Biol. Stud. 2026, 20(3), 27–38 • https://doi.org/10.30970/sbi.2003.901
www.https://publications.lnu.edu.ua/journals/index.php/biology

UDC: 577.35+576.32+615.275

TIME-DEPENDENT MODULATION OF REACTIVE OXYGEN SPECIES IN LYMPHOMA CELLS BY A THIAZOLE DERIVATIVE AND ITS COMPLEX WITH A POLYMERIC NANOCARRIER

Yaryna Shalai [1], ***Marta Ilkiv*** [2], ***Yurii Koval*** [1], ***Vira Budzyn*** [2], ***Andriy Babsky*** [1]

[1] *Ivan Franko National University of Lviv, 4 Hrushevsky St., Lviv 79005, Ukraine*

[2] *Ivan Boberskyi Lviv State University of Physical Culture 11 Kostiushko St., Lviv 79000, Ukraine*

Shalai, Ya., Ilkiv, M., Koval, Yu., Budzyn, V., & Babsky, A. (2026). Time-dependent modulation of reactive oxygen species in lymphoma cells by a thiazole derivative and its complex with a polymeric nanocarrier. *Studia Biologica*, 20(3), 27–38. doi:10.30970/sbi.2003.901

Background. Thiazole-based molecules are promising anticancer candidates that disrupt the redox balance of tumor cells, but the impact of polymer carriers on their activity remains poorly understood. This study evaluated how a 2-amino-5-benzylthiazole derivative (BF1) and its complex with a PEG-based polymer (Th4) influence reactive oxygen species (ROS) generation in Nemeth–Kellner lymphoma (NK/Ly) cells, using the free polymer (Th3) as a control.

Materials and Methods. NK/Ly lymphoma cells obtained from ascitic tumors in mice were incubated with BF1, the free polymer carrier Th3, or the BF1–polymer complex Th4 at equal concentrations. After 30, 60, and 120 minutes of incubation, intracellular ROS levels were evaluated by fluorescence microscopy using a ROS-sensitive probe, and fluorescence intensity was quantified with image analysis software. Group differences were assessed by standard statistical tests, and correlation analysis was applied to examine the relationship between incubation time and ROS levels.

Results. Treatment with BF1 led to a significant, time-dependent increase in intracellular ROS compared with untreated control cells, indicating that this thiazole derivative effectively enhances oxidative stress in lymphoma cells. The free polymer Th3 did not cause meaningful changes in ROS at any time point, supporting its role as an inert carrier. In contrast, cells exposed to the BF1–polymer complex Th4 consistently showed a more pronounced elevation of ROS than those treated with BF1 alone at all incubation times.

Correlation analysis revealed a moderate positive association between incubation time and ROS levels for BF1, and a stronger positive association for Th4, suggesting that polymer complexation intensifies and prolongs ROS accumulation in tumor cells.

Conclusions. A 2-amino-5-benzylthiazole derivative markedly increases ROS levels in lymphoma cells, an effect further amplified by its polymer complexation without additional toxicity from the free carrier. These findings indicate that induction of oxidative stress is a key mechanism of the derivative's antitumor action. The inert nature of the free polymer confirms its suitability as a nanocarrier, while the enhanced ROS generation supports further development of polymer-based thiazole formulations for cancer therapy.

Keywords: lymphoma, thiazole derivative, polymeric carrier, polyethyleneglycol, reactive Oxygen species

INTRODUCTION

Lymphoma is a malignant hematologic neoplasm of lymphoid tissue characterized by enlargement of lymph nodes and extensive accumulation of malignant lymphocytes in internal organs. Lymphomas are the most aggressive and most common form of hematologic malignancy, accounting for 55.6 % of all neoplastic diseases. The development of novel small molecules that selectively target malignant cells while sparing normal tissues remains a major objective in oncology. Thiazole-containing heterocycles have emerged as a particularly promising chemotype, exhibiting potent cytotoxic and pro-apoptotic activity across a variety of tumor models, including hematologic malignancies. Thiopyrano[2,3-d]thiazole structures have been shown to suppress the viability of human leukemia T-cells and glioblastoma cells via ROS-mediated mitochondrial apoptosis and PARP-1 inhibition, establishing thiazole scaffolds as promising candidates for anticancer drug design (Finiuk *et al*., 2022).

A key mechanism underlying the antitumor action of many thiazole derivatives is modulation of cellular redox homeostasis and induction of reactive oxygen species (ROS). It was reported that representative thiopyrano[2,3-d]thiazole derivatives induce accumulation of endogenous ROS, leading to mitochondrial dysfunction and apoptosis in leukemia models (Finiuk *et al.*, 2022). This mode of action is consistent with the broader concept of redox-based cancer therapy, where tumor cells characterized by elevated basal ROS and reprogrammed antioxidant defenses are pushed beyond their adaptive capacity by additional oxidative stress. Wang *et al*. reviewed the design principles and applications of ROS-responsive drug delivery systems, emphasizing that ROS-rich tumor microenvironments can be exploited for selective activation of therapeutics (Liang *et al.*, 2016). Against this background, thiazole derivatives that enhance intracellular ROS generation represent rational tools for targeted redox modulation in cancer cells.

In parallel, polymer-based delivery platforms have been intensively developed to improve the pharmacokinetics, stability, and tumor selectivity of small-molecule drugs. Folate-modified pH/ROS dual-responsive polymeric micellar systems have demonstrated enhanced intracellular delivery and controlled release of doxorubicin in cancer cells, thereby increasing therapeutic efficacy while potentially limiting systemic toxicity (Dai *et al.*, 2024). Other studies have shown that ROS-responsive and actively targeted polymeric nanoparticles can further improve tumor selectivity and on-demand activation

of chemotherapeutics in oxidatively stressed microenvironments (Zhang *et al.*, 2021). These data provide a strong rationale for combining redox-active thiazole derivatives with polymer carriers to modulate their cellular uptake, intracellular distribution, and ROS-dependent mechanisms of action.

Despite these advances, experimental data on the interplay between newly synthesized thiazole derivatives, polymer carriers, and ROS generation in lymphoma cells remains limited. Our previous studies showed that a thiazole derivative and its complexes with PEG-containing polymeric nanoparticles significantly increase ROS generation in NK/Ly lymphoma cells, while maintaining the oxidative status of non-tumor tissues within a tolerable range. Also, changes in bioenergetic characteristics and mitochondrial function of NK/Ly cells under the action of thiazole derivatives in complex with polymeric nanoparticles have been documented, suggesting that polymer-assisted delivery can significantly influence mitochondrial respiration and membrane potential in lymphoma cells (Ilkiv *et al.*, 2022). However, a detailed quantitative analysis of time-dependent ROS dynamics and the relative contribution of free versus polymer-complexed thiazole derivatives in NK/Ly lymphoma cells remains incomplete.

In this context, the present study investigates the effect of a thiazole derivative (BF1) and its polymer complex (Th4) on intracellular ROS generation in NK/Ly lymphoma cells, using a free polymer (Th3) as a control carrier. Quantitative analysis of ROS levels over different incubation periods allows us to evaluate how polymer complexation influences the pro-oxidant activity of BF1, as well as the temporal dynamics of oxidative stress in tumor cells. By correlating incubation time with fluorescence-based ROS readouts, we aim to clarify whether polymer-assisted delivery enhances or modifies the redox-dependent mechanism of BF1 compared to the free compound.

MATERIALS AND METHODS

The 2-amino-5-benzylthiazole derivative (hereafter referred to as BF1) was synthesized at the Department of Organic Chemistry of Ivan Franko National University of Lviv. A polyethylene glycol (PEG)-based polymer carrier, a homopolymer of PEG methacrylate with a PEG side-chain molecular weight of 475 kDa (poly(PEGMA), hereafter designated Th3) was synthesized at the Department of Organic Chemistry of Lviv Polytechnic National University.

The compounds were dissolved in dimethyl sulfoxide (DMSO), and aqueous dispersions of a polymer nanoparticle, Th3, and its complex with BF1 (hereafter designated Th4), were used.

The Nemeth–Kellner lymphoma (NK/Ly) model, a transplantable murine lymphoma, was used in this study. The NK/Ly strain was obtained from the tumor strain collection of the Institute of Experimental Pathology, Oncology and Radiobiology of the National Academy of Sciences of Ukraine (Kyiv, Ukraine). Animal handling and experimental procedures were conducted in accordance with the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (1998) and the Law of Ukraine “On Protection of Animals from Cruel Treatment”, as well as approved by the Ethics Committee of Ivan Franko National University of Lviv, Ukraine (Protocol of 01.06.2026 No 58-06-2026). The lymphoma was maintained in outbred male mice by intraperitoneal inoculation of 200 µL of ascitic fluid. The injected ascitic fluid contained 100–150 million tumor cells per 200 µL. Tumor growth was monitored throughout the experiment, and the mice were weighed daily from the day of

lymphoma inoculation. Over the course of the experiment, the tumors increased in size over a period of 10–14 days, and the rate of tumor growth and body weight gain were monitored. In order to obtain ascitic fluid for further analysis, the ascitic tumor was drained. Drainage of ascitic fluid was performed when the body weight of the mice reached 140–170 % of their pre-inoculation body weight. Prior to the procedure, the mice were anesthetized with diethyl ether. The abdominal cavity was then drained using a sterile syringe. Tumor cell counts were determined using a Goryaev hemocytometer.

Intracellular ROS levels were assessed by fluorescence microscopy using dihydroethidium (DHE), a fluorescent probe for ROS detection. The samples were incubated with DHE for 15 min, and the final dye concentration was 100 nM. Images were acquired using an Olympus IX73 inverted microscope equipped with a DP74 digital camera (Ilkiv *et al.*, 2022). Fluorescence microscopy was using an excitation filter of 540–585 nm, a 595 nm dichroic mirror, and a 600 nm emission (barrier) filter. Oxidized DHE products exhibit fluorescence with excitation and emission maxima within the ranges of 500–530 nm and 590–620 nm, respectively (Ilkiv *et al.*, 2022).

The incubation medium contained the following components (mM): KCl, 90.0; NaCl, 15.0; EGTA, 1.0; and HEPES, 10.0, adjusted to pH 7.4. Ascitic lymphoma cells were washed and diluted 10-fold in the incubation medium. BF1, the polymeric carrier Th3, and the BF1–Th3 complex (Th4) were added to the cell suspension at a final concentration of 10 μM. Rotenone (final concentration 5 %) was used as a positive control in a separate sample. Cells were incubated for 15 min at 37 °C. Following incubation, the cells were washed and stained with 10 μL of dihydroethidium (DHE), followed by an additional 15 min incubation at 37 °C. Several microliters of each sample were placed onto a microscope slide and covered with a coverslip. The preparations were examined using an Olympus IX73 microscope at ×12.6 magnification. Multiple fields of view were selected for analysis. Images were first acquired under bright-field illumination and subsequently under fluorescence illumination.

Changes in intracellular ROS levels were assessed by measuring fluorescence intensity. The photographs were analyzed using ImageJ software. After obtaining the quantitative indicators, the mean value was calculated using GraphPad Prism software. All data are presented as mean ± standard error of the mean (SEM). To determine statistically significant differences between the independent groups, a one-way analysis of variance (ANOVA) followed by Tukey4's post-hoc test for multiple comparisons was performed. $P < 0.05$ was considered statistically significant. To determine the statistical relationships between the variables, Pearson correlation analysis was performed, and the statistical significance of the correlation coefficients was evaluated ($P < 0.05$). (Hazra *et al*., 2016).

RESULTS AND DISCUSSION

Quantitative analysis of intracellular levels of ROS under the influence of a thiazole derivative in complex with polymer carriers showed that treatment of cells with compound BF1 at a concentration of 10 μM led to a 28.7 % increase in ROS production compared to control values (**Fig. 1**). This indicates a potential ability of BF1 to modulate the oxidative status of tumor cells. At the same time, the free polymer Th3 did not induce statistically significant changes in ROS levels in lymphoma cells, confirming its neutrality with respect to pro-oxidant processes and supporting its consideration as an inert carrier for bioactive molecules.

In contrast, investigation of the Th4 complex revealed a more pronounced increase in ROS production – by 36.3 % relative to the values obtained for the free compound (**Fig. 1**). This trend may indicate changes in intracellular localization or the kinetics of BF1 uptake upon its encapsulation within the polymer matrix, which likely enhances its pro-oxidant activity.

To validate the sensitivity of our assay to ROS induction, we included rotenone (Rot), a mitochondrial complex I inhibitor widely used as a positive control for oxidative stress (Li *et al.*, 2003), in all experimental series. Rotenone treatment induced a marked increase in ROS levels compared with untreated control cells, confirming that the applied DHE-based fluorescence protocol reliably detects mitochondrial ROS overproduction in NK/Ly lymphoma cells.

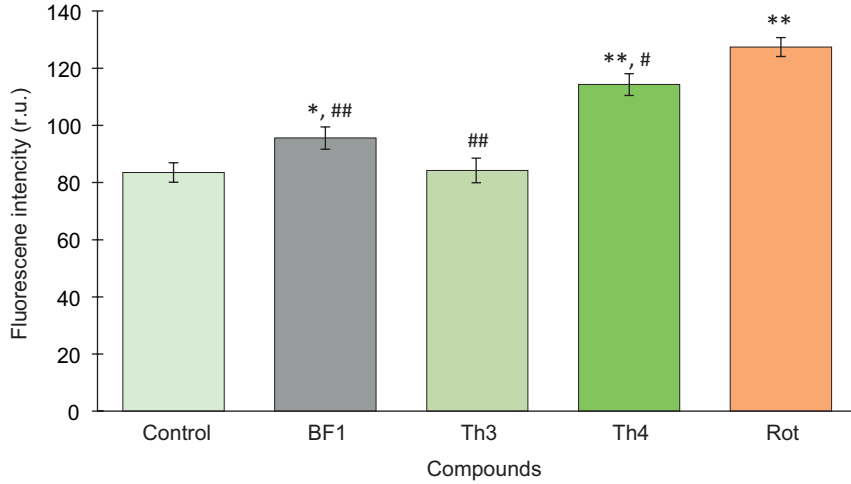

Fig. 1. ROS content in lymphoma cells under the action of BF1, Th3 polymer carrier, BF1 + polymer carrier (Th4), and rotenone (Rot) after 30 minutes of incubation. M ± SEM; n = 5. *, # – P < 0.05; **, ## – P < 0.01 (* – vs Control, # – vs Rot)

Thus, the conducted studies demonstrated that treatment of cells with the BF1 derivative is accompanied by a significant increase in intracellular ROS levels. This trend suggests a possible involvement of ROS as intermediate or effector components in the mechanism of action of the studied compound. The elevated generation of radical species may reflect activation of oxidative stress–dependent signaling pathways, mitochondrial dysfunction, or other processes that alter cellular redox homeostasis.

After 60 minutes of incubation of lymphoma cells with the tested compounds, treatment with the BF1 derivative at a concentration of 10 μM resulted in a 32.5 % increase in ROS levels compared to the control. In contrast, the free polymer Th3 did not show a noticeable effect on ROS levels in lymphoma cells (**Fig. 2**).

Application of the polymer complex Th4 led to an even more pronounced increase in ROS levels – by 39.1 % (**Fig. 2**), indicating enhanced intracellular oxidative stress under the action of the complex. These results allow tracking of intracellular response patterns to Th4 exposure.

Fig. 3 presents changes in fluorescence intensity in NK/Ly lymphoma cells after 120 minutes of incubation with the studied substances. After prolonged exposure, the

BF1 derivative showed a substantial increase in ROS levels by 35.4 % compared to the control, indicating persistence or even enhancement of its pro-oxidant effect over time.

The free polymer Th3 again did not cause statistically significant changes in fluorescence intensity, consistent with the 60-minute incubation data and confirming its neutral effect on ROS levels.

The most pronounced increase in ROS was observed with the Th4 complex. After 120 minutes of incubation, fluorescence intensity exceeded control values by 42 %, indicating intensified intracellular oxidative stress in the presence of the polymer complex. This effect may suggest more efficient cellular uptake of the complex or a modification of the mechanism of action of BF1 when incorporated into the polymer matrix.

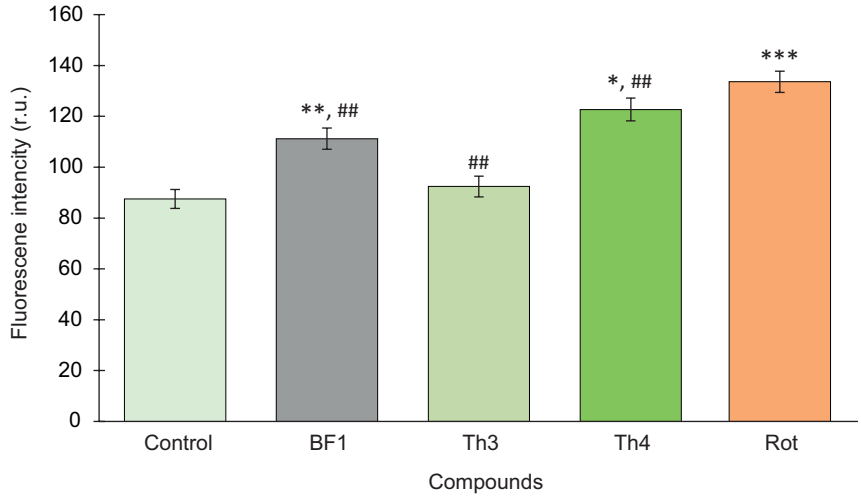

Fig. 2. ROS content in lymphoma cells under the action of BF1, Th3 polymer carrier, BF1 + polymer carrier (Th4), and rotenone (Rot) after 60 minutes of incubation. M ± SEM; n = 5. **, ## – P < 0.01; *** – P < 0.001 (* – vs Control, # – vs Rot)

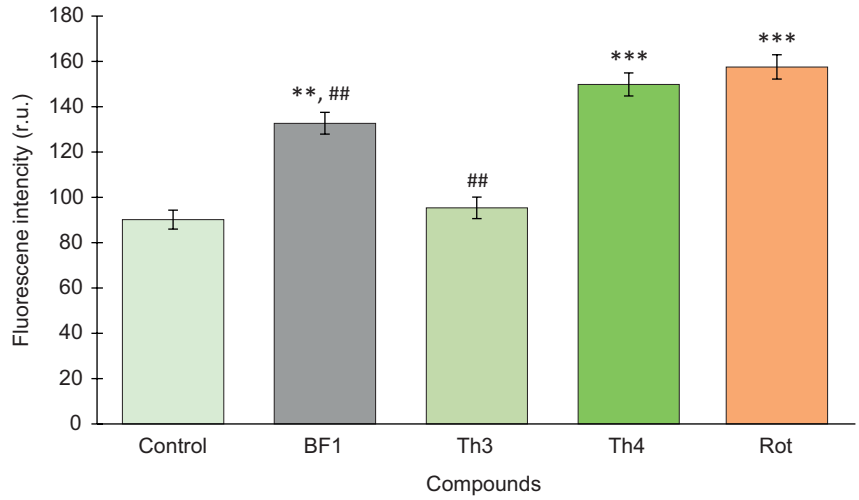

Fig. 3. ROS content in lymphoma cells under the action of BF1, Th3 polymer carrier, BF1+ polymer carrier (Th4), and rotenone (Rot) after 120 minutes of incubation. M ± SEM; n = 5.; **, ## – P < 0.01; *** – P < 0.001 (* – vs Control, # – vs Rot)

Correlation analysis revealed a positive relationship between incubation time and fluorescence intensity in NK/Ly lymphoma cells under the action of the BF1 derivative (**Fig. 4**). The correlation coefficient value of R = 0.69 (P < 0.05) indicates a moderate-to-strong positive correlation, suggesting a gradual increase in intracellular ROS levels with increasing exposure time.

For the Th4 complex, correlation analysis demonstrated an even more pronounced direct relationship between incubation duration and ROS levels in tumor cells. The coefficient value of R = 0.82 (P < 0.05) indicates a strong positive correlation, reflecting a substantial increase in fluorescence intensity with prolonged exposure to the complex (**Fig. 4**).

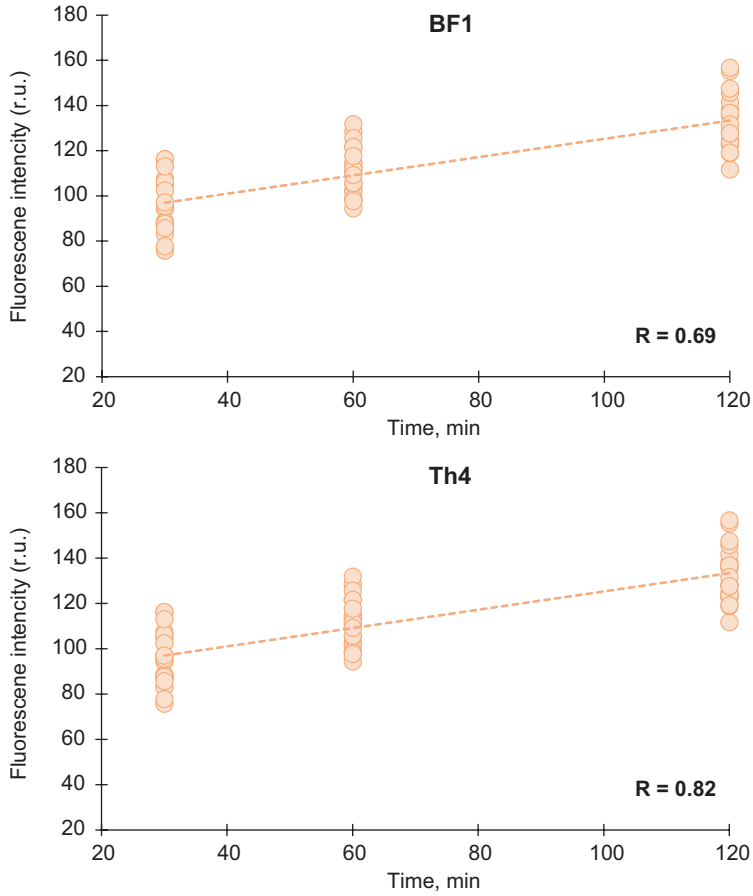

Fig. 4. Correlation analysis of the effects of BF1 and the BF1-polymer carrier complex (Th4) after 30, 60, and 120 minutes of incubation (P < 0.05)

Compared to BF1, the Th4 complex provides a more intensive accumulation of ROS, which may result from increased bioavailability, enhanced penetration, or prolonged interaction of the active substance within the polymer carrier. This aligns with the hypothesis regarding a potentially enhanced therapeutic effect of the derivative upon its encapsulation.

Within the scope of this study, the effects of the 2-amino-5-benzylthiazole derivative (BF1), the Th3 polymer carrier, and their Th4 complex on the ROS level in Nemeth–Kellner lymphoma cells were comprehensively characterized. It was previously shown that BF1 is capable of significantly increasing ROS content in tumor cells, indicating its pro-oxidant properties (Ilkiv *et al.*, 2022). Importantly, both the free form of BF1 and its complex with the Th4 polymer caused a statistically significant increase in the levels of lipid peroxidation products, which may indicate the initiation or intensification of oxidative stress in the cellular environment.

Within the framework of this study, new experimental data were obtained, allowing a deeper understanding of the potential mechanisms of biological action of the studied compounds. It is essential to consider the chemical reactivity of ROS and their fundamental difference from other signaling molecules (Liu *et al.*, 2023). The biological effects of ROS are largely determined by their concentration: at low concentrations, they act as regulators of intracellular processes, participating in the mechanisms of proliferation, differentiation, and signal transduction. Conversely, excessive accumulation of ROS leads to damage to cellular structures, including proteins, lipids, and DNA. An increase in ROS levels in oncogenic cells is associated with compromised integrity of genetic material and the development of carcinogenesis (Chen *et al.*, 2025).

It is logical to assume that changes in ROS concentration directly correlate with structural and functional changes in the cell, particularly ultrastructural disruption, altered direction of differentiation, and activation of programmed cell death pathways. Excessive or uncontrolled generation of ROS can substantially disrupt the normal functioning of cellular systems (Rivadeneira *et al.*, 2025).

Our experimental results confirm that BF1 induces a significant increase in the total ROS level in NK/Ly cells compared to control samples that were not exposed to this derivative. This suggests that BF1 can modulate the oxidative status of the cell and potentially affect its viability and metabolic activity.

In the course of the study, it was found that under the influence of BF1, as well as its complex with Th4-polymer, the ROS levels in NK/Ly lymphoma cells increased significantly compared to the control. This indicates that the induction of oxidative stress may be one of the key mechanisms of the cytotoxic effect of this thiazole derivative. At the same time, free Th3-polymer did not cause any changes in the level of ROS, which confirms the leading role of BF1 in mediating the biological effect, while the carrier polymer exhibits neutral properties. The increase in the levels of ROS after treatment of cells with BF1 and Th4-complex indicates the possible participation of the studied compound in the activation of apoptosis or other forms of programmed cell death, which is probably associated with DNA damage (Meriç *et al*., 2024).

It is particularly significant that the polymeric carrier in its unbound form did not induce an increase in the ROS level, demonstrating its good biocompatibility and the absence of negative effects on cellular metabolism. This aspect is of fundamental importance, since polymeric materials are widely used as nanostructured carriers for targeted delivery of therapeutic agents, and their own toxicity should be minimal (Jiaying *et al*., 2023)

Summarizing the obtained results, it can be argued that the activation of ROS generation is an integral components of the antitumor mechanism of action of BF1 and its complex with the polymer carrier. These effects were not observed in response to the action of the free polymer, which further emphasizes the leading role of BF1 as the primary biologically active component. At the same time, the results indicate that polymer

carriers are capable of enhancing the effect of the derivative, probably by increasing its stability or prolonging its residence time in the cellular environment.

Taken together, our results extend current knowledge on thiazole derivatives as ROS-modulating anticancer agents and demonstrate that polymer complexation can significantly amplify their pro-oxidant activity in NK/Ly lymphoma cells. By clearly differentiating the inert behavior of the free polymer Th3 from the enhanced ROS generation induced by the Th4 complex, this study provides mechanistic evidence that polymer carriers may act not only as passive vehicles, but also as modulators of redox-dependent antitumor effects. In a broader context, these data support the further development of polymer-assisted formulations of thiazole derivatives and other redox-active small molecules as promising, prospective approaches for targeted oxidative stress modulation in hematologic malignancies.

CONCLUSIONS

A 2-amino-5-benzylthiazole derivative (BF1, 10 μM) significantly elevates intracellular ROS levels in NK/Ly lymphoma cells at 30, 60, and 120 minutes, indicating robust pro-oxidant activity and redox modulation as a key component of its antitumor mechanism. Complexation of BF1 with the PEG-based polymer (Th4) enhances and prolongs ROS accumulation in lymphoma cells, producing a greater increase in ROS than free BF1 at all time points and showing a stronger positive correlation between incubation time and ROS levels. These findings support the concept that targeted modulation of oxidative stress is an integral part of the anticancer potential of thiazole derivatives and justify further development of PEG-based polymer complexes of BF1 and related redox-active small molecules as promising candidates for cancer therapy.

ACKNOWLEDGMENTS AND FUNDING SOURCES

The authors wish to acknowledge all those who collaborated on this work, and the members of the Faculty of Chemistry, Ivan Franko National University of Lviv and Institute of Chemistry and Chemical Technology, Lviv Polytechnic National University.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of Interest: the authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Human Rights: this article does not contain any studies with human subjects performed by any of the authors.

Animal studies: all international, national and institutional guidelines for the care and use of laboratory animals were followed.

AUTHOR CONTRIBUTIONS

Conceptualization, [Ya.Sh.]; methodology, [M.I; Ya.Sh.]; validation, [Ya.Sh.; Yu.K.]; formal analysis, [Ya.Sh.; A.B.].; investigation, [Ya.Sh.; M.I.]; resources, [V.B.; Yu.K.]; data curation, [A.B.]; writing – original draft preparation, [Ya.Sh.; Yu.K.; M.I.]; writing – review and editing, [Ya.Sh.; A.B.; V.B.]; visualization, [Ya.Sh.]; supervision, [A.B.]; project administration, [A.B.]; funding acquisition, [-].

All authors have read and agreed to the published version of the manuscript.

REFERENCES

Dai, F., Chen, F., Zhang, J., Chen, X., Liang, H., Liang, Z., Zhang, S., Tan, H., & Zhao, L. (2024). Folate-modified pH and ROS dual-responsive polymeric nanocarriers for targeted anticancer drug delivery. *ACS Applied Nano Materials*, 7(7), 7289–7299. doi:10.1021/acsanm.4c00021
Crossref ● Google Scholar

Finiuk, N., Zelisko, N., Klyuchivska, O., Yushyn, I., Lozynskyi, A., Cherniienko, A., Manko, N., Senkiv, J., Stoika, R., & Lesyk, R. (2022). Thiopyrano[2,3-d]thiazole structures as promising scaffold with anticancer potential. *Chemico-Biological Interactions*, 368, 110246. doi:10.1016/j.cbi.2022.110246
Crossref ● PubMed ● Google Scholar

Hazra, A., & Gogtay, N. (2016). Biostatistics series module 6: correlation and linear regression. *Indian Journal of Dermatology*, 61(6), 593. doi:10.4103/0019-5154.193662
Crossref ● PubMed ● PMC ● Google Scholar

Ilkiv, M. V., Shalai, Ya. R., Manko, B. O., Ostapiuk, Yu. V., Mitina, N. E., Zaichenko, A. S., & Babsky, A. M. (2022). Generation of ROS under the influence of thiazole derivative and its complexes with PEG-based polymeric nanoparticles. *Biopolymers and Cell*, 38(3), 158–168. doi:10.7124/bc.000a7d
Crossref ● Google Scholar

Jiaying, Y., Bo, S., Xiaolu, W., Yanyan, Z., Hongjie, W., Nan, S., Bo, G., Linna, W., Yan, Z., Wenya, G., Keke, L., Shan, J., Chuan, L., Yu, Z., Qinghe, Z., & Haiyu, Z. (2023). Arenobufagin-loaded PEG-PLA nanoparticles for reducing toxicity and enhancing cancer therapy. *Drug Delivery*, 30(1), 2177362. doi:10.1080/10717544.2023.2177362
Crossref ● PubMed ● PMC ● Google Scholar

Li, N., Ragheb, K., Lawler, G., Sturgis, J., Rajwa, B., Melendez, J. A., & Robinson, J. P. (2003). Mitochondrial complex I inhibitor rotenone induces apoptosis through enhancing mitochondrial reactive oxygen species production. *The Journal of Biological Chemistry*, 278(10), 8516–8525. doi:10.1074/jbc.m210432200
Crossref ● PubMed ● Google Scholar

Liang, J., & Liu, B. (2016). ROS-responsive drug delivery systems. *Bioengineering & Translational Medicine*, 1(3), 239–251. doi:10.1002/btm2.10014
Crossref ● PubMed ● PMC ● Google Scholar

Meriç, N., Kar, E., & Kar, F. (2024). 4-Methylthiazole triggers apoptosis and mitochondrial disruption in HL-60 cells. *Molecular Biology Reports*, 51(1), 997. doi:10.1007/s11033-024-09939-y
Crossref ● PubMed ● Google Scholar

Zelisko, N., Demchk, R., & Lesyk, R. (2016). New thiopyrano[2,3-d][1,3]thiazole derivatives as potential antiviral agents. *The Ukrainian Biochemical Journal*, 88(Special Issue), 105–112. doi:10.15407/ubj88.si01.105
Crossref ● Google Scholar

Zhang, Z., Lu, Z., Yuan, Q., Zhang, C., & Tang, Y. (2021). ROS-Responsive and active targeted drug delivery based on conjugated polymer nanoparticles for synergistic chemo-/photodynamic therapy. *Journal of Materials Chemistry B*, 9(9), 2240–2248. doi:10.1039/d0tb02996c
Crossref ● PubMed ● Google Scholar

Zhao, H., Kalivendi, S., Zhang, H., Joseph, J., Nithipatikom, K., Vásquez-Vivar, J., & Kalyanaraman, B. (2003). Superoxide reacts with hydroethidine but forms a fluorescent product that is distinctly different from ethidium: potential implications in intracellular fluorescence detection of superoxide. *Free Radical Biology & Medicine*, 34(11), 1359–1368. doi:10.1016/s0891-5849(03)00142-4
Crossref ● PubMed ● Google Scholar

ЧАСОЗАЛЕЖНА МОДУЛЯЦІЯ ВМІСТУ АКТИВНИХ ФОРМ ОКСИГЕНУ В КЛІТИНАХ ЛІМФОМИ ЗА ДІЇ ПОХІДНОГО ТІАЗОЛУ ТА ЙОГО КОМПЛЕКСУ З ПОЛІМЕРНИМ НАНОНОСІЄМ

***Ярина Шалай*[1], *Марта Ільків*[2], *Юрій Коваль*[1], *Віра Будзин*[2], *Андрій Бабський*[1]**

[1] *Львівський національний університет імені Івана Франка*
вул. Грушевського, 4, Львів 79005, Україна

[2] *Львівський державний університет фізичної культури імені Івана Боберського*
вул. Костюшка, 11, Львів 79007, Україна

Обґрунтування. Тіазолові низькомолекулярні сполуки розглядають як перспективні протипухлинні кандидати, оскільки вони здатні порушувати окисно-відновний баланс пухлинних клітин та індукувати окиснювальний стрес і опосередковану загибель клітин. Водночас полімерні носії розробляють для покращення доставки, стабільності й посилення внутрішньоклітинної дії біологічно активних сполук, однак їхній вплив на редокс-модулюючу дію тіазолових похідних у клітинах лімфоми залишається недостатньо вивченим. Метою цього дослідження було оцінити, як похідне 2-аміно-5-бензилтіазолу (БФ1) та його комплекс із полімером на основі поліетиленгліколю (Th4) впливають на продукцію активних форм Оксигену (АФО) у клітинах лімфоми Немета–Келлнера (NK/Ly) з використанням вільного полімеру (Th3) та ротенону як контролю.

Матеріали та методи. Клітини NK/Ly, отримані з асцитних пухлин у мишей, інкубували з БФ1, вільним полімерним носієм Th3 або комплексом Th4 в однакових концентраціях. Через 30, 60 та 120 хв інкубації внутрішньоклітинний рівень АФО оцінювали методом флуоресцентної мікроскопії з використанням чутливого до АФО зонда дигідроетидію, а інтенсивність флуоресценції кількісно аналізували за допомогою програмного забезпечення. Відмінності між групами визначали за допомогою стандартних статистичних тестів, а кореляційний аналіз застосовували для оцінки зв'язку між тривалістю інкубації та рівнем АФО.

Результати. Обробка клітин БФ1 спричиняла достовірне, часозалежне підвищення внутрішньоклітинного рівня АФО порівняно з інтактним контролем, що вказує на ефективне посилення окиснювального стресу в клітинах лімфоми цим тіазоловим похідним. Вільний полімер Th3 не зумовлював суттєвих змін рівня АФО на жодному з часових інтервалів, що підтверджує його роль як інертного носія. Натомість у клітинах, інкубованих із комплексом Th4, на всіх термінах інкубації реєстрували більш виражене підвищення АФО, ніж за дії БФ1 у вільній формі. Кореляційний аналіз виявив помірний позитивний зв'язок між тривалістю інкубації та рівнем АФО для БФ1 і сильніший позитивний зв'язок для Th4, що вказує на посилення та пролонгацію накопичення АФО у пухлинних клітинах за умов комплексоутворення з полімером.

Висновки. Похідне 2-аміно-5-бензилтіазолу істотно підвищує рівень АФО у клітинах лімфоми, а його включення до складу полімерного комплексу додатково підсилює цей прооксидантний ефект. Отримані результати демонструють, що активація утворення АФО є ключовою складовою протипухлинної дії тіазолового

похідного, тоді як полімер-опосередкована доставка підвищує його редокс-модулюючий потенціал. Посилене утворення АФО за дії комплексу обґрунтовує подальше вивчення комплексів тіазолових похідних з полімерними носіями як кандидатів для терапії пухлин спрямованою модуляцією окиснювального стресу.

Ключові слова: лімфома, похідне тіазолу, полімерний носій, поліетиленгліколь, активні форми Оксигену

Received / Одержано 22 June, 2026 | Revision / Доопрацьовано 02 July, 2026 | Accepted / Прийнято 23 September, 2026 | Published / Опубліковано 30 September, 2026