Міністерство охорони здоров'я України
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Міжнародна internet-конференція

Modern chemistry of medicines

25 вересня 2024 р.
м. Харків, Україна

Посвідчення Державної наукової установи «Український інститут науково-технічної експертизи та інформації» № 263 від 16.04.2024 р.

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Ministry of health of Ukraine
Ministry of education and science of Ukraine
National university of pharmacy
Pharmaceutical chemistry department
General chemistry department

MODERN CHEMISTRY OF MEDICINES

Матеріали
Міжнародної Internet-конференції «Modern chemistry of medicines»,
до 85-річчя з дня народження професора Петра Овксентійовича Безуглого
25 вересня 2024 року

Materials
of the International Internet Conference 'Modern chemistry of medicines',
dedicated to the 85th Anniversary of Professor Petro O. Bezuglyi
September 25, 2024

ХАРКІВ
KHARKIV
2024

Validation of the method of standardization of concomitant impurities in "Carbatryl" tablets

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Introduction. It is important to create medicines based on fixed combinations containing compatible physico-chemical and pharmacological characteristics of an antioxidant and a drug of basic therapy, which determines their higher therapeutic efficiency and safety compared to the use of individual components of complex treatment. Carbamazepine is currently the main drug in the treatment of focal epilepsies. But the large number of side effects that limit its use in the clinic are clearly evident. The solution to this problem is the creation of a new, more effective antiepileptic drug that exhibits pronounced antidepressant, nootropic, neuroprotective and antioxidant properties based on a fixed combination of carbamazepine and thiotriazoline, which will also significantly reduce the amount of side effects. All medicinal products must meet quality standards. And the developed analytical methods included in the regulatory documentation for a pharmaceutical substance or a finished dosage form must be validated.
The purpose of our work is to validate the methodology for quantitative determination of accompanying impurities in "Carbatryl" tablets.
Materials and methods: The following analytical equipment was used during the validation study:
Chromatograph: LC-20 ProminenceShimadzu models in the following configuration: two LC-20AD pumps, SIL-20A autosampler, SPD-20AV detector, CTO-20A thermostat, CBM-20 ALITE system controller; Column: polymer column (Peek), size 100 mm x 4.6 mm, "ChromolithSpeedRODRP-18e" cat. No. 1.02129.0001 production of the firm "MerkKGaA", Germany; Analytical balance model AUW 220D, manufactured by Shimadzu, Germany, uncertainty of weighing results 0.033 mg.
Limits: the content of a single impurity of thiotriazoline is normalized within 1%, the sum of impurities is no more than 2%. For carbamazepine impurities, the following content limits are established: individual - no more than 0.5%, sum - no more than 2%. The suitability criteria of the validation characteristics of the method were calculated for a 16% tolerance of the content of active substances in the preparation.
Preparation of samples and conducting tests for the study of the "Specificity" characteristic, the tested solution and the comparison solution of thiotriazoline and carbamazepine and the comparison solutions A and B were prepared according to the project methodology. Samples for studying the characteristics of correctness, convergence (precision) and range of application were prepared similarly to comparison solution B, only 0.25 ml, 0.50 ml, 0.75 ml, 1.00 ml and 1.25 ml of the original solution of 3-methyl-1,2,4-triazolyl-5-thione and impurity A of carbamazepine. These amounts correspond to impurity concentrations equal to 50%, 75%, 100%, 125% and 150% of the maximum permissible amount.
Results and discussion: the method is characterized by sufficient convergence, since the found value of the relative confidence interval of the value Δ_Z for the impurities of thiotriazoline and carbamazepine does not exceed the critical value for the convergence of the results. The method is characterized by sufficient accuracy, as the criterion of insignificance of the systematic error of the method is fulfilled. The systematic error of the method meets the requirements of statistical (for the admixture of thiotriazoline) and practical (for the admixture of carbamazepine) insignificance.The high value of the correlation coefficient r = 0.99994 and 0.9998 satisfies the requirements of the acceptance criterion (r = 0.9998) and confirms the linear relationship between the taken and found amounts of thiotriazoline and carbamazepine impurities in the range from 50% to 150% relative to its nominal content in drugs.
Conclusions: the method of standardization of accompanying impurities in "Carbatryl" tablets was validated according to the following indicators: specificity, range of application, correctness and precision (convergence).