Introduction. Acute infections of the upper respiratory tract (URT) are one of the most widespread pathologies both in Ukraine and worldwide. Among other factors the efficacy of the treatment to a large extent is affected by the right choice of a dosage form, which should provide the maximum therapeutic effect and promote the compliance of the patient.

Among medical preparations intended for the treatment of infectious-inflammatory diseases of the URT, compressed lozenges have become very popular. They are solid single-dose dosage forms that dissolve or disintegrate slowly in the mouth to release the drug into the saliva, usually for the purpose of local action in the mouth or throat, and for systemic effect if the drug is well absorbed through the mucous membrane of the cheeks. Compared with other oromucosal dosage forms, compressed lozenges have significant advantages: as it was shown by γ-scintigraphy, compared to aerosols and rinses, the use
of medicated lozenges allows to maximize the residence time and concentration of the drug on the throat mucosa and mouth. Compared to conventional tablets, compressed lozenges differ in that they are non-porous and do not contain disintegrants. Because this dosage form should remain in the oral cavity for a certain period of time, its taste and tactile characteristics play a significant role.

Therefore, considering the way of administration of compressed lozenges, a very important attribute of their quality is the rate of dissolution in the oral cavity. With the rapid dissolution or disintegration of compressed lozenges in the oral cavity, there are conditions for the active substances to be washed away by the saliva into the lower parts of the digestive tract that reduces the efficacy of the treatment of local inflammation. On the other hand, with the excessively long time required for a lozenge to be completely dissolved in the oral cavity, the comfort of treatment decreases, which negatively affects the patient's compliance. However, up to date, the leading world pharmacopoeias, as well as the State Pharmacopoeia of Ukraine (SPhU), do not have any specific criteria and methods for quality attributes determination of compressed lozenges of local therapeutic action.

**Aim.** Our work was devoted to pharmaceutological and biopharmaceutical studies of compressed lozenges for sore throat treatment available in the pharmaceutical market of Ukraine in order to determine the optimal values of the quality attributes of this dosage form, which will allow to achieve the maximum therapeutic effect and treatment compliance at the same time.

**Materials.** The following drugs were selected for the studies: LYSOBACT (Bosnalijek d.d., Bosnia and Herzegovina), FARINGOSEPT with lemon taste (S.C. Terapia S.A., Romania), EFISOL (Balkanpharma-Dupnitsa AD, Bulgaria), LIZAK (Farmak JSC, Ukraine), SEPTEFRIL-Darnitsa (Pharmaceutical Firm “Darnitsa” PrJSC, Ukraine), CHLOROPHYLLIPT tablets 25 mg (“Pilot Plant “State Scientific Centre on Medicinal Products” LLC, Ukraine).

The abovementioned preparations were investigated by the attributes: average mass, geometric dimensions of the dosage units (diameter and height), resistance to crushing (according to SPhU chapter 2.9.8, using a tablet hardness tester of Monsanto type), disintegration/dissolution time (DT) (according to SPhU chapter 2.9.1, using disintegration tester BJ-2 MINHUA Pharmaceutical Machinery Co. Ltd., China, and purified water as the disintegration medium). Six healthy volunteers (3 females and 3 males) were recruited to determine the dissolution time of the drugs in vivo. Such attributes as taste and optimality of in-mouth residence time according to the experts' opinions were assessed on a five-point scale, where 1 is very bad and 5 is excellent. The obtained data were processed in Microsoft Excel 2010.

**Results.** One of the ways to slow down the dissolution/disintegration of tablets is to increase their mechanical strength. Particularly, according to the available literature, the recommended resistance to crushing for compressed lozenges should be at least 100 N, providing in such a manner the gradual dissolution of a dosage unit in the mouth during 5-10 min.

According to our results, the mean value of crushing strength of four preparations that were tested exceeded 100 N and ranged from 115.2 to 126.3 N, while the mean DT in vitro values for these samples were in the range of 12.7–16.7 min. An abnormally prolonged time in testing in vitro was needed for complete dissolution of CHLOROPHYLLIPT tablets – in average, it took 94.3 minutes. Crushing resistance values below 100 N were obtained for SEPTEFRIL-Darnitsa and LYSOBACT tablets – 72.7 and 39.6 N, respectively, while the average DT in vitro values were 9.3 and 12.2 min, respectively. All medical preparations except LYSOBACT were characterized by an average mass of tablets more than 700 mg (747–1013 mg). For LYSOBACT this value was 202 mg.

The fastest in vivo dissolution was observed for SEPTEFRIL-Darnitsa – the average time was 4.2 min (3.0–5.7 min); while EFISOL had the longest residence time in the oral cavity – 14.0 min (13.6–14.9 min). It is interesting to note, that the average in-mouth residence time of CHLOROPHYLLIPT, which was characterized by an abnormally long DT under in vitro testing conditions, was only 8.6 min (4.9–12.1 min).

The taste preferences of the experts can be ranged as EFISOL > SEPTEFRIL-Darnitsa > FARINGOSEPT with lemon taste > LYSOBACT > LIZAK = CHLOROPHYLLIPT. The range characterizing the experts' assessment of the optimality of in-mouth residence time is as follows:
FARINGOSEPT with lemon taste > SEPTEFRIL-Darnitsa = LYSOBACT > EFISOL > LIZAK > CHLOROPHYLLIPT.

Thus, our studies have shown that medical preparations in the form of compressed lozenges have specific features, which distinguishes them from conventional tablets. Most of these formulations are characterized by higher mechanical strength or the presence of certain binders that prevent rapid dissolution (for example, tragacanth in LYSOBACT tablets). The assessment of the optimality of in-mouth residence time according to the subjective feelings of the experts showed that this attribute is affected not only by time, but also the taste of the lozenges. In instance, time required for dissolving of LIZAK and CHLOROPHYLLIPT in the oral cavity was assessed as the least comfortable for the experts, and at the same time these preparations received the lowest scores in the taste assessment.

The analysis of the obtained results has revealed that if the taste is pleasant for the patient, the most comfortable duration of dissolution in the oral cavity does not exceed 8 min. Correlation with the in vitro testing data showed that, when using the procedure of SPhU chapter 2.9.1 this time corresponds to about 13 min. In such a way, taking into account the recommendations on the dissolution time of compressed lozenge in the oral cavity of 5–10 min, the approximate time criteria may be set as 11–15 min when using the pharmacopoeial disintegration tester.

Conclusions. The studies have allowed us to provide specific recommendations for the quality attributes of compressed lozenges that can be used by pharmaceutical development laboratories to create new drugs in this dosage form.

RECEIVING WATER FOR INJECTIONS ON A COMPLEX «STILMAS»
Lukina A. A., Orlova E. V., Kylosova I. A.
Perm State Pharmaceutical Academy, Perm, Russia
inna_kylosova@mail.ru

Introduction. The saved-up practical experience of producers of medicines in Russia and abroad shows that used water of unsatisfactory quality is the reason of a seizure of production and a source of its pollution in most cases. Water is widely used as an auxiliary substance as a part of medicines, the medical substances, and also at various technological needs, for example a sink of bottles, ampoules, cleaning of rooms and preparation of disinfecting solutions, etc. Therefore water systems are the main components of any pharmaceutical production. Problems with quality or number of preparation of water can lead to decrease in a product yield or discrepancy of this product to norms and it will inevitably entail losses on sales or even shares of the market.

Aim. The purpose of work is the opportunity assessment receiving water for injections (WFI) on a water-purifying complex «Stilmas».

Materials and methods. Objects of research are WFI and complex «Stilmas». The specific conductivity was chosen as the main indicator of quality of WFI.

Results and discussion. Water from water supply system moves on the filter for a rough filtration, sodium hypochlorite is dosed in parallel in the pipeline. Then via the lamellar heat exchanger water goes for operation of preliminary cleaning in the deferrization block. Further it arrives on the duplex block of softening. When passing drinking water through system of preliminary cleaning it is exempted from impurity of iron, salts of rigidity, the weighed particles and organic substances. Softened water arrives on the following operation – demineralization on installation of the return osmosis. From accumulative capacity water is pumped by the pump of a high pressure on the filter, then the pump of low pressure pumps it on the membrane`s block of installation of return osmosis. There are 2 streams after this membrane’s block: concentrate and permeate. Permeate comes further to the block of an electrodeionization (EDI) for finishing tertiary treatment. Permeate comes to system of storage.