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Review Article

Balancing oxidative stress: Antioxidants as Allies and adversaries in cancer treatment

Geeta Shinde[1], Snehal Kadam[1], Shivani Kale[1], Aman Upaganlawar[1]*, Manojkumar Mahajan[1], Chanrashekhar Upasani[1]

[1]Dept. of Pharmacology, SNJBs SSDJ College of Pharmacy, Chandwad, Nashik, Maharashtra, India

Abstract

The medical repercussions of cancer span globally because genetic disposition and environmental elements together with life choices play a role in its development. Oxidative stress functions as a primary development factor because it emerges when reactive oxygen species (ROS) amount exceeds antioxidant defenses thereby producing DNA and lipid and protein damage that drives tumor initiation and tumor growth. The variations in chemical structure between endogenous and dietary antioxidants (including vitamins C and E, polyphenols, carotenoids) make them eligible for cancer therapy supplementation because of their capability to alter redox-sensitive biochemical processes and activate apoptosis and angio-inhibition and minimize inflammatory responses. Multiple studies based on preclinical and clinical investigations conclude that antioxidant-rich dietary intake helps decrease cancer susceptibility alongside improving therapeutic responses. The use of antioxidants encounters difficulties related to dosage-dependent pro-oxidant effects and determination of best supplement timing and possible tumor cell protection mechanisms. This review discusses the actual mechanisms of antioxidant use in cancer therapy while reviewing appropriate therapeutic applications together with exploration of their limitations and directions for further research.

Keywords: Cancer, oxidative stress, Reactive oxygen species (ROS), antioxidants, Redox balance, Chemotherapy, Radiotherapy, Phytochemicals, Antioxidant-rich diet, Cancer prevention, Precision medicine.

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1. Introduction

Despite strides in science and research, cancer still remains one of the most formidable health challenges this world has to face today, by the fact of abnormal cells proliferating with the capacity to invade or spread to other tissues and organs.[1] This disease is extremely complex as it involves a very broad range of malignancies involving virtually every organ system of the human body. Unlike most acute diseases having a sudden onset and early cure, cancer is usually of a chronic type, with attendant high morbidity and mortality in populations.[2] The World Health Organization (WHO) says that cancer is one of the leading causes of death worldwide today, claiming over 10 million deaths so far in 2020. A significant percentage of this global mortality is caused by the most common forms of cancer such as lung, breast, colorectal, prostate, and stomach cancers. Addition to the increasing burden of modifiable risk factors such as tobacco use, unhealthy dietary habits, inactivity and exposure to environmental carcinogens, the burden of cancer is further complicated. Lifestyle changes, urbanization and ageing populations have all contributed to steady rise in cancer incidence in both the developed and developing countries.[3] Until recently, it has been observed that cancer rates are higher in developed countries because of higher diagnostic capabilities and longer life expectation, but recent trends indicate an alarming rise of cancer cases in low- and middle-income countries. The high needs is due to the adoption of Westernized lifestyles, as well as lack of suitable cancer prevention and control strategies in these regions. Along with having a tremendous toll on human life, cancer also costs healthcare systems worldwide an enormous amount of money. Diagnosis, treatment and palliative care are expensive and therefore put huge pressure on both individual patients and national healthcare budgets. Much of the cost of cancer therapies like chemotherapy, radiation,

*Corresponding author: Aman Upaganlawar
Email: amanrxy@gmail.com

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immunotherapy, and targeted treatments means that the cost of high quality care is substantial, and that many people are unable to access effective treatment when they are most in need, in resource limited settings.[3] At the same time, the social and psychological consequences of cancer are also important because patients are commonly burdened by a lowered quality of life, emotional distress, and social stigmatization.[4]

1.1. Link between oxidative stress and cancer progression

There has been a lot of attention on oxidative stress being a critical element in the pathogenesis and progression of cancer. It is a consequence of dysfunctional antioxidant defenses of the body and the production of reactive oxygen species (ROS). ROS, hydrogen peroxide (H_2O_2), and •OH radicals generate under physiological condition as secondary metabolites induced by normal cellular metabolism and perform indispensable role in cell signaling, immune response and homeostasis. But when the levels are too high for their capacity to be resolved by the cells' endogenous antioxidant systems, cells undergo oxidative stress and experience damage at the molecular and cellular levels.[5] All of cancer development stages including initiation, promotion and progression are greatly contributed by the oxidative stress. Finally, ROS may directly damage DNA, as it induces strand breaks, modifications of bases and crosslinking. Such genotoxic insults serve to mutate important oncogenes and tumor suppressor genes, thus promoting malignant transformation of normal cells.[6] In addition, oxidative damage to proteins and lipids can interfere with the signaling pathways and cell membrane by disrupting the cellular membranes. Consequently, this process can impair cellular proliferation and promote resistance to the apoptosis. Cancer cells in turn generate high levels of ROS, in the tumor microenvironment due to dysfunction in mitochondria, oncogene activation as well as inflammatory responses.

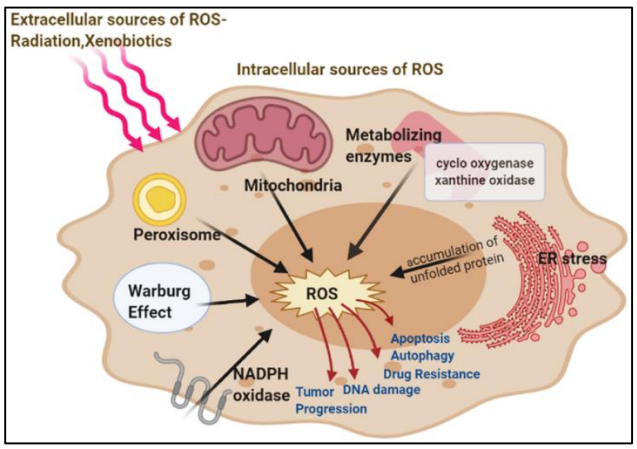

Figure 1: Diagram showing how ROS contribute to different stages of carcinogenesis.[9]

These elevated ROS levels paradoxically promote tumor promotion and progression by activation of redox sensitive transcription factors NF-κB and AP-1.[7] Transcription factors regulate expression of genes that are crucial for involvement of malignant cells in angiogenesis, invasion, metastasis and survival. Furthermore, ROS leads to activation of matrix metalloproteinases (MMPs) that degrade the extracellular matrix to facilitate tumor cell invasion of surrounding tissues and metastasis to distant organs.[8] ROS contribution to different stages of carcinogenesis is shown in **Figure 1**.

2. Antioxidants: Classification and Mechanisms

2.1. Endogenous antioxidants

Body's inherent defense against the reactive oxygen species (ROS) and the oxidative stress is formed by endogenous antioxidants. And these naturally occurring enzymatic and non-enzymatic molecules coordinate to keep redox homeostasis, that is to neutralize any excess ROS in order to act as free radical scavengers and thus prevent the oxidative damage of the cell components. Super to out of the numerous endogenous antioxidants in existence, three of the more important players in this protective network are superoxide dismutase (SOD), catalase, and glutathione.[10] **Table 1** shows classification of antioxidants. One of the first defensives lines of enzymatic protection against oxidative stress is superoxide dismutase (SOD). It is a dismutase for superoxide anions (O_2•−), a primary ROS produced in relation to mitochondrial respiration and other O_2•− producing processes, into molecular oxygen (O_2) and hydrogen peroxide (H_2O_2). The assembly of SOD can occur in multiple isoforms, because Cu Zn-SOD (SOD1) is cytoplasmic, Mn-SOD (SOD2) is mitochondrial matrix, and extracellular SOD (SOD3) can work extracellular.[11] SOD reduces the body count of superoxide radicals, which if left unchecked, can act with nitric oxide to form peroxynitrite, a very destructive chemical combining serving to induce protein nitration and lipid peroxidation.[12] Names of some antioxidants are shown in **Figure 2**.

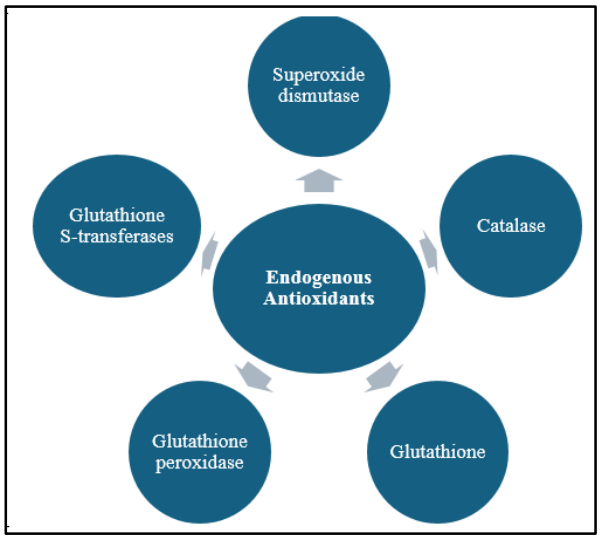

Figure 2: Endogenous antioxidants

2.2. Exogenous antioxidants

Exogenous antioxidants are obtained from outside the body and this is mainly from oral sources, and they contribute significantly to complementing the body's endogenous systems of defense against oxidative stress. The natural compounds with the antioxidant activity tend to be found abundantly in many fruits, vegetables, herbs, nuts and other plant foods and are playing a significant role in human health as they are neutralizing reactive oxygen species (ROS) and effectively deflecting oxidative damage.[13] Vitamins C and E, polyphenols, and carotenoids among the most well researched exogenous antioxidants have distinct biochemical properties and mechanisms of action that protect cells from oxidative injury.[14]

Water soluble antioxidant vitamin C (ascorbic acid) plays a key role of strong free radical scavenging capacity. It can directly neutralize a variety of ROS, such as superoxide, reactive oxygen radicals (hydroxyl radicals, hydrogen peroxide), etc. Vitamin C is principally hydrophilic and largely exists in aqueous body solutions (plasma and the cytosol). Apart from its antioxidant properties, vitamin C is important in protecting the other antioxidants such as vitamin E, to maintain redox cycling, as well as preventing propagation of oxidative damage.[15] It also plays an essential role as an essential cofactor in collagen synthesis, immune function, and wound healing. In the context of cancer, vitamin C has been investigated for its ability to inhibit tumor growth through modulation of redox sensitive signalling pathways and induction of oxidative stress in cancer cells at pharmacological concentrations.[16]

Vitamin E (α-tocopherol) is the most abundant molecule of the lipid soluble antioxidant protected polyunsaturated fatty acids (PUFAs) from lipid proofing. Vitamin E scavenges lipid peroxyl radicals to terminate the lipid oxidation chain reaction and preserve membrane integrity to prevent cellular dysfunction. Vitamin C also combines synergistically with vitamin E, as an oxidized form of vitamin E can be regenerated back to its active form by vitamin C, thus meeting again the free radical defensive requirement of these two vitamins.[17] The vitamin E also has been shown to modulate inflammatory response and immune functions and to be considered as a means of reducing cancer risk through preventing cell membrane and signaling molecule damage with oxidative attack.[18]

Another important class of exogenous antioxidants are carotenoids, substances responsible for the red, orange and yellow pigmentation in many fruits and vegetables. Beta carotene, lycopene, lutein, and zeaxanthin are common dietary carotenoids. These are lipid soluble compounds that quench singlet oxygen and scavene peroxyl radicals and repress oxidative degradation of lipids within the cellular membranes. Carotenoids possess additional antioxidant activities, aging some as vitamin A precursor vital for vision, defense and integrity of the epithelium. Most of the epidemiological studies have shown that high dietary intake of carotenoids is associated with reduced risk of many different types of cancers such as lung, prostate and gastrointestinal cancers and this is attributed to their antioxidant and anti-inflammatory properties.[19]

2.3. Mechanisms of action: ROS scavenging, metal chelation, and gene regulation

Mechanisms that collectively mediate their protective effects across overlapping mechanisms to maintain redox balance and protect cells from oxidative damage include antioxidants. Scavenging of reactive oxygen species (ROS) by direct mechanisms, chelation of transition metals that catalyze ROS production, and gene regulation of redox homeostasis, inflammation, and cell death are these mechanisms. The path the antioxidants take to reduce oxidative stress, prevent biomolecular damage and alter cell fate, particularly in the context of cancer biology, are through these interconnecting pathways.[20]

2.3.1. A. ROS scavenging

Direct neutralization of free radicals and reactive oxygen species is one of the main actions of the antioxidants. Due to the unpaired electrons on free radicals, they cannot simply exist and are thus highly unstable; free radicals can initiate damaging chain reactions within biological macromolecules. The reactive species are stabilized by donating electrons or hydrogen atoms to them, without becoming pro-oxidants themselves, by antioxidants including vitamins C and E, glutathione, and polyphenols. For example, vitamin C yields electrons to reduce the hydroxyl radicals and the superoxide anions, while vitamins such as vitamin E terminate lipid peroxidation chain reactions by preventing lipid peroxyl radicals from spreading out of its cellular membrane. This ROS scavenging capacity prevents oxidative modification of DNA, protein and lipid to maintain genomic integrity and cellular function.[21,22]

2.3.2. B. Metal chelation

The chelation of transition metals like iron (Fe^{2+}) and copper (Cu^{2+}), that participate in Fenton and Haber-Weiss reactions to promote conversion of relatively stable hydrogen peroxide into highly reactive hydroxyl radicals is the secondary, although crucial, antioxidant mechanism. Flavonoids, phenolic acids, and some thiol containing compounds (e.g. glutathione) can act as antioxidants binding to these metal ions and sequestering them as inactive complexes reducing the metal's catalytic availability. Antioxidants effectively attenuate ROS generation at its source by limiting the free pool of redox active metals within cells, which consequently decreases oxidative stress and reduces further biomolecular (damage). As this mechanism is crucial in the context of breast cancer biology, where the iron biology is perturbed and ROS are produced at high levels, it is particularly important.[23,24]

2.3.3. C. Gene regulation

In regulation of intracellular signaling pathways and gene expression profiles associated with oxidative stress, inflammation, cell proliferation and apoptotic responses, many antioxidants act beyond their role as chemical reactivity with ROS. Nuclear factor erythroid 2 related factor 2 (Nrf2) is one of the most important transcriptional regulators affected by antioxidants. Under oxidative stress Nrf2 translocates to the nucleus, where Nrf2 binds to antioxidant response elements (ARE) in the promoter elements of various cytoprotective genes and their products include heme oxygenase-1 (HO-1), glutathione S-transferases (GSTs), NAD(P) H:quinone oxidoreductase 1 (NQO1), and glutamate cysteine ligase (GCL), all of which within the networks of cellular anti-oxidant defense.[25] Furthermore, they can also influence pro-inflammatory transcription factors such as nuclear factor kappa B (NF-κB). As a good example of how ROS induces NF-κB activation that contributes to chronic inflammation and tumor progression, ROS induces the expression of cytokines, adhesion molecules, MMPs, anti-apoptotic genes. Antioxidants can inhibit ROS and interfere with NF-κB signaling to reduce inflammation and sensitize cancer cells to apoptotic stimuli. In addition, some of the same antioxidants also affect other signals: mitogen activated protein kinases (MAPKs), phosphoinositide 3 kinase (PI3K)/Akt, and p53 dependent pathways that are essential for controlling cellular growth, survival, and death. Antioxidants do not only limit cellular oxidative damage, but they also modulate these pathways and induce apoptosis, suppress angiogenesis and metastasis, and arrest cells in the cell cycle. Together, these mechanisms, when taken together, regulate and direct ROS scavenging, metal chelation, and redox sensitive genes to convey the multiplicity of antioxidant action. However, redox imbalance is a key driver of pathology in diseases such as cancer and their ability to act at multiple levels of cellular defense indicates their potent modulators of oxidative stress and their therapeutic potential in such diseases.[26,27]

3. Antioxidants in Cancer Prevention

3.1. Epidemiological evidence linking antioxidant intake and reduced cancer risk

Studies over the last several decades have consistently pointed out the association between high consumption of antioxidants in diet and decreased chances of getting different kinds of cancers. Compared to diets low in bioactive food constituents such as exogenous antioxidants (vitamins C, E, carotenoids, polyphenols) from fruits, vegetables, whole grains, etc. populations with diets rich in plants foods (fruits, vegetables, whole grains, etc.) have lower cancer incidence rates.[32] Across diverse geographical regions and ethnic groups, there has been this inverse relationship between the consumption of antioxidant and the cancer risk, indicating the universality significance of antioxidants in cancer prevention.[33]

Table 1: Classification of antioxidants with representative examples, sources, and mechanisms of action

Category	Antioxidant	Source	Mechanism of Action	References
Endogenous (Enzymatic)	Superoxide dismutase (SOD)	Cytoplasm, mitochondria	Converts superoxide anion (O_2•−) to hydrogen peroxide (H_2O_2) and oxygen (O_2).	[28]
	Catalase	Peroxisomes	Breaks down hydrogen peroxide into water and oxygen.	[28]
	Glutathione peroxidase (GPx)	Cytoplasm, mitochondria	Reduces H_2O_2 and lipid hydroperoxides using glutathione (GSH).	[28]
Endogenous (Non-enzymatic)	Glutathione (GSH)	Cytosol	Direct scavenging of ROS; cofactor for GPx; regenerates antioxidants.	[29]
Exogenous (Vitamins)	Vitamin C (Ascorbic acid)	Citrus fruits, vegetables	Scavenges ROS; regenerates vitamin E; reduces oxidized biomolecules.	[30]
	Vitamin E (α-tocopherol)	Nuts, seeds, vegetable oils	Inhibits lipid peroxidation by scavenging lipid peroxyl radicals.	[30]
Exogenous (Polyphenols)	Quercetin, Resveratrol, EGCG	Fruits, tea, grapes	Scavenges ROS, chelates metals, modulates Nrf2 and NF-κB pathways.	[31]
Exogenous (Carotenoids)	β-carotene, Lycopene	Carrots, tomatoes	Quenches singlet oxygen, prevents lipid peroxidation in cell membranes.	[30]
Synthetic	BHA, BHT	Food preservatives	Free radical scavenging; prevents oxidative spoilage in processed foods.	[31]

3.2. Role of dietary antioxidants in cancer prevention

Dietary antioxidants fortified in plant foodstuffs including fruits, vegetables, herbs, legumes, nuts, and whole grains have beneficial effect on reducing oxidative stress and cancer development. Such bioactive compounds are external supplements to body's endogenous antioxidant defense systems and enhance protective effects by acting in several different ways such as free radical scavenging, metal chelation, and modulation of cells' signaling pathways involved in inflammation, cell proliferation and death or apoptosis.[34] The most abundant dietary antioxidants and the sources of supply of vitamins (e.g. vitamin C and E), carotenoids (e.g. β-carotene, lycopene, lutein), flavonoids (e.g. quercetin, kaempferol), and other polyphenolic compounds are fruits and vegetables. These natural compounds neutralize directly reactive oxygen species (ROS) formed during metabolic processes or as a result of environmental carcinogens and thereby decrease oxidative damage to DNA, proteins and lipids inherited events associated with the initiation of carcinogenesis. In addition, these antioxidants have anti-inflammatory effects, by suppressing proinflammatory cytokines or inhibiting redox sensitive transcription factors such as nuclear factor kappa B (NF-κB), which is usually activated in chronic inflammation, and is associated with promoting various cancers.[35-37]

3.3. Preclinical and clinical studies on antioxidant-rich diets

The effects of antioxidant rich diet on cancer prevention and therapy have already been considered by a large body of preclinical and clinical research. Evidence accumulated from animal models and human trials and shows modulating key hallmarks of cancer: reducing oxidative stress, inhibiting tumor growth, and modulating molecular pathways in cancer related to inflammation, proliferation, and apoptosis via antioxidant dense foods and phytochemicals. Dietary antioxidants have consistently been shown to protect against chemically induced carcinogenesis by preclinical studies, mostly performed in 'rodent model'. Examples include experimental studies in which flavonoid rich diets have been used, like diets containing quercetin, kaempferol or catechins, have demonstrated reduced tumor incidence in colorectal, lung and breast cancer models. ROS accumulation was inhibited by these bioactive compounds, DNA damage prevented, and pro-carcinogenic signaling pathways (NF-κB, MAPK and PI3K/Akt) down regulated. Likewise, murine models of prostate, breast and skin cancers have shown that polyphenols such as resveratrol and curcumin arrest cancer cell proliferation, induce apoptosis, inhibit angiogenesis and metastasis. These models also showed that dietary antioxidants associated with antioxidant rich diets also up regulated the detoxifying enzymes such as glutathione S transferase (GST) and SOD, in demonstrating that the dietary antioxidants have the ability to further enhance the cellular antioxidant defenses.[38,39]

4. Antioxidants in Cancer Therapy

4.1. Synergistic role of antioxidants with chemotherapy and radiotherapy

Interest in using antioxidants in cancer therapy has appreciably increased because of their capacity to improve the efficacy and tolerability of such approved treatments as chemotherapy and radiotherapy. The main anticancer effects of chemotherapeutic agents and ionizing radiation are the induction of oxidative stress, high levels of reactive oxygen species (ROS) to damage DNA, proteins and lipids causing cancer cell death. Nevertheless, this oxidative burst is indiscriminate and often leads to collateral damage of healthy tissues including mucositis, cardiotoxicity, nephrotoxicity, neurotoxicity, and myelosuppression.[40] In this context, antioxidants have become promising adjunctive agents that could mitigate these side effects and also increase the anticancer activity of standard therapy through redox modulation. Antioxidants are well documented to play a synergistic role with chemotherapy in preclinical and clinical studies. For instance, N-acetylcysteine (NAC), other antioxidants like glutathione and vitamin E, have been shown to reduce normal cells from chemotherapy induced oxidative damage but without compromising their cytotoxicity to killing cancer cells. In patients given alkylating agents such as cyclophosphamide or cisplatin, NAC primarily replenishes intracellular antioxidant stores and reduces chemotherapeutic toxicity. In addition, vitamin E has been employed to manage anthracycline-induced cardiotoxicity of breast cancer patients without diminishing the anti-cancer effect of the chemotherapy regimen.[41]

4.2. Reduction of therapy-induced oxidative damage and side effects

Chemotherapy and radiotherapy are among the most important clinical challenges in cancer management because of their adverse side effects. These conventional treatments are highly successful at causing oxidative stress in rapidly dividing cancer cells, but also kill healthy tissues non-selectively. The major cause of this off target toxicity is excessive generation of reactive oxygen species (ROS) during therapy thus causing oxidative damage to the DNA, proteins and lipids of nonmalignant cells.[42] However, the treatment of cancer induces multiple other side effects including cardiotoxicity, nephrotoxicity, mucositis, neurotoxicity, myelosuppression and gastrointestinal disturbances that often reduce the tolerability of treatment, require dose reductions, and reduce the quality of patient life. As promising agents to mitigate therapy-induced oxidative damage and minimize treatment-related toxicities, antioxidants have emerged as agents that can preserve anticancer efficacy of standard therapies. As a potent precursor of glutathione, N acetylcysteine (NAC) is widely considered to be cytoprotective against chemotherapy induced toxicity. NAC replenishes intracellular glutathione stores and increase cellular antioxidant capacity, thereby

reassuring the oxidative injury to normal tissues, and has been successfully used for prevention of cisplatin induced nephrotoxicity in both preclinical and clinical settings.[43]

4.3. Enhancement of therapeutic efficacy via redox modulation

Redox modulation has provided both a means to mitigate therapy-induced toxicity with the use of antioxidants but also to manipulate the efficacy of anticancer treatments with a strategic strategy. Because cancer cells have elevated intrinsic levels of ROS due to mitochondrial dysfunction, oncogene activation and increased metabolic activity, they are characterized. To promote the survival with this pro-oxidant environment, tumor cells increase antioxidant defense systems, for example the glutathione (GSH) system and the Nrf2 pathway, to avoid ROS-triggered apoptosis. The redox adaptation of cancer cells allows them to adapt to stress but at the same time grants a vulnerability that can be therapeutically exploited.[44] Redox modulation occurs by targeting appropriate modification of intracellular ROS levels to drive cancer cells past their oxidative capability, or in the case of unique tumor types, to weaken their antioxidant defense systems to increase their sensitivity to conventional forms of therapy such as chemotherapy and radiotherapy. Most antioxidants and phytochemical that usually are considered as ROS scavengers respond in a dual manner, that is, as pro oxidants under certain conditions, such as in tumor microenvironment.[45]

5. Challenges and Controversies

Antioxidants have traditionally been known to neutralize the reactive oxygen species (ROS) and reducing the oxidative damage, but in the realm of oncology, another concern is that antioxidants may actually prevent the ROS from damaging the cancer cells. This paradoxical effect poses an important dogma in regard to the use of antioxidants as adjuncts in cancer therapy, as the non-selectivity of the antioxidants could oppose the very mechanisms that most chemotherapeutic agents and radiotherapy use to elicit their antitumor effect. Aberrant metabolism of cancer cells, mitochondrial dysfunction and heightened proliferative signaling increase basal ROS levels in cancer cells.[46] Thus, this renders them at risk of oxidative damage, but cancer cells adapt to this by upregulating antioxidant systems, including glutathione (GSH) system, superoxide dismutase (SOD) and the Nrf2 mediated antioxidant response, which allows them to maintain redox homeostasis and escape apoptosis induced by ROS.[37] Exogenous antioxidants are easily given indiscriminately; however, when provided, they can further enhance these adaptive mechanisms, and thus tumor cells are better equipped to withstand oxidative stress generated from anticancer therapies. For instance, as has been shown, NAC or vitamin E may under appropriate conditions diminish the ability of ROS producing chemotherapies (e.g., alkylating agents, anthracyclines) and radiotherapy to ciliate lethal damage to cancer cells through their conversion to ROS. When used in experimental models, antioxidants have been found to prevent the damage oxidative DNA damage inflicts on cancer cells, disrupting the pro-apoptotic signaling cascade that's essential for adequate tumor removal. For example, in animal models, high doses of antioxidant supplement were shown to accelerate tumor progression of existing tumors, pointing out the possibility for oxidative and antioxidant supplement to favor tumor survival if oxidants and antioxidants are misused.[47]

6. Future Perspectives

Redox balance is a critical determinant of cellular homeostasis which is balanced well between the generation of reactive oxygen species (ROS) by the electron transport chain and the antioxidant defense system. This balance is frequently disrupted in cancer biology, as tumor cells often work within a persistent state of oxidative stress induced by aberrant metabolic activity and mitochondrial dysfunctions. Nevertheless, the same tumor cells use adaptive responses to antioxidants to neutralize ROS and supply survival. The duality of redox regulation means it is a key precision medicine therapeutic target where therapeutic interventions are formulated on the basis of an individual's tumor molecular and biochemical characteristics.[48] The objective of precision medicine is to improve the therapeutic outcome by tailoring treatment strategies to a patient's genetic, molecular, and environmental profile. Several pathways that affect carcinogenesis, tumor progression, metastasis and response to therapy are intricately linked to redox homeostasis. Clinically, this means that modulating redox status at the individual level helps clinicians determine cancer cell vulnerabilities without compromising normal tissue function.[49]

7. Conclusion

Antioxidants formulate an essential defense system against cancer because they stop oxidative damage while dealing with inflammation along with tumor progression through ROS scavenging, metal chelation and redox-sensitive gene regulation. Endogenous as well as exogenous antioxidants function to guard normal tissues against chemotherapy and radiotherapy damage and selected phytochemicals demonstrate additional anticancer action through redox modulation. Research on antioxidants needs careful evaluation because these compounds protect sensitive cells alongside oncological cells. Research demands precise strategies to evaluate cancer type alongside treatment plans and a patient's redox status and specific characteristics because current clinical findings differ. The upcoming research into personalized redox profiling together with targeted delivery methods integrated with immunotherapy should become the focus while establishing therapeutic windows to improve antioxidant benefits in cancer treatment.

8. Source of Funding

None.

9. Conflict of Interest

None.

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