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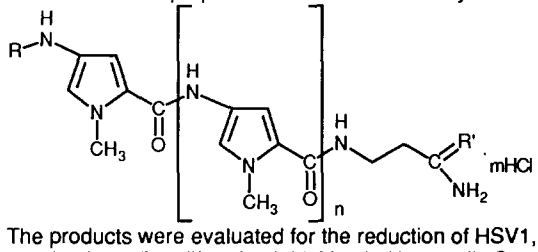
Anti-herpes activity of biscationic distamycin analogues E. M. Iafrate, F. Animati, G. Giannini, P. Lombardi and S. Manzini Menarini Ricerche Sud S.p.a., Via T. Speri 10, 00040 Pomezia, Roma, Italy

Distamycin (**1**, n=2) a pyrrole-amidine oligopeptide isolated from the mycelium of Streptomices distallicus, inhibits the multiplication of a number of viruses (vaccinia, herpes simplex, Rous sarcoma) probably by binding to A-T rich regions in DNA.Since the distamycin is cationic and the minor groove AT-rich regions of DNA bear a high negative potential, the electrostatic interaction seems to play a key role in the drug-DNA recognition.With the aim to investigate the effect of the electrostatic binding on the antiviral activity, analogues (**2**) of distamycin bearing a positive charge at N-terminus chain have been prepared and tested for their cytotoxicity and anti-herpes activity.



	R	R'	n	m
1:	HCO	NH	2,3	1
2:	H, HCNH	NH, O	0, 2,3	1,2

The products were evaluated for the reduction of HSV1, strain HF, cytopatic effect on Hep2 cell line and for the cell proliferation inhibition in Hep2 cells.Compounds with a second amidine group (**2**, R=HCNH, R'=NH, n=2,3) retain the antiviral effect although at a lower degree than the parent drugs (**1**), whereas the presence of the amidine group on the sole N-terminus chain (**2**, R=HCNH, R'=O, n=2) causes total loss of activity. On the other hand biscationic derivatives (**2**, R=H, R'=NH, n=2,3) bearing the second positive charge not delocalized show activity comparable to those of reference compounds (**1**). These results suggest the following structure-activity relationship: a) antiviral activity is enhanced by increasing the number of the pyrrole residues from 3 to 4; b) the C-terminal amidine group is essential for this biological activity; c) the N-formyl group does not seem to be a major prerequisite for the anti-herpes activity.

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ANTIVIRAL ACTIVITY OF THE BENTHIC ALGAE FROM THE PIRAN BAY

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Experiments were performed to evaluate the antiviral activity of selected macroalgae from the north Adriatic sea (Piran Bay). Algal extracts were prepared in saline from the following algae:(a) Chlorophyta: Ulva rigida, Enteromorpha compressa, Codium coralloides, (b) Paheophyta: Halopteris scoparia, Dictyota dichotoma, Dictyota linearis, Dyctyopteris membranacea, Scytosiphon lomentaria, Fucus virsoides, Cystoseira crinita, Cystoseira compressa, (c) Rhodophyta: Coralina granifera, Gracilaria compressa, Chylocladia kaliformis, Anthitamnion sp., Ceramium diaphnum, Gulsonia nodulosa, Nytophillum punctatum, Polysiphonia subulifera. Obtained extracts were tested for antiviral activity against: Herpes simplex virus type 1 and 2, Adenovirus and Poliovirus on VERO cells. Cytotoxicity tests were performed on VERO and WiREF cells. Data were evaluated using LETDOZA (BIA,Ltd. Adamičeva 4, 61000 Ljubljana, Slovenia) computer programme. Antiviral activity in vitro against Herpes simplex virus type 1 and 2 was found in the extracts from:Codium corraloides, Dyctiota linearis, Scytosiphon lomentaria Fucus virsoides, Cystoseira crinita and Cystoseira compressa. Antiviral activity against Adenovirus was found in the same extract, except these obtained from Cystoseira compressa. Antiviral activity against Poliovirus was found in the extracts from the: Fucus virsoides and cystoseira crinita.