ECMC 2023

MDPI

Abstract

Antithrombin activity of a new triazolopyrimidine derivative†

Kseniia Gaidukova [1*], Aida Kucheryavenko [2]

[1] Department of Pharmacology and Bioinformatics, Volgograd Medical University, Russia 1; ksenijagajjdukva@rambler.ru
[2] Department of Pharmacology and Bioinformatics, Volgograd Medical University, Russia 2; aidakucheryavenko@yandex.ru
* Correspondence: ksenijagajjdukva@rambler.ru; Tel.: (+79272540407)
† Presented at the title, place, and date.

Abstract: In the pathogenesis of inflammatory processes caused by viral and bacterial infections, there are various disorders of many systems of the organism, including pathology of hemostasis system characterized by prethrombotic state. According to clinical recommendations, the use of new oral anticoagulants is aimed at reducing the risk of hypercoagulation disorders, that's why the search and study of new direct anticoagulant compounds is relevant. Pyrimidine derivatives have been shown to exhibit various types of pharmacological activity, including anticoagulant activity. To study the effect of a new condensed triazolopyrimidine derivative in vitro and in vivo on coagulogram parameters (without and in conditions of hypercytokinemia). Dabigatran etexilate was studied as a comparison drug. For in vitro studies, the test samples were studied in a dose-dependent manner. In the in vivo test, the triazolopyrimidine derivative and the comparison drug were administered to rats once intragastrically at doses of 5.5 mg/kg and 12 mg/kg, respectively, 2 h before the study. Hypercytokinemia was created by lipopolysaccharide by intravenous injection at a dose of 2 mg/kg into the tail vein of the rat. The effect of the tested compound and the comparison drug on rat blood coagulogram parameters (APTT, TT, PT) was determined chronometrically on a SOLAR hemocoagulometer (Belorussia). It was shown that the tested sample and the comparison drug manifested antithrombin activity comparable in terms of IC50 in in vitro test. Triazolopyrimidine derivative in in vivo experiments at a single intragastric administration to rats prolonged thrombin time 5.6 times relative to control values, but was 2 times inferior to the comparison drug dabigatran etexilate. However, under conditions of hypercytokinemia the tested compound was 1.3 times superior to the comparison drug in antithrombin activity. The new triazolopyrimidine derivative in in vitro and in vivo experiments showed high antithrombin activity in sepsis-mediated conditions causing a systemic inflammatory response, which may make a significant contribution to reducing the risk of thrombosis in viral and bacterial infections.

Keywords: dabigatran etexilat, anticoagulant activity, antithrombin effect, triazolopyrimidine derivative.

Citation: Lastname, F.; Lastname, F.; Lastname, F. Title. *Med. Sci. Forum* **2023**, *2*, x. https://doi.org/10.3390/xxxxx

Academic Editor: Firstname Lastname

Published: date

Supplementary Materials:

Author Contributions: Conceptualization, A.K.; methodology, A.K.; software, K.G.; validation, K.G.; formal analysis, A.K.; investigation, K.G.; resources, A.K.; data curation, A.K.; writing—original draft preparation, K.G.; writing—review and editing, A.K.; visualization, K.G.; supervision, A.K.; project administration, A.K.; funding acquisition, A.K. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Ministry of Science and Higher Education of the Russian Federation (Agreement on the provision of grants from the federal budget in

the form of subsidies under paragraph 4 of Article 78.1 of the Budget Code of the Russian Federation, Moscow, October 1, 2020 No, 075-15-2020-777).

Institutional Review Board Statement: All animal procedures in the study were performed in accordance with generally accepted ethical standards for animal manipulation adopted by the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (1986) and considering the International Recommendations of the European Convention for the Protection of Vertebrate Animals Used for Experimental Research (1997). The study was approved by the Regional Ethical Committee of Volgograd State Medical University (Registration No. IRB 00005839 IORG 0004900, OHRP), Certificate No. 2022/097 dated 21.01.22. All sections of this study comply with the ARRIVE Guidelines for Reporting Animal Research [17].

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: This research was funded by Grant according to the Agreement No. 075-15-2020-777, October 1, 2020, on the provision of grants from the federal budget in the form of subsidies in accordance with paragraph 4 of Article 78.1 of the Budget Code of the Russian Federation, Moscow.

Conflicts of Interest: The authors declare no conflict of interest.