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Usage of HPLC in analysis of tetrahydropyrimidine Biginelli derivative

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Abstract

The search for new compounds exhibiting a significant pharmacological effect with low toxicity is an actual problem of modern organic and medical chemistry. One solution to this problem is the synthesis of heterocyclic compounds containing in their structure the pyrimidine cycle, a one-step three-component Biginelli reaction. This method of synthesis, with proper selection of initial reagents and conditions of the reaction, allows obtaining compounds with the predicted structure and high yield of the target product. Among the products of the Biginelli reaction, compounds that possess a broad spectrum of biological activity were found. The compound 3,4-dimethyl-6-(3-pyridyl)-*N*-phenyl-2-oxo-1,2,3,6-tetrahydropyrimidine-5-carboxamide, synthesized in the Perm State Pharmaceutical Academy, exhibits antifungal and anti-inflammatory activity and is a promising object for detailed research. It was studied that this compound is formed as a result of three-component Biginelli condensation upon fusion of acetoacetanilide with a mixture of 3-pyridinecarboxaldehyde and *N*-methyl urea. The development of analytical methods for assessing the quality of the substance of the obtained compound is an important stage of preclinical testing. The purpose of this work is to select the conditions for HPLC to standardize the substance of the biologically active compound. The studies were performed on a *Shimadzu LC Prominence* high performance liquid chromatograph (Japan) with an SPD diode array detector. The separation was carried out on a chromatographic column (250×4.6 mm). In the course of the experiment, chromatographic conditions were selected that allow the standardization of the substance 3,4-dimethyl-6-(3-pyridyl)-*N*-phenyl-2-oxo-1,2,3,6-tetrahydropyrimidine-5-carboxamide according to the parameters "authenticity", "related impurities" and "quantitation". A technique for quantitative determination of a specific acetoacetanilide impurity has been developed and validated, and the possibility of using the HPLC method for the quantitative determination of the studied compound in its dosage forms has been demonstrated.

References

[1] C.O. Kappe. Biologically active dihydropyrimidones of the Biginelli-type – a literature survey. *Eur. J. Med. Chem.* **2000**. Vol.35. P.1043. DOI: 10.1016/S0223-5234(00)01189-2
[2] S.V. Vdovina, V.A. Mamedov. New potential of the classical Biginelli reaction. *Rus. Chem. Rev.* **2008**. Vol.77. No.12. P.1091. DOI: 10.1070/RC2008v077n12ABEH003894 (russian)
[3] M. Brands, R. Endermann, R. Gahlmann. Dihydropyrimidinones – a new class of anti-Staphylococcal antibiotics. *Bioorg. Med. Chem. Lett.* **2003**. Vol.13. P.241. DOI: 10.1016/S0960-894X(02)00880-6
[4] T.M. Zamaraeva, T.F. Odegova, A.Y. Fedotov, M.V. Tomilov, V.L. Gein, P.A. Slepukhin. Synthesis and antimicrobial activity 6-aryl-3,4-dimethyl-N-phenyl-2-oxo-1,2,3,6-tetrahydropyrimidine-5-carboxamide. *Jour. Gen. Chem.* **2014**. Vol.84. Iss.10. P.1672-1675. (russian)