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Antiviral Properties of Platinum(II) and Palladium(II) Complexes Containing Antiviral Nucleoside Analogs. R.C. Taylor and S.G. Ward, Department of Chemistry, Oakland University, Rochester, MI 48309-4401, USA, and J. Balzarini and E. De Clercq, Rega Institute for Medical Research, Katholieke Universiteit Leuven, Minderbroedersstraat 10, B-3000 Leuven, Belgium.

Cisplatin, in addition to its potent and broad-based antitumor activity, is effective both in vitro and in vivo as an antiherpetic agent. In an effort to enhance the antiherpes activity, to broaden the spectrum of antiviral activity, and to develop a new class of potentially useful antiviral agents, we have synthesized a number of multifunctional complexes containing various platinum(II) and palladium(II) moieties chemically bound to a selected series of antiviral nucleoside analogs including, acyclovir, 9-(1,3-dihydroxy-2-propoxymethyl)guanine (DHPG), 9-(3,4-dihydroxybutyl)guanine (DHBG), 9beta-D-arabinofuranosyladenosine (Ara-A), tubercidin, ribavirin, neplanocin A, and 3-deazaaristeromycin (C-c^{3}Ado). These complexes have the general formula, $(N_2M(Nu)_2)^{2+}$, where N_2= $2NH_3$, 1,2-diaminocyclohexane or ethylenediamine, M= Pt or Pd, and Nu= an antiviral nucleoside. We wish to report the results for the broad spectrum antiviral activities of these complexes against HSV-1, HSV-2, vaccinia virus, vesicular stomatitis virus, Coxsackie virus B4, parainfluenza virus type 3, Sindbis virus, Semliki forest virus, and HIV-1. Also, the cytotoxicities of these complexes have been determined. The coupling of the cytotoxic metal-containing precursor with the relatively non-toxic nucleosides eg, acyclovir, DHPG, and DHBG, produces species with comparable cytotoxic behavior to the free nucleosides but with diminished antiviral activity. On the other hand, when toxic nucleosides are incorporated, eg, neplanocin A and tubercidin, complexes with significantly diminished cytotoxicities and comparable antiviral activities (to the free nucleoside) are produced. This yields species with improved therapeutic indices.

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SYNTHESIS AND ANTIVIRAL ACTIVITY OF AVARONE AMINOACIDIC DERIVATIVES

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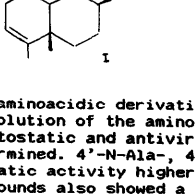

I

R = H
= Alanine
= Serine
= Phenylalanine
= Leucine
= Cysteic acid

Avarone aminoacidic derivatives (I) were synthesized adding a NaHCO3 solution of the aminoacids to a solution of Avarone in EtOH. Cytostatic and antiviral effects of the title compounds were determined. 4'-N-Ala-, 4'-N-Phe-, 4'-N-Leu-Avarone showed a cytostatic activity higher than that of Avarol and Avarone. Some compounds also showed a selective activity against various DNA and RNA viruses.