IN VITRO ACTIVITY OF NOVEL OXAZOLE DERIVATIVES AGAINST HUMAN PAPILOMAVIRUS

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Until recent years, there were rather few chemotherapies for HPV infections, for example, cidofovir (CDV) [1,2], imiquimod, sinecatechins (Veregen), podophyllotoxin, and some other compounds [3].

Various substituted oxazoles have significant antiviral activity [4]. Recently, we have synthesized novel 1,3-oxazole-4-and 5-sulfonamides and their antiviral activities against human papillomavirus were evaluated *in vitro* [5]. These compounds exhibited considerably higher antiviral activity (EC_{50} = 2.43-47.28μM) against a normal laboratory strain than Cidofovir (EC_{50} = 148.0 μM). These data indicate that 1,3-oxazole derivatives are promising compounds in the search for design of new antiviral drugs.

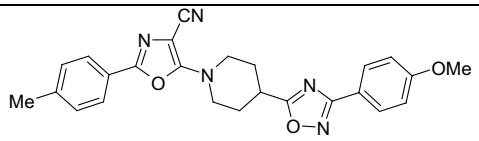
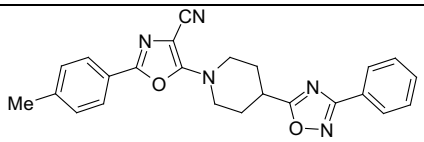
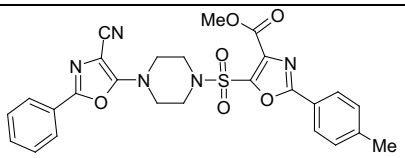
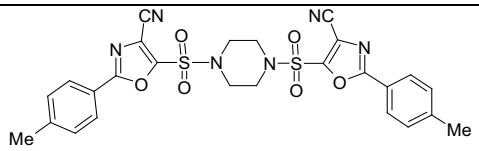
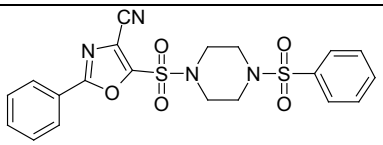
In this work a set of novel 2-aryl-4-cyano-5-amino-1,3-oxazoles and 1,3-oxazole-5-sulfonylamides as potential anti-HPV agents generated and screened using the QSAR model were synthesized in V.P. Kukhar Institute of Bioorganic Chemistry and Petrochemistry, NAS of Ukraine and evaluated *in vitro*. The antiviral activity of the compounds **1** and **2**was predicted as 4.6 -log(M) unit, while the activity of the rest compounds was predicted in the range of 3.8-4.0 -log(M) units.

The all cytotoxicity and efficacy tests performed at UAB. The evaluation was carried out under the auspices of the National Institute of Allergy and Infectious Diseases (USA) and its Collaborative Antiviral Testing Group. The effects of the 1,3-oxazole derivatives on antiviral activity against a normal laboratory HCMV strain, AD-169, and their cytotoxicity was evuated on HFF cells using CellTiter-Glo (Cytopathic effect/Toxicity) assay (Table 1).

Control and drug concentrations ranges are 0.048-150 μM. Vehicle is DMSO. EC_{50} and CC_{50} are compound concentrations that reduce viral replication and cell viability, respectively, by 50% in CellTiter-Glo (Cytopathic effect/Toxicity) assay. Selectivity Index (SI_{50}) is calculated as the CC_{50} value divided by the EC_{50} value.

Compounds exhibited different antiviral activityagainst HE611260.1strainof human papillomavirus 11 and, with the exception of **5**, had EC_{50} values of >17 μM. Compound **5** showed the best activity with EC_{50} =3.68 μM. Compounds **1-4** have shown moderate antiviral activity.

Table 1 The antiviral activity and cytotoxicity of the 1,3-oxazole derivatives against HE611260.1strainof human papillomavirus 11, in C-33A cell line. Compound concentrations are in μM.

No	Compound	Strain HE611260.1		
		EC_{50}	CC_{50}	SI_{50}
1		>150	>150	1
2		21	>150	>7
3		17.21	103.04	6
4		>30	105.44	<4
5		3.68	88.10	24
9-[2-phosphono-metoxy)ethyl]guanine		1.77	>150	>85

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