методикою Фармакопеї, без урахування вартості на електропостачання, заробітну плату персоналу та утилізацію викидів.

За аналітичною шкалою AGREE, методики є надзвичайно зеленими з числовими значеннями 0,77, 0,82 та 0,82 в середовищі метанолу, 0,1 М розчину кислоти хлористоводневої та 0,1 М розчину натрію гідроксиду, відповідно.

Висновки. Для ідентифікації міноксидилу в лікарських та косметичних засобах рекомендовано метод абсорбційної спектрофотометрії в інфрачервоній ділянці спектра, кількісне визначення проводити методом спектрофотометрії в ультрафіолетовій ділянці в середовищі 0,1 М розчину кислоти хлористоводневої, або 0,1 М розчину натрію гідроксиду, або метанолу. Через те, що обрані методики є експресними, екологічними, економічними, чутливими та специфічними.

THE CHOICE OF OPTIMAL METHODS OF DETERMINATION OF CLONAZEPAM FOR THE TASKS OF FORENSIC PHARMACEUTICAL ANALYSIS

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Introduction. Clonazepam, a benzodiazepine, is commonly used in treating various conditions, including anxiety disorders and epileptic seizures. Due to its low price and easy availability, however, it has become a commonly misused medication, both in medical and recreational contexts. Clonazepam, alone or in combination with other psychoactive substances, can lead to unwanted effects on health, such as motor and cognitive impairment, sleep disorders, and aggravation of mood and anxiety disorders. Prolonged use of clonazepam may lead to physical dependence and tolerance. Therefore, very often, the use of clonazepam leads to criminal acts. Therefore, it is often found in toxicological and forensic analysis in case files.

In this regard, it is important to select methods for the determination of clonazepam in substances, finished medicinal products, and mixtures in the presence of other components. It should be borne in mind that these methods must meet the requirements of the Pharmacopoeia for pharmaceutical analysis and the Ministry of Justice for the use of methods in forensic and toxicological analysis so that the results obtained have legal force and serve as evidence in court.

Therefore, the methods should be validated, and their choice should be justified by the following parameters: validation characteristics suitable for court cases, environmental friendliness, and cost-effectiveness.

The aim of the study. The aim of the study is to select a method for the determination of clonazepam for forensic pharmaceutical analysis, consideration of validation characteristics, material costs and environmental friendliness.

Materials and methods. compilation of data from reports on clonazepam analysis methods suitable for forensic pharmaceutical analysis, mathematical calculations and statistical processing of the results.

Research results. To conduct the study, we considered the liquid chromatography (HPLC) method, which is approved by the US Pharmacopeia for the analysis of clonazepam in substance and finished medicinal products, and was also used to determine clonazepam in forensic materials, and the ultra-performance liquid chromatography–tandem mass spectrometry (UPLC–MS-MS) method, which is widely used in forensic and toxicological analysis due to the fact that it allows the determination of a substance in mixtures and biological fluids, including metabolites.

The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 15-cm column that contains packing L7. Mobile phase – mixture of buffer solution (pH of 8.0), methanol, and tetrahydrofuran (60:52:13). The sample is diluted in a mixture of water, methanol, and tetrahydrofuran (60:52:13).

In ultra-performance liquid chromatography–tandem mass spectrometry, the sample is analyzed using a Waters Acquity UPLC and TQ detector using positive electrospray ionization and multiple reaction monitoring mode. The capillary voltage is 3 kV and the desolvation temperature is 400°C. The desolvation gas flow is set at 800 L/h and the source temperature is 120°C. An Acquity UPLC BEH C18 column with dimensions of 2.1 × 100 mm and a 1.7-µm particle size is used; column temperature is maintained at 50°C. The mobile phase flow rate was 0.40 mL/min, and the injection volume is 10 µL. The mobile phase is 0.1% formic acid in water (A) and 0.1% formic acid in methanol (B). The sample is diluted in a mobile phase A.

The results of the analysis were validated statistically and also by recovery studies. The validation and critical parameters, calculated by using HPLC and UPLC–MS-MS for Clonazepam, are shown in Table 1.

Table 1. Comparison of validation characteristics of HPLC and UPLC–MS-MS methods for clonazepam determination

Parameter	HPLC	UPLC–MS-MS
Pressure, bar	400	750
Volume of mobile phase, ml	40	21.5
Volume of sample injection, ml	20	5
Flow rate, ml/min	1	0.7
Retention time, min	15 ± 0.036	4.4 ± 0.017
Total run time, min	40	15
Linearity with R^2	> 0.991	> 0.996
Limit of detection, µg/ml	0.07	0.001

Based on the methods and results obtained, the UPLC–MS-MS method takes less time, requires less sample and has a sample limit of 0.001 µg/ml, but the HPLC method also meets the requirements for methods to be used in forensic analysis in all validation parameters.

As for the cost of analysis, the analysis of one sample of clonazepam by the HPLC method will cost EUR 25.04, and the UPLC–MS-MS method will cost EUR 0.84.

The overall AGREE scale to calculate the ecological indicator for the proposed analytical methods HPLC, UPLC–MS-MS was calculated as 0.54, 0.78, respectively, indicating that the proposed UPLC–MS-MS method for the analysis of clonazepam is extremely green, but the HPLC method is not.

The ecological compatibility of the HPLC method was affected by the large number of reagents and volumes that would need to be disposed of, the analysis time (40 minutes), since only one analysis can be performed in 1 hour, and the lengthy multi-operational sample preparation. Therefore, in comparison with the HPLC method, it cannot be recommended as a green method.

Conclusions. The UPLC–MS-MS method proved to be the optimal method for the forensic pharmaceutical analysis of clonazepam in terms of accuracy, environmental friendliness and cost-effectiveness. As for the HPLC method proposed by the US Pharmacopeia, it can also be used in laboratories for suitable tasks, as it meets all the requirements for methods set out in the Pharmacopoeias and legal legislation, but it requires more time for analysis and is more costly. In sum, the methods are interchangeable depending on the equipment of the laboratories.

USING PHARMACOPOEIAL METHODS FOR IDENTIFICATION AND ASSAY OF DOSAGE FORMS BASED ON CHLORHEXIDINE GLUCONATE

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Introduction. The use of antiseptics has increased significantly in various medical and professional settings, as well as in the home, due to their antiviral properties in the context of the ongoing coronavirus disease 2019 (COVID-19) pandemic. Also, the use of this class of drugs is widely used by consumers to prevent infection during seasonal colds and flu. In connection with such popularity of use, the aspect of studying the quality of this group of agents is very important, since the appearance of cheap analogues of many antiseptics in recent years indicates the use of low-quality substances or counterfeit products. Such actions can lead to undesirable side effects. Another aspect of poor quality, in addition to determining the authenticity of the active ingredients, is its quantitative content, which must correspond to that stated in the regulatory documentation or quality certificates. Failure to comply with this parameter can lead to a decrease in the antimicrobial and antiviral properties of the antiseptics used. Therefore, the study of existing and possible methods of quality control of known antiseptic agents is an urgent study.

Aim. Using of pharmacopoeial methods for the identification and assay of dosage forms based on Chlorhexidine gluconate in order to introduce potential quality control methods into the development.

Materials and methods. As objects, antiseptics based on Chlorhexidine gluconate (solution and gel) were chosen, which are widely used in dermatology, dentistry, surgery, as well as in everyday life for the treatment of wounds and skin disinfection. For the study, pharmacopoeias methods of analysis were used.

Results and discussion. For the identification and quantification (assay) of Chlorhexidine gluconate in dosage forms for topical use, the quality control methods of the European (Ph. Eur.) and American Pharmacopoeia (U.S.P.) monographs were used. The table systematizes the data of quality parameters for the solution and gel of Chlorhexidine gluconate.