



3

4

5

6 7

8

10

11

12

13

15

16

17

18

19

20

21

23

24

25

26

27

28

29

30

31

32 33

34

35

36

37

38

40

41

Abstract

Novel anthranilic acid hybrids – an alternative weapon against inflammatory pathologies

Miglena Milusheva 1,2,*, Mina Todorova 2, and Stoyanka Nikolova 2

- Bulgaria, Medical University of Plovdiv, Faculty of Pharmacy, Department of Bioorganic Chemistry, 15A Vassil Aprilov blv., <u>miglena.milusheva@mu-plovdiv.bg</u>
- ² Bulgaria, The Paisii Hilendarski University of Plovdiv, Faculty of Chemistry, Department of Organic Chemistry, 24 Tzar Assen str., <u>miglena.milusheva@uni-plovdiv.bg</u>; <u>minatodorova@uni-plovdiv.bg</u>, <u>tanya@uni-plovdiv.bg</u>
- * Correspondence: miglena.milusheva@mu-plovdiv.bg
- † Presented at the title, place, and date.

Abstract: Non-steroidal anti-inflammatory drugs are used to relieve pain, fever, and inflammation while also protecting the cardiovascular system. However, the side effects of currently available anti-inflammatory medications, which include gastric ulcer, bronchospasm, and cardiovascular problems, have limited their usage. Due to the adverse effects of these drugs, there is a high demand for the search of new drugs with lesser or no side effects. In the context, current trend of research has shifted towards synthesis of new anthranilic acid hybrids. Having in mind the variety of biological activities, we have synthesized a new hybrid molecule of anthranilic acid and 2-(3,4-dimethoxyphenyl)ethylamine. The synthesis of a new molecule, attached to a 2-phenylethylamine or substituted 2-phenylethylamines, is extremely interesting in view of what properties the newly obtained molecule would inherit from both fragments. The synthesized hybrid is then used in acylation with various acyl chlorides. A number of new hybrid anthranildiamides were synthesized as a result. The novel molecules were tested *in vitro* to estimate their anti-inflammatory effect preventing albumin denaturation. The results showed that all the compounds exhibit a preventive effect on albumin denaturation higher than common non-steroidal anti-inflammatory drugs. To confirm the presence of anti-inflammatory effect in the diamides, we conducted additional tests evaluating their effect on Interleukin-1 expression, and similar results were observed. Based on the experimental data, we can conclude that a collection of novel 2-phenylethilamine hybrids were successfully synthesized and they can be considered as anti-inflammatory drug candidates – alternatives to current therapeutics.

Keywords: synthesis; hybrid molecules; anthranilic acid; diamides; anti-inflammatory activity; denaturation of albumin

Author Contributions: Conceptualization, S.N.; methodology, M.M., M.T.; investigation, M.M, M.T., and S.N.—synthesis; writing—original draft preparation, S.N., M.M.; writing—review and editing, S.N. and M.M.; visualization, S.N., M.M., and M.T.; supervision, S.N.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Citation: Milusheva, M.; Todorova, M.; Nikolova, S Novel anthranilic acid hybrids – an alternative weapon against inflammatory pathologies *Med. Sci. Forum* **2023**, 2, x. https://doi.org/10.3390/xxxxx

Academic Editor: Firstname Lastname

Published: date

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2023 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

Med. Sci. Forum **2023**, 2, x

| Acknowledgments: This research is supported by the Bulgarian Ministry of Education and Science |
|--|
| under the National Program "Young Scientists and Postdoctoral Students – 2". |
| Conflicts of Interest: The authors declare no conflict of interest. |