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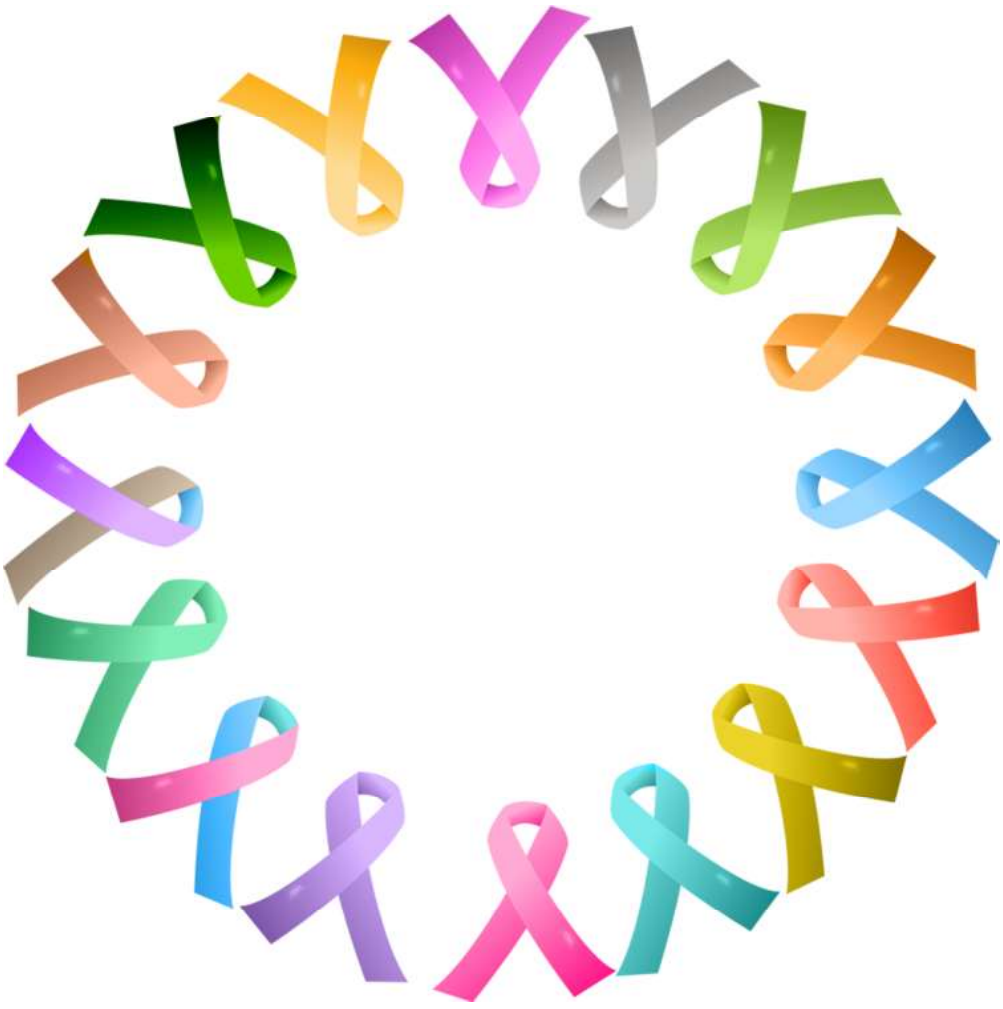
Official Journal of the Serbian Association for Cancer Research



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ONCOLOGY INSIGHTS

Aims and Scope

Oncology Insights is a yearly oncological open-access peer-reviewed journal that publishes new research from different areas of oncology. It strives to provide a platform for the exchange of cutting-edge research and knowledge in the field of oncology. This journal aims to advance the understanding, prevention, diagnosis and treatment through the dissemination of high-quality scientific discoveries.
The journal applies a fair and accurate peer review process, employing double-blind review methodologies. Acceptance of manuscripts is based on their scientific merit, originality, clarity, and contribution to the field.

Topics

Oncology Insights covers a wide spectrum of topics within the field of oncology, including but not limited to:

- Basic and Translational Research
- Clinical Oncology
- Radiation Oncology
- Surgical Oncology
- Pediatric Oncology
- Hematologic Oncology
- Palliative Care
- Epidemiology and Public Health
- Cancer Genetics
- Immunotherapy and Targeted Therapies
- Experimental Therapeutics
- Computational Biology and Artificial Intelligence

About/Information

Oncology Insights welcomes various types of contributions including original research articles, review articles, case reports, case studies, clinical trials, registered reports, comments, brief communications, editorials, letters to the editor, perspectives, and conference papers from a wide range of disciplines related to cancer research.
Through encouraging interdisciplinary collaborations, the journal welcomes contributions that integrate oncology with related fields such as immunology, genetics, biochemistry, radiology, and other relevant disciplines. The journal places a special emphasis on publishing research that highlights emerging trends, novel technologies, and innovative approaches in cancer research and clinical practice.
Oncology Insights is intended for a diverse readership, including oncologists, researchers, clinicians, nurses, allied healthcare professionals, patients, patient advocates, policymakers, and all stakeholders involved in the prevention, diagnosis, and treatment of cancer. It adopts a global perspective, encompassing research from diverse regions addressing oncological challenges that may vary across different populations.
The journal is committed to upholding the highest ethical standards in research and publication provided by established international guidelines.
Periodically, Oncology Insights may publish special issues focusing on specific topics to highlight particular areas of interest or emerging needs.
Authors are provided with clear and comprehensive guidelines for manuscript preparation, including structure, formatting, and other specific requirements.

Esteemed colleagues,

It is a rare honor and privilege in a scientist's career to shape joint efforts and dedication of a group of scientific enthusiasts into a tangible outcome - ***Oncology Insights, the Official Journal of the Serbian Association for Cancer Research*** (srp. Srpsko društvo istraživača raka, SDIR).

The first volume of Oncology Insights has been derived from years of scientific contributions of many individuals and institutions who have selflessly devoted their expertise, ideas and time to establish the SDIR society that today resonates with integrity and charm. In the future, we will strive to maintain those standards, always aiming higher. Thus, we encourage researchers, physicians, nurses, laboratory technicians, as well as patients, survivors, caregivers, and patient advocates to offer their valuable expert insights that will stimulate future progress of oncology in Serbia and worldwide.

Over the last 20 years, we have witnessed remarkable progress in the field of cancer research. Oncology Insights aims to play an integral role in supporting that progress by providing a platform for sharing cutting-edge research, creating a space for new collaborations, partnering established researchers with young investigators, and serving as a home for oncology professionals of various specialties dedicating their careers to this challenging research field.

Oncology Insights pledges to evolve, adapt, reinvent, redefine, and reshape its content to serve its members and inevitable advances in the field. We hope you will be a part of its success story by providing evidence-based, unbiased multidisciplinary content, feeling both an honor and a duty to treat cancer research with the same care, passion, and dedication which individuals with cancer deserve and expect.

Please tune all your senses to enjoy the intellectual feast spread through the pages of this inaugural journal volume. The future of Oncology Insights will be shaped by you.

With kind regards,

Milena Čavić, SDIR President
Editor-in-Chief
Oncology Insights
Official Journal of the Serbian Association for Cancer Research

The first number of Oncology Insights includes
PROCEEDINGS BOOK of
THE SIXTH CONGRESS OF THE SERBIAN ASSOCIATION FOR CANCER RESEARCH
with international participation

From Collaboration to Innovation in Cancer Research

2nd – 4th October 2023
Royal Inn Hotel, Belgrade

SDIR-6 ORGANIZER
Srpsko društvo istraživača raka (SDIR)
Serbian Association for Cancer Research (SACR)
www.sdir.ac.rs

Dear colleagues,

We are very pleased to welcome you to the 6th Congress of the Serbian Association for Cancer Research (SDIR) with international participation "From Collaboration to Innovation in Cancer Research" which will be held on October 2-4 2023, at the Royal Inn Hotel, Kralja Petra 56, Belgrade, Serbia.
During the three-day congress, lectures will be given by distinguished Serbian and international researchers, covering the following topics:

- Tumour metabolism and biology
- Epigenetics and gene regulation in cancer
- Bioinformatics and artificial intelligence in cancer research
- Omics approaches in cancer research
- Therapy response and resistance
- Clinical and translational oncology
- Immunooncology
- New and challenging drug targets
- Pathways to innovation in cancer research

We are pleased to announce that our sixth congress is actively supported by the European Association for Cancer Research (EACR). National and regional cooperation is also important, and so representatives from our friend societies will be attending our congress.
The timing of the organisation of SDIR-6 is important for the establishment of our national society's journal Oncology Insights. The abstracts of the sixth congress will be published in the very first issue of the journal.
Advances and innovations in cancer research are based on growing scientific knowledge and collaboration. We believe you will enjoy the lively atmosphere of the congress and that fruitful scientific discussions will help you build new collaborations and develop new ideas.

We look forward to welcoming you in Belgrade!

Kind regrads,

on behalf of the SDIR-6 Organizing Committee

Prof. dr Katarina Zeljić
Faculty of Biology, University of Belgrade
President of the SDIR-6 Organizing Committee

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Anticancer activity of diphenyltin(IV) compounds bearing carboxylato N-functionalized 2-quinolones

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Background: The limited efficacy of conventional metal-based chemotherapeutic drugs is attributed to resistance, high toxicity, and numerous side effects, thus providing a platform for the design of new metal-based drugs with enhanced properties. Organotin(IV) compounds have already been recognized as promising agents due to their ability to inhibit tumor growth both *in vitro* and *in vivo*. Following this concept, new diphenyltin(IV) complexes incorporating carboxylato N-functionalized 2-quinolones ligands were assessed on different cancer cell lines. **Material and Methods:** Evaluation of anticancer activity *in vitro* of the newly synthesized diphenyltin(IV)complexes bis (3-(4-methyl-2-oxoquinolin-1(2H)-I)propanoato)diphenyltin(IV), and bis (2-(4-hydroxy-2-oxoquinolin-1(2H)-yl)ethanoato)diphenyltin(IV) (1−3, respectively) as well as ligand precursors (HL1, HL2, and HL3) was determined after 72 h on a panel of cancer cell lines of human and mouse origin (MCF-7, A375, HCT116, 4T1, B16, CT26) using MTT and CV assays.Complex 1 and HCT116 cells were selected for further analysis of the potential mechanism, Flow cytometry for the assessment of cell death, proliferation, caspase activation and production of active oxygen/nitrogen species as well as fluorescent microscopy for detection of nuclei morphology were employed. **Results:** Obtained results showed a dose-dependent viability decrease in all cell lines exposed to complexes 1−3 with IC50 values in the low micromolar range. Ligand precursors, HL1−HL3 showed no activity up to 200 μM. Complex 1 inhibited cell proliferation and provoked caspase-dependent apoptosis in HCT116 cells. The enhanced presence of autophagosomes determined after the treatment with complex 1 was found to be protective, opposing apoptosis. The scavenging potential of tested complex 1 on ROS/RNS production can be connected with abolished viability and suppressed proliferation, since HCT116 cells are potent producers of ROS. **Conclusion:** Taking all together, novel diphenyltin(IV) complexes present promising anticancer agents and should be further tested *in vivo*.
Keywords: apoptosis, cancer, cytotoxicity, melanoma

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Bismuth ferrite nanoparticles increase ROS production and p62 expression in A375 melanoma and HeLa cells

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Background: Cancer nanomedicine is a rapidly developing field that uses nanoparticles (NPs) for the diagnosis and treatment of cancer. Currently, many nanomaterials with different shapes, sizes, structures, and compositions have been investigated to produce effective anticancer NPs. The interest in the biomedical applications of bismuth-containing nanoparticles, such as bismuth ferrite (BFO-NP) is a result of their promising properties such as cost-effectiveness, chemical inertness, high stability, and simplicity of functionalization. **Material and Methods:** A375 human melanoma and HeLa cervical carcinoma cells were used to study the antitumor activity of BFO-NP. Clonogenicity of treated cells was analyzed by colony forming assay, while cell death was examined using flow cytometry. DCF-DA fluorescent assay was applied to measure ROS production. Protein expression of p62 and TfR1 was detected by Western blot. Cell migration was analyzed using a wound scratch assay, while an SRB assay was used to assess cell adhesion. **Results:** BFO-NP (200 ng/μL) significantly reduced the clonogenicity of A375 and HeLa cells by 46 and 60%, respectively. Detected ROS production was increased considerably, especially for A375 melanoma cells, and amounted to 400%. The number of late apoptotic and/or necrotic cells increased by 10-12%, compared to the control. Significantly increased expression of autophagy-related protein p62 was observed in both cell lines after BFO-NP treatment. Ferroptosis-related transferrin

receptor (TfR1) expression was slightly increased in treated A375 end HeLa cells (~14%). The noticed increase in cell adhesion ranged from 20-30% followed by a decrease in cell migration. **Conclusion:**BFO-NP is a promising antitumor agent with a significant inhibitory effect on A375 and HeLa cell growth and metastatic potential. Molecular mechanisms involved in these processes include ROS production and increased p62 expression. Reduced metastatic potential resulted from the inductionof cell adhesion and decreased cell migration.
Keywords: bismuth ferrite nanoparticles, cell death, cell migration, ROS.

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Stimulation and inhibition of NF-kB by repurposed drugs – effects on hamster fibrosarcoma

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Background: NF-kB transcription factors are key regulators of apoptosis, autophagy, necroptosis and turns up everywhere in cancer life and death. This study investigated how the regulation of NF-kB by repurposed drugs in oncology affect experimental fibrosarcoma development and progression in hamsters. **Material and Methods:** Anticancer efficacy of certain drugs was tested on fibrosarcoma experimentally induced by BHK21/C13 cells in Syrian golden hamsters. Used repurposed drugs with in vitro verified NF-kB inhibitory effect were: metformin, caffeine, itraconazole, nitroglycerin. Used drug with known NF-kB stimulatory effect was mebendazole. Tumor biophysical characteristics, histology and immunohistochemistry were assessed. Blood samples were collected for hematological and biochemical analyses and the main organs were toxicologically analyzed. **Results:** Our study showed that combinations of NF-kB inhibitors: metformin with caffeine, metformin with itraconazole and metformin with nitroglycerin, in human equivalent doses could be efficacious ($p < 0.05$) against fibrosarcoma growth, which can rescued by mebendazole, without toxicity and influence on biochemical and hematological tests. **Conclusion:** Combinations of repurposed drugs with NF-kB inhibitory effect: metformin with caffeine, metformin with itraconazole and metformin with nitroglycerin could be an important therapeutic option in oncology.
Keywords: BHK-21/C13 cell culture, drug effects, fibrosarcoma, hamsters, NF-kB

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Targeting Tumor pH: The Role of Sodium Bicarbonate in Cancer Treatment

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Background: Tumor acidity is a hallmark of cancer that promotes cancer progression and treatment resistance. It is associated with metabolic reprogramming and the use of glycolysis, which results in high lactic acid production. Sodium bicarbonate (SB) potentially can alkalize the tumor microenvironment, and SB per oral administration has shown promising anticancer effects in numerous preclinical studies and some clinical reports. However, the question of local or systemic use of SB in cancer therapy is unclear. Buffering therapy does not counteract standard treatment and can be used in combination to increase effectiveness. For some manifestations of the tumor process, like malignant ascites (MA), clinicians would have been able to transfer the local use of SB from preclinical studies to the clinic quickly. In this study, we evaluated the effect of MA local treatment with SB. **Material and Methods:** We performed the intraperitoneal perfusion procedure with SB/sodium chloride (SC) solution in ICR (CD-1) mice with Erlich ascites carcinoma one week after tumor cells injection. The perfusion procedure consisted of tumor ascites evacuation,