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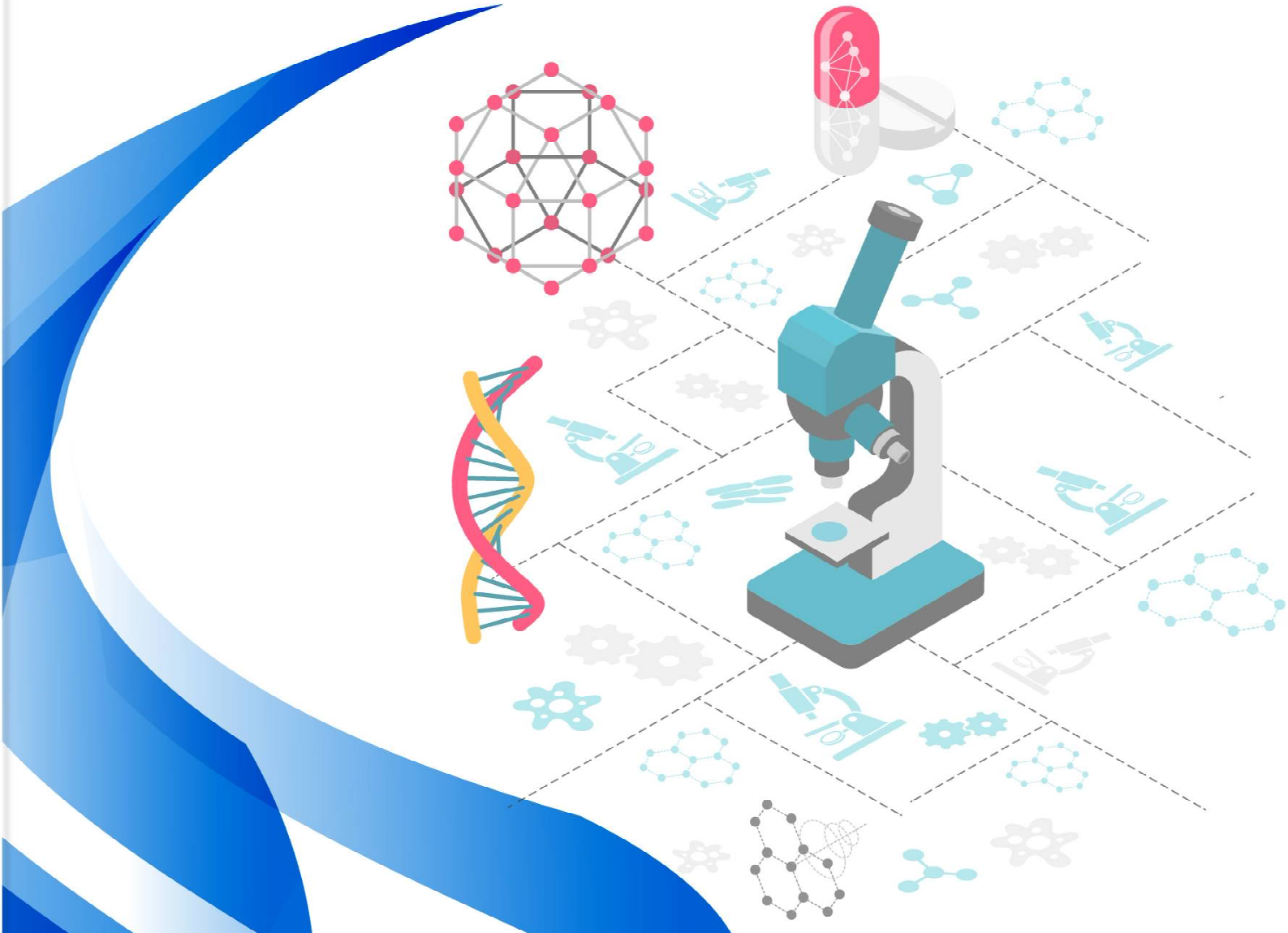

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STUDY OF STABILITY OF "GEPAFLOX" CAPSULES BASED ON A DRY EXTRACT

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Abstract: The article provides the results of experimental researahes on study of stability and establishment of shelf life of the capsules "Gepaflox".

Keywords: stability, shelf life, capsules, shelf life, packaging, storage conditions.

Introduction. The staff of the Tashkent Pharmaceutical Institute obtained a dry extract based on the choleretic polyherbal tea "Triflos", assessed the qualitative and quantitative indicators for compliance with the requirements of regulatory documents. At the next stage, the composition was selected and the technology of capsules based on this extract was developed.

Currently, encapsulated drugs are gaining an importance due to their advantages over other dosage forms. The shelf life of a dosage form of a drug is the main quality indicator that determines its stability during an appropriate shelf life. The length of time during which the quality of the drug changes is called the degradation rate constant. In this case, toxic decomposition products should not be formed or the physicochemical properties of the active substance should not change. A decrease in the quantitative content of a active substance y 10% should not occur within 2.5-3 years in finished dosage forms based on medicinal plants. The expiration date is the period of time during which a given drug fully retains its therapeutic activity, safety and meets the requirements of ND in quality. After the expiration date, the quality of the medicinal product is re-checked, and the shelf life can be extended. The term "shelf life" has a time sense, and the term "stability" has the meaning of drug resistance. During storage, both chemical and physical changes of the active substancecan occur. In this case, pharmacological activity is gradually lost or impurities appear that change the pharmacological activity [1, 2].

The purpose of studying the stability of drugs is to obtain information on how their quality changes over time under the influence of environmental factors (temperature, humidity, lighting). Various methods are used for this: stress tests, accelerated stability tests and real-time studies, or long-term studies. The data obtained is used to establish the recommended storage conditions, retest periods (for substances) and shelf life (for finished forms). In addition, these results are taken into account in the process of developing a specification for a drug substance or dosage form in terms of setting limits and choosing analytical methods that can reliably determine the substance and its degradation products in a mixture with each other [2, 3].

Thus, the development of dosage forms that are convenient to use and stable during storage is one of the main problems of modern pharmaceutical technology. The study of the shelf life of dosage forms is one of the main tasks in the development of drug technology [4-15].

Purpose of the study: study of the influence of different conditions on the stability of the capsules "Gepaflox", establishing the shelf life and storage conditions.

Experimental part.

At the initial stage of the research, the qualitative and quantitative indicators of the obtained capsules were evaluated in accordance with the requirements of regulatory documents. We studied the appearance, authenticity, average weight of the capsule and the contents of the capsule, as well as deviations from these indicators, disintegration, dissolution, microbiological purity, the quantitative content of total flavonoids in terms of

quercetin.

Studies on the microbiological purity of the "Gepaflox" capsules were carried out on the basis of the research department of Scientific Center for Standardization of Medicines " LLC. The results of studying the quality indicators of the developed capsules are shown in Table 1

Table 1
Results of determining the quality indicators of capsules "Gepaflox"

Determined indicator	ND requirements	Analysis results
Description	White capsules №0, with light brown contents	pass
Identification	Qualitative reaction to flavonoids (reddish brown coloration)	pass
Average capsule weight, g ± and deviations from it,%	0.459-0.561 g ± 10.0%	0.520 g ± 2.0%
Average mass of capsule contents, g ± and deviations from it,%	0.378-0.462 g ± 10.0%	0,432 g ±2,86%
Disintegration	Must disintegrate within no more than 20 minutes	9 min 25 sec
Dissolution	Not less than 75% for 45 minutes at a basket rotation speed of 150 rpm	91,7%
Microbiological purity	In 1 g of the preparation, the total number of aerobic bacteria is allowed no more than 10^4, the total number of fungi is not more than 10^2, enterobacteria and some other gram-negative bacteria are not more than 10^2 in the absence of Pseudomonas aeruginosa, Escherichiacoli, Staphyloccocu saureus, Salmonella	pass

Determination of the quantitative content of the total flavonoids in terms of quercetin was determined spectrophotometrically at a wavelength of 430 ë 2 nm. The average values of 5 determinations were calculated both for the tested solutions and for solutions of standard samples.

The results of the determinations are presented in table 2.

Table 2

Results of quantitative determination of total flavonoids in terms of quercetin in capsules "Gepaflox" (n = 5)

Weighed amount, mg	Found amount of active substance, mg	Metrological characteristics
2, 0045	7,34	X_{av}=7,4
2,0060	7,42	f=4 T(95%,4)=2,78
2,0086	7,58	S^2=0,0124 S=0,111
2,0035	7,29	S_x=0,050
2,0050	7,37	e_{av}=1,87 %

Researches to study the stability of capsules were carried out by natural storage in a room at a temperature of 20 ± 2^0C. Samples of capsules were packed in the following types of packaging materials: blisters according to Branch Standart 64-074-91 from polyvinyl chloride film according to State Standart 25250-88; blister packaging according to Branch Standart 64-074-91 of printed aluminum foil varnished according to TC 48-21-270-78; gars of colorless glass, type according to TC 13-7308001-477-85; gars of sun-protective glass melt type BDS-25 according to TC 64-228-84. At the beginning of the experiment, as well as every 6 months, qualitative and quantitative indicators were determined, such as appearance, average weight of capsules and deviations from it, average weight of capsule contents and deviations from it, disintegration, quantitative content of active substance, dissolution.

The data obtained for samples of capsules packed in a blister according to Branch Standart 64-074-91 from a polyvinyl chloride film according to State Standart 25250-88) are shown in Table 3.

Results. According to the data given in Table 1, the analyzed capsules "Gepaflox" № 0 have a light brown contents. The average weight of the investigated capsules was 0.520 g, and the average weight of the encapsulated weight was 0.432 g. In both cases, the deviations did not exceed 10%, as required by the regulatory documents. The ident was determined by a qualitative reaction to flavonoids: when magnesium powder and concentrated hydrochloric acid were added to the alcohol extract, a reddish-brown color gradually appeared.

Disintegration of the encapsulated dosage form was 9 minutes 25 seconds, and the amount of the released amount of flavonoids in terms of quercetin for 45 minutes was 91.7%.

The results of determining the microbial purity of the "Gepaflox" capsules indicate the absence of bacteria of the family Pseudomonas aeruginosa, Escherichia coli, Staphyloccocus aureus, Salmonella, and the total number of aerobic bacteria and fungi does not exceed the permitted limit.

The quantitative content of the total flavonoids in terms of quercetin was 0.0074

g. It was decided to set the limit for their content in one capsule at least 0.006 g.

Thus, according to the results of the studies carried out, the capsules "Gepaflox" for the analyzed qualitative and quantitative indicators meet the requirements of the regulatory documentation.

The results of the stability study showed that the analyzed parameters met the requirements for encapsulated dosage forms for two years. So, for example, the developed white capsules № 0, the contents of a light brown color, did not change their appearance over the entire time of the experiment. Such an indicator as the average mass of capsules and encapsulated mass, as well as deviations from it, were also within the specified limits. The maximum dissolution time of the capsules was 11 minutes, which did not exceed the 20 minutes specified in the ND. When conducting research on dissolution, it was found that this indicator in 45 minutes ranged from 91.7% to 94.5%, i.e. significantly more than the threshold of 75%.

The quantitative content of the total flavonoids in terms of quercetin varied from 0.0063 g to 0.0074 g.

The results of studying the quality indicators of capsules packed in other materials also met the requirements of regulatory documents for 2.5 years.

Findings: the results of the assessment of the quality of the capsules "Gepaflox" testify to their compliance with the requirements of ND. And the study of the stability of the "Gepaflox" capsules of choleretic action made it possible to establish the shelf life in the approved types of packaging materials equal to 2 years.

Table 2

The results of establishing the shelf life of the capsules "Gepaflox" packed in a blister according to Branch Standart 64-074-91 from polyvinyl chloride film according to State Standart 25250-88)

The name of indicators	Norms for NTD	Results by date					
		original sample	after 6 months	after 12 months	after 18 months	after 24 months	after 30 months
Description	White capsules № 0, light brown content	pass	pass	pass	pass	pass	pass
average weight, g ± dev. from average mass,%	0,459-0,561 g ±7,5%	0,520 g ±2.0%	0,511g ±0,20%	0,518 g ±1.57%	0,506 g ±0,78%	0,493 g ±3,33%	0,496 g ±2,75%
average mass of content, g ± dev. from average mass contents, %	0,378-0,462 g ±7,5%	0,432 g ±2,78%	0,426 g ±1,43%	0,417 g ±0,71%	0,408 g ±2,86%	0,414 g ±1,43%	0,410 g ±2,38%
disintegration, min	Must disintegrate within no more than 20 minutes	9 minutes 25 sec	10 minutes 05 sec	8 minutes 50 sec	9 minutes 35 sec	10 min 05 sec	11 minutes 10 sec
dissolution,%	Not less than 75% for 45 minutes at a basket rotation speed of 150 rpm	91,7%	92,3%	92,6%	91,8%	94,5%	92,2%
Quantitative content	Not less than 0.0060 g in the 1st capsule	0,0074 g	0,0071 g	0,0067 g	0,0072 g	0,0069 g	0,0063 g

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