UDC 616.314.17:612.08:577.115:599.323.4 https://doi.org/10.15407/biotech18.02.103

PERIODONTOPROTECTIVE EFFECT OF NIMESULIDE AND NaHS UNDER SIRS CONDITIONS

O.T. TKACHENKO, V.V. PLETNOV, A.O. MYKYTENKO

Poltava State Medical University, Poltava, Ukraine

E-mail: yixelo.tkachenko@gmail.com

Received 2025/03/24
Revised 2025/03/03
Accepted 2025/04/30

Hydrogen sulfide donors can protect the gastric mucosa from nimesulide damage, but their combined effect is unknown.

Aim. The work purposed to determine the concentration of peroxynitrites ($ONOO^-$), nitrites (NO_2^-), and malondialdehyde (MDA) in the periodontal soft tissues of rats under the conditions of administration of nimesulide and NaHS during systemic inflammatory response syndrome (SIRS) modeling.

Materials and Methods. Thirty sexually mature male Wistar rats were divided into groups: I — control, II — intraperitoneal injection with 0.4 μg/kg of bacterial lipopolysaccharide *S.typhi* (SIRS group), III — 18 mg/kg/day nimesulide gavage during SIRS, IV group — 5 mg/kg/day NaHS injection during SIRS, V group — NaHS and nimesulide administration during SIRS. We studied concentrations of $ONOO^-$ and NO_2^- and MDA.

Results and Discussion. During SIRS, ONOO- concentration in soft periodontal tissues increased by 1.12 times, NO_2^- by 7.02 times, and MDA by 4.51 times compared to the control ($P < 0.05$). Nimesulide lowers ONOO- content by 1.04 times, NO_2^- by 1.22 times, and MDA by 1.5 times compared to the SIRS group ($P < 0.05$). NaHS lowers NO_2^- by 11.79 times and MDA by 1.46 times compared to the SIRS group ($P < 0.05$). The combination of NaHS and nimesulide increases $ONOO^-$ content by 1.4 times, lowers NO_2^- content by 6.7 times, and MDA by 1.36 times compared to the SIRS group ($P < 0.05$).

Conclusions. The combination of nimesulide and NaHS lowers the intensity of lipid peroxidation in soft periodontal tissues during SIRS modeling.

Keywords: nitrites, peroxynitrite, lipid peroxidation, lipopolysaccharide, hydrogen sulfide, nimesulide.

It is known that under conditions of systemic inflammatory response syndrome (SIRS), periodontal tissues are damaged by the mechanism of oxidative stress. The reaction between the superoxide anion radical and nitric oxide forms peroxynitrite. The biochemistry of peroxynitrite is multifaceted, including one- or two-electron oxidation and nitration reactions. Experimental studies confirm that peroxynitrite is an essential mediator in physiological and pathological processes [1]. Nimesulide is an effective anti-inflammatory drug for the treatment of periodontitis, but it has an ulcerogenic effect [2]. Hydrogen sulfide donors can protect the gastric mucosa from the adverse impacts of nimesulide. Still, such a combined effect on periodontal tissues has not previously been studied, and the role of peroxynitrite under these conditions is unknown.

Aim. The work was purposed to establish the concentration of peroxynitrite, nitrites, and malondialdehyde in the periodontal soft tissues of rats under the conditions of administration of nimesulide and NaHS against the background of modeling of systemic inflammatory response syndrome.

Citation: Tkachenko, O. T., Pletnov, V. V., Mykytenko, A. O. (2025). Periodontoprotective effect of nimesulide and NaHS under SIRS conditions. *Biotechnologia Acta*, 18(2), 103–105. https://doi.org/10.15407/biotech18.02.103

Materials and Methods. The experiments were performed on 30 sexually mature male Wistar rats weighing 190–210 g. Group I — control, Group II — rats that were injected intraperitoneally with 0.4 μg/kg of bacterial lipopolysaccharide (LPS) *S.typhi*, simulating SIRS, with a frequency of 3 times in the first 7 days, then once a week, for 30 days, Group III — animals that were injected intragastrically with 18 mg/kg nimesulide once a day in the last 7 days of SIR's simulation, Group IV — rats that were injected intraperitoneally with 5 mg/kg NaHS once a day in the previous 7 days of SIRS simulation, Group V — animals that were injected intragastrically with 18 mg/kg nimesulide and intraperitoneally with 5 mg/kg NaHS once a day in the last 7 days of SIRS simulation. The object of the study was the soft periodontal tissues of rats, where the concentration of peroxynitrite and nitrites [3] and malondialdehyde (MDA) [4] was determined. The data were statistically processed using a nonparametric method – the Mann-Whitney test.

Results and Discussion. Administration of *S. typhi's* LPS led to an increase of peroxynitrite concentration by 1.12 times compared to the control ($P < 0.05$). Nimesulide administration during SIRS reduced the concentration of peroxynitrite in the periodontal soft tissues of rats by 1.04 times compared to the SIRS group ($P < 0.05$). Under the conditions of administration of the hydrogen sulfide donor NaHS and nimesulide, the concentration of peroxynitrites increased by 1.56 times compared to the control group and by 1.4 times compared to the SIRS group ($P < 0.05$). Under the conditions of administration of *S. typhi's* LPS, the concentration of nitrites in the soft periodontal tissues of rats increased by 7.02 times compared to the control ($P < 0.05$). The administration of nimesulide during SIRS reduced the concentration of nitrites by 1.22 times compared to the control group and by 8.54 times compared to the SIRS group ($P < 0.05$). Under the conditions of administration of the hydrogen sulfide donor NaHS, the concentration of nitrites decreased by 1.68 times compared to the control group and by 11.79 times compared to the SIRS group ($P < 0.05$). Under the conditions of administration of the hydrogen sulfide donor NaHS and nimesulide, the concentration of nitrites increased by 1.05 times compared to the control. It decreased by 6.7 times compared to the SIRS group ($P < 0.05$). Under the conditions of *S. typhi's* LPS administration, the concentration of MDA increased by 4.51 times compared to the control ($P < 0.05$). The administration of nimesulide during SIRS reduced the concentration of MDA by 1.5 times compared to the SIRS group and was 3.01 times higher compared to the control group ($P < 0.05$). Under the conditions of administration of the hydrogen sulfide donor NaHS, the concentration of MDA decreased by 1.46 times compared to the SIRS group. It was 3.09 times higher compared to the control group ($P < 0.05$). Under the conditions of administration of the hydrogen sulfide donor NaHS and nimesulide, the concentration of MDA decreased by 1.36 times compared to the SIRS group. It was 3.32 times higher compared to the control group ($P < 0.05$).

One of the essential properties of H_2S is its bell-shaped (or biphasic/bimodal) pharmacological mode of action. At low concentrations, H_2S exhibits physiological, regulatory, or modulating effects and acts as a cytoprotective, antioxidant, and anti-inflammatory agent. At high concentrations, H_2S can have harmful effects, including pro-oxidant effects and cytostatic or cytotoxic reactions. To exert its cytoprotective effects, H_2S engages a multitude of molecular pathways and mechanisms. Molecular targets and signaling pathways of H_2S include K-ATP channels, Akt, AMPK, PTEN, NF-κB, Nrf2, proline-rich kinase 2, as well as the adenylate cyclase and guanylate cyclase systems, etc. [5]. Numerous studies have shown that H_2S activates Nrf2, which provides antioxidant effects, playing a significant role in the development of respiratory diseases such as COPD, asthma, acute lung injury, etc. According to Wang Y. et al., intraperitoneal administration of NaHS alleviates emphysema and airway inflammation by restoring redox balance and inhibiting ferroptosis by regulating the Nrf2-PPAR-ferritinophagy signaling pathway [6].

Nitration does not always have a negative impact, as previously believed. Nitration reactions can modify other compounds, altering their bioactivity and perhaps even forming new signaling molecules. Unsaturated fatty acids (FA) in lipids, including oleic and linoleic acids, are modified to form nitrolipids (NO_2-FA), which make them electrophilic. Through this mechanism, NO_2-FA potently antagonizes NF-κB and activates Nrf2 signaling, two significant effects that explain their broad anti-inflammatory and antioxidant activities [7]. The role of peroxynitrite and its metabolites in the development of various pathological conditions still requires more detailed study.

Conclusions: the combined effect of nimesulide and the hydrogen sulfide donor NaHS on the soft tissues of periodontal tissues of rats under conditions of modeling systemic inflammatory response syndrome reduces the intensity of lipid peroxidation, the content of nitrites, and increases the content of peroxynitrites.

Authors' contribution

Tkachenko O. T. — data acquisition, data analysis, writing the original draft; Pletnov V. V. — data acquisition, data analysis, writing the original draft; Mykytenko A. O. — project administration, project supervision, data analysis, writing original draft, review of the original draft.

All authors approved the final version of the article.

REFERENCES

1. Prolo, C., Piacenza, L., Radi, R. (2024). Peroxynitrite: a multifaceted oxidizing and nitrating metabolite. *Current Opinion in Chemical Biology*, 80, 102459. https://doi.org/10.1016/j.cbpa.2024.102459.
2. Salvi, G., Lang, N. (2005). The Effects of Non-Steroidal Anti-Inflammatory Drugs (Selective and Non-Selective) on the Treatment of Periodontal Diseases. *Current Pharmaceutical Design*, 11(14), 1757–1769. https://doi.org/10.2174/1381612053764878.
3. Akimov, O. Y., Kostenko, V. O. (2016). Functioning of nitric oxide cycle in gastric mucosa of rats under excessive combined intake of sodium nitrate and fluoride. *Ukrainian biochemical journal*, 88(6), 70–75. https://doi.org/10.15407/ubj88.06.070.
4. Gérard-Monnier, D., Erdelmeier, I., Régnard, K., Moze-Henry, N., Yadan, J. C., Chaudière, J. (1998). Reactions of 1-methyl-2-phenylindole with malondialdehyde and 4-hydroxyalkenals. Analytical applications to a colorimetric assay of lipid peroxidation. *Chemical research in toxicology*, 11(10), 1176–1183. https://doi.org/10.1021/tx9701790.
5. Dilek, N., Papapetropoulos, A., Toliver-Kinsky, T., Szabo, C. (2020). Hydrogen sulfide: An endogenous regulator of the immune system. *Pharmacological Research*, 161, 105119. https://doi.org/10.1016/j.phrs.2020.105119.
6. Wang, Y., Liao, S., Pan, Z., Jiang, S., Fan, J., Yu, S., Xue, L., Yang, J., ..., Chen, Y. (2022). Hydrogen sulfide alleviates particulate matter-induced emphysema and airway inflammation by suppressing ferroptosis. *Free Radical Biology and Medicine*, 186, 1–16. https://doi.org/10.1016/j.freeradbiomed.2022.04.014.
7. Lundberg, J. O., Weitzberg, E. (2022). Nitric oxide signaling in health and disease. *Cell*, 185(16), 2853–2878. https://doi.org/10.1016/j.cell.2022.06.010.