



Talanta 47 (1998) 891–898

---

---

**Talanta**

---

---

## Reversed-phase liquid chromatographic determination of isoniazide in human urine as a test of the genetically predetermined type of biotransformation by acetylation

M.I. Evgen'ev <sup>a,\*</sup>, S.Yu. Garmonov <sup>a</sup>, I.I. Evgen'eva <sup>a</sup>, S.M. Goryunova <sup>b</sup>,  
V.I. Pogorel'tsev <sup>b</sup>, F.S. Levinson <sup>a</sup>

<sup>a</sup> Department of Analytical Chemistry, Kazan State Technological University, 420015, K. Marx str. 68, 420015 Kazan, Russia

<sup>b</sup> Department of Clinical Pharmacology, Kazan State Medical University, 420012, Butlerov str. 49, Kazan, Russia

Received 22 July 1997; received in revised form 30 January 1998; accepted 21 April 1998

---

### Abstract

A new method of determination of genetically predetermined type of biotransformation by acetylation rate using reversed-phase liquid chromatography (RP-HPLC) was described. The method is based on determination of isonicotinic hydrazide (INH) which is excreted with the patient's urine during 24 h period after oral administration of 0.4 g of the drug. INH is used as pharmacogenetic marker. Precolumn derivatization of 4-chloro-5,7-dinitrobenzofurazan is used at RP-HPLC determination of INH and a new drug phosphabenzide (diphenylphosphinylacetic hydrazide, DPPAH) with spectrophotometric detection in urine. The limit of INH detection was  $0.27 \mu\text{g ml}^{-1}$  and the one of DPPAH was  $0.82 \mu\text{g ml}^{-1}$ . As a result of pharmacokinetic investigation it was discovered that bimodal distribution by acetylation rate for DPPAH is less apparent than in the case of INH. It is shown, that immunomodulator xymedone (*N*-( $\beta$ -oxyethyl)-4,6-dimethyldihydropyrimidin-2) is the acetylation inductor of xenobiotics. © 1998 Elsevier Science B.V. All rights reserved.

**Keywords:** RP-HPLC; Derivatization; 4-Chloro-5,7-dinitrobenzofurazan; Drugs

---

### 1. Introduction

Clarification of the connection between concentration of xenobiotics, their metabolites and pharmacological effect is the base of effective and secure application of drugs as well as diagnostics

and treatment of personnel exposed to industrial toxicants [1–4]. In connection with this, the task of the development of sensitive and selective methods of determination of drugs and other xenobiotics in biological substrates of a human being is very urgent. The availability of relatively simple and clinically applicable methods for the determination of drugs in biological substrates for diagnostics of genetically predetermined type of

---

\* Corresponding author. Tel.: +7 8432 399566; fax: +7 8432365768; e-mail: [evgen@cnit.ksu.ras.ru](mailto:evgen@cnit.ksu.ras.ru)