV genotype is dominant in younger women (aged 25–30 years) and with at least one high-risk or probably high-risk HPV genotype. According to the results of our research we believe that in active search of women, who are more likely to develop cervical cancer, it necessary to do the tests that are able to detect broader spectrum of high-risk HPV genotypes. Sensitive detection of multiple HPV genotypes in patients is, also, especially important for the determination of persistence of infection and timing of usage type-specific vaccines.

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Enhanced Cellular Penetration of ODE-(S)-MPMPA Accounts for Its Prolonged Post-exposure Anti-HCV Activity

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Background: Octadecyloxyethyl 9-(*S*)-[3-methoxy-2-(phosphonomethoxypropyl)]adenine (ODE-MPMPA) exhibits potent anti-HCV replicon activity (EC50 1–2 μM) with a high selectivity (CC50 > 150 μM). In vitro resistance selection experiments demonstrated a high barrier to resistance with selection of low fold-change variants (A/Q49L 1.3-fold, K50N 1.6-fold) and/or unfit variants that do not replicate in vitro (Q58L). Continued selection at higher concentrations (9 μM) resulted in reversion to wild type replicon sequences while maintaining a resistant cell