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EVALUATION OF METROLOGICAL CHARACTERISTICS OF SPECTROPHOTOMETRIC QUANTITATIVE DETERMINATION OF PARACETAMOL IN TABLETS BY SPECIFIC ABSORBANCE

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Key words: paracetamol; quantitative determination; spectrophotometry; specific absorbance method; validation

The validation characteristics of the spectrophotometric quantitative determination of paracetamol in tablets by specific absorbance according to the British Pharmacopoeia (BPh) have been evaluated. The results of paracetamol content of 83.59% and 84.39% in terms of the average mass of one tablet do not meet the permissible limits B ±5.0%. The peculiarities of the sample preparation method for quantitative determination of the active pharmaceutical ingredient in tablets has been discussed, and comparative analysis of "Dissolution" and "Assay" tests for paracetamol tablets according to the BPh has been conducted. We have suggested to make such changes at the stage of the sample preparation as "… place the flask in an ultrasonic bath for 30 min…" instead of "…shake for 15 minutes…". The acceptance criteria of the assay method for paracetamol tablets have been calculated for permissible limits of ±5.0%, ±7.5%, ±10.0%. The results of the convergence and linearity research of the method meet requirements for the permissible limits of ±5.0%. The results of the intermediate precision research of the method meet requirements for the permissible limits of ±7.5%. The results of the accuracy research of the method meet requirements for the permissible limits of ±10.0%. Taking into account the technical capabilities of the Ukrainian producers and a diverse list of excipients used in the manufacture of the drug, the spectrophotometric quantitative determination of paracetamol tablets by specific absorbance is recommended to use with the permissible limits of ±10.0%. The prognosis of the total uncertainty of the analysis results is consistent with requirements to the maximum permissible uncertainty of the analysis $\Delta_{As}^{10.0\%} = 2.6 \leq max\ \Delta_{As}^{10.0\%} = 3.2\%$ *and with results of the 3rd round of the Professional Testing Programme (PTP) of "Pharma-test" laboratories in the system of the State Inspection for Medication Quality Control of the Ministry of Public Health of Ukraine.*

Paracetamol belongs to the group of non-steroidal anti-inflammatory drugs, it is a nonselective COX inhibitor, and over 50 years it has already been used as an antipyretic and analgesic [10]. Monocomponent formulations based on paracetamol tablets, capsules, solutions, suppositories, suspensions, granules, gel are produced by pharmaceutical industry. Paracetamol is part of many combined medicines with antipyretic and analgesic effects. The research concerning the use of paracetamol to treat pain in neonates as an alternative to opiates is being performed [12].

Quantitative determination of paracetamol in the substance according to the monographs of the State Pharmacopoeia of Ukraine (SPhU) [7], European [11], British [9] pharmacopoeias and Pharmacopoeia of the Republic of Belarus [3] is carried out by the ceriometry method, American [16], Japan [14] Korea [15] pharmacopoeias by the spectrophotometric method (by standard), China [13] – by specific absorbance.

UV-spectrophotometry by standard [7] and specific absorbance methods [9, 13], HPLC [16] are used for pharmacopoeial quantitative assessment of paracetamol tablets.

Thanks to the introduction of quality assurance systems for results of analysis, equipment qualification the specific absorbance method has been widely used in pharmacopoeial analysis. At present the specific absorbance method is recommended by the SPhU not only for quantitative determination of 10 substances [7], but also for 21 types of medicinal plants [6]. A standardized procedure of validation of spectrophotometric methods for quantitative determination of drugs by specific absorbance has been developed [4] and successfully approved on the quantitative determination methods for prednisolone and riboflavin substances [18].

The aim of this research is to evaluate the metrological characteristics of spectrophotometric quantitative determination of paracetamol in tablets by specific absorbance, which is recommended by the British Pharmacopoeia (BPh) and to determine acceptable permissible limits for this method.

Experimental Part

Tablets "Paracetamol", 200 mg, manufactured by the pharmaceutical company "Darnitsya", batch UA / 4369/01/01 were chosen as an object of the research.

The following analytical equipment was used: a "SPECORD 200" spectrophotometer, AV 204 S / A METTLER TOLEDO analytical balance. Reagents, measuring glassware of class A (first class) and excipients meeting the requirements of the SPhU were used for the work.

The assay method for paracetamol in tablets according to the British Pharmacopoeia [9]: weigh and powder 20 tablets.

Table 1

The critical values of the systematic error ($max\ \delta_{tot}$), total uncertainty of the analysis ($max\Delta_{As}$) and parameters of the linear dependence $Y_i = b \cdot X_i + a^*$

Permissible limits, *B*%	λ, nm	$A_{1cm}^{1\%}$	C_{nom}, mg/100 ml	A_{nom}	max$\Delta_{,As}$%	maxδ_{tot} = max$\Delta_{prec,}$%	$RSD_{o,}$ %	min R^2_c	max*a*, %	max$\delta_{A,}$%
±5.0%	257	715	0.75	0.536	1.6	1.15	0.60	0.9981	2.34	2.6
±7.5%					2.4	1.7	0.90	0.9957	3.5	
±10.0%					3.2	2.3	1.20	0.9924	4.7	

* the number of points 9, for the range of 80-120%.

Add an accurately weighed powder containing 0.15 g of paracetamol to 50 ml of 0.1 M sodium hydroxide, dilute with 100 ml of water, shake for 15 minutes and dilute to 200 ml with a sufficient amount of water. Mix, filter and dilute 10 ml of the filtrate to 100 ml with water. Add 10 ml of the solution obtained to 10 ml of 0.1M sodium hydroxide, dilute to 100 ml with water and measure the absorbance of the solution obtained at the maximum at 257 nm. Calculate the content of $C_8H_9NO_2$ taking 715 as the value of A ($A_{1cm}^{1\%}$) at the maximum at 257 nm.

The nominal content of paracetamol b_{nom} is 200 mg; the average weight of one tablet is 256.02 mg. The content of paracetamol in one tablet in terms of the average weight of one tablet in percentage of the prescribed amount was calculated by the formula:

$$X\ (\%) = \frac{10 \cdot A_1}{A_{1cm}^{1\%}} \cdot D \cdot m_t \cdot \frac{100}{b_{nom}}\ ;\ D = \frac{V_D}{m}\ ,$$

where: D – is dilution of the sample analyzed, m – is the mass of the sample for analysis. In our case, dilution is:

$$D = \frac{V_D}{m} = \frac{200}{0.1952} \times \frac{100}{10} \times \frac{100}{10} = \frac{20000}{0.1952} \cdot$$

Results and Discussion

According to the specific absorbance method it is possible to obtain the correct results using a high level of equipment, its qualification and compliance with the requirements of the SPhU [7]. Taking this into account the qualification spectrophotometer characteristics were evaluated before the experiment. The control of cells, absorbance accuracy, absorbance convergence with removing cells, the limit of stray light have been carried out. The results obtained meet requirements of the SPhU.

The acceptance criteria of the assay method for paracetamol tablets was calculated considering the peculiarities of spectrophotometry by the specific absorbance method [4] for permissible limits of 95-105% (B = ±5.0%) and ±7.5%, ±10.0% according to the monograph (Tab. 1).

At first quantitative determination of paracetamol tablets in the concentration of 100% in accordance with the prescribed amount was carried out. To control correctness of the results and accuracy of the sample preparation two parallel studies of the tablet powder were conducted. Immediately after preparing analytical solutions according to the method, absorbance (A) was measured at the absorbance maximum of 257 nm three times with removing the cells. The results of the paracetamol content of 83.59% and 84.39% in terms of the average mass of one tablet do not meet the permissible limits (Tab. 2).

According to the results of the accuracy control of the sample preparation $|X_1\text{-}X_2| = 0.80\% < \Delta_{As}1.60\%$; the negative result cannot be associated with the analyst's errors.

Peculiarities of the sample preparation of quantitative determination methods for the active pharmaceutical ingredient (API) in tablets. Determination of the quantitative content of the API in tablets has certain features that must be considered in standardization of methods. An accurately weighed quantity is dissolved in a suitable solvent in one or several steps using measuring glassware in quantitative determination of substances. Each step of the sample preparation is a part of uncertainty, which is calculated from the values of permissible uncertainty of measuring glassware and weighing according to the SPhU. In addition to the abovementioned sample preparation steps the method includes such additional operations as weighing of 20 tablets, powdering, dissolving and filtering, which bring more uncertainty to the total uncertainty of the sample preparation in quantitative determination of the API in tablets.

The relationship of "Dissolution" and "Assay" tests for paracetamol tablets according to the BPh. It should be noted that according to the BPh monograph control of dissolution of paracetamol tablets and "Assay" test for the API in tablets are carried out by UV-spectrophotometry using specific absorbance [9]. "Dissolution" and "Assay" tests are quite similar in operations, but differ in terms of dissolution, the purpose and test evaluation.

"Dissolution" test determines the minimum quality requirements for pharmaco-technological properties of paracetamol tablets regardless of the manufacturer (the composition of excipients, technology (Tab. 3)) based on the API quantitative determination after dissolution.

Conditions for "Dissolution" test: place one tablet in Apparatus II (paddle apparatus), rotate the paddle at 50 rpm (tolerance ±4%); the medium is phosphate buffer, pH 5.8 (±0.05 units), carry out dissolution at a temperature from 36.5° to 37.5°C; assess the API release in 45 minutes; dilute 20 ml of the filtrate with 0.1M sodium hydroxide to the concentration of 0.00075% (w/v); measure the absorbance of this solution; the amount of

Table 2

The results of the spectrophotometric quantitative determination of paracetamol tablets by specific absorbance

Description / parameter	The BPh method			
	sample preparation without changes		sample preparation with changes	
	Test 1	Test 2	Test 1	Test 2
The nominal content of paracetamol in one tablet of the prescribed amount b_{nom}, mg	200		200	
Permissible limits of paracetamol, %	95.0-105.0			
B, %	5			
The average mass of one tablet m_t, mg	256.02			
The mass of the tablet powder for analysis $m_н$, mg	195.2	196.8	196.3	195.9
Mean absorbance, A_i	0.4557	0.4638	0.5358	0.5363
Standard deviation, $S_{as,}$ %	0.0006	0.0010	0.0003	0.0002
Relative standard deviation, $S_{as,r,}$ %	0.12	0.21	0.06	0.04
The paracetamol content in terms of the average mass of one tablet, $X_{mean,}$ %	83.59	84.39	97.74	98.03
Control of accuracy of the sample preparation, % $\|X_1-X_2\|<\Delta_{As}$	0.80		0.29	

the active ingredient in the solution should be not less than 70% of the prescribed amount.

Conditions for "Assay" test: add an accurately weighed quantity of the powder to 50 ml of 0.1 M sodium hydroxide, dilute with 100 ml of water, shake for 15 minutes; dilute 10 ml of the filtrate with 0.1 M sodium hydroxide to the concentration of 0.00075% (w/v); measure the absorbance of this solution; the amount of the active ingredient in the solution should be within the range of 95%-105% of the prescribed amount.

The question is if the API of paracetamol can be completely released under the following conditions for 15 minutes. Paracetamol belongs to the 1st class of the biopharmaceutical classification system (BCS) and is considered to be very instant (at least 85% of the prescribed amount of the API passes into the solution for 15 min when using the paddle apparatus (50 or 75 rpm) or basket apparatus (100 rpm)) [2, 17]. The quality of 17 batches of 10 names of paracetamol tablets made in Russia and Western Europe was comparatively assessed in terms of the content of the API and the rate of dissolution (quantitative determination of the API for each batch was performed by HPLC (n = 10) according to the EuPh monograph "Paracetamol"). The results show that in 30 min 44.0±3.3% of the API of paracetamol was released for one batch; for 6 batches the dissolution percentage was in the range of 88.0±1.3% – 94.0±1.1%; for 10 batches it was 96.0±0.7% – 100.0±0.4% [1]. Thus, the difference in the release of the API may be associated with the composition of the excipients of tablets and their different formulations that each manufacturer sets independently.

Considering the facts described above the stage of the sample preparation of the method – "…shake for 15 minutes…" should be changed to "… place the flask in an ultrasonic bath for 30 min…". Two parallel experiments were conducted with the tablet powder. The results concerning the paracetamol content in terms of the average mass of one tablet of 97.74% and 98.03% meet the permissible limits (Tab. 2). Thus, too low results ob-

Table 3

Comparative analysis of the excipients when producing paracetamol tablets by the Ukrainian manufacturers

Manufacturer	How supplied	Excipients
"Lubnyfarm" JSC, Lubni, Poltava region	Tablets, 0.2 g No.10 in the blister card	Potato starch, calcium stearate, colloidal anhydrous silica, methylcellulose
"Lugansk Pharmaceutical Plant" JSC, Lugansk	Tablets, 0.2 g No. 10 in the strip	Sugar, corn starch, stearic acid, gelatin
"Agrofarm" LLC, Irpin, Kyiv region	Tablets, 0.2 g No.10	Potato starch, corn syrup, calcium stearate
"Styrolbiofarm" Ltd., Gorlovka, Donetsk region	Tablets, 0.325 g No.6 in the blister card	Croscarmellose sodium, povidone, pregelatinized starch, corn starch, stearic acid
"Pharmaceutical company" Darnitsa" PJSC, Kiev	Tablets, 0.2 g No.10 in the blister card	Potato starch, povidone, calcium stearate, aerosil
"Galychpharm", JSC, Lviv	Tablets, 0.2 g No.10 in the blister card	Sodium carboxymethyl starch, low molecular weight polyvinyl pyrrolidone, calcium stearate

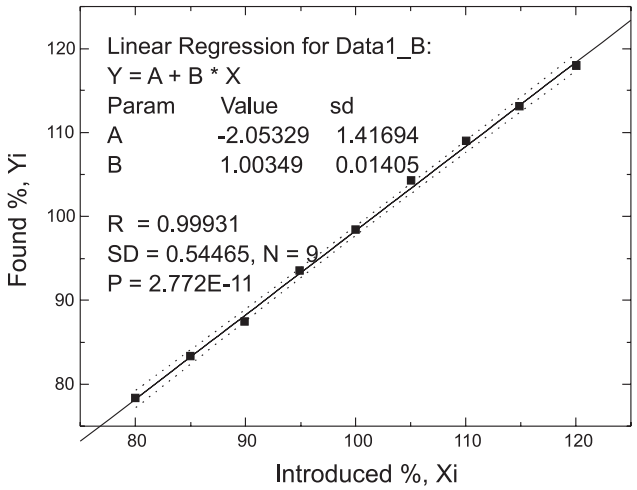

Fig. 1. The plot of linear dependence of absorbance on the concentration of paracetamol in the normalized coordinates.

tained in the first experiment caused by incomplete release of the active substance when dissolving.

Further research and evaluation of validation characteristics of quantitative determination methods for paracetamol tablets by specific absorbance (the sample preparation with changes) were performed according to the standardized procedure of validation of spectrophotometric methods of quantitative determination of drugs by specific absorbance [4].

The prognosis of the total uncertainty of the analysis results (Δ_{As})

The prognosis of uncertainty of the sample preparation. The approach and requirements for maximum permissible errors for volumetric glassware, balances and devices were used to assess uncertainty of the sample preparation [7, 8]:

$$\Delta_{Sp} = \sqrt{0.10^2 + 0.10^2 + 0.5^2 + 0.12^2 + 0.5^2 + 0.12^2} = 0.74\%.$$

The prognosis of the total uncertainty of the analysis result for the permissible limits of ±5.0%; ±7.5%; ±10.0% was conducted according to the standardized procedure of validation of spectrophotometric methods by specific absorbance [4]:

$$\Delta_{As}^{5.0\%} = \sqrt{\max\delta_{tot}^2 + \Delta_{SP}^2 + \Delta_{FAO}^2} =$$

$$= \sqrt{1.15^2 + 0.74^2 + 0.49^2} = 1.7\%;$$

$$\Delta_{As}^{7.5\%} = 2.1\%; \ \Delta_{As}^{10.0\%} = 2.6\%.$$

The total uncertainty should be insignificant compared with the maximum permissible uncertainty of the analysis results:

$$\Delta_{As} \le \max \Delta_{As}^{5.0\%} = 1.6\% : \ \Delta_{As}^{5.0\%} = 1.7 \ge 1.6\%;$$

$$\Delta_{As}^{7.5\%} = 2.1 \le \max \Delta_{As}^{7.5\%} = 2.4\%;$$

$$\Delta_{As}^{10.0\%} = 2.6 \le \max \Delta_{As}^{10.0\%} = 3.2\%.$$

The total uncertainty of the analysis results exceeds the maximum permissible uncertainty for the permissible limits of ±5.0% and meets requirements for the permissible limits of ±7.5% and ±10.0%.

Accuracy, linearity, repeatability, intermediate precision were investigated using 9 model solutions within the whole range of the method application from 80 to 120% of the prescribed amount. The assessment of linearity was performed in the normalized coordinate system (Fig. 1). The results are shown in Tab. 4. The Table shows that the requirements for the parameters of the linear dependence are performed for permissible limits of ±5.0%.

The assessment of the validation parameters of the method is given in Tab. 5. Parameters of the accuracy and convergence are shown graphically in Fig. 2.

The results of the convergence research of the method meet requirements for the permissible limits of ±5.0%. The results of the intermediate precision research of the method meet requirements for the permissible limits of ±7.5%. The results of the accuracy research of the method meet requirements for the permissible limits of ±10.0%. In this case without the other tests results (e.g. Art. 2.9.3. "Dissolution", Art. 2.9.6. "Uniformity of the content of the active ingredient per unit dosage of a medicinal pro-

Table 4

The metrological characteristics of the linear dependence

Parameters	Value		Criteria (for tolerances of 95-105%, the number of points 9)	Conclusion
	test 1	test 2		
b	1.0034	0.9798	–	–
s_b	0.0141	0.0077	–	–
a	-2.05	-0.36	statistical insignificance $a \le t(95\%, g-2) \cdot s_a = 1.89 \cdot s_a = 2.67\%$ $a \le t(95\%, g-2) \cdot s_a = 1.89 \cdot s_a = 1.47\%$	satisfied
			practical insignificance $\lvert a_{\delta A} \rvert \le \max \delta A = 0.71 \cdot \max \Delta_{As} = 1.15\%$	satisfied
			$\max a = 2.34\%$	satisfied
s_a	1.4172	0.7787	–	–
RSD_0	0.54	0.30	$RSD_o \le 0.60\%$	satisfied
r	1.0000	1.0000	$\min R^2_c = 0.9981$	satisfied

Table 5

The results of the accuracy and convergence research of the spectrophotometric quantitative determination of paracetamol tablets by specific absorbance

Validation parameters	Research 1	Research 2
$\overline{X}$%	**98.27**	**97.61**
RSD_x%	0.60	0.31
$\Delta_{prec}\% = t(95\%,8)\cdot RSD_x =$	**1.12**	**0.59**
Critical value for $\Delta_{prec} \le 1.15\%$	satisfied	satisfied
$\delta = \lvert X - 100 \rvert$	**1.73**	**2.39**
Criterion of the systematic error insignificance $\delta \le \Delta_{prec}/3$ if it is not satisfied 1), then 2) $\delta \le max\delta_{tot} = 1.15$ *for permissible limits ±7.5%* $\delta \le max\delta_{tot} = 1.7$; *for permissible limits ±10.0%* $\delta \le max\delta_{tot} = 2.3$	$\delta \le 0.37$ unsatisfied satisfied satisfied	$\delta \le 0.20$ unsatisfied unsatisfied satisfied
The conclusion of the method	**correct**	**correct**
Intermediate precision		
$Z_{intra}\% =$	**97.94**	
$SD_{z\text{-}intra}\% =$	**1.07**	
$\Delta_{intra}\% = t(95\%,n\cdot m\text{-}1)\cdot SD_{z\text{-}intra}\% = 1.75\, SD_{z\text{-}intra}\%$	**1.87**	
Critical value for $\Delta_{prec} \le 1.15\%$	unsatisfied	
Intermediate systematic error $\delta =$	**2.06**	
Criterion of the systematic error insignificance $\delta \le \Delta_{prec}/\sqrt{18}$ if it is not satisfied 1), then 2) $\delta \le max\delta_{tot} = 1.15$ *for permissible limits ±7.5%* $\delta \le max\delta_{tot} = 1.7$; *for permissible limits ±10.0%* $\delta \le max\delta_{tot} = 2.3$	$\delta \le 0.24$ unsatisfied unsatisfied satisfied	
The overall conclusion of the method	**correct**	

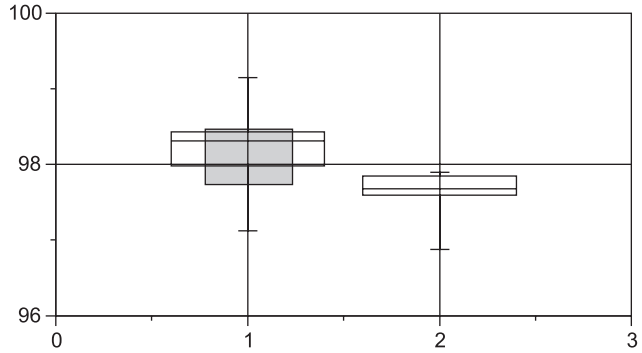

Fig. 2. The plot of the accuracy and convergence research results of the spectrophotometric quantitative determination of paracetamol tablets by specific absorbance.

duct") conclusions about the quality of the tablets cannot be done. Taking into account the technical capabilities of the Ukrainian producers and a diverse list of excipients used in the manufacture of the drug, the spectrophotometric quantitative determination of paracetamol tablets by specific absorbance is recommended to use for quantitative determination of the API in the drug with the permissible limits of ±10.0%, while the permissible limits of ±7.5% results may be doubtful. The prognosis of the total uncertainty of the analysis results is consistent with requirements to the maximum permissible uncertainty of the analysis $\Delta_{As}^{10.0\%} = 2.6 \le \max\ \Delta_{As}^{10.0\%}\ 3.2\%$ and with results of the 3rd round of the Professional Testing Programme (PTP) of "Pharma-test" laboratories in the system of the State Inspection for Medication Quality Control of the Ministry of Public Health of Ukraine [5].

CONCLUSIONS

The validation characteristics of the spectrophotometric quantitative determination of paracetamol in tablets by specific absorbance according to the British Pharmacopoeia have been evaluated. We have suggested to make such changes at the stage of the sample preparation as "… place the flask in an ultrasonic bath for 30 min…" instead of "…shake for 15 minutes…". Taking into account the technical capabilities of the Ukrainian producers and a diverse list of excipients used in the manufacture of the drug, the spectrophotometric quantitative determination of paracetamol tablets by specific absorbance is recommended to use for quantitative determination of API in the drug with the permissible limits of ±10.0%.

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ОЦІНКА МЕТРОЛОГІЧНИХ ХАРАКТЕРИСТИК МЕТОДИКИ СПЕКТРОФОТОМЕТРИЧНОГО КІЛЬКІСНОГО ВИЗНАЧЕННЯ ПАРАЦЕТАМОЛУ У ТАБЛЕТКАХ МЕТОДОМ ПОКАЗНИКА ПОГЛИНАННЯ

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Ключові слова: *парацетамол; кількісне визначення; спектрофотометрія; метод показника поглинання; валідація*

Здійснено оцінку метрологічних характеристик методики кількісного визначення парацетамолу у таблетках методом показника поглинання (МПП), яка рекомендується Британською фармакопеєю (БФ). Отримані результати у перерахунку на середню масу однієї таблетки 83.59% та 84.39% не відповідають допускам вмісту 95-105% (В ±5.0%). При встановленні можливих причин негативного результату обговорені особливості пробопідготовки методик кількісного визначення активного фармацевтичного інгредієнта у таблетках та здійснено порівняльний аналіз випробувань «Розчинення» та «Кількісний вміст» парацетамолу у таблетках відповідно до монографії БФ. Запропоновано внести зміни в етап пробопідготовки: «…перемішувати на протязі 15 хв…» змінити на «помістити колбу в ультразвукову баню на 30 хв». З метою визначення прийнятних допусків розраховані критерії прийнятності для В ±5.0%, ±7.5% та ±10.0%. Результати вивчення лінійності та збіжності відповідають вимогам при В±5,0%; внутрішньолабораторної прецизійності для В ±7.5%. Результати правильності методики обох дослідів перевищують критерії для В ±5.0%; результати досліду 1 відповідають критеріям для В ±7.5%; результати досліду 2 та результат внутрішньолабораторної правильності відповідають критеріям для В ±10.0%. Враховуючи технічні можливості українських виробників та різноманітний перелік допоміжних речовин, які застосовуються при виробництві препарату, рекомендується використовувати методику кількісного визначення парацетамолу у таблетках за МПП при В ±10.0%. Прогноз невизначеності результатів аналізу узгоджується з вимогами до максимально припустимої невизначеності аналізу $\Delta_{As}^{10.0\%} = 2.6 \leq max\ \Delta_{As}^{10.0\%} = 3.2$ *та з результатами 3-го раунду Програми професійного тестування лабораторій «Фарма-тест».*

ОЦЕНКА МЕТРОЛОГИЧЕСКИХ ХАРАКТЕРИСТИК МЕТОДИКИ СПЕКТРОФОТОМЕТРИЧЕСКОГО КОЛИЧЕСТВЕННОГО ОПРЕДЕЛЕНИЯ ПАРАЦЕТАМОЛА В ТАБЛЕТКАХ МЕТОДОМ ПОКАЗАТЕЛЯ ПОГЛОЩЕНИЯ

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Ключевые слова: *парацетамол; количественное определение; спектрофотометрия; метод показателя поглощения; валидация*

Осуществлена оценка метрологических характеристик методики количественного определения парацетамола в таблетках методом показателя поглощения (МПП), которая ре-

комендуется Британской фармакопеей (БФ). Полученные результаты в пересчете на среднюю массу одной таблетки 83.59% и 84.39% не соответствуют допускам содержания 95-105% (В ±5.0%). При установлении возможных причин отрицательного результата обсуждены особенности пробоподготовки методик количественного определения активного фармацевтического ингредиента в таблетках и осуществлен сравнительный анализ испытаний «Растворение» и «Количественное определение» парацетамола в таблетках согласно монографии БФ. Предложено внести изменения в этап пробоподготовки: «... перемешивать в течение 15 мин...» изменить на «поместить колбу в ультразвуковую баню на 30 мин». С целью определения приемлемых допусков рассчитаны критерии приемлемости для В ±5.0%, ±7.5% и ±10.0%. Результаты изучения линейности и сходимости соответствуют требованиям при В ±5.0%; внутрилабораторной прецизионности – для В ±7.5%. Результаты правильности методики обоих опытов превышают критерии для В ±5.0%; результаты опыта 1 соответствуют критериям В ±7.5%; результаты опыта 2 и результат внутрилабораторной правильности соответствуют критериям В ±10.0%. Учитывая технические возможности украинских производителей и разнообразный перечень вспомогательных веществ, которые применяются при производстве препарата, рекомендуется использовать методику количественного определения парацетамола в таблетках МПП при В ±10.0%. Прогноз неопределенности результатов анализа согласовывается с требованиями к максимально допустимой неопределенности анализа $\Delta_{As}^{10.0\%} = 2.6 \leq max\ \Delta_{As}^{10.0\%} = 3.2\%$ *и с результатами 3-го раунда Программы профессионального тестирования лабораторий «Фарма-тест».*