METROLOCAL ASSESSMENT OF THE REFRACTOMETRICY METHOD FOR QUANTITATIVE DETERMINATION OF PHARMACY COMPOUNDING SOLUTION

Zeytun Ali, Taran S. G., Yevtifieva O. A.
National University of Pharmacy, Kharkiv, Ukraine
jevt.23@gmail.com

Introduction. In the pharmaceutical analysis refractometry method is used to identify of substances, assess their purity and for quantitative analysis. The refractometry method is used widely in the practice of pharmacy control to assess the quality of the preparation of concentrated solutions, liquid dosage forms made for the future compounding.

Monograph 2.2.6 of State Pharmacopoeia of Ukraine (SPhU) "The refractive index (refractive index)" is harmonized with the requirements of the European Pharmacopoeia (EPh) and gives a description of the method, the instrument calibration rules, standard terms and conditions for carrying out tests to refractometric analysis and requirements for the refractometric equipment that must be met. The national part of this monograph contains additional conditions for the application of the method for quantification of the substance in the solution: the accuracy of the measurement of the refractive index must be not less than $\pm 2\times10^{-4}$. Allowed calibration with purified water, for which the refractive index is $n_D^{20} = 1{,}3330$, the value of the temperature coefficient must not exceed ($\frac{\Delta_n}{\Delta_t} = 0{,}000085$).

Aim. The aim of our work is experimental determination of the metrological characteristics of refractometry method for the quantitative determination of model solution of sodium hydrogencarbonate 5% according to the requirements of SPhU.

Materials and methods. The analytical balance AV 204 S/A METTLER TOLEDO was used. Reagents, measuring glass-ware of class A (first class) and excipients meeting the requirements of the SPhU were used for the work. The refractometer RL 3 was used in the work. The refractometer RL 3 is characterized by the scale of the refractive index from 1.3 to 1.7; scale division is equal 0.001; the accuracy of determination - $\pm 2\times10^{-4}$ meeting the requirements of the SPhU. The substance of sodium hydrogencarbonate manufactured by Biesterfeld Siemsgluss International GmbH" Hamburg, Germany No. 060125 meeting the requirements of the BPh 98/USP30/SPhU was used in the experimental researches. The measurements were performed with at ambient temperature 20 °C±0.5 °C.

The validation parameters - linearity, precision, accuracy, reproducibility was investigated throughout the range of application methods performed by a standardized procedure. In the process of determining the refractive index of purified

water (n_0) and model solution (n) with concentration (C_x) was measured three times. The content of sodium hydrogen carbonate C_x is calculated by the formula: $C = \frac{n-n_0}{F}$, in which C – the concentration of substance: n - the refractive index of solution; n_o - the refractive index of purified water; F - the value of the refractive index growth of sodium hydrogencarbonate with increasing concentration by 1%.

Preparation of the test solution. 4.9411 g (exact sample) RS placed in a volumetric flask of 100 ml, added 40 ml of purified water and stirred until dissolved sodium hydrogencarbonate, dilute with water to volume, and mix.

Preparation of model solutions. Model solutions were prepared according to the range of concentration from 60 to 140% of the concentration specified (60, 80, 100, 120, 140%). Sample weights 3.0330 g; 4,0150 g; 4.9411 g, 5.9680 g and 7.0265 g were accurately weighed. Prepared like a test solution.

Results and discussion. The results of quantitative determination of sodium hydrogencarbonate 5% in aqueous solution by refractometry allow to conclude that if content tolerances is ±2% it is not possible to conduct a correctly quantitative definition by this method. The validation characteristics of the refractometry method (Table) for quantitative determination of hydrogencarbonate 5% in aqueous solution have been investigated. These results allow recommending the refractometry method for quantity control of sodium hydrogencarbonate with the permissible limits of ±5%.

Table

The results of the statistical evaluation of the metrological characteristics of methods of quantitative determination of sodium hydrogencarbonate by refractometry.

Test data			Theoretical data			
Relative confidence interval of single results			Maximum permissible uncertainty of the method, $max\Delta_{As}\%$		Prognosis of total uncertainty, $\Delta_{As}\%$	Permissible limits, B%
Lab. 1	Lab. 2	Inter laboratory				
$\Delta_{x,r}^1$	$\Delta_{x,r}^2$	$\Delta_{x,r}^{intra}$	±2%	±5%		
3.3	1.6	3.0	0.64	1.6	3.2	10

Conclusions. The prognosis of total uncertainty $\Delta_{As}\% = 3{,}2\%$ exceeds the maximum permissible uncertainty for the permissible limits of ±5%. For correct quantitative determination of sodium hydrogencarbonate by refractometry is recommended to use with the permissible limits of ±10% or to use refractometer with limit of permissible error of the refractive index which is not higher $\mathbf{n_D}$ - $\pm 1\times10^{-4}$.