

Editorial

Redox Active Molecules in Cancer Treatments

Višnja Stepanić^{1,*}  and Marta Kučerová-Chlupáčová^{2,*} 

¹ Laboratory for Machine Learning and Knowledge Representation, Ruđer Bošković Institute, Bijenička 54, 10000 Zagreb, Croatia

² Department of Pharmaceutical Chemistry and Pharmaceutical Analysis, Faculty of Pharmacy in Hradec Králové, Charles University, Ak. Heyrovského 1203/8, 500 05 Hradec Králové, Czech Republic

* Correspondence: visnja.stepanic@irb.hr (V.S.); kucerom@faf.cuni.cz (M.K.-C.); Tel.: +385-1-457-1356 (V.S.); +420-495-067-372 (M.K.-C.)

Cancer is one of the leading causes of death worldwide, with nearly 10 million deaths in 2020 [1]. Redox active molecules in the diet, dietary supplements, or in approved drug preparations are used to prevent and treat cancer.

The main objective of this Special Issue, “Redox Active Molecules in Cancer Treatments”, in the journal *Molecules* is to present the results of in vitro, in vivo, and/or in silico studies on the biological effects and activities of anti- and pro-oxidant molecules observed in original research studies or collected and discussed in review articles. This goal is achieved by compiling seventeen articles. They present antioxidative or targeted oxidative effects of miscellaneous small-molecular-weight compounds or proteins against a variety of cancer types:

- An endogenous compound—melatonin [2].
- Natural plant compounds (naringenin [3], papaverine [4], polyphenols isolated from *Myrciaria trunciflora* [5] or *Anneslea fragrans* [6], and seed-derived peptides [7]), natural compounds also found in animals (melatonin [2,8]), and peptides as well as proteins from Jellyfish venom [9].
- Synthetic compounds, i.e., alkyl thiols [10], dimethyl sulfoxide [11], metformin and S63845 [12], the ruthenium complex [Ru(Phen)₃]²⁺ [13], and copper-based compounds—Casiopéinas [14].
- Different formulations, i.e., peptide fractions from germinated soybeans conjugated to Fe₃O₄ nanoparticles [15] and astaxanthin microparticles in combination with pentoxifylline [16].
- Proteins (aquaporins [17]) and nuclear factor erythroid-2-related factor 2 (NRF2) [8].

The studies explored diverse anticancer mechanisms of action of redox-active molecules in association with specific signaling pathways by using in vitro and in vivo methods. Some studies investigated the use of redox-active compounds to alleviate radiation-induced fibrosis, which is a side-effect of radiotherapy [16], or to detect oxygen in vitro and in vivo [13]. Most studies examined the effect of the tested compounds on cancer cell viability/proliferation assays [2–4,6,11,12] and/or analyses of reactive oxygen species concentrations [2,3,6,11,15,16]. Some other studies used in vitro assays such as cell cycle analyses [2–4,9], DNA fragmentation assays [3,9], analyses of the expression of apoptosis-related proteins and/or genes [9,11,12], etc. The two included studies are based on the application of state-of-the-art chemoinformatic analysis and modeling approaches—molecular docking and molecular dynamics [7,18].

The whole series of thirteen experimental investigations and one computational study is accompanied by three review articles focusing on aquaporins as redox regulators in breast cancer [17], natural compounds affecting ferroptosis [18], and modulation of NRF2 expression at the mRNA and protein levels [8].

We hope that readers will enjoy the book and glean interesting and useful information from the particular studies.



Citation: Stepanić, V.;

Kučerová-Chlupáčová, M. Redox Active Molecules in Cancer Treatments. *Molecules* **2023**, *28*, 1485. <https://doi.org/10.3390/molecules28031485>

Received: 29 January 2023

Accepted: 31 January 2023

Published: 3 February 2023



Copyright: © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Funding: This research received no external funding.

Acknowledgments: We would like to thank all of the authors who contributed to this Special Issue.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. World-Health-Organization. Cancer. Available online: <https://www.who.int/news-room/fact-sheets/detail/cancer> (accessed on 11 January 2023).
2. Chok, K.C.; Koh, R.Y.; Ng, M.G.; Ng, P.Y.; Chye, S.M. Melatonin Induces Autophagy via Reactive Oxygen Species-Mediated Endoplasmic Reticulum Stress Pathway in Colorectal Cancer Cells. *Molecules* **2021**, *26*, 17. [[CrossRef](#)] [[PubMed](#)]
3. Lee, C.W.; Huang, C.C.Y.; Chi, M.C.; Lee, K.H.; Peng, K.T.; Fang, M.L.; Chiang, Y.C.; Liu, J.F. Naringenin Induces ROS-Mediated ER Stress, Autophagy, and Apoptosis in Human Osteosarcoma Cell Lines. *Molecules* **2022**, *27*, 16. [[CrossRef](#)] [[PubMed](#)]
4. Gomes, D.A.; Joubert, A.M.; Visagie, M.H. In Vitro Effects of Papaverine on Cell Proliferation, Reactive Oxygen Species, and Cell Cycle Progression in Cancer Cells. *Molecules* **2021**, *26*, 19. [[CrossRef](#)] [[PubMed](#)]
5. Augusti, P.R.; Quatrin, A.; Mello, R.; Bochi, V.C.; Rodrigues, E.; Prazeres, I.D.; Macedo, A.C.; Oliveira-Alves, S.C.; Emanuelli, T.; Bronze, M.R.; et al. Antiproliferative Effect of Colonic Fermented Phenolic Compounds from Jaboticaba (*Myrciaria trunciflora*) Fruit Peel in a 3D Cell Model of Colorectal Cancer. *Molecules* **2021**, *26*, 13. [[CrossRef](#)] [[PubMed](#)]
6. He, S.Y.; Cui, X.Y.; Khan, A.; Liu, Y.P.; Wang, Y.D.; Cui, Q.M.; Zhao, T.R.; Cao, J.X.; Cheng, G.G. Activity Guided Isolation of Phenolic Compositions from *Anneslea fragrans* Wall. and Their Cytoprotective Effect against Hydrogen Peroxide Induced Oxidative Stress in HepG2 Cells. *Molecules* **2021**, *26*, 14. [[CrossRef](#)] [[PubMed](#)]
7. Chai, T.T.; Koh, J.A.; Wong, C.C.C.; Sabri, M.Z.; Wong, F.C. Computational Screening for the Anticancer Potential of Seed-Derived Antioxidant Peptides: A Cheminformatic Approach. *Molecules* **2021**, *26*, 21. [[CrossRef](#)] [[PubMed](#)]
8. Aliyev, A.T.; Panieri, E.; Stepanić, V.; Gurer-Orhan, H.; Saso, L. Involvement of NRF2 in Breast Cancer and Possible Therapeutical Role of Polyphenols and Melatonin. *Molecules* **2021**, *26*, 18. [[CrossRef](#)]
9. Tawfik, M.M.; Eissa, N.; Althobaiti, F.; Fayad, E.; Abu Almaaty, A.H. Nomad Jellyfish *Rhopilema nomadica* Venom Induces Apoptotic Cell Death and Cell Cycle Arrest in Human Hepatocellular Carcinoma HepG2 Cells. *Molecules* **2021**, *26*, 14. [[CrossRef](#)] [[PubMed](#)]
10. Heymans, V.; Kunath, S.; Hajieva, P.; Moosmann, B. Cell Culture Characterization of Prooxidative Chain-Transfer Agents as Novel Cytostatic Drugs. *Molecules* **2021**, *26*, 12. [[CrossRef](#)] [[PubMed](#)]
11. Sangweni, N.F.; Dlodla, P.V.; Chellan, N.; Mabasa, L.; Sharma, J.R.; Johnson, R. The Implication of Low Dose Dimethyl Sulfoxide on Mitochondrial Function and Oxidative Damage in Cultured Cardiac and Cancer Cells. *Molecules* **2021**, *26*, 15. [[CrossRef](#)] [[PubMed](#)]
12. Valiuliene, G.; Vitkeviciene, A.; Skliute, G.; Borutinskaite, V.; Navakauskiene, R. Pharmaceutical Drug Metformin and MCL1 Inhibitor S63845 Exhibit Anticancer Activity in Myeloid Leukemia Cells via Redox Remodeling. *Molecules* **2021**, *26*, 13. [[CrossRef](#)] [[PubMed](#)]
13. Huntosova, V.; Horvath, D.; Seliga, R.; Wagnieres, G. Influence of Oxidative Stress on Time-Resolved Oxygen Detection by Ru(Phen)(3)(2+) In Vivo and In Vitro. *Molecules* **2021**, *26*, 24. [[CrossRef](#)]
14. Ramirez-Palma, L.G.; Espinoza-Guillen, A.; Nieto-Camacho, F.; Lopez-Guerra, A.E.; Gomez-Vidales, V.; Cortes-Guzman, F.; Ruiz-Azuara, L. Intermediate Detection in the Casiopeina-Cysteine Interaction Ending in the Disulfide Bond Formation and Copper Reduction. *Molecules* **2021**, *26*, 12. [[CrossRef](#)]
15. Augusto-Jimenez, Y.E.; Gonzalez-Montoya, M.; Naranjo-Feliciano, D.; Uribe-Ramirez, D.; Cristiani-Urbina, E.; Diaz-Aguila, C.; Yee-Madeira, H.; Mora-Escobedo, R. Antioxidant Activity of Bioactive Peptide Fractions from Germinated Soybeans Conjugated to Fe₃O₄ Nanoparticles by the Ugi Multicomponent Reaction. *Molecules* **2021**, *26*, 15. [[CrossRef](#)] [[PubMed](#)]
16. Binatti, E.; Zoccatelli, G.; Zannoni, F.; Dona, G.; Mainente, F.; Chignola, R. Effects of Combination Treatments with Astaxanthin-Loaded Microparticles and Pentoxifylline on Intracellular ROS and Radiosensitivity of J774A.1 Macrophages. *Molecules* **2021**, *26*, 11. [[CrossRef](#)] [[PubMed](#)]
17. Milković, L.; Čipak Gašparović, A. AQP3 and AQP5-Potential Regulators of Redox Status in Breast Cancer. *Molecules* **2021**, *26*, 14. [[CrossRef](#)] [[PubMed](#)]
18. Stepanić, V.; Kučerová-Chlupáčová, M. Review and Chemoinformatic Analysis of Ferroptosis Modulators with a Focus on Natural Plant Products. *Molecules* **2023**, *28*, 475. [[CrossRef](#)] [[PubMed](#)]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.