medical sciences forum

MDPI

Abstract

The Synthesis and Biological Activity of Amidrazone Derivatives Obtained in Reaction with *cis*-1,2,3,6-Tetrahydrophthalic Anhydride †

Renata Paprocka [1,*], Małgorzata Wiese-Szadkowska [2], Jolanta Kutkowska [3] and Adam Kowalewski [4,5]

[1] Department of Organic Chemistry, Faculty of Pharmacy, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Jurasza Str. 2, 85-089 Bydgoszcz, Poland
[2] Department of Immunology, Faculty of Pharmacy, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, M. Curie-Sklodowska Str. 9, 85-094 Bydgoszcz, Poland
[3] Department of Genetics and Microbiology, Institute of Biological Sciences, Maria Curie-Skłodowska University, Akademicka Str. 19, 20-033 Lublin, Poland
[4] Department of Clinical Pathomorphology, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, M. Curie-Sklodowska Str. 9, 85-094 Bydgoszcz, Poland
[5] Department of Tumor Pathology and Pathomorphology, Oncology Centre—Prof. Franciszek Łukaszczyk Memorial Hospital, Romanowskiej Str. 2, 85-796 Bydgoszcz, Poland
* Correspondence: renata.bursa@cm.umk.pl
† Presented at the 8th International Electronic Conference on Medicinal Chemistry, 1–30 November 2022; Available online: https://ecmc2022.sciforum.net/.

Abstract: Amidrazones are known for the broad biological activity of their derivatives (antimicrobial, anti-inflammatory, antiparasitic, antitumor and others). While searching for new drugs, twelve new derivatives of N^3-substituted amidrazones were obtained in the reaction with *cis*-1,2,3,6-tetrahydrophthalic anhydride. The structures of obtained linear compounds and 1,2,4-triazole derivatives were confirmed by ^{1}H NMR, ^{13}C NMR and MS. Toxicity and inflammatory activity of obtained compounds (at concentrations of 10, 50 and 100 µg/mL) were studied in human peripheral blood mononuclear cells (PBMC). The influence of new derivatives on cytokine production (TNF-α, IL-6 and IL-10) was examined in PBMC cultures stimulated by LPS. Antiproliferative activity of compounds was studied in PBMC cultures stimulated by phytohaemagglutinin. Minimal inhibitory activity of compounds was studied by broth microdilution method on Gram-positive (*S. aureus*, *M. smegmatis*) and Gram-negative (*E. coli*, *Y. enterocolitica*, *K. pneumonia*) bacterial and fungal *C. albicans* strain. Obtained 1,2,4-triazole derivatives were not toxic to PBMC at a concentration range of 10–100 µg/mL. Only one 1,2,4-triazole derivative showed significant antiproliferative activity at the highest dose. Five 1,2,4-triazole derivatives showed significant, stronger than ibuprofen, inhibition of pro-inflammatory TNF-α production at concentrations 10 and 50 µg/mL, as well as significant elevation of levels of anti-inflammatory cytokine IL-10 at each used dose. Two linear compounds showed antibacterial activity against Gram-positive bacteria. In conclusion, five obtained compounds showed a strong anti-inflammatory effect and deserve further research.

Keywords: amidrazones; anti-inflammatory; antibacterial; anthelmintic; PBMC; drug research

Citation: Paprocka, R.; Wiese-Szadkowska, M.; Kutkowska, J.; Kowalewski, A. The Synthesis and Biological Activity of Amidrazone Derivatives Obtained in Reaction with *cis*-1,2,3,6-Tetrahydrophthalic Anhydride. *Med. Sci. Forum* **2022**, *14*, 139. https://doi.org/10.3390/ECMC2022-13453

Academic Editor: Maria Emília Sousa

Published: 1 November 2022

Supplementary Materials: The presentation material of this work is available online at https://www.mdpi.com/article/10.3390/ECMC2022-13453/s1.

Author Contributions: Conceptualization, R.P.; methodology, M.W.-S. and J.K.; investigation, R.P., M.W.-S. and J.K.; resources, R.P.; writing—original draft preparation, R.P.; writing—review and editing, A.K. and M.W.-S.; visualization, R.P.; supervision R.P.; project administration, R.P.; funding acquisition, R.P. All authors have read and agreed to the published version of the manuscript.

Funding: This work has been supported by Nicolaus Copernicus University, Collegium Medicum (IDUB IDE HS-2020 Renata Paprocka).

Institutional Review Board Statement: Experiments using peripheral blood mononuclear cells (PBMC) ware conducted according to the guidelines of the Declaration of Helsinki and were approved by the Collegium Medicum of Nicolaus Copernicus University Bioethical Commission (KB 39/2019).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Data is available from the authors.

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