

This article was downloaded by:

On: 27 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



## Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597286>

## Electrochemical Analysis of 3'-Azidothymidine (AZT)

Barbara Czocharlska<sup>a</sup>; Bozena Sapok<sup>a</sup>; David Shugar<sup>a</sup>

<sup>a</sup> Department of Biophysics, Institute of Experimental Physics, University of Warsaw, Warsaw, POLAND

**To cite this Article** Czocharlska, Barbara , Sapok, Bozena and Shugar, David(1990) 'Electrochemical Analysis of 3'-Azidothymidine (AZT)', *Nucleosides, Nucleotides and Nucleic Acids*, 9: 3, 443 — 444

**To link to this Article:** DOI: 10.1080/07328319008045166

**URL:** <http://dx.doi.org/10.1080/07328319008045166>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

### ELECTROCHEMICAL ANALYSIS OF 3'-AZIDOTHYMININE (AZT)

Barbara Czochralska, Bozena Sapok and David Shugar

Department of Biophysics, Institute of Experimental Physics, University of  
Warsaw, Zwirki i Wigury 93, 02-089 Warsaw, POLAND

Abstract: 3'-Azido-3'-deoxythymidine (AZT) exhibits a two-electron diffusion-controlled polarographic reduction wave, with conversion to 3'-amino-3'-deoxythymidine. The mechanism of reduction, analytical and clinical applications, and its use for one-step synthesis of amino from azido nucleosides, are described.

The thymidine analogue 3'-azido-3'-deoxythymidine (AZT); a potent inhibitor of retroviruses and human immunodeficiency virus (HIV), is currently clinically approved for treatment of selected patients with AIDS and AIDS-related complex (1). However, the source(s) of its toxic side-effects remains to be clarified, and lends interest to studies of its chemical and biochemical reactivities. Thiol reduction of alkyl and aryl azides, long known, has been shown, in the case of AZT, to lead to conversion to the 3'-amino-3'-deoxy congener (2).

In a continuation of studies on electrochemical reduction of purine and pyrimidine analogues (3), we have found that AZT is readily reduced at the dropping mercury electrode. With both d.c. polarography and d.p.p. (differential pulse polarography), AZT exhibits a diffusion-controlled two-electron reduction wave over the pH range 2 - 12. Dependence of the half-wave potential ( $E_{1/2}$ ) and limiting current ( $I_g$ ) of the reduction wave of AZT is shown in Fig.1. The height of the wave is linearly dependent on the AZT concentration, permitting of its analytical determination in aqueous medium by d.p.p. in the range  $1 \times 10^{-3}$  to  $2 \times 10^{-7}$  M.

Electrolysis of AZT (as well as AZdU) conducted on  $10^{-4}$  M solutions buffered at pH 7 at a potential of -1.1 V, was accompanied by disappearance of the cathodic wave at  $E_{1/2} = -1.05$  V, with simultaneous appearance of an anodic wave at  $E_{1/2} = -0.15$  V, identical to that exhibited by 3'-deoxy-3'-aminothymidine. The initial UV absorption maximum of the solution at 266.5 nm shifted from 266.5 nm to 265 nm, the minimum from 234.5 nm to 233 nm, and the ratio of maximum to minimum from 4.5 to 4.0, the final spectrum corresponding to 3'-deoxy-3'-aminothymidine, further confirmed by appearance chromatographically of a single product with the mobility of authentic 3'-deoxy-3'-aminothymidine.

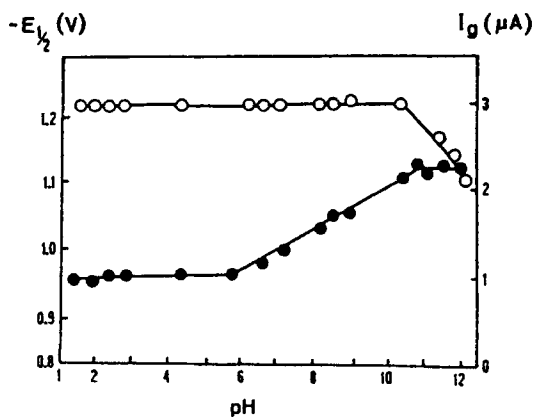


Fig. 1: pH-dependence of half-wave potential ( $E_{1/2}$ , ●-●-) and limiting current ( $I_0$ , ○-○-) of ( $2 \times 10^{-4}$  M) AZT.

From the height of the anodic wave  $E_{1/2} = -0.15$  V for 3'-deoxy-3'-aminothymidine, and the spectral changes accompanying formation of this product from AZT, the reaction was virtually quantitative (96-98%). Furthermore, electrolysis of AZT in acid medium (pH 2) turns out to be a convenient procedure for the large-scale preparation of 3'-deoxy-3'-aminothymidine, probably applicable more generally to one-step conversion of various azido nucleosides to their amino derivatives, as in the case of reduction of azido derivatives of cinnamic acids (4).

Analytical determination. Levels of AZT were determined by d.p.p. in 0.1 M phosphate buffer pH 7. In aqueous medium the height of the reduction peak was linearly dependent on AZT concentration over the range  $10^{-3}$  M -  $10^{-7}$  M. With serum samples, following deproteinization with trichloroacetic acid, neutralization with 1 M NaOH, and 10-fold dilution with 0.1 M phosphate buffer, the lower detection limit was  $5 \times 10^{-6}$  M. Samples of urine were diluted 10-fold with 0.1 M KCl prior to polarography, the lower limit of detection being then also  $5 \times 10^{-6}$  M. Attempts to improve sensitivity are under way.

Acknowledgments: We are indebted to Dr. T-S Lin for a sample of AZdU. This work was supported by the Ministry of Higher Education, project CPBP 01.06/10.01

#### REFERENCES

1. J. Balzerini and S. Broder in "Clinical Use of Antiviral Drugs" (De Clercq E., ed.) Martinus Nijhoff Publishing (1988) 362-385.
2. A.L. Handlon and N.J. Oppenheimer, *Pharmaceut. Res.* **5** (1988) 297-302.
3. B. Czochralska, M. Wrona and D. Shugar, *Topics Curr. Chem.* **30** (1986) 133-181.
4. D. Knittel, *Monatsch. für Chemie* **115** (1984) 1335-1343.