UV-SPECTROPHOTOMETRIC DETERMINATION OF TINIDAZOLE, ORNIDAZOLE AND NIMORAZOLE IN ACID MEDIUM IN THE VARIANT OF THE METHOD OF ADDITIONS

Grishna N. V., Maslov O. Yu.
Scientific supervisors: assoc. prof. Shovkova Z. V., assoc. prof. Klimenko L. Yu.
National University of Pharmacy, Kharkiv, Ukraine
lina_klimenko@nuph.edu.ua

Introduction. Tinidazole (1-[2-(ethylsulfonyl)ethyl]-2-methyl-5-nitro-1*H*-imidazole), ornidazole (1-chloro-3-(2-methyl-5-nitroimidazol-1-yl)propan-2-ol) and nimorazole (4-[2-(5-nitroimidazol-1-yl)ethyl]morpholine) are the derivatives of 5-nitroimidazole and the medicines from the group of antiprotozoal compounds widely used for treatment of infectious diseases.

Aim. To develop UV-spectrophotometric procedure of tinidazole, ornidazole and nimorazole quantitative determination using 0.1 M HCl solution as a solvent and carry out step-by-step validation of the developed procedure in the variant of the method of additions.

Materials and methods. Tinidazole, ornidazole and nimorazole were of pharmacopoeial purity. All spectrophotometric measurements were carried out using a single beam UV/VIS spectrophotometer SPEKOL®1500 (Analytik Jena AG, Germany).

The stock and model solutions, and also solution of addition were prepared by dissolving the substances in 0.1 M hydrochloric acid solution.

The absorbance of all solutions was measured 3 times with randomization of cell position. 0.1 M hydrochloric acid solution was used as a compensation solution.

Results and discussion. UV-spectra of the solutions of tinidazole, ornidazole and nimorazole in 0.1 M HCl have the absorption maximum at 277, 277 and 298 nm respectively. The values of specific absorbance have been calculated and equal 195 (tinidazole, concentration range: 6 – 42 μg/mL), 212 (ornidazole, concentration range: 5 – 35 μg/mL), 159 (nimorazole, concentration range: 7 – 49 μg/mL).

Validation of the developed procedures has been carried out by model solutions in the variant of the method of additions. The analytical range *D* of the methods application is 25 – 175%; the number of concentration levels *g* equals 7 in constant increments of 25%. Such validation parameters as in process stability, linearity/calibration model, precision and accuracy have been estimated by model solutions.

To estimate precision and accuracy the model solutions with and without addition were analysed within 1 run; the concentrations of model solutions without addition were recalculated:

$$X_{ad}^{model} = \frac{C_{ad}^{model} \cdot V_{ad}}{C_{reference}^{model} \cdot V_{m.f}} \cdot 100\%; \quad X_{i,fact}^{model\,MA} = \frac{C_i^{model\,MA}}{C_{reference}^{model}} \cdot 100\%; \quad X_{i,calc}^{model\,MA} = X_{ad}^{model} \cdot \frac{A_i^{model\,MA}}{A_{i+ad}^{model\,MA} - A_i^{model\,MA}}.$$

The values «found/given» $RR_i^{model\,MA}$ were calculated and used to determine the confidence interval $\Delta_{RR}^{model\,MA}$ and the systematic error $\delta^{model\,MA}$ respectively:

$$RR_i^{model\,MA} = \frac{X_{i,calc}^{model\,MA}}{X_{i,fact}^{model\,MA}} \cdot 100\%;$$

$$\Delta_{RR}^{model\,MA} = t(95\%; n-1) \cdot RSD_{RR}^{model\,MA} \le \max \Delta_{As}^{model} = 6.40\%;$$

$$\delta^{model\,MA} = \left| 100 - \overline{RR}^{model\,MA} \right| \le \max \delta^{model} = 2.05\%$$

The validation results obtained within one analytical run are presented in Table 1.

Table 1. The validation results of UV-spectrophotometric procedures of tinidazole, ornidazole and nimorazole quantitative determination in the variant of the method of additions

Parameter	Values			Acceptability criterion
	tinidazole	ornidazole	nimorazole	
stability				
$\delta^{model\ stability}$,%	1,37 (24 h)	0,95 (24 h)	0,68 (48 h)	$\leq 2.05\%$
linearity/calibration model				
b^{model}	0,980	1,006	0,959	–
s_b^{model}	0,005	0,015	0,004	–
a^{model}	1,068	0,079	2,695	$\leq 2.73\%$
s_a^{model}	0,542	1,650	0,485	$a^{model} \leq 2.015 \cdot s_a^{model}$
RSD_0^{model}	0,642	1,952	0,574	$\leq 3.18\%$
R_c^{model}	0,9999	0,9995	0,9999	≥ 0.9983
precision and accuracy				
$\overline{RR}^{model\ MA}$,%	101,24	99,43	102,39	–
$\delta^{model\ MA}$,%	1,24	0,57	2,39	$\leq 2.05\%$
$RSD_{RR}^{model\ MA}$,%	1,65	2,45	1,47	–
$\Delta_{RR}^{model\ MA}$,%	3,33	4,93	2,96	$\leq 6.40\%$

The total results of validation allow to point to the conclusion about acceptable stability, linearity, accuracy and precision of the developed UV-spectrophotometric procedures of tinidazole, ornidazole and nimorazole quantitative determination in the variant of the method of additions.

Conclusions. New procedures of tinidazole, ornidazole and nimorazole quantitative determination by the method of UV-spectrophotometry have been developed using 0.1 M HCl solution as a solvent; their acceptability for application in the variant of the method of additions has been shown.

APPLICATION OF THIN LAYER CHROMATOGRAPHY IN ANALYSIS OF EFAVIRENZ

Kabbaj Abdelmounaaim, Slabiak O. I.
Scientific supervisors: assoc. prof. Ivanchuk I. M., assoc. prof. Mykytenko O. Ye.
Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine
National University of Pharmacy, Kharkiv, Ukraine
lynnne2@ukr.net

Introduction. HIV infection is usually treated with drug combinations consisting of at least three different antiretroviral medicines. Essential components of this highly active antiretroviral therapy are non-nucleoside reverse transcriptase inhibitors presented by five medicines (nevirapine, delavirdine, efavirenz, etravirine and rilpivirine). Efavirenz is recommended currently as preferred first-line medicine with a low pill burden, once daily dosing, a long half-life allowing for relatively stable plasma concentrations and some forgiveness for doses not taken exactly on schedule. There are cases of acute poisoning due to administration of efavirenz, including cases of suicide attempts. The method of thin layer chromatography (TLC) is widely used in the process of forensic toxicological examinations for screening and confirming investigations – with the purpose of analytes detection and identification respectively. The main focus is the chromatographic behaviour of the substances using standard mobile