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ESI MS, NMR and PM5 semiempirical studies of oligomycin A and its complexes with Li^+ and Na^+ cations

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Abstract

The ability to complex formation of oligomycin A (OLA) with monovalent cations was studied by the ESI mass spectrometry, ^1H, ^{13}C, ^7Li and ^{23}Na NMR spectroscopic and PM5 semiempirical methods. The ESI MS spectra indicated that OLA formed stable 1:1 complexes with all monovalent cations irrespective of the stoichiometry and cone voltage values used. With increasing cone voltages only the degradations of the OLA–Li^+ and OLA–Na^+ complexes with formation of fragmentary metal cation complexes were found. For OLA complexes with K^+, Rb^+ and Cs^+ cations, with increasing cone voltage the fragmentation of these complexes occurred without the formation of fragmentary metal cation complexes. On the basis of the NMR studies the assignment of the signals of hydroxyl groups in the spectrum of OLA was made and the spectra of its complexes evidenced the involvement of certain oxygen atoms in the complexation process. The PM5 semiempirical calculations allowed visualizations of all structures of the OLA—monovalent cation complexes as well as the fragmentary cations. The most interesting structure was found for OLA–Li^+ complex, in which the Li^+ cation is fully isolated from the interactions with the environment.

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1. Introduction

Oligomycines are closely related group of 26-membered macrolides with lactone moieties and double bonds produced by various strains of streptomyces. These compounds show a wide spectrum of biological activity, especially antifungal, antibacterial and their anticancer effects arise from the inhibition of the oxidative phosphorylation in mitochondria membrane [1–3]. Some specific oligomycins are rutamycin, peliomycin, and botrycidin. A mixture of A:B:C—oligomycins at the ratio ca. 75:10:8 (HPLC) is the so called macrolide antibiotic complex. The major component in this complex is oligomycin A [4–8]. The structures of the basic oligomycins have been studied by the X-ray and NMR spectroscopy [9–13].

Oligomycin A includes some oxygen atoms within its structure, which should be able to form complexes with metal cations. In many cases such properties of biomolecules and natural products are essential for their biological activity, e.g. for ionophores or ion channels. On the other hand, the formation of complexes with metals cations can change the conformation or electron density within the biomolecules, which influences their biological activity. In our previous works we have studied a complexation of some metal cations by synthetic and natural ionophores [14–17].

In this paper, we study the complex formation of oligomycin A with monovalent cations and make an attempt at determination the structures of these complexes using ESI MS, ^1H, ^{13}C, ^7Li and ^{23}Na NMR and PM5 semiempirical methods.

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Table 1
Mass spectrometry data (ESI) for complexes of oligomycin A with monovalent cations

M^+	m/z		
	$[OLA+M]^+$	$[OLA+2M]^{2+}$	$[2OLA+M]^+$
H^+	–	–	–
Li^+	798	–	–
Na^+	814	–	–
K^+	830	–	–
Rb^+	876	–	–
Cs^+	924	–	–

OLA, oligomycin A.

2. Experimental

Oligomycin A was purchased from Aldrich.

2.1. ESI MS spectrometry

The ESI (Electrospray Ionization) mass spectra were recorded on a Waters/Micromass (Manchester, UK) ZQ mass spectrometer equipped with a Harvard Apparatus syringe pump. All sample solutions were prepared in acetonitrile. The measurements were performed for two types of samples being the solutions of: (a) oligomycin A (2×10^{-6} mol dm^{-3}) with perchlorates of the H^+, Li^+, Na^+, K^+, Rb^+, Cs^+ cations (2×10^{-6} mol dm^{-3}) used separately and (b) oligomycin A (2×10^{-6} mol dm^{-3}) with perchlorates of the monovalent cations used as a mixture (the concentration of each cation perchlorate was 2×10^{-6} mol dm^{-3}). The samples were infused into the ESI source using a Harvard pump at a flow rate of 20 μl min^{-1}. The ESI source potentials were: capillary 3 kV, lens 0.5 kV, extractor 4 V. In the case of standard ESI mass spectra the cone voltage was 30 V. The source temperature was 120 °C and the dessolvation temperature was 300 °C. Nitrogen was used as the nebulizing and dessolvation gas at flow-rates of 100 and 300 l h^{-1}, respectively.

2.2. NMR measurements

The ^{1}H and ^{13}C spectra were measured in [^{2}H]$_3$-acetonitrile and the sample concentrations was 5 mg of oligomycin A in 600 μl of solvent. The anhydrous equimolar amount of lithium or sodium perchlorate was added to the dissolved sample of oligomycin A to obtain 1:1 stoichiometry of the mixture. The ^{1}H and ^{13}C NMR spectra were recorded at 298 K on a Bruker Avance DRX 600

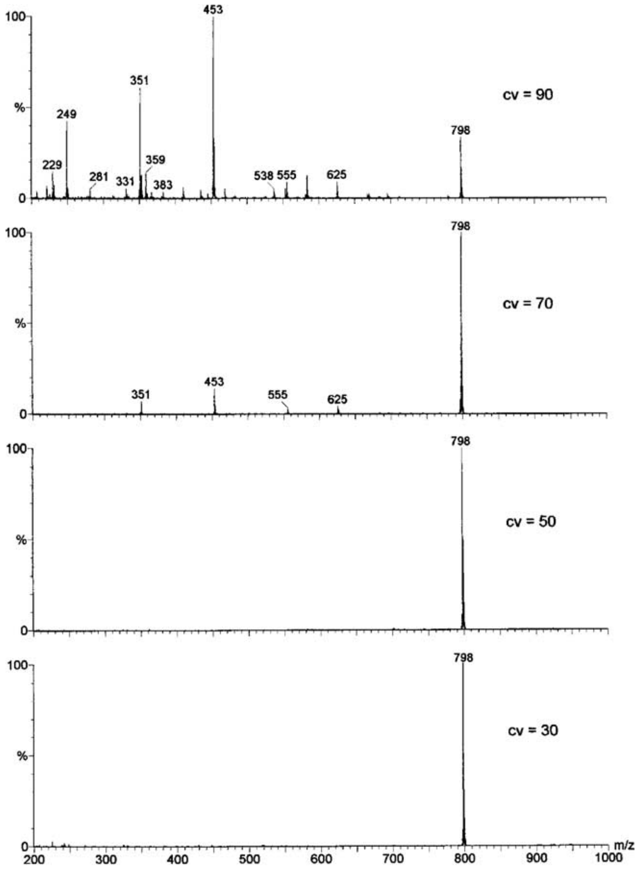

Fig. 1. ESI MS spectra of the 1:1 complex of OLA with $LiClO_4$ in acetonitrile at various cone voltages cv = 30, 50, 70 and 90 V.

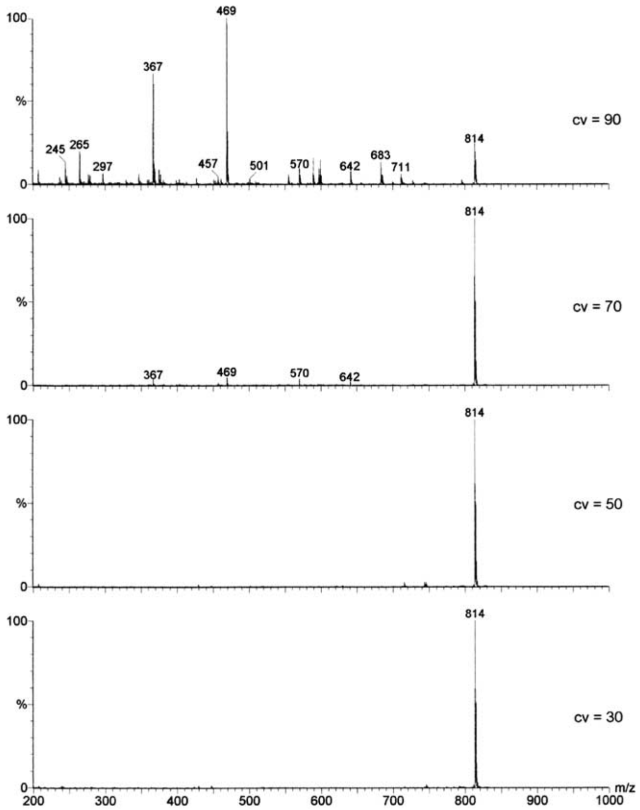

Fig. 2. ESI MS spectra of the 1:1 complex of OLA with $NaClO_4$ in acetonitrile at various cone voltages cv = 30, 50, 70 and 90 V.

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