IN VITRO ACTIVITY OF NOVEL 1,3-OXAZOLE DERIVATIVES AGAINST HUMAN PAPILLOMAVIRUS

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Chemotherapeutic approaches to the control of HPV (human papillomavirus) infection suffer from a lack of specificity. For most existing HPV inhibitors, the weak antiviral effects observed in cellular assays suggest that further improvements in selecting targets, in drug potency, and in bioavailability and cell uptake are required. Substituted 1,3-oxazoles can exert various biological effects and have significant antiviral activity.

The present study is an exploratory investigation of anti-HPV activity by novel 1,3-oxazole derivatives (1,3-oxazol sulfonamides and 5-amino-1,3-oxazole-4-carbonitriles) designed and synthesized in Kyiv, with all the cytotoxicity and efficacy tests performed in the the National Institute of Allergy and Infectious Diseases (USA).

The influence of the 1,3-oxazol sulfonamide derivatives on transient replication of HPV origin-containing plasmid was first evaluated in transfected HEK293 cells by human papillomavirus−11 replication origin−containing plasmid. All compounds exhibited potent anti-replication activity and were more active than Cidofovir in this assay. Two compounds, which showed high activity against HPV-11 in the primary assay, were chosen for the secondary assay (HPV-18 DNA amplification in an organotypic squamous epithelial raft culture of primary human keratinocytes freshly prepared from neonatal foreskins). In contrast to the HPV-11 in HEK293 cells, the cytotoxicity, EC_{50} and EC_{90} of both compounds for HPV-18 were the same in PHK raft cultures.

At present, the reasons for the difference in the anti-HPV effect of 1,3-oxazole derivatives in HEK29 cells versus the HPV-18 are not understood. Perhaps, the compounds are metabolized differently in the two distinct culture systems. This discrepancy points to the importance of the raft cultures in verifying putative anti-HPV compounds. This study does provide useful information on specific analogs with antiviral activity *in vitro* that can be further modified to identify more active inhibitors.