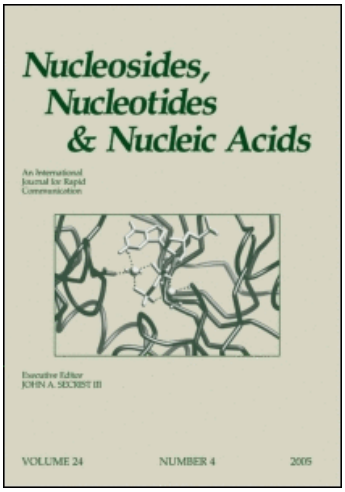

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Electroanalytical Study on Nicotinamide 7-Methylguanine Dinucleotide (Nm^7GD), Analog of Coenzyme NAD and Related Compounds

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ELECTROANALYTICAL STUDY ON NICOTINAMIDE 7-METHYLGUANINE DINUCLEOTIDE (Nm^7GD^+), ANALOG OF COENZYME NAD^+ AND RELATED COMPOUNDS

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Abstract: Electrochemical methods (direct-current polarography, cyclic voltammetry and differential pulse polarography) were used for analysis of 7-methylguanine nucleosides and nucleotides.

Among the mutagenic and carcinogenic compounds, alkylating agents are a group of substances that disturb the biological function of cellular DNA and RNA. The major products of endogenous alkylation are methylated base adducts, including 7-methylguanine. It has been observed that a high level of 7-methylguanine in mitochondrial and nuclear DNA could contribute to ageing and cancer (1). Furthermore, 7-methyl GMP is a key component of the cap of various eukaryotic mRNA's (2).

We have studied polarographic behaviour of 7-methylguanine derivatives: 7-methylguanosine (m^7Guo), 7-methyl GMP (m^7GMP), methyl esters of 7-methyl GDP and 7-methyl GTP (m^7ester GDP and m^7ester GTP), acyclo 7-methyl GMP (m^7acyclo GMP), nicotinamide 7-methylguanine dinucleotide (Nm^7GD^+) and nicotinamide guanine dinucleotide (NGD^+), analogs of coenzyme NAD^+, in which the adenine moiety has been replaced by 7-methylguanine and guanine, respectively.

It is known that 7-methylguanosine readily undergoes electrochemical reduction, both in the free state (3) and when incorporated into DNA (4). Electrochemical reduction of 7-methylguanosine occurs in the imidazole ring (3).

Three polarographic techniques were used for analysis of 7-methylguanine derivatives: direct current polarography (d.c.), cyclic voltammetry (c.v.) and differential pulse polarography (d.p.p.).

It was found that 7-methylguanine nucleosides and nucleotides exhibit in aqueous solutions one d.c. polarographic wave (or one c.v. and d.p.p. peak) in the potential range -1.7 V to -1.8 V (pH 4.5 - 8.5). The data presented on Fig.1 indicate that there is no significant difference between polarographic behaviour

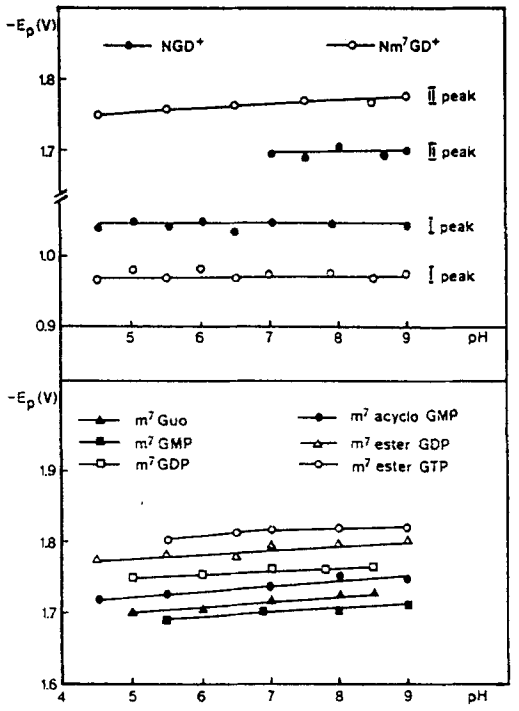

Fig. 1. pH dependence of d.p.p. potential peaks of 1 x 10^{-4} M 7-methylguanine derivatives (phosphate buffers).

of acyclo-7-methyl GMP and other compounds (cyclo derivatives). However, their adsorption properties are quite different. On the basis of an additional a.c. polarographic study it was shown that acyclo derivatives of 7-methylguanine adsorb weakly in comparison with cyclo derivatives.

Nm^7GD^+ and NGD^+ exhibit two polarographic waves (or two d.p.p. peaks) in the pH region 7-10 which can be ascribed to nicotinamide reduction. In slightly acidic medium (pH 4.5 - 6.0) the polarographic behaviour of both compounds differs. NGD^+ exhibits only one reduction wave (peak) due to the nicotinamide ring, whereas Nm^7GD^+ undergoes a two step reduction, the first identical with that for NGD^+ and the second due to reduction of 7-methylguanine moiety (Fig. 1).

The heights of the polarographic waves (peaks) are lineary dependent on the 7-methylguanine derivative concentrations in the range 2 x 10^{-4} M - 1 x 10^{-6} M (pH 5-7), which might be of use for analytical applications.

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