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A CRITICAL REVIEW ON THERAPEUTIC METHODS OF CANCER TREATMENT

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ABSTRACT: ***In cancer cells, reactive oxygen species (ROS) are developed as a consequence of increased metabolic rate, mitochondrial dysfunction, elevated cell signaling, oncogene expression and increased peroxisome activity. Cancer cells need a certain level of ROS, above or below, leading to cytotoxicity in cancer cells. It is possible to leverage this biochemical aspect to develop novel therapeutic agents to kill cancer cells preferentially and selectively. We searched for peer-reviewed English-language publications in different electronic databases, including PubMed, Web of Science, and Google Scholar. Selected articles were reviewed, ranging from research papers, clinical studies and review articles on the production of ROS in living systems, its role in the development and treatment of cancer, and the role of microbiota in the treatment of ROS-dependent cancer. This review highlights tumour oxidative stress, the underlying mechanisms of various ROS and cancer cell relationships, various therapeutic strategies mediated by ROS, and the evolving role of microbiota in cancer therapy.***

KEYWORDS: Cancer, Clinical, Life, Oxygen, ROS.

INTRODUCTION

Life without oxygen is difficult to picture, but its use has certain effects that threaten the balance of life. Molecules called reactive oxygen species or ROS may give rise to cellular respiration. ROS are by-products of oxygen that in their outermost shell contain single or more unpaired electrons and are produced from molecular oxygen. In the outermost shell, molecular oxygen comprises two unpaired electrons that are in the ground state. Oxygen is not in a very reactive state owing to the identical spinning of these electrons. Conversely, when one of these two unpaired electrons becomes excited, oxygen becomes highly reactive as two electrons with different spins will react with other electrons immediately, particularly with double bonds. It results in the development of comparatively stable intermediates when oxygen is reduced by one electron at a time. As a result of oxygen metabolism in living organisms, ROS is developed and plays a significant role in cell signaling and homeostasis[1].

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Normally, in order to avoid cell disruption, ROS balance is retained. However, some environmental sources, such as ultraviolet rays or heat exposure, can contribute to an increase in the level of ROS[2]. This disease is known as oxidative stress. Several factors in cancer cells, including increased metabolic activity, mitochondrial dysfunction, increased cell signaling, elevated peroxisome activity, and oncogene activity, can result in elevated ROS levels. Cellular proliferation and survival may be caused by a moderate elevation in cellular ROS levels. Conversely, it overcomes the cell's antioxidant function when the amount of ROS exceeds a toxic threshold and may trigger cell death. By preserving the balance between ROS production and removal, normal cells maintain redox equilibrium. Because of their conserved antioxidant mechanism, cells can tolerate certain levels of oxidative stress under physiological conditions. Increased ROS production in cancerous cells due to increased signaling cascades and metabolic activities will encourage a ROS adaptation reaction, resulting in cellular antioxidant regulation to maintain redox homeostasis[3].

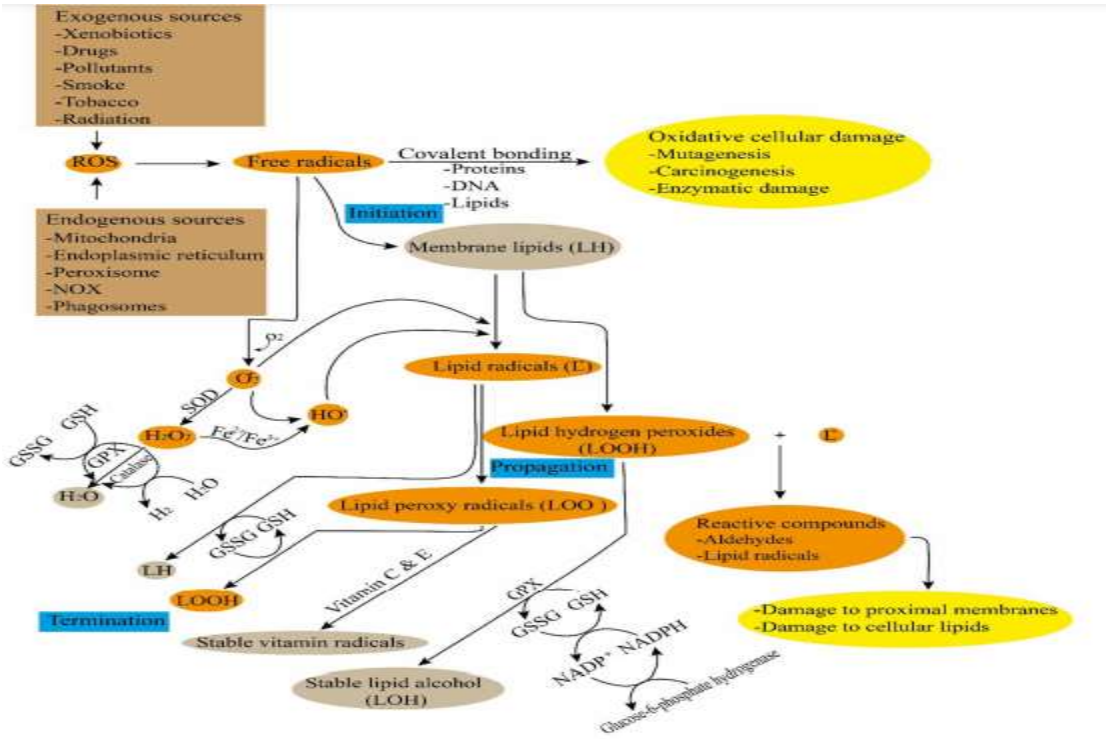

Figure 1: Illustrates the engineering view of pharmaceutical development[4]**.**

Table 1: Illustrates ROS scavenging agents[5]**.**

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Agents	Mode of action
Vitamin C and E, β-carotene, selenium	Common antioxidants
PEG, SOD, glutathione peroxidase, catalase	Antioxidant enzymes
Minodronate, histamine	NADPH oxidase blockers
Tempol	Nitroxide derivative manipulator

DISCUSSION

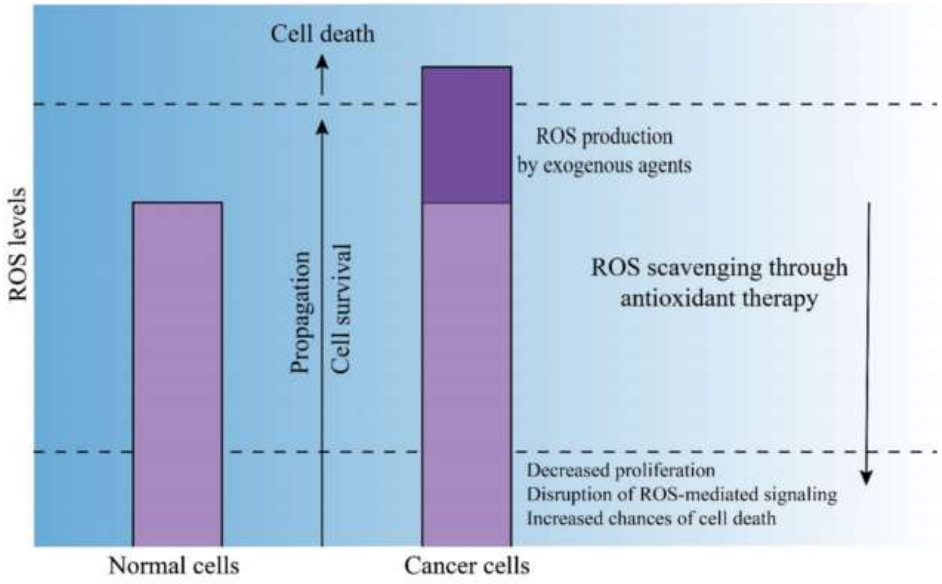

Figure 2: Depicts double edged sword function of ROS[5]**.**

Table 2: Shows agents under development for ROS generating anticancer therapy[6]**.**

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Agent	Mode of action	Type of cancer and current status
Imexon	Targets GSH	Lung cancer (Phase I clinical trials) Follicular lymphoma (Phase II clinical trials) Pancreatic cancer (Phase II clinical trials)
Tetrathiomolybdate	Blocks cytosolic SOD1	Melanoma, myeloma, prostate and breast cancer (Phase II clinical trials)
2-Methoxyesradiol	Blocks SOD and inhibits synthesis of tubulin	Renal cell carcinoma, metastatic and hormone-refractory prostate cancer (Phase II clinical trials)
Mangafodipir	Mimetic of SOD, GSH reductase and catalase, elevates H_2O_2 generation in tumors	Colon cancer stage Dukes' C (Phase II clinical trials)
B-lapachone	Goes through cellular redox cycles carried out by intracellular NQO1	Advanced solid tumors (Phase I clinical trials)
Elesclomol	Induces apoptosis in cancer cells by promoting ROS accumulation	Prostate cancer (Phase I clinical trials) Melanoma (Phase II clinical trials)
Phenylethyl isothiocyanate	Blocks GPx and NF-κB	Hematological malignant cancer (preclinical trials)
Gadolinium texaphyrin	Blocks TrxR and promotes superoxide production in cancer cells	Brain cancer and hematological malignant cancer (Phase III clinical trials
G202	Blocks endoplasmic reticulum calcium ATpase pump which induces apoptosis, ROS induction owing to ER stress	Liver cancer, prostate cancer (Phase II clinical trials)
Photodynamic therapy	Promotes ROS generation after stimulation of photosensitizer by light	Skin cancer (Phase II clinical trials) Basal cell carcinoma (Phase I clinical trials) Choroidal melanoma (Phase II clinical trials)

ROS has a role in the initiation, growth and maintenance of cancer cells' phonotypical characteristics in cancer. Compared to their normal counterparts, increased ROS generation in tumour cells is due to the involvement of oncogenes that are also involved in malignant transformation[7]. The relationship between the increase in levels of ROS and oncogene activation is still unclear. Inflammation plays an etiological role in cases of some malignancies, such as lung and oral carcinomas. However, the stress induces ROS generation that cause chronic inflammation. Another most commonly implicated mechanism is oxidative DNA damage. ROS can activate various signaling pathways related to persistent tumour survival, metastasis, vascularization and proliferation in cancer cells, in addition to oxidative DNA damage, which can promote cancer growth[8].

CONCLUSION

It is not only a theoretical approach to guiding ROS to target cancer cells, but has also gone to the beds of patients. In vitro and in vivo clinical trials have proven the effectiveness of both ROS producing and ROS depleting therapies. For accurate selectivity, difference in redox levels of normal and cancerous cells can be used. Nevertheless, it is necessary to develop a combination of variables including oxidative stress status, enzymatic antioxidant production, signaling cascades, and transcription factor promoters that can subsequently be used as a suggestive for ROS boosting

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or ROS scavenging therapy targeting only cancer cells. Tumors show increased oxidative stress that can promote metastasis of the tumor and, in some cases, cell survival and resistance to chemotherapy. A promising strategy that can modulate drug selectivity and decrease chemotherapeutic resistance is to guide therapeutic agents towards these biochemical characteristics of tumors with ROS-mediating approaches. Based on the function of ROS in tumour metastasis and oxidative damage, two diverse therapeutic approaches are postulated. One is to increase the scavenging of ROS by antioxidant intake, thereby disrupting ROS-mediated signaling cascades and inhibiting metastasis of cancer. However, during clinical trials, the ingestion of several antioxidant agents was associated with increased tumour growth.

REFERENCES

[1] M. H. Raza *et al.*, "ROS-modulated therapeutic approaches in cancer treatment," *Journal of Cancer Research and Clinical Oncology*. 2017, doi: 10.1007/s00432-017-2464-9.

[2] E. N. Kumar and E. S. Kumar, "A Simple and Robust EVH Algorithm for Modern Mobile Heterogeneous Networks- A MATLAB Approach," 2013.

[3] S. Kumar, A. Gupta, and A. Arya, *Triple Frequency S-Shaped Circularly Polarized Microstrip Antenna with Small Frequency-Ratio*. 2016.

[4] J. Drews, "Drug discovery: A historical perspective," *Science*. 2000, doi: 10.1126/science.287.5460.1960.

[5] S. J. Ralph, S. Rodríguez-Enríquez, J. Neuzil, and R. Moreno-Sánchez, "Bioenergetic pathways in tumor mitochondria as targets for cancer therapy and the importance of the ROS-induced apoptotic trigger," *Molecular Aspects of Medicine*. 2010, doi: 10.1016/j.mam.2009.12.006.

[6] J. M. Matés, J. A. Segura, F. J. Alonso, and J. Márquez, "Oxidative stress in apoptosis and cancer: An update," *Archives of Toxicology*. 2012, doi: 10.1007/s00204-012-0906-3.

[7] C. Benavente, M. Jacobson, and E. Jacobson, "NAD in Skin: Therapeutic Approaches for Niacin," *Curr. Pharm. Des.*, 2009, doi: 10.2174/138161209787185760.

[8] E. Spyratou, M. Makropoulou, E. A. Mourelatou, and C. Demetzos, "Biophotonic techniques for manipulation and characterization of drug delivery nanosystems in cancer therapy," *Cancer Letters*. 2012, doi: 10.1016/j.canlet.2011.12.039.