4. Yan Q., Xing Q., Liu Z., Zou Y., Liu X., Xia H. The phytochemical and pharmacological profile of dandelion // Biomed Pharmacother. 2024. Vol. 179. P. 117334. doi: 10.1016/j.biopha.2024.117334.

5. Younger S., Jang H., Davies H.A., Niemiec M.J., Garcia J.G.N., Nussinov R., Migrino R.Q., Madine J., Arce F.T. Medin Oligomer Membrane Pore Formation: A Potential Mechanism of Vascular Dysfunction // Biophys J. 2020. Vol. 118(11). P. 2769-2782. doi: 10.1016/j.bpj.2020.04.026.

УЁКПЕЙИ ОГХЕНЕМАРО ЭММАНУЭЛЬ, ФЕЛИКС АНГЕЛ ЧИСОМ, КОВАЛЬ А.Н.

ДИСФУНКЦИЯ МИТОХОНДРИЙ И G-КВАДРУПЛЕКСЫ ПРИ ХРОНИЧЕСКИХ РЕСПИРАТОРНЫХ ЗАБОЛЕВАНИЯХ: НОВЫЕ ТЕРАПЕВТИЧЕСКИЕ МИШЕНИ И ПОДХОДЫ К ЛЕЧЕНИЮ НА ОСНОВЕ РАСТЕНИЙ

Гомельский государственный медицинский университет, г. Гомель, Республика Беларусь
e-mail: akovalj@ya.ru

UYOKPEYI OGHENEMARO EMMANUEL, FELIX ANGEL CHISOM, KOVAL A.N.

MITOCHONDRIAL DYSFUNCTION AND G-QUADRUPLEXES IN CHRONIC RESPIRATORY DISEASES: NOVEL THERAPEUTIC TARGETS AND PLANT-BASED INTERVENTIONS

Gomel State Medical University, Gomel, Belarus
e-mail: *akovalj@ya.ru*

Аннотация. Хронические респираторные заболевания (ХРЗ), такие как хроническая обструктивная болезнь легких (ХОБЛ), астма и легочный фиброз, представляют серьезные глобальные проблемы здравоохранения. Данное исследование изучает роль митохондриальной дисфункции и гуаниновых квадруплексов (G-квадруплексов) в митохондриальной ДНК (мтДНК) в патогенезе ХРЗ, уделяя внимание окислительному стрессу, метаболическому перепрограммированию и воспалению. На основе систематического анализа литературы оценивается терапевтический потенциал вторичных метаболитов растений и подходов лечения на основе G-квадруплексов. Результаты подчеркивают общие механизмы между радиационным повреждением митохондрий и ХРЗ, предлагая новые стратегии лечения. Будущие исследования должны сосредоточиться на биоинформатике и клинической валидации этих подходов.

Ключевые слова: митохондриальная дисфункция, G-квадруплексы, хронические респираторные заболевания, окислительный стресс, растительные метаболиты

Abstract. Chronic respiratory diseases (CRDs), such as chronic obstructive pulmonary disease (COPD), asthma, and pulmonary fibrosis, pose significant global health challenges. This study investigates the role of mitochondrial dysfunction and guanine quadruplexes (G4) in mitochondrial DNA (mtDNA) in CRD pathogenesis, focusing on oxidative stress, metabolic reprogramming, and inflammation. Using a systematic literature analysis, we evaluate the therapeutic potential of plant-based secondary metabolites and G4-targeted interventions. The findings highlight shared mechanisms between radiation-induced mitochondrial damage and CRDs, suggesting novel treatment strategies. Future research should prioritize bioinformatics and clinical validation of these approaches.

Keywords: mitochondrial dysfunction, G-quadruplexes, chronic respiratory diseases, oxidative stress, plant-based metabolites

This study explores how mitochondrial dysfunction and G-quadruplexes (G4) drive chronic respiratory diseases (CRDs) like COPD, asthma, and pulmonary fibrosis. We aim to find shared pathways between radiation-induced and CRD-related mitochondrial damage, focusing on oxidative stress, energy disruption, and inflammation, while assessing plant-based compounds and G4-targeted therapies as potential treatments for those affected.

Materials and Methods. This study employs a systematic literature review to analyze the mechanisms of mitochondrial dysfunction and G4 in CRDs. The following steps were undertaken:

1) Literature search: Relevant studies were identified using PubMed, Scopus, and Web of Science databases, covering the period from 2000 to 2025. Search terms included «mitochondrial dysfunction», «G-quadruplexes», «chronic respiratory diseases», «oxidative stress», «COPD», «asthma», «pulmonary fibrosis», and «plant-based metabolites».

2) Inclusion criteria: Peer-reviewed articles and conference proceedings in English or Russian, focusing on mitochondrial dysfunction, G4, or plant-based therapies in CRDs or related stress models (e.g., radiation exposure).

3) Data extraction: Key findings were extracted regarding oxidative stress, metabolic reprogramming, NLRP3 inflammasome activation, G4 roles in mtDNA, and therapeutic interventions.

4) Data analysis: A comparative analysis was conducted to identify parallels between radiation-induced mitochondrial damage and CRD pathogenesis. Therapeutic strategies were evaluated based on their mechanistic relevance and potential clinical applicability.

For completing the research, five key studies were selected for in-depth analysis, including two works on radiation-induced mitochondrial dysfunction and plant-based G4 modulation [1, 2], and three studies on CRD mechanisms and inflammation [3, 4, 5].

Results and Discussion. The analysis of the sources revealed that mitochondrial dysfunction is a central feature of CRD pathogenesis. And it is driven by three key mechanisms:

1) Oxidative stress: Excessive reactive oxygen species (ROS) production in CRDs overwhelms antioxidant defenses, such as superoxide dismutase, leading to mitochondrial damage and inflammation [4]. Similar ROS-driven mitochondrial impairments were observed in radiation stress models, where prolonged ^{137}Cs exposure disrupted mitochondrial ultrastructure and energy metabolism in rat myocardium [1]. This suggests that oxidative stress is a shared pathway across stress-induced mitochondrial pathologies, amplifying tissue damage in CRDs like COPD and asthma [3].

2) Metabolic reprogramming: Hypoxia in CRDs shifts cellular metabolism toward glycolysis, reducing ATP production and increasing lactate accumulation [5]. Comparable disruptions in oxidative phosphorylation were reported in chronic ^{137}Cs exposure models, indicating energy deficits as a common feature [1]. In asthma, allergen-induced mitochondrial ROS exacerbate Th2-mediated immune responses, further impairing metabolic homeostasis [3]. These findings highlight the role of mitochondrial energy metabolism in CRD progression.

3) Inflammasome activation: Mitochondrial DNA (mtDNA) release into the cytosol activates the NLRP3 inflammasome, driving IL-1β-mediated inflammation in CRDs [5]. G4 in mtDNA may regulate this process by modulating mtDNA stability and gene expression [2]. Dysregulation of G4 was linked to changes in cellular energy status (some radiation stress models, suggesting their relevance in CRD-related inflammation [2].

Therapeutic strategies targeting mitochondrial dysfunction showed promise:

1) Antioxidants: Mitochondrial-targeted compounds like MitoQ and plant-derived flavonoids reduced ROS-mediated damage [2]. Plant-based secondary metabolites, such as those studied in cancer models, stabilized mtDNA G4, offering potential for CRD treatment [2].

2) AMPK activators: Metformin restored energy homeostasis by enhancing mitochondrial function [5].

3) G4-targeted therapies: Stabilizing G4 in mtDNA could mitigate inflammation and energy deficits, a novel approach inspired by radiation biology [2].

The similarities between mitochondrial damage caused by radiation and that seen in chronic respiratory diseases (CRDs) offer a hopeful bridge for new discoveries. Studies like those by Koval and colleagues [1, 2] show that lessons from radiation biology could guide us toward better understanding CRDs, potentially improving the lives of millions. Yet, we face hurdles: much of this research relies on animal models, which don't fully capture human complexity, and therapies targeting G-quadruplexes (G4) still need testing in real patients. Moving forward, researchers could harness bioinformatics to explore how G4 structures work in CRDs and test plant-based treatments, like those derived from nature's antioxidants, in people struggling with these conditions.

Conclusions. Mitochondrial dysfunction lies at the heart of CRDs, fueling oxidative stress, disrupting energy production, and sparking inflammation through pathways like the NLRP3 inflammasome. G-4 in mitochondrial DNA emerge as promising new targets, as their imbalance seems to worsen inflammation and energy shortages. Plant-based compounds, such as flavonoids, offer exciting potential – not only as antioxidants but also as stabilizers of these G4 structures. The overlap between radiation-related mitochondrial damage and CRDs opens doors to innovative treatments by combining insights from different fields. However, to truly help patients, we need more research, using tools like bioinformatics and real-world clinical trials, to create tailored therapies that address the unique challenges of living with CRDs.

References

1. Koval A.N. Changes in the energy metabolism of rat myocardium under the influence of ionizing radiation // Problems of Health and Ecology. – 2024. – Vol. 21, No. 1. – P. 89–92.
2. Koval A.N., Litvinchuk A.V., Logvinovich O.S., Sergeenko S.M., Geldimamedov Ch.A., Belous E.M., Gromyko M.V., Shaforost A.S. Secondary plant metabolites and mitochondrial G-quadruplexes: therapeutic potential in cancer treatment // Modern Achievements of Chemical-Biological Sciences. – 2024. – P. 175–180.
3. Qian L., et al. Mitochondria signaling pathways in allergic asthma // Journal of Investigative Medicine. – 2022. – Vol. 70, No. 4. – P. 863–882. – DOI: 10.1136/jim-2021-002060.
4. Rahman I., Adcock I.M. Oxidative stress and redox regulation of lung inflammation in COPD // European Respiratory Journal. – 2006. – Vol. 28, No. 1. – P. 219–242. – DOI: 10.1183/09031936.06.00014506.

Zhou R., et al. A role for mitochondria in NLRP3 inflammasome activation // Nature. – 2011. – Vol. 469, No. 7329. – P. 221–225. – DOI: 10.1038/nature09663