The study of stability of suppositories with the glifazin herbal complex during storage

The result of the search in the direction of creating an effective and save drug for the treatment of type 2 diabetes mellitus (DM) was development of suppositories with the glifazin herbal complex obtained from the herb of bean (*Phaseolus vulgaris*) and mung bean (*Phaseolus aureus*).

**Aim.** To study stability of suppositories with glifazin during storage.

**Materials and methods.** The study objects were rectal suppositories with the hypoglycemic activity containing the glifazin herbal complex in its composition and made on the hydrophilic polyethylene oxide base by the molding method. While storing suppositories their quality parameters (description, uniformity of mass, average weight, dissolution time, pH, microbiological purity, quantitative content of phenolic compounds) were determined using physical, physicochemical, pharmacotechnological and microbiological methods in accordance with the requirements of the State Pharmacopeia of Ukraine (SPhU).

**Results and discussion.** It has been experimentally proven that all quality parameters of the drug meet the requirements of the draft of the Quality Control Methods (QCM).

**Conclusions.** The results of the studies conducted have shown that suppositories are stable when stored in a dry, dark cool place for 2 years.

**Key words:** suppositories; glifazin herbal complex; diabetes mellitus; stability
Diabetes mellitus (DM) is a serious health problem, and does not depend on the age and nationality of a patient. As evidenced by the UN resolution, DM has been recognized as one of the most dangerous diseases in the world [1]. Currently, more than 380 million people suffering from DM have been registered. According to the State Center of Statistics of Ukraine today 2.9 % of the country’s total population are people with the confirmed diagnosis of DM, among them 90 % are patients with type 2 DM. In the EU almost 4-6% of the population suffers from type 2 DM. Therefore, a great attention is paid to prevention and treatment of DM in national health programs of all countries worldwide [2, 3].

According to modern concepts the increase in the concentration of glucose in the blood of patients with type 2 DM is caused by two processes: reduced sensitivity of the liver and tissues to the action of insulin (insulin resistance) and dysfunction of β-cells of pancreatic islets [4].

Taking into account multifactorial pathogenesis of type 2 DM the pathogenetic pharmacotherapy of this disease is considered to be the most appropriate, it involves correction of the pathological links of DM [4, 5, 6, 7].

However, all antidiabetic medicines have certain disadvantages in varying degrees, and it complicates the effectiveness of DM treatment [5, 8]. Creation of products based on medicinal plants with the antidiabetic properties is of great interest. Due to the content of many biologically active substances (BAS) medicinal plants exhibit diverse properties, including the antidiabetic ones, and reduce the glucose level in the blood, normalize the lipid and protein metabolism, reveal the antioxidant, anti-inflammatory, hypolipidemic properties, proving reasonability of their use in the complex therapy of type 2 DM [9, 10, 11].

In the National University of Pharmacy (NUPh) the complex drug with the hypoglycemic activity under the conditional name glifazin was obtained from the herb of bean (Phaseolus vulgaris) and mung bean (Phaseolus aureus). Its biological properties were studied in detail by prof. Sytnik A. G. and prof. Maloshtan L. M. [8]. Using this herbal substance a number of drugs has been developed.

The aim of the work was to study stability of suppositories with glifazin during storage.

**Materials and methods**

The study objects were rectal suppositories with glifazin made on the hydrophilic polyethylene oxide base by the molding method [12]. Suppositories were stored at two temperature conditions:
1. at the temperature of 11.5 ± 3.5 °C;
2. at the temperature of 20.0 ± 5.0 °C and the relative humidity of 60 ± 5 %.

While storing suppositories such quality parameters as description, uniformity of mass, average weight, dissolution time, pH, microbiological purity, quantitative content of phenolic compounds were determined using physical, physicochemical, pharmaceutotechnological and microbiological methods in accordance with the requirements of the State Pharmacopoeia of Ukraine (SPhU) [2, 13, 14, 15, 16].

Microbiological studies were performed at the premises of the State Institution “Institute of Microbiology and Immunology named after I. I. Mechnikov of the National Academy of Medical Sciences of Ukraine” according to the requirements of the SPhU. The quantitative determination of phenolic compounds of glifazin in suppositories was conducted by UV spectrophotometry at a wave length of 271 ± 2 nm; as a standard onoside (7-O-[3,0-glucopyranoside-3’,4’-methylenedioxy-6’-methoxyisoflavanone) with the absorption maximum at 271 nm was used [17].

**Results and discussion**

The quality parameters of the samples of suppositories with glifazin controlled by the draft of the Quality Control Methods (QCM) are given in Tab. 1.

![Table 1](image-url)

The quality parameters of suppositories with glifazin
To determine the stability of the suppositories developed during storage and their shelf life, several batches of the drug were prepared and stored.

The studies on compliance of the drug to the requirements of the draft of QCM were performed every 3 months during the first year, every 6 months during the second year, and at the end point of control – 27 months. The data were processed using MS Excel and Statistika 6.0 software. The results of the analysis of suppositories are given in Tables 2 and 3.

According to the results obtained, suppositories with glifazin stored at temperatures of 11.5 ± 3.5 °C and 20.0 ± 5.0 °C and the relative humidity of 60 ± 5 % were consistent with the requirements of the draft of QCM by all quality parameters for 27 months.

However, it should be noted that the pH value of suppositories stored within the temperature range of 15.0-25.0 °C was slightly higher compared to the pH value of suppositories stored at the temperature of 8.0-15.0 °C within 27 months.

### Table 2

The results of studying the stability of suppositories with glifazin during storage (with the storage temperature of 11.5 ± 3.5 °C and the relative humidity of 60 ± 5 %)

| Quality parameter according to QCM | Shelf life, months |
|------------------------------------|--------------------|
| Description                        |                    |
| Suppositories of a light brown color, homogeneous, with a slight characteristic odor |                    |
| Identification:                    |                    |
| Phenolic compounds                 | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy |
| Polyethylene oxide base            | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy |
| Average weight, g                  | 3.92 ± 0.02 | 3.96 ± 0.04 | 4.06 ± 0.02 | 3.95 ± 0.08 | 3.96 ± 0.04 | 4.10 ± 0.05 | 4.02 ± 0.06 | 3.95 ± 0.04 |
| Uniformity of mass                 | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy |
| pH                                 | 6.12 ± 0.04 | 6.04 ± 0.05 | 5.96 ± 0.06 | 6.20 ± 0.04 | 5.92 ± 0.06 | 6.16 ± 0.04 | 6.08 ± 0.08 | 6.18 ± 0.06 |
| Dissolution time, min              | 42.05 ± 0.25 | 46.10 ± 0.20 | 45.50 ± 0.25 | 43.25 ± 0.20 | 46.75 ± 0.25 | 50.10 ± 0.20 | 44.25 ± 0.20 | 45.20 ± 0.25 |
| Quantitative content of the total amount of phenolic compounds, g | 0.0037 ± 0.0003 | 0.0039 ± 0.0002 | 0.0036 ± 0.0002 | 0.0037 ± 0.0003 | 0.0038 ± 0.0003 | 0.0037 ± 0.0003 | 0.0039 ± 0.0002 | 0.0037 ± 0.0002 |
| Microbiological purity             | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy |

To determine the stability of the suppositories developed during storage and their shelf life, several batches of the drug were prepared and stored.

The studies on compliance of the drug to the requirements of the QCM draft were performed every 3 months during the first year, every 6 months during the second year, and at the end point of control – 27 months. The data were processed using MS Excel and Statistika 6.0 software. The results of the analysis of suppositories are given in Tables 2 and 3.

### Table 3

The results of studying the stability of suppositories with glifazin during storage (with the storage temperature of 20.0 ± 5.0 °C and the relative humidity of 60 ± 5 %)

| Quality parameter according to QCM | Shelf life, months |
|------------------------------------|--------------------|
| Description                        |                    |
| Suppositories of a light brown color, homogeneous, with a slight characteristic odor |                    |
| Identification:                    |                    |
| Phenolic compounds                 | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy |
| Polyethylene oxide base            | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy |
| Average weight, g                  | 3.90 ± 0.04 | 3.95 ± 0.03 | 4.02 ± 0.06 | 3.92 ± 0.05 | 3.98 ± 0.06 | 4.12 ± 0.06 | 3.96 ± 0.04 | 3.92 ± 0.04 |
| Uniformity of mass                 | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy |
| pH                                 | 6.12 ± 0.06 | 5.88 ± 0.04 | 5.90 ± 0.06 | 6.02 ± 0.06 | 5.92 ± 0.05 | 6.12 ± 0.06 | 6.25 ± 0.08 | 6.36 ± 0.06 |
| Dissolution time, min              | 40.02 ± 0.30 | 43.12 ± 0.25 | 42.50 ± 0.15 | 40.25 ± 0.30 | 44.25 ± 0.12 | 45.50 ± 0.25 | 41.15 ± 0.30 | 44.50 ± 0.30 |
| Quantitative content of the total amount of phenolic compounds, g | 0.0038 ± 0.0002 | 0.0039 ± 0.0002 | 0.0037 ± 0.0003 | 0.0038 ± 0.0003 | 0.0039 ± 0.0003 | 0.0037 ± 0.0003 | 0.0038 ± 0.0003 | 0.0037 ± 0.0003 |
| Microbiological purity             | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy | satisfy |
CONCLUSIONS
The results of the studies conducted have shown that suppositories are stable when stored in a dry, dark cool place for 2 years.

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