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STANDARDIZATION OF GLIGISCIN TABLETS

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Abstract---*The research work states the results of standardization and quality control of Gligiscin tablets. As it is known, the national medicine policy is aimed at reducing the dependence of Uzbekistan's health care on the import of medicines by full using of its own production capacities, raw materials and scientific and technical potential, developing at the same time its pharmaceutical and medical industry. Based on the pharmaceutical and physiological features of both Zinc and glycyrrhizic acid, a high specific hepatoprotective activity can be expected at their combination. Considering the demandfor creating a new hepatoprotective preparation based on local plant raw materials, particularly glycyrrhizic acid obtained from the Licorice root, a new coordination compound of Zinc with glycyrrhizic acid and histidine has been synthesized, which has hepatoprotective and hypolipidemic properties, conventionally named Gligiscin.* ***The aimand tasks*** *of the research and the further stage of development is to determine chemical and biological safety indicators of Gligiscin tablets in accordance with the General Technical Regulation on Medicines Safety (Annex to the Resolution of CMRUz dated 27.10.2016 for № 365).* ***Materials and methods of research****. For determination of quality indicators, the following equipment was used in the process of work: devices Erweka TBH 30and Erweka ZT 44 (Germany2004); tester for determination of solid medicines abrasion TAR 200, Erweka (Germany 2004). Besides, spectrophotometric and photocolorimetric methods were applied on thedevice UV-spectrophotometr 8453 by Agilent Technologies (Germany).****Results and their discussion****. Standardization of Gligiscin tablets considering chemical and biological safety indicators, such as: average weight and deviation from average weight, degradability, abrasion strength, fracture strength, was performed according to General Technical Regulation on Medicines Safety (Annex to Regulation of CMRUz by №365 dated 27.10.2016). The quality of the produced tablets was determined by such indicators asorganoleptic, physical, chemical, bacteriological and biological. Quality control of ready-made tablets was carried out according to the requirements of pharmacopoeia article "Tablets," as well as private pharmacopoeia articles, by the following indicators: description, authenticity, average weight and deviation from average weight, degradability, abrasion strength, fracture strength, dissolution, microbiological purity, foreignimpurities, quantitative definition.****Conclusion.*** *The standardization limits for Gligiscin tablets have been established in accordance with SP XI and SP XII. On the basis of the obtained results, a draft of standard documentation for Gligiscin tablets has been developed. The tested indicators are included into the draft of standard documentation for Gligiscin tablets.*

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Keywords---*tablets, Gligiscin, quality indicators, description, authenticity, average weight and deviation from average weight, degradability, abrasion strength, fracture strength, dissolution, microbiological purity, foreign impurities, quantitative definition, normative document.*

I. Introduction

Supplying thepopulation with effective and safe medicines is one of the main tasks of health care. Therefore, the national medicine policy of pharmaceutical and medical industry development is aimed at reducing the dependence of Uzbekistan 's health care on the import of medicines byfull using of its own production capacities, raw materials and scientific and technical potential. At the present time, taking into account Uzbekistan's rich raw materials sources, the main efforts are focused on the production of substances and ready-made medical forms made ofraw materials of plant origin.

Nowadays, among other medicinal plants, Licorice is the leading one in the number of offered and used medicinal preparations. Preparations made of Licorice root are used in medicine for the treatment of a number of autoimmune, allergic, immunodeficiency, viral, tumor, inflammatory, infectious and other diseases [1]. The high biological activity of the Licorice root is generallycaused by the presence of triterpene glycoside - glycyrrhizic acid (GA). It should be noted that although the medicinal plant raw material does not havea high toxicity, but in most cases it is generally not characterized by high biological activity. In this regard, researches aimed at the comprehensive study of the active components of Licorice root and the products of their chemical modifications obtain great relevance, in order to create new highly effective medications.

Zinc and other 3d-metals, despite of their low content in the human body, are vital, as they are considered to be important components of a number of metal-containing enzymes and in therapeutic doses have beneficial effect on the course of the most important bioprocesses in the body [2,3]. However, their use as a "plain" inorganic salt is not effective because of their relatively high toxicity and low biological activity and stability. The ability of 3d-metals to participate in complexation processes with organic molecules explains an extremely wide range of their involvement in different biological processes of the body.

In modern pharmacology intensive scientific research worksare aimed generally at searching of the medicineswhich are similar by their action mechanism to the natural compounds. For this purpose, metal coordination links with bio-ligands present awide scope for application of biometals in medicine. Complexes of Zinc with glycyrrhizic acid can serve as perspectivemedications of hepatoprotective activity; besides, the combination of bioeffects of 3d-metals and physiologically active organic ligands in many cases leads to reduction of toxicity and increase of bioactivity of metal ions, which gives total and specific biological qualities, which are not characteristic to the initial components [4]. Biocomplexes of 3d-metals, synthesized outsidethe body, unlike its constituent components, are not able to destroy metal organelles.This fact allows to use them more prospectively in medicine.

Based on the pharmaceutical and physiological features of both Zinc and GA, a high specific hepatoprotective activity can be expected at their combination in a coordination compound. Considering above stated, as well as significance of creating a new hepatoprotective preparation based on local plant raw materials, particularly glycyrrhizic acid obtained from the Licorice root, we have synthesized a new coordination compound of Zinc with glycyrrhizic acid and histidine, which has hepatoprotective and hypolipidemic properties, provisionally named Gligiscin. Based on this substance, a medicinal form of tablets has been developed.

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The aimand tasksof the present study and the further stage of development is to determine chemical and biological safety indicators of Gligiscin tablets in accordance with the General Technical Regulation on Medicines Safety (Annex to the Resolution of CMRUz dated 27.10.2016 for № 365).

II. Materials and methods of research

The following equipment was used in the process of research work:

- Determination of diameter and fracture strength of tablets, Erweka TBH 30, Germany; 2004

-Tester for determination of solid medicinesabrasion, TAR 200, Erweka, Germany; 2004

- A device for determination of degradability, Erweka ZT 44, Germany; 2004.

- Spectrophotometric and photocolorimetric method - on the device UV-spectrophotometr 8453 by Agilent Technologies (Germany).

Besides, accessory measuring devices are also used in the work: magnetic mixers, electronic scales CAS MW-II 300 Sr№0505034, by CAS Corporation(South Korea); electronic analytical scales BP-310S by Sartorius (Germany), hygrometer MV 35 Halogen OHAUS R (Switzerland), an air sterilizer HS 32 ACwith automatic equipment, pH-meters Seven Easy by Mettler Toledo (Switzerland) and 766 Calimatic Knick (Germany). Also thesolvents and reagents by MERCK (Germany) and ready-made nutrients by HIMEDIA Laboratories Pvt. Ltd" (India) were used.

As a research material, 5 experimental-industrial series of Gligiscin tablets were used.

III. Results and their discussion

In accordance with modern requirements, according to the General Technical Regulation on Medicines Safety (Annex to Regulation of CMRUz by No.365 dated 27.10.2016), we have conducteda standardization of Gligiscin tablets considering chemical and biological safety indicators, such as: average weight and deviation from average weight, degradability, abrasion strength and fracture strength.

One of the main conditions of industrial production of tablets is a conformity of ready-made products with the requirements of the current regulatory and technical documentation. The quality of the produced tablets is determined by various indicators, which are divided into the following groups:

1. Organoleptic
2. Physical
3. Chemical
4. Bacteriological
5. Biological

Determination of tablets' quality begins with evaluation of their appearance (organoleptic properties).

Chemical indicators include authenticity, dissolution, quantification and stability of chemical composition, activity of medicine substance, shelf life of tablets, their stability during storage, etc.

Bacteriological quality indicators areseeding of tablets with microorganisms, spores and bacteria of a non-pathogenic nature with a content of not more than a specified amount.

Quality control of ready-made tablets is performed according to the requirements of pharmacopoeia article "Tablets," as well as private pharmacopoeia articles by the following indicators:

1. Description
2. Authenticity

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3. Average weight and deviation from average weight
4. Degradability
5. Abrasion strength
6. Fracture strength
7. Dissolution
8. Microbiological purity
9. Foreign impurities
10. Quantitative definition

Some additional requirements for the tablet quality are stated in private pharmacopoeia articles [5-8].

Evaluation of tablets appearance

(Description) 20 tablets are viewed and a conclusion is made on its surface defects or absence. The tablet size (diameter, height) is measured by calipers, and the tablet type is determined according to the OST64-072-89, as well as color and separation matchmark

Description of Gligiscin tablets. Round flat-cylindrical tablets, of yellow color. The appearance should comply with the requirements of SP XI, edit. 2, p.154.

The results are given in the Table 1.

Table 1. Results on evaluation ofGligiscin tablet appearance

№ of series	Description of the tablets appearance in accordance with the draft of ND	Results	Conclusion
Series 1	Round flat-cylindrical tablets, of yellow color.	Complies with the requirements of SP XI, edition 2, p.154.	Meets the requirements of the ND draft
Series 2	Round flat-cylindrical tablets, of yellow color.	Complies with the requirements of SP XI, edition 2, p.154	Meets the requirements of the ND draft
Series 3	Round flat-cylindrical tablets, of yellow color.	Complies with the requirements of SP XI, edition 2, p.154	Meets the requirements of the ND draft
Series 4	Round flat-cylindrical tablets, of yellow color.	Complies with the requirements of SP XI, edition 2, p.154	Meets the requirements of the ND draft
Series 5	Round flat-cylindrical tablets, of yellow color.	Complies with the requirements of SP XI, edition 2, p.154	Meets the requirements of the ND draft

Authenticity. 1. 0.13g of grated tablets powder was placed in a conical flask with capacity 50 ml, 2 ml of sulfuric concentrated acid and 5 ml of nitric concentrated acid were added and heated on a sand bath until complete mineralization

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of the preparation. The obtainedresidue after mineralization was cooled and dissolved in 10 ml of water. The solution made characteristic reactions to Zinc (SP XI, edition 1, p.165).

2. 0.13 gr of grated tablets powder was dissolved in 10 ml of 0.25% ammonium hydroxide solution and stirred to form an abundant foam (glycyrrhizic acid).

3. 0.06 gr of grated tablets powder was dissolved in 10 ml of water, filtered. 1 ml of 10% alcohol solution of phosphoric molybdenum acid and 1 ml of concentrated sulfuric acid was addedto the filtrate, after that a dirty violet coloration with a blue tint (glycyrrhizic acid) appeared.

4. Solution A prepared for quantified determination of histidine with water solution of ninhydrin in an equal proportionat heatingon a boiling water bath gives a specific blue-violet coloration (histidine).

The results of the five series of Gligiscin tablets by the indicator "Authenticity" complies the requirements of the draft of normative document.

The average weigh tand deviations from average weight

The average weight should be 0.2 gr ± 7.5% (SP XI, edition 2, p.154). 20 tablets were weighed with accuracy to 0.001 grand the result was divided into 20. The weight of the separate tablets was determined by weighing 20 tablets separately to accuracy of 0.001 gr, the weight deviation of the separate tablets.

The results of five series of Gligiscin tablets are given in the Table 2.

Table 2. Results on determination of average weight and deviation **from average weight of Gligistsin tablets**

Numbers of series	Norm on the indicator“The average weight and deviations from average weight” according to ND draft	Results	Conclusion
Series 1	Should be 0,2 gr ± 7,5 % (SP XI, edit.2, p.154)	0,2044gr +5,2% -4,8%	Meets the requirements of the draft ND
Series 2	Should be 0,2 gr ± 7,5 % (SP XI, edit. 2, p.154)	0,2058gr +4,2% -5,8%	Meets the requirements of the draft ND
Series 3	Should be 0,2 gr ± 7,5 % (SP XI, edit. 2, p.154)	0,2032gr +3,2% -3,8%	Meets the requirements of the draft ND
Series 4	Should be 0,2 gr ± 7,5 % (SP XI, edit. 2, p.154)	0,2015gr +3,4% -4,1%	Meets the requirements of the draft ND
Series 5	Should be 0,2 gr ± 7,5 % (SP XI, edit. 2, p.154)	0,2022gr +2,2% -3,6%	Meets the requirements of the draft ND

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Determination of tablets degradability.

The most appropriate way to determine the tablets degradability was to observe itsproceeding in the human stomach by obtaining X-ray images. However, in the mass production of tablets, this is difficult task, that why conventional methods for determining tablet degradabilityperformed outside the human body are adopted worldwide.

Gligistsin tablets degradability. It should not exceed 15 min (SP XI, edit. 2, p.154).

The results of the five series are given in the Table 3.

Table 3. Results on Gligiscin tabletsdegradability

Numbers of series	Norm of the indicator «Degradability» according to draft ND	Results	Conclusion
Series 1	Should not exceed 15 min	5 minutes	Meets the requirements of the draft ND
Series 2	Should not exceed 15 min	6 minutes	Meets the requirements of the draft ND
Series 3	Should not exceed 15 min	6 minutes	Meets the requirements of the draft ND
Series 4	Should not exceed 15 min	7 minutes	Meets the requirements of the draft ND
Series 5	Should not exceed 15 min	8 minutes	Meets the requirements of the draft ND

Determination of abrasion strength

Mechanical strength is characterized by the degree of tablets abrasion. The abrasion is observed atpacking, packaging and transportation, being especially strengthen onfilling machines.The sign of abrasion is the formation of powdered dust on tablets and packaging. 10 tablets, dusted-free and weighed to the accuracy of 0.001 grwere placed in the drum, the lid was screwed and the device was turned on for 5 minutes, which corresponded to 100 revolutions of the drum. After the specified time, the tablets were dusted-free and their weight was determined with accuracy up to 0.001 gr. The abrasion strength of the tablets was calculated by the formula in percentage:

$$П = 100 - \frac{P_{нач.} - P_{кон.}}{P_{нач.}} \times 100$$

where Pbef., Paft were the weight of tablets before and after abrasion, respectively; in gr.

The shape of the tablets should not change during abrasion. Abrasion strength should be not less than 97%.

The results of the five series of Gligiscin tablets are given in the Table 4.

Table 4. Results on abrasion strength of Gligiscin tablet

Numbers of series	Norm of the indicator «Abrasion» according to draft ND	Results	Conclusion
Series 1	Should be not less than 97%.	99,7%	Meets the requirements of the draft

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			ND
Series 2	Should be not less than 97%.	99,4%	Meets the requirements of the draft ND
Series 3	Should be not less than 97%.	99,6%	Meets the requirements of the draft ND
Series 4	Should be not less than 97%.	99,5%	Meets the requirements of the draft ND
Series 5	Should be not less than 97%.	99,4%	Meets the requirements of the draft ND

Determination of fracture strength

The test determines the pressure resistance of tablets under certain conditions by measuring the strength required to crash the tablets. Determination and rationalization of the mechanical strength of tablets is necessary both in industrial production conditions (e.g. tablet coating process and packaging) and to ensure the consumer properties of the preparation (preserving the integrity of the tablet when removed from the package).

The device consists of two opposite clamps, one of which moves towards the other. Planes of clamps surfaces are perpendicular to direction of movement. The compressing surfaces of the clamps should be flat and larger than the contact area with the tablet. The device shouldstop compressionin case of any violation of tablet integrity.

The tablet was placed between the clamps by a rib in relation to the moving part of the device. The tablet placed on the rib was compressed to disintegration. Measurements were made for 10 tablets. Before each measurement, all fragments of the previous tablet were carefully removed. Tests were carried out five times on five series of Gligiscin tablets, at the same time the norm - not less than 30 H - was experimentally established.

The results are given in the Table 5.

Table 5. Results on determination of fracture strength of Gligiscin tablets

Numbers of series	Norm of the indicator «Fracture strength» according to draft ND	Results	Conclusion
Series 1	Should be not less than 30 H	38 H	Meets the requirements of the draft ND
Series 2	Should be not less than 30 H	40H	Meets the requirements of the draft ND
Series 3	Should be not less than 30 H	42H	Meets the requirements of the draft ND
Series 4	Should be not less than 30 H	44H	Meets the requirements of the draft ND
Series 5		40H	Meets the requirements of the draft ND

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Dissolution

The tests werecarried out in accordance with the requirements of SP XI, edit. 2, p.154. The device of "Rotating basket" type was used. Dissolution medium - pure water, volume - 900 ml, rotation speed -100 rpm, dissolution time -45 minutes. A tablet was placed into the basket. After 45 minutes, the solution was filtered; discarding the first 20 ml of filtrate, 10 ml of sample solution was taken, which was filtered through a paper filter (GOST 1206-76) or through Millipor with a pore diameter of 0.45 mcm. The optical density of the solution was measured on a spectrophotometer at a wavelength of 258±2 nm in a cuvette with a layer thickness of 1 nm. Water was used as a comparison solution.

At the same time optical density of standard Gligiscin solution was measured. Content of gligiscin transferred into solution was calculated by formula:

$$X = \frac{D * a_{st} * 900 * 100\%}{D_{st} * a * 100} = \frac{D * a_{st} * 900}{D_{st} * a}$$

D - Optical density of testing solution, nm;

D_{st} - Optical density of WSS solution,nm;

a - Content of Gligiscin ina tablet, g;

a_{st} - Sample weight with WSS , in g;

Not less than 75% ofGligiscin should transfer to the solution after 45 minutes.

Note. Preparation of working standard sample (WSS) of Gligiscin: 0,015 g of Gligiscin WSS was dissolved in water in a flask with capacity 100 ml, the volume was dissolved to the mark with water and stirred.

Microbiological purity

The tests were carried out by an agar two-layer method in Petri dishes with a diameter of 90-100 mm. The substance in aamountof 10 gr was suspended in a phosphate buffer solution pH 7.0 so that the final volume of the solution was 100 ml. To determine the total number of bacteria, the prepared suspension was added by 1 ml to every of two test tubes with 4 ml of medium No. 1, melted and cooled to the temperature 45 ºC. Then it was quicklystirred and transferred to thePetri dish containing 20 ml of frozen growth medium № 1, at the same time evenly spreading the top layer of agar. After solidification of the medium, the dishes were turned over and incubated during 5 days at temperature of 30-35 ºC. Inoculations were looked through daily. After 5 days, the number of bacterial colonies in two dishes was counted, the average value was found, and multiplying it by the dilution index, the number of bacteria in 1 gr of the sample was counted.

For determination of the total number of fungi, the similar tests were carried out by theagar two-layer method using medium № 2. The inoculations were incubated for 5 days at 20-25 ºC andlooked through daily. After 5 days, the total number of yeast and mold fungi colonies in two dishes was counted, the average value was found, and multiplying it by the dilution index,the number of fungi in 1 g of the sample was counted.

To detect enterobacteriaceae, the sample was transferred to 100 ml of growth medium № 3, stirred and incubated at 30-35 ºC for 48 hours. In comparison with the control sample, no gas bubbles release and dreg formation were visually

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detected. Considering this fact, further identification and subculture of loops to the media № 4 and № 5 were not carried out.

For determination of Pseudomonas aeruginosa, Staphylococcus aureus, the sample was added to 100 ml of growth medium № 8, stirred and incubated at 30-35 ºC for 48h. No turbidity and change in the medium colorwas detected visually,in comparison to the control sample, that indicated about the growth absence. Therefore, no further loops subculture was carried out to the media № 9 and № 10.

Experimentally obtained results for 5 series of Gligiscin substance are shown in the table below.

Table 6

№	Indicators	Norm by ND (BP/EP)	Tests results				
			series 1	series 2	series 3	series 4	series 5
1	The total number of aerobic bacteria, in 1g	Not more than 1000	20 CFU	30 CFU	50 CFU	Less than 10 CFU	Less than 10 CFU
2	Total number of fungi, in 1 g	Not more than 100	Less than 10 CFU	Less than 10 CFU	Less than 10 CFU	Less than 10 CFU	Less than 10 CFU
3	Enterobacteria, in 1 g	Should be absent	absent	absent	absent	absent	absent
4	Pseudomonas aeruginosa, Staphylococcus aureus, in1g	Should be absent	absent	absent	absent	absent	absent

On the basis of the experimental data obtained, it is obvious that the samples of 5 series of Gligiscin tablets comply with SP XII standards.

Foreign impurities. *1. Free histidine*.

5 mcl of the test and standard solutions were applied on the start line of the chromatographic plate silica gel GF 254. The plate was dried up on air and put in previously sated camera with combination of solvents iced acetic acid - water - butanol in proportion 20:20:60. When the solvent front was 15 cm high, the plate was removed and dried in air. Then it was sprayed with ninhydrin solution and heated at 100-105 ºC within 15 min. Any spot obtained on thechromatogram of the testing solution should not be more intensivethan spots obtained on the chromatogram of the standard solution (0.5%).

Preparation of the test solution 0.133g of the medication was stirred with 10 ml of water for 1 minute, centrifuged at 5000 rpm for 5 minutes, and the clear solution was separated.

Preparation of the standard histidine solution 0.013g of the standard histidine sample was dissolved in 10 ml of water. 2.5 ml of the resulting solution was diluted to 50 ml with water.

2. Free glycyrrhizic acid.

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5 mcl of the tested and standard solutions were applied on the start line of the chromatography plate "Silufol UV-254". The plate was air-dried and placed in a pre-saturated chamber with solvent mixture of chloroform-methanol-water in proportion of 30:17: 3. When the solvent front passed 11 sm high, the plate was removed and dried in air. Then sprayed with phosphoric molybdenum acid solution. The peculiar zones should appear as a blue spot on a yellowish background. The quality of the chromatogram was improved by chromatography at 20-25 ºC and heating the plate to 40 ºC. Any spot or spots obtained on the chromatogram of the test solution should not be more intensive than the spot obtained on the chromatogram of the standard solution (0.5%).

Preparation of the test solution. 0.133 g of the medication was stirred with 10 ml of ethyl alcohol for a minute, then filtered through a filter paper.

Preparation of standard glycyrrhizic acid solution. 0, 013g of the standard glycyrrhizic acid sample was dissolved in 10 ml of ethyl alcohol. 2.5 ml of the resulting solution was diluted with alcohol to 50 ml.

Table 7. Results of analysis on the foreign impurities content

№ of series	№	Glycyrrhizic acid	Histidine
1.1	1	Not more than 0,5 %	Not more than 0,5 %
	2	Not more than 0,5 %	Not more than 0,5 %
	3	Not more than 0,5 %	Not more than 0,5 %
	4	Not more than 0,5 %	Not more than 0,5 %
	5	Not more than 0,5 %	Not more than 0,5 %
1.2	1	Not more than 0,5 %	Not more than 0,5 %
	2	Not more than 0,5 %	Not more than 0,5 %
	3	Not more than 0,5 %	Not more than 0,5 %
	4	Not more than 0,5 %	Not more than 0,5 %
	5	Not more than 0,5 %	Not more than 0,5 %
1.3	1	Not more than 0,5 %	Not more than 0,5 %
	2	Not more than 0,5 %	Not more than 0,5 %
	3	Not more than 0,5 %	Not more than 0,5 %
	4	Not more than 0,5 %	Not more than 0,5 %
	5	Not more than 0,5 %	Not more than 0,5 %
1.4	1	Not more than 0,5 %	Not more than 0,5 %
	2	Not more than 0,5 %	Not more than 0,5 %
	3	Not more than 0,5 %	Not more than 0,5 %
	4	Not more than 0,5 %	Not more than 0,5 %
	5	Not more than 0,5 %	Not more than 0,5 %

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1.5	1	Not more than 0,5 %	Not more than 0,5 %
	2	Not more than 0,5 %	Not more than 0,5 %
	3	Not more than 0,5 %	Not more than 0,5 %
	4	Not more than 0,5 %	Not more than 0,5 %
	5	Not more than 0,5 %	Not more than 0,5 %

Quantitative definition.

1. About 0.66g (exact sample weight) of the grated tablets were placed in a conical flask with capacity 250 ml, adding 100 ml of water, 10 ml of ammonia buffer solution and 0.1 g of eriochrome black indicator mixture. Then it was titrated with 0.05 mol/L by Trilon-B solution from dark cherry to green coloring.

The Zinc content of the tablets (X) is calculated by the formula:

$$X = \frac{V*M*65,38*Rob}{a*1000}$$

where V – is the volume of solution, used for titration of the sample weight, in ml;

M – molarity of titrated Trilon-B solution;

65,38 – Zinc atomic mass;

a – sample weight of the test sample in g;

Rob - average weight of the tablet

The Zinc content in the tablets should be from 0.0066g to 0.0081g.

2. About 0.026 g (exact sample weight) of the grated tablet powder was dissolved in 15 ml of 50% ethyl alcohol with 2-3 drops of concentrated hydrochloric acid in a measuring flask with capacity 25 ml, and the volume of solution was adjusted to the mark with the same solvent (solution A).

1 ml of the solution A was transferred to the measuring flask with capacity 25 ml and the volume solution was adjusted to the mark by 50% ethyl alcohol, then stirred (solution B). The optical density of the solution B was measured on a spectrophotometer at a wavelength of 251$\pm$2 nm in a cuvette with a layer thickness of 10 mm. 50% ethyl alcohol was used as a comparison solution. At the same time optical density of the standard glycyrrhizic acid solution was measured.

The content of Glycyrrhizic acid in tablets (X) is calculated by the formula:

$$X = \frac{D*a_{st}*Rob}{D_{st}*a}$$

where D - optical density of the test solution, nm;

Dst - optical densityof the standard solution, nm;

a - sample weight of the medication in g;

a_{st} - sample weight of standard, in g;

Rob- average weight of the tablet

The content of glycyrrhizic acid in the tablets should be from 0.0887g to 0.09345g.

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Preparation of standard glycyrrhizic acid solution. About 0.02g (exact sample weight) of glycyrrhizic acid was dissolved in 15 ml of 50% ethyl alcohol with 2-3 drops of concentrated hydrochloric acid in a measuring flask with capacity 25 ml and the volume of the solution was adjusted to the mark with the same solvent. 1 ml of the resulting solution was transferred to themeasuring flask with capacity 25 ml and the volume of the solution was adjusted to the mark by 50% ethyl alcohol.

3. About 0.066g (exact sample weight) of the grated tablets were dissolved in 20 ml of 50% ethyl alcohol with 2-3 drops of concentrated hydrochloric acid in a measuring flask with capacity 50 ml, adding 1 ml of 10% NaOH to pH 6.0-7.0, and the volume of the solution was adjusted to mark with water (solution A). 5.0 ml of the resulting solution A was transferred to themeasuring flask with capacity 25 ml, adding 5 ml of ninhydrin solution and heatingon a boiling water bath for 10 minutes; then it was cooled and the volume of the solution was adjusted with water to the mark.At once the optical density of the test solution was measured on the spectrophotometer at 568±2 nm in a cuvette of 10 mm thickness. Water was used as the comparison solution. The optical density of the standard histidine solution was measured at the same time.

The content of histidine (X) in the tablets was calculated by the formula:

$$X = \frac{D^{*}ast^{*} Rob}{D_{st}{*}a}$$

where D - optical density of the test solution, nm;

Dst - optical density of the standard solution, nm;

a - sample weight of medication, in g;

a_{st} - sample weight of standard, in g;

Rob- average weight of the tablet

The content of histidine in the preparation should range from0.0334g to 0.0364g.

Preparation of the standard histidine solution. About 0.012 g (exact sample weight) of base histidine by Merck (Germany) was dissolved in 30 ml of water in a measuring flask with capacity 50.0 ml and the volume of the solution was adjusted to the mark with water. 5.0 ml of the resulting solution was transferred to a measuring flask with a capacity of 25.0 ml, and thenthe preparation of the test solution was made starting with the words "addition of 5 ml of ninhydrin solution."(see information stated above).

Results on the quantitative content of active substances in Gligiscin tablets comply with the requirements of the draft of normative documentation.

IV. Conclusions

On the basis of the experimental studies carried out and stated above, the quality parameters of Gligiscin tablets were determined according to the indicators: description, authenticity, average weight and deviation from the average weight, degradability, abrasion strength, fracture strength, dissolution, microbiological purity, foreign impurities, quantitative determination. Their standardization limits have been established in accordance with SP XI and SP XII. On the basis of the obtained results, the draft ofstandard documentation for Gligiscin tablets has been developed. The tested indicators are included into the draft of standard documentation for Gligiscin tablets.

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