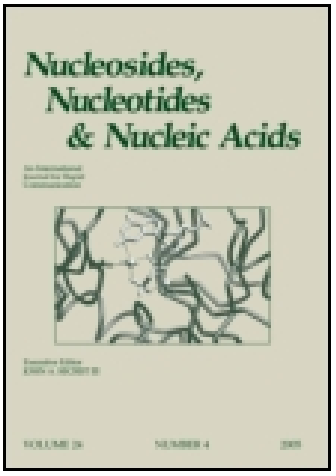

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Determination Of 2-Chloro-2′-deoxyadenosine (Antileukemic Agent) and Related Compounds by Electrochemical Method

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DETERMINATION OF 2-CHLORO-2'-DEOXYADENOSINE (ANTILEUKEMIC AGENT) AND RELATED COMPOUNDS BY ELECTROCHEMICAL METHOD

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ABSTRACT: Electrochemical method for determination of 2-chloro-2'-deoxy-adenosine and related compounds modified in exocyclic 6-NH_2 group is described. Electrochemical detection of investigated compounds, based on the electrooxidation process of the adenine moiety, has been performed in aqueous solutions, in the pH range 2-9, on a glassy carbon electrode

Characterization of any therapeutic agents for use both research and clinical programs is essential for the pharmaceutical and medical applications. A particularly important aspects of the chemical characterization of new drugs include the identification of various byproducts and structurally related derivatives of investigated therapeutic agents. All techniques that can provide informations without complicated step of preparations are particularly valuable for medical applications.

The objective of this work was to develop an electrochemical method for determination of 2-chloro-2'-deoxyadenosine (2CldAdo, Cladribine) and related compounds modified in exocyclic 6-NH_2 group: 2-chloro-9-(2'-deoxy-β-D-erythro-*pentofuranosyl*)-6[(hydroxyethyl)amino]-9H-purine, 2-chloro-9-(2'deoxy-β-D-*pento-furanosyl*)-6-methoxypurine and 2-chloro-6-(cyclohexyloamino)-9-(2'deoxy-β-D-erythro-*pentofuranosyl*)-9H-purine. 2CldAdo is an adenosine-deaminase resistant nucleoside widely used for the treatment of lymphoid and autoimmunoaggressive diseases [1,2]. The investigated 2CldAdo analogs substituted at the exocyclic amino group exhibited cytotoxic activity against leukemia cell lines[3] and were also substrates for the *E. coli* PNP[4].

2CldAdo and its analogs were synthesized by Dr Z. Kazimierczuk[3]. Electrochemical analysis, differential pulse voltammetry (DPV) was conducted with Autolab Electrochemical Analyzer (Eco-Chemie, Netherlands). Electrochemical detection of 2-chlorosubstituted purine nucleosides, based on the electrooxidation process of the adenine moiety, has been performed in aqueous buffer solutions in the pH range 2-9, on a glassy-carbon electrode, in acetate, phosphate and carbonate buffers.

All investigated deoxynucleosides undergo electrochemical oxidation with formation one, pH dependent peak. Direct electrochemical analysis of these compounds provides limits of detection at 1 μM, because oxidation peaks appeare close to the background discharge, due to the strong adsorption on the surface of the electrode. Acid catalyzed hydrolysis of all compounds (1M acetic acid, pH 2.3), lead to the formation of respective bases[5] (2-chloroadenines), which undergo electrochemical oxidation at potentials about 200 mV less positive in comparison with investigated nucleosides. This makes the electrochemical analysis more sensitive detecting (100 nM).

The electrochemical method can be applied for monitoring concentration of Cladribine in human plasma during the treatment and for detection of 2CldAdo degradation products.

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