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Verification of "Dissolution" Test for Famotidine Tablets with UV-spectrophotometric Determination

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Abstract: Famotidine is a new generation of antiulcer drugs. There are 14 different dosage forms are registered in Ukraine, and 50% of them are produced by Ukrainian pharmaceutical factories. That is why it is necessary to include into the first supplement of the second edition of the State Pharmacopeia of Ukraine monographs for regulating quality control of dosage forms with famotidine. Methods of quality control for famotidine tablets are present in the United States Pharmacopeia, and do not require complete validation procedure, but only their verification. The USP method for "Dissolution" test for famotidine tablets with UV-spectrophotometry determination was verified for including to the State Pharmacopeia of Ukraine. Specificity, linearity, convergence, as well as the accuracy were determined for this method and confirmed its correctness. The total uncertainty of the method is 1.12% that not more than critical value of total uncertainty for the "Dissolution" test (3.00%).

Keywords: Famotidine Tablets, Verification, Dissolution, UV-spectrophotometry

1. Introduction

Famotidine is a new generation of antiulcer drugs of histamine receptors antagonists. Lately it was prescribed by doctors frequently due to high efficiency and low toxicity in comparison with its predecessors [5, 6, 8, 10]. There are 14 different dosage forms with famotidine are registered in Ukraine for today. 50% of them are produced on the pharmaceutical factories of Ukraine. Also, manufacturing compounded drugs with using prefabricated ones is a modern international practice. State Pharmacopoeia of Ukraine is a member of the European Pharmacopoeia Commission [2, 7]. It has national part that includes among the others monographs for finished dosage forms. That monographs are developed for preparations produced in Ukraine. Therefore, it was advisable to include to the first supplement of the second edition of the State Pharmacopoeia of Ukraine monograph that would regulate the requirements for quality control of dosage forms with famotidine [7]. Methods of quality control of the finished dosage forms included in the World Pharmacopeias (such as USP, British Pharmacopeia etc., for example), do not require complete validation procedures, but only verification procedures of these methods [1, 7, 9].

The aim of this work was verification of "Dissolution" test for famotidine tablets from USP pharmacopoeia monograph for including into the 2nd edition of the State Pharmacopoeia of Ukraine "Famotidine tablets".

2. Experimental Methods

2.1. Materials

The object of study is famotidine tablets "Famotidine" with the content of the active substance constituting 20 mg (manufactured by PJSC Kievmedpreparat, Arterium Corporation, Kyiv, Ukraine, batch: 106810, 133634, 127728).

Substance of famotidine (manufactured by NAKODA CHEMIKALS LTD, Telangana, India, batch: FM-1507002) was used as the working standard sample for prepare famotidine standard solution and sample solutions for the linearity.

Lactase monohydrate, Potato Starch, Calcium Stearate, Silicon Dioxide, Povidone as the excipients in known amounts were used for preparing placebo solution.

The "Specord 200" UV-Vis.-Spectrophotometer (Germany), the "PharmaTest PT-70" device for

"Dissolution" test (Germany), the AB 204 S/A METTLER TOLEDO analytical balances (USA) as well as the class A measuring vessel and reagents that conform to the State Pharmacopeia of Ukraine [7], were used in the study.

Investigation was carried out at the State scientific-research laboratory for medicinal substances quality control, National University of Pharmacy, Kharkiv, Ukraine.

Statistical analysis of the results was performed according to the State Pharmacopeia of Ukraine monograph "5.3.N.1. Statistical analysis of the results of chemical experiments" [7]. Microsoft Office Excel was used for calculations and statistical analysis of obtained data.

2.2. Method of «Dissolution» Test for Famotidine Tablets [USP 37, 2014]

Dissolution medium: 0.1 M phosphate buffer; prepared by dissolving 13.6 g of monobasic potassium phosphate in 1 L of water, adjusted with phosphoric acid to pH 4.5.

Volume of dissolution medium: 900 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Determine the amount of famotidine ($C_8H_{15}N_7O_2S_3$) dissolved employing UV-spectrophotometric method [9].

2.3. Spectrophotometric Method of Determination

Standard solution: Famotidine RS is prepared in the Dissolution medium in a concentration similar to the one expected in the sample solution (0.022 mg/ml).

Sample solution: A portion of the sample under test was passed through a suitable filter, and diluted with the Dissolution Medium if it necessary. Concentration of famotidine in the sample solution is 0.022 mg/ml.

Determination: UV-spectrophotometry at the wavelength of maximum absorbance at about 265±2 nm.

Tolerances: Not less than 75% (Q) of the labeled amount of famotidine ($C_8H_{15}N_7O_2S_3$) is dissolved [9].

2.4. Calculation Formula

Calculate the amount of famotidine dissolved by the formula [9]:

$$Result = \frac{r_u \cdot C_s \cdot V \cdot 100}{r_s \cdot L},$$

r_u – absorption from the Sample solution;

r_s – absorption from the Standard solution;

C_s – concentration of Famotidine RS in the Standard solution (mg/ml);

L – label claim, mg/Tablet (20 mg);

V – volume of Dissolution medium, 900 ml.

2.5. Verification Procedure

Specificity, accuracy, precision as well as linearity were studied in model mixtures of the series of samples containing the known amounts of active substances and excipients. The investigation was carried out in application range of 50%-130% method with 10% increments. Absorbance was measured three times with the cell removed. The average value was used for the results calculation [3, 7, 9].

3. Results and Discussion

"Dissolution" test is one of the important pharmaco-technological tests for solid finished dosage forms. It allows verifying the completeness of the release of active substance from the dosage form at application. It is essential that pharmaceutical producers were assured of proper quality of products, which provide an effective of patients' treatment. Conditions of the stomach (temperature, pH, etc.) are simulating in vitro for carrying out of this test [4].

First of all, total uncertainty should be calculated for each verifying test. It should to confirm insignificant of the sample preparation error as well as the error of the total test.

The projected total uncertainty of results of "Dissolution" test for famotidine tablets for spectrophotometric procedure (Table 1) is 1.12% and does not exceed the critical value (3.00%) [7], which is insignificant. Therefore, verified method can be used in laboratories for quality control for medical products in Ukraine in the proposed conditions.

Defining the parameters of specificity for the verified method of "Dissolution" test is necessary to confirm that the error introduced by excipients in the determination of active substance is not significant. For the spectrophotometric method of determining the error is:

$$\delta_{esc} = \frac{100 \cdot 0.005}{0.7043} = 0.71\% \leq 0.32 \cdot 3.0 = 0.96\%$$

Thus, the determination method is specific and can be used to determine famotidine at carrying out the "Dissolution" test for famotidine tablets.

Table 1. *The prognosis of the total uncertainty of results of test "Dissolution" method.*

№	Operation of the sample preparation	Uncertainty of the operation	The value of the operation	The value of the uncertainty of the operation, %
Preparation of the standard solution				
1	Weighing on the analytical balances, mg	0.2 mg	55.0 mg	0.36 %
2	Dilution in the volumetric flask, 50.0 ml	-	50.0 ml	0.17 %
3	Sampling aliquots by pipette, 2.0 ml	-	2.0 ml	0.57 %
4	Dilution in the volumetric flask, 100.0 ml	-	100.0 ml	0.12 %
Preparation of the sample solution				
5	Taking the volume of with a graduated cylinder, 1000 ml	-	1000.0 ml	0.5 %
6	Sampling aliquots by pipette, 20.0 ml	-	20.0 ml	0.18%
The uncertainty of the sample preparation: $\Delta_{SP} = \sqrt{0.36^2 + 0.17^2 + 0.57^2 + 0.12^2 + 0.5^2 + 0.18^2} = 0.88\%$				
The total uncertainty of results for the spectrophotometric measurement: $\Delta_{AS} = \sqrt{\Delta_{SP}^2 + \Delta_{FAO}^2} = \sqrt{0.88^2 + 0.70^2} = 1.12\% \leq max\Delta_{AS} = 3.0\%$				

Table 2. *Eligibility criteria of metrological characteristics.*

Eligibility criteria	Critical values, %
Content tolerances, Q	75 %
Critical value of the total uncertainty, max Δ_{AS}	3.0 %
Systematic error, δ_{max}	0.96 %
Critical value of the relative standard deviation, RSD_0	1.58 %
The correlation coefficient, min R_0	0.9987
Critical practically insignificant value of free member, a_{max}	1.92

Graph (Fig. 1) confirms the linear dependence for determination method. The calculation of the linear dependence for famotidine was performed by the least squares method. According to Table 3, the parameters of linear dependence correspond to the requirements, confirming the linearity of the verified method.

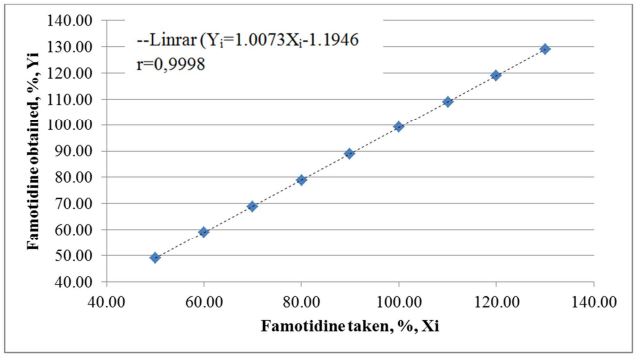

Figure 1. *The plot of linear dependence of absorbance on the concentration of famotidine in the normalized coordinates Yi = b*Xi + a.*

Table 3. *The metrological characteristics of linear dependence for famotidine.*

Parameter	Value	Criterion, n = 9	Conclusion
b	1.0015	-	-
S_b	0.0071	-	-
a	|-1.1877|	1) $\leq 1.8946 \cdot S_a = 1.1409$ 2) if not executed 1), then ≤ 2.60	corresponds
S_a	0.6670	-	-
S_o	0.5518	-	-
r	0.9998	≥ 0.9987	corresponds

The criterion of practical uncertainty for systematic error was 0.69%, executed at δ, % = 0.69≤0.96. This data characterize the accuracy of the procedure in the range of applying the 50%-130% method.

This method is characterized by convergence, as the relative confidence interval, Δ_Z, %=t (95%, 8)·S_z = 1.6616 are below the critical value for convergence of results 3.00% (Table 4) [7].

Thus, obtained in the study results confirm the specificity, linearity, accuracy as well as convergence for "Dissolution" test for famotidine tablets. The total uncertainty for verified method is not more than 3.00%. Given method can be used for analysis of solid finished dosage forms with famotidine in laboratories for quality control for medical products in Ukraine.

4. Conclusions

1. Verification of the "Dissolution" test for famotidine tablets with UV-spectrophotometry determination was carried out.
2. The researched validation characteristics confirmed specificity, linearity, convergence, as well as the accuracy of the verified method.
3. The calculation of total uncertainty of the verified method meets the eligibility criteria, which confirms the possibility of using this method in other laboratories.
4. "Dissolution" test with UV-spectrophotometric determination for famotidine tablets is correct and could be included into the first supplement of the second edition of the State Pharmacopeia of Ukraine.

Table 4. *The results of famotidine model mixtures analysis.*

№	Aliquot, ml	Introduced to nominal amount, (X_i, %)	Absorbance, A_i	Obtained for the nominal volume (Y_i, %)	Obtained in % to introduced $Zi = 100 \cdot \frac{Yi}{Xi}$
1	0.50	50	0.3328	50.25	100.50
2	0.60	60	0.3873	58.49	97.48
3	0.70	70	0.4566	68.94	98.49
4	0.80	80	0.5257	79.38	99.23
5	0.90	90	0.5920	89.39	99.32
6	1.00	100	0.6584	99.43	99.43
7	1.10	110	0.7250	109.48	99.53
8	1.20	120	0.7920	119.59	99.66
9	1.30	130	0.8625	130.25	100.19
Average value, Z, %					99.31
Relative standard deviation, S_Z, %					0.8936
Relative confidence interval, Δ_Z, %=t(95%,8)·S_z					1.6616
Critical values for convergence of results, Δ_{AS}, %					3.00
Systematic error, δ, %					0.69
Criterion of systematic error statistical uncertainty, δ, %					0.55
Criterion of systematic error practical uncertainty, δ, %					0.96
Overall conclusion about the method					correct

References

[1] British Pharmacopoeia 2009 / London. The Stationary Office. – 2008. – Vol. 1-4. – pp. 8826-8829.

[2] European Pharmacopoeia eighth edition. Directorate for the Quality of Medicines & HealthCare of the Council of Europe (EDQM). – 2013. – pp. 2211-2212.

[3] Gryzodub O. I., Standard procedures for the validation of methods of quality control of medicines. Kharkiv: Farmakom, 2006; 1/2, pp. 35-44.

[4] Guide 42-7.1:2014. Guidelines on Clinical Research. Drugs. Investigation of Bioavailability. Kyiv:MPHU; 2014.

[5] Ivashkin V. T., Lapina T. L., et al. Rational pharmacotherapy of diseases of the digestive system. Moscow:Literra; 2003 – 16 p.

[6] Pharmacist's protocols / edited by VP Chernykh, IA Zupanets, OM Lischyshyna – Kharkiv: Golden Pages, 2014. – 232 p.

[7] State Pharmacopoeia of Ukraine, 2nd ed., vol.1. State Enterprise "Ukrainian scientific pharmacopoeia center of quality of medicines", 2015; pp. 910-930.

[8] Unified clinical protocols of primary, secondary (specialized) medical care for peptic ulcer of the stomach and duodenum in adults. Available from: http://www.dec.gov.ua/mtd/_peptychvyrazka

[9] United States Pharmacopeia 37, 2014. – USP Convention Inc. – [Electronic version].

[10] Zupanets I. A., Chernykh V. P., Kupnovytska I. G., et al. Clinical pharmacy. Kharkiv: Golden pages; 2013. – 970 p.