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STUDYING PHARMACOTECHNOLOGICAL ASPECTS AND STABILITY OF "ORTOF-S" TABLETS

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ABSTRACT

Biopharmaceutical methods for evaluating the quality of drugs include methods for studying the kinetics of dissolution of medicinal substances from various dosage forms, especially oral solid dosage forms (tablets, granules, dragees, capsules, powders), since, often with their absorption, the dissolution rate of the active substance is much less than the speed suction, and then dissolution becomes the determining factor of bioavailability. General requirements for determining the dissolution rate were introduced in the USP XIX (1970) and are retained in subsequent editions (USP XX-XXIII). In the last XXIII edition of the United States Pharmacopeia, the quality of more than 600 oral dosage solid dosage forms is assessed by individual dissolution tests. In 1983, Dissolution was introduced in the UK pharmacopoeia (BP XIX), and in addition to the German Pharmacopoeia (DAV X 1992), in the French, Japanese and European pharmacopoeias. This indicator is widely used in regulatory documents of pharmaceutical companies. This indicator is widely used in regulatory documents of pharmaceutical companies. In 1985, the "dissolution" index was introduced in the second volume of the GF XI edition (a section of the general article "Tablets"), which allowed to more objectively evaluate the quality of solid dosage forms. To study the rate of dissolution of medicinal substances from tablets, powders, dragees, capsules and other solid dosage forms, devices such as a "rotating basket" and a "rotating blade" are used, more rarely a "rotating bulb" device. The results of research in the field of the development of tablets "ORTOF-S" are presented. Pharmacotechnological aspects were studied and the conditions and shelf life of recommended tablets were determined.

KEYWORDS: Tablets, solubility, pharmacological aspects, accelerated aging, biopharmacy.

INTRODUCTION

The prerequisite for the emergence of biopharmacy as a science has become numerous facts of therapeutic non-equivalence of the same dose of drug substance. Biological equivalence of drugs is a comparison of the bioavailability of synonymous drugs. The study of the bioavailability of drugs, drugs or their dosage forms usually begins with in vitro experiments, and ends with in vivo experiments with further research in clinical settings.[1,2,3]

Modern technologies and a variety of auxiliary substances with wide parameters of properties make it possible to vary the characteristics of medicinal substances to a considerable extent when they are formulated into medicinal forms, providing directed development of compositions and technologies for the creation of medicaments with the desired pharmacokinetic and therapeutic properties.[3,4,6]

One of the main biopharmaceutical characteristics that largely determines the bioequivalence of the drug is considered the solubility of the drug substance, which determines the possibility of creating a dosage form with an effective dose of the drug, the kinetics of its release from the dosage form, speed and completeness of absorption. The dissolution test in in vitro experiments is an important tool for characterizing the biopharmaceutical quality of drugs.[2,4]

Stability is one of the most important characteristics of the drug. The medical industry enterprise must guarantee the maintenance of the therapeutic dose of the active substance in dosage forms for a certain period. This is reflected in the FS or FSP. Stability (sustainability) of medicinal substances and its quality are closely related. The study of the stability of drugs depending on various factors, the establishment of the shelf life of medicinal substances is one of the most important problems, which are solved by specialists in various fields of pharmacy. Under the influence of external factors, changes in physical properties and chemical composition can occur in medicinal preparations, which in turn affects their stability and therapeutic effectiveness. One of the main problems of modern pharmaceutical technology is the development of dosage forms convenient to use, stable during storage.[5,6,7,8]

The physical state of the substance, the storage temperature, the surrounding atmosphere, light, packaging, the method of preparation, the selection of auxiliary substances, etc., are of

great influence on the stability of dosage forms. The study of the shelf life of dosage forms is one of the main and final stages in the development of drug technology.[5,9,10]

The purpose of this stage of the work was to determine the release rate of the active substances from the tablets "ORTOF-S" by in vitro method, also to determine the storage conditions and establish the shelf life of the recommended tablets.

MATERIALS AND METHODS

The materials of the study was the tablets "ORTOF-S" obtained by our recommended composition and technology. The main way to evaluate the biopharmaceutical properties of drugs in experiments in vitro is the "Rotating basket" method included in GF XI. Therefore, to determine the release rate of the active substance from the recommended tablets, the experiments were carried out by this method. It should be noted that various factors influence the release rate of the active substance: the auxiliary substances used, the volume and pH of the dissolving medium, the rotational speed of the basket.

Solvent media with different pH values were used to select the optimal pH of the dissolving medium. As neutral - purified water, acidic - 0.1 N solution of hydrochloric acid and alkaline - 0.1 N sodium hydroxide solution. In experiments, the volume of the dissolution medium was standard - 1000 ml. This volume was established, taking into account the sensitivity of our method of quantitative determination of active substances in tablets "ORTOF-S".

To study the stability, the experiments were carried out by the method of ordinary storage and by the method of "accelerated aging" according to the time instruction I-42-2-82 at a temperature of 60°C. Of the physical factors, the greatest influence on the stability of drugs is temperature, light and humidity. The first stage of the study was the study of physic-chemical, qualitative and quantitative parameters of the initial samples of tablets. At the same time, qualitative indicators such as external appearance, average mass and deviation from the average mass, solubility, disintegration, abrasion, humidity, microbiological purity, quantitative content of the active substance were evaluated.

All listed indicators were determined according to GF XI. At the next stage of the experiment, the tablets were packaged in the following 4 types of packaging approved for use in medicine: jars of colorless glass (TU-64-228-84) with screw-on plastic caps and gasket (TU-64-2-250-75); jars of orange glass (OST 64-2-71-8) with screwed plastic covers and

gasket (TU 64-2-250-75), contour - without a cellular package made of laminated paper with polyethylene coating according to TU13-7308001-477-85 , contour-cell packaging made of polyvinyl chloride film of EP-73 grade and aluminum lacquered foil (TU 48-21-270-78).

RESULTS AND DISCUSSION

Figure 4.1. The results of the study of the effect of the pH of the dissolution medium on the dissolution rate of GLS tablets are presented.

Based on the results obtained to study the effect of pH of the medium on the rate of dissolution of “ORTOF-S” tablets for further studies, we recommended the use of a neutral medium - purified water.

In experiments, in the development of the "dissolution" test, the study to determine the optimum rotation speed of the basket was carried out at 50, 100, 150 and 200 rpm. **Figures 1, 2, 3** and **4** show the results of the experiment. From the results obtained, it can be seen that the release of active substances from tablets “ORTOF-S” at different rotation speeds of the basket is intense.

It should be noted that at a basket rotation speed of 100 rpm the concentration of active substances passed into the solution in 45 minutes is more than 75%, which meets the requirements of GF XI. In such conditions, the kinetics of the release of the active substance by the first-order equation is observed. Proceeding from the foregoing, in order to further study the quality of the finished product from the biopharmaceutical point of view, a basket rotation speed of 100 rpm is recommended.

Thus, based on the results obtained to study the effect of pH of the medium on the dissolution rate of ORTOF-S tablets, the use of a neutral medium is recommended for further studies, water is purified, and a basket rotation speed of 100 rpm is recommended for further study of the quality of finished products.

Stability of drugs largely depends on the chemical composition and properties of the packaging material. When investigating the use of a packaging material, preliminary physical, chemical and biological testing is necessary. Especially high requirements are imposed on packaging materials intended for storage of medicinal products. Of great importance is not only the stability of the packaging material, but also its ability to protect medicines from the effects of temperature, light, and humidity of the environment. Therefore,

after studying the stability of the packaging material, the stability of samples of drugs or dosage forms placed in the same package is examined. On the basis of this, the expiration dates of the medicinal products in the respective packaging are established. Packaged in different types of packaging tablet "ORTOF-S" after the experiment met the requirements for tablets. For example, the appearance of the tablets did not change over 3 years of the study, the deviations from the average mass were up to 3.95%, the disintegration was 8 to 11 minutes, the abrasion strength 98.5 to 99.5%, the fracture strength of 60- 70H, and the quantitative content of the active substance was in the range from 98.7-101.2%.

Thus, the recommended composition and technology for the preparation of ORTOF-S tablets, as well as the types of packaging used, ensure the stability of the tablets for 3 years, both in studies using the "accelerated aging" method and during storage under normal conditions.

Table and figure titles and legends

Table 1: Stability and indices of “Ortof-S” tablets are natural at 22±20°C learning outcomes.

Table 2: Stability of the “Ortof-S” tablet and its acceleration to “accelerated depreciation” at 60°C learning results.

Fig. 1: The release of diclofenac sodium from tablets "ORTOF-S".

Fig. 2: The release of omeprazole from tablets "ORTOF-S".

Fig. 3: The results of studying the influence of the basket rotation speed on the intensity of diclofenac sodium release from tablets “ORTOF-S”.

Fig. 4: The results of studying the effect of the rotation speed of the basket on the intensity of omeprazole release from tablets “ORTOF-S”.

Table 1: Stability and indices of "Ortof-S" tablets are natural at 22 ± 20°C learning outcomes.

Detected indicators		Period of storage, days	Type of packet			
			colorless bottle with plastic lid (TU-64-2-250-75) (TU-64-228-84)	flame glass with plastic lid (TU-64-2-250-75) (OST 64-2-71-8)	stainless steel polyethylene laminated paper TU13-7308001-477-85	polyurethane polyurethane polyurethane (EP-73) and aluminum foil (TU 48-21-270-78)
Appearance		Primary sample	White or light creamy, all tablets on the edges	White or light creamy, all tablets on the edges	White or light creamy, all tablets on the edges	White or light creamy, all tablets on the edges
Average weight and pinch,%		#	0,299±3,7	0,301±3,3	0,299±3,4	0,301±4,6
Rivalry, min		#	8,40	9,00	10,03	9,10
Hardness of fracture, N		#	65,00	55,60	57,50	49,10
Hardness hardness,%		#	97,89	98,05	97,78	98,59
Amount of the active substance,%	D	#	99,89	99,56	99,68	98,98
	O	#	99,15	99,70	99,59	98,95
Dissolution,%		#	91,12	90,65	97,11	97,30
Appearance		6 months	Did not change	Did not change	Did not change	Did not change
Average weight and pinch,%		#	0,299±4,0	0,296±4,2	0,299±4,1	0,300±3,9
Rivalry, min		#	9,10	9,45	9,02	9,15
Hardness of fracture, N		#	51,8	49,2	56,5	51,7
Hardness hardness,%		#	97,15	98,78	97,80	99,10
Amount of the active substance,%	D	#	99,58	99,88	99,99	99,95
	O	#	98,99	99,67	98,99	98,95
Dissolution,%		#	90,83	94,55	90,16	90,56
Appearance		12 months	Did not change	Did not change	Did not change	Did not change
Average weight and pinch,%		#	0,301±3,4	0,299±3,8	0,298±4,7	0,301±4,1
Rivalry, min		#	9,05	9,55	8,28	9,45
Hardness of fracture, N		#	58,1	56,3	55,5	49,5
Hardness hardness,%		#	97,57	97,45	97,43	98,05
Amount of the active substance,%	D	#	99,78	99,65	99,54	99,20
	O	#	99,45	99,69	99,66	99,54
Dissolution,%		#	91,45	90,32	93,00	94,72
Appearance		18 months	Did not change	Did not change	Did not change	Did not change
Average weight and pinch,%		#	0,299±4,1	0,298±3,5	0,299±3,3	0,299±3,3
Rivalry, min		#	8,89	9,00	9,35	9,05
Hardness of fracture, N		#	50,9	50,7	49,3	45,9
Hardness hardness,%		#	98,61	97,56	98,37	98,07

Amount of the active substance,%	D	#	99,92	98,98	99,90	99,58
	O	#	98,98	99,67	99,09	99,12
Dissolution,%			85,32	90,77	94,38	92,39
Appearance		30 months	Did not change	Did not change	Did not change	Did not change
Average weight and pinch,%		#	0,299±4,1	0,297±3,5	0,297±3,5	0,300±3,2
Rivalry, min		#	9,00	9,35	9,55	10,05
Hardness of fracture, N		#	55,3	53,0	4898	53,9
Hardness hardness,%		#	97,63	97,63	97,88	97,09
Amount of the active substance,%	D	#	99,35	99,38	99,84	98,99
	O	#	98,98	99,08	99,45	99,34
Dissolution,%		#	99,15	92,67	93,05	92,38
Appearance		36 months	Did not change	Did not change	Did not change	Did not change
Average weight and pinch,%		#	0,299±3,7	0,298±3,6	0,296±3,2	0,301±3,4
Rivalry, min		#	9,35	9,25	9,51	10,05
Hardness of fracture, N		#	53,5	52,9	59,0	55,9
Hardness hardness,%		#	99,63	98,17	98,55	99,83
Amount of the active substance,%	D	#	98,99	99,48	99,78	99,49
	O	#	99,45	99,43	98,37	99,03
Dissolution,%		#	91,34	91,00	90,55	91,28

Table 2: Stability of the “Ortof-S” tablet and its acceleration to "accelerated depreciation" at 60°C learning results.

Detected indicators		**Period of storage, days**	**Type of packet**			
			colorless bottle with plastic lid (TU-64-2-250-75) (TU-64-228-84)	**flame glass with plastic lid (TU-64-2-250-75) (OST 64-2-71-8)**	**stainless steel polyethylene laminated paper TU13-7308001-477-85**	**polyurethane polyurethane polyurethane (EP-73) and aluminum foil (TU 48-21-270-78)**
Appearance		Primary sample	White or light creamy, all tablets on the edges	White or light creamy, all tablets on the edges	White or light creamy, all tablets on the edges	White or light creamy, all tablets on the edges
Average weight and pinch,%		#	0,298±4,5	0,299±4,7	0,301±4,4	0,303±3,6
Rivalry, min		#	9,40	9,15	9,50	9,10
Hardness of fracture, N		#	55,00	50,60	53,50	47,10
Hardness hardness,%		#	98,54	99,05	98,78	99,60
Amount of the active substance,%	D	#	99,34	99,56	98,68	99,98
	O	#	98,98	99,11	98,99	98,98
Dissolution,%		#	90,18	94,45	96,78	95,79

Appearance		46 days	Did not change	Did not change	Did not change	Did not change
Average weight and pinch,%		#	0,304±4,5	0,295±3,5	0,298±3,9	0,297±4,9
Rivalry, min		#	9,15	8,45	9,22	8,40
Hardness of fracture, N		#	51,85	49,28	56,51	61,36
Hardness hardness,%		#	98,35	97,78	98,80	97,10
Amount of the active substance,%	D	#	99,56	99,76	99,60	98,95
	O	#	98,94	98,68	99,65	98,99
Dissolution,%		#	91,83	84,55	92,11	94,56
Appearance		92 days	Did not change	Did not change	Did not change	Did not change
Average weight and pinch,%		#	0,300±3,5	0,298±3,3	0,298±4,7	0,302±5,1
Rivalry, min		#	9,00	8,55	9,20	8,67
Hardness of fracture, N		#	48,9	54,3	51,5	49,5
Hardness hardness,%		#	97,56	98,92	99,43	99,00
Amount of the active substance,%	D	#	98,69	99,25	100,58	99,26
	O	#	98,65	99,77	99,78	99,21
Dissolution,%		#	90,24	94,22	94,00	93,71
Appearance		138 days	Did not change	Did not change	Did not change	Did not change
Average weight and pinch,%		#	0,299±3,6	0,298±3,9	0,297±3,9	0,296±4,3
Rivalry, min		#	8,56	9,10	9,35	10,05
Hardness of fracture, N		#	52,7	53,8	46,9	46,6
Hardness hardness,%		#	97,68	98,25	97,41	97,57
Amount of the active substance,%	D	#	98,96	99,28	98,99	98,56
	O	#	99,77	99,04	98,78	98,96
Dissolution,%		#	90,33	93,65	95,34	94,57
Appearance		184 days	Did not change	Did not change	Did not change	Did not change
Average weight and pinch,%		#	0,295±4,7	0,296±4,1	0,296±3,9	0,300±3,9
Rivalry, min		#	9,35	9,50	9,55	10,00
Hardness of fracture, N		#	53,7	56,1	49,8	56,6
Hardness hardness,%		#	98,67	97,77	97,57	97,89
Amount of the active substance,%	D	#	99,59	99,46	99,99	99,76
	O	#	99,44	98,99	99,00	99,22
Dissolution,%		#	89,60	90,64	91,51	90,22
Appearance		230 days	Did not change	Did not change	Did not change	Did not change
Average weight and pinch,%		#	0,295±4,7	0,296±4,1	0,296±3,9	0,300±3,9
Rivalry, min		#	9,35	9,50	9,55	10,00

Hardness of fracture, N		#	53,7	56,1	49,8	56,6
Hardness hardness,%		#	98,67	97,77	97,57	97,89
Amount of the active substance,%	D	#	99,59	99,46	99,99	99,76
	O	#	99,59	99,46	99,99	99,76
Dissolution,%		#	89,60	90,64	91,51	90,22
Appearance		276 days	Did not change	Did not change	Did not change	Did not change
Average weight and pinch,%		#	0,295±4,7	0,296±4,1	0,296±3,9	0,300±3,9
Rivalry, min		#	9,35	9,50	9,55	10,00
Hardness of fracture, N		#	53,7	56,1	49,8	56,6
Hardness hardness,%		#	98,67	97,77	97,57	97,89
Amount of the active substance,%	D	#	99,59	99,46	99,99	99,76
	O	#	98,44	99,02	89,99	99,35
Dissolution,%		#	89,60	86,64	91,51	90,22

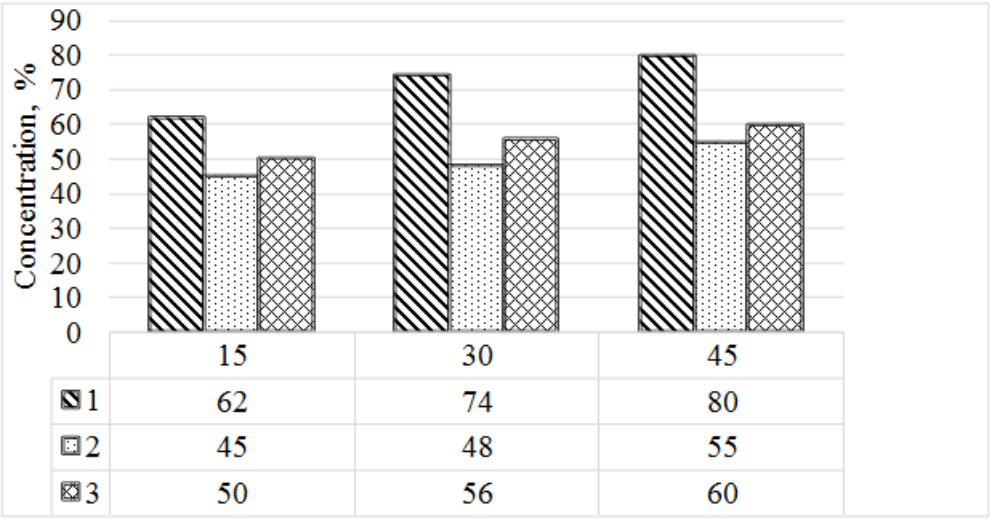

Fig. 1: The release of diclofenac sodium from tablets "ORTOF-S".

1-neutral medium (purified water)

2-acidic medium (0.1 N HCl solution)

3-alkaline medium (0.1 N NaOH solution)

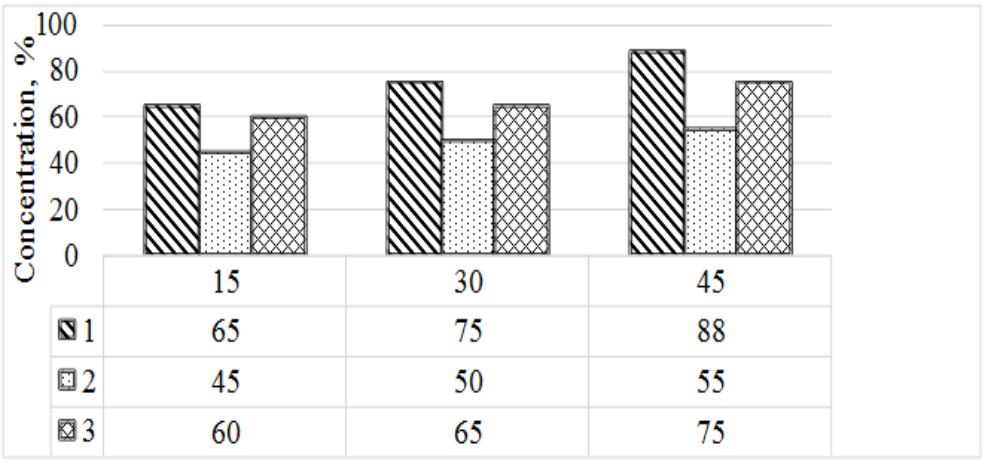

Fig. 2: The release of omeprazole from tablets "ORTOF-S".

1-neutral medium (purified water)

2-acidic medium (0.1 N HCl solution)

3-alkaline medium (0.1 N NaOH solution)

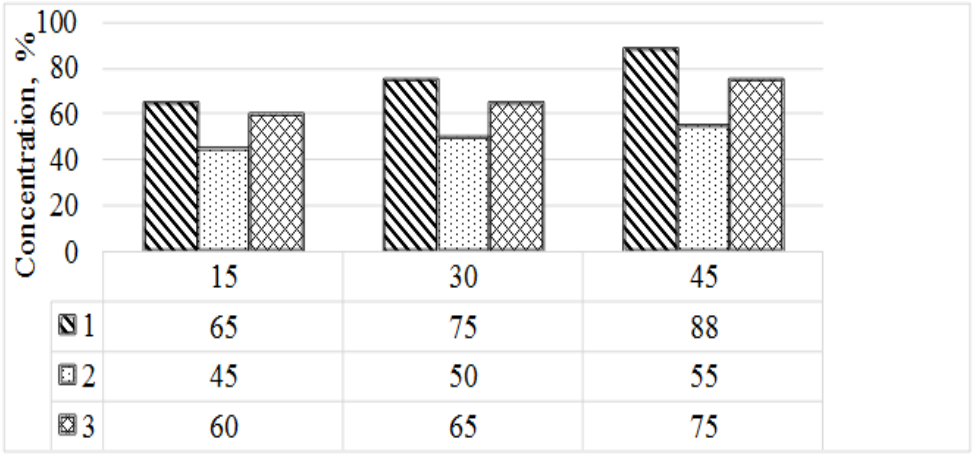

Fig. 3: The results of studying the influence of the basket rotation speed on the intensity of diclofenac sodium release from tablets “ORTOF-S”.

1-rotation speed of the basket 50 rpm

2- rotation speed of the basket 100 rpm

3- rotation speed of basket 150 rpm

4- rotation speed of the basket 200 rpm

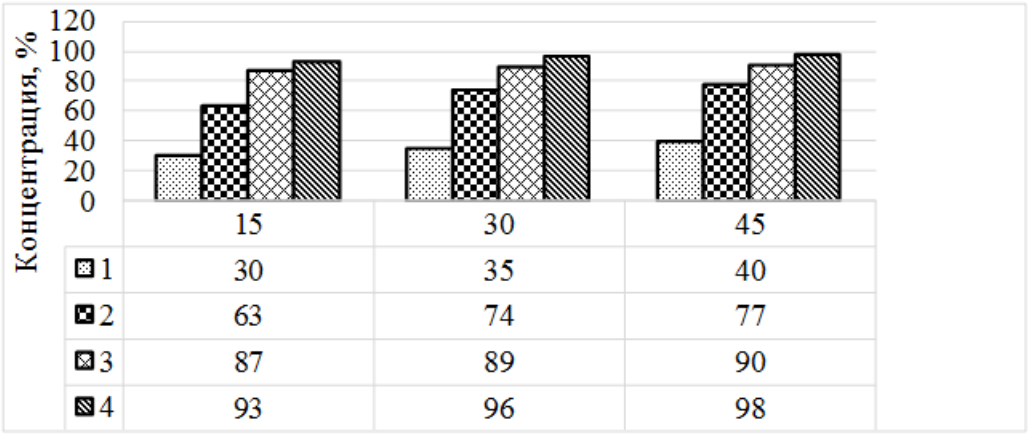

Fig. 4: The results of studying the effect of the rotation speed of the basket on the intensity of omeprazole release from tablets "ORTOF-S".

1-rotation speed of the basket 50 rpm

2- rotation speed of the basket 100 rpm

3- rotation speed of basket 150 rpm

4- rotation speed of the basket 200 rpm

CONCLUSION

1. Based on the results obtained to study the effect of pH of the medium on the dissolution rate of ORTOF-S tablets, a neutral medium, purified water, is recommended for further studies.

2. In experiments, the volume of the dissolution medium was set at 1000 ml, which was chosen taking into account the sensitivity of the method of quantitative determination of the active substances developed by us.

3. Based on the data obtained, a basket rotation speed of 100 rpm is recommended from the biopharmaceutical point of view to further investigate the quality of the finished product.

4. The types of packaging used ensure the stability of "ORTOF-S" tablets, for 3 years both in studies using the "accelerated aging" method and during storage under normal conditions.

REFERENCES

1. Azimova I.D., Teplyakova N.G., Dorofeev V.L. Dissolution test in the evaluation of generic drugs omeprazole / / Pharmacy, 2009; 1: 9-11.
2. Arzamastsev AP, Sadchikova NP, Luttseva T.Yu. Comparative evaluation of the level of requirements for the test "Dissolution" / / Chem.-Pharm. Journal-Moscow, 2003; 1: 39-45.

3. Karieva Y.Y. Yunusova, m, Comparative study of meloxicam drugs bioequi-valence Medical and Health Science Journal (Prague), 2011; 5: 112-114.
4. The current state of creation, production and research of tableted medicinal preparations. / M.M. Vasenda, N. M. Belei, M.B. Demchuk, V. Trigubchak, M.B. tore off the top, S.M. Gureeva, A. Melnik, V.Ya. Shalata, T. A. Denezhny / / Pharmaceutical Journal, 2009; 4(9): 77-80.
5. Guidelines for stability testing of pharmaceutical products containing well-established drugs. WHO Technical Report Series No. 863. Geneva, 2010.
6. Stability study and storage conditions for Piracetam-SM tablets / NB Shodieva, Kh. M. Yunusova // Proceedings of the scientific-practical conference "Integration of education, science and production in pharmacy" Tashkent, 2012; 178.
7. V. Dash, A. Kesari. // Role of Biopharmaceutical Classification System in Drug Development Program // J. Current Pharm. Res., 2011; 5(1): 28-31.
8. Smekhova I.E. Investigation of the bioequivalence of solid dosage medications // Pharmacy, 2009; 4: 38-40.
9. Setkina, S.B. Biopharmaceutical aspects of drug technology and ways to modify bioavailability / S.B. Setkina, O.M. Hishova // Bulletin of Vitebsk State Medical University, 2014; 13(4): 162-172.
10. M.S. Makieva, Yu.A. Morozov Development of quality standards, the study of stability and the establishment of expiration dates of cosmeceutical forms of the Chinese magnolia vine // Pharmacy and Pharmacology, 2015; 1(8): 95-97.