Chapter

The Two Sides of Dietary Antioxidants in Cancer Therapy

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Abstract

Cancer is a major cause of mortality around the world, representing about 13% of deaths on the planet. Among the available cancer treatments, chemotherapy is most frequently utilized compared to other treatments such as surgery and radiotherapy. Many dietary antioxidants have proven to effectively prevent oxidative stress, which has been noted in many disease pathogeneses, including cancer. However, during chemotherapy or radiotherapy treatment of cancer patients, antioxidants are used as an adjuvant treatment. The use of a proof-based technique is advised in determining the supplements most suited to cancer patients. Though there are numerous opinions about the dangers and advantages of antioxidants, it is reasonable to conclude that side effects caused by antioxidants, for now, remain unclear for patients during cancer treatment, aside from smokers during radiotherapy. In this report, details of the effectiveness of antioxidants on cancer treatment aiding in the reduction of cancer therapy side effects are discussed.

Keywords: antioxidants, chemotherapy, dietary supplements, polyphenolics, radiotherapy

1. Introduction

Cancer is a wide collection of diseases that can begin in practically any organ or tissue of the body when abnormal cells develop and move beyond their space to attack surrounding areas and also spread to different organs [1]. There are numerous types of cancer such as breast cancer, skin cancer, bone cancer, lung cancer, colon cancer, prostate cancer and if left untreated, it results in serious harm and could eventually lead to death [2]. Different causes of cancer include hereditary variables, way of life, diet, exposure to various kinds of synthetic compounds, and radiation. The American Cancer Society has estimated the number of new cancer cases for the year 2020 in the United States is 1,806,590 cases and 606,520 deaths. Previously, the cancer death rate increased up until the year 1991, at which point, the numbers dropped ceaselessly from 2017, bringing about a general decrease of about 29% which is equivalent to 2.9 million fewer cancer deaths than as projected. This was attributed to the long-term decrease in death rates for the 4 main cancer types (colorectal, prostate, breast, and lung cancer) [3]. Among the reasons that can be mentioned for the reduction in the mortality rate of cancer patients are the

various techniques being used for treatment such as chemotherapy, surgery, and radiotherapy. Various kinds of cancer can proceed in abnormal ways, develop at different rates, and react to treatment differently, hence, each cancer treatment is focused on the specific cancer type. Cancer therapy used in the treatment of cancer patient includes surgery, chemotherapy, radiotherapy and more recently antioxidant have been proposed to benefit cancer patients during cancer therapy [2].

Antioxidants are substances that can neutralize the production of free radicals and counteract the oxidation process. Antioxidants can be classified based on their source; endogenous source (enzymes) and exogenous diets (carotenoids, flavonoids, phenolics, minerals, and vitamins) [4]. Antioxidants are naturally found abundant in dietary sources, and their consumption possesses great health benefits [5]. The use of dietary antioxidants mitigates oxidative stress which contributes majorly to several diseases. Plant nutrients including organic products, vegetables, tea, grains, red wine, nuts, spices, and flavors give a huge sum and variety of antioxidants by preventing diseases. Dietary antioxidants are also a complex mixture of minerals (selenium, zinc, or copper) and micronutrients (vitamins A, C, and E) [6]. There are recommended antioxidants intake either as a diet with antioxidant activities or combined with antioxidant enzymes. Metals such as iron, zinc, manganese, copper, and selenium are considered cofactors of various enzyme antioxidants, and some nutrients (β-carotene, α-tocopherol, ascorbic acid, and folic acid) as sequestrate of reactive oxygen species (ROS) [7]. In light of this, this review discusses dietary antioxidants in cancer therapy in light of merits and demerits.

2. Oxidative stress

A free radical is a particle capable of existing independently and has at least one unpaired electron in its outer shell. Most free radicals are profoundly reactive and unsteady as a result of the number of electrons. Therefore, they rapidly react with different substances to attain stability. Free radical attacks the nearest steady particle and acquire its electron, meanwhile, the attacked particle can turn into a free radical by loosing its electron and start a chain reaction course harming the living cells. Examples of free radicals are superoxide anion, lipid alkoxyl, lipid peroxide, lipid peroxyl, and hydroxyl radical. Reactive oxygen species (ROS) are radical subordinates, for example, hydrogen peroxide and singlet oxygen [8]. Free radicals are fundamentally reactive oxygen species (ROS) or reactive nitrogen species (RNS) comprising of singlet oxygen, hydrogen peroxide, superoxide radicals, intermediary nitrite, and nitric oxide (NO) [9]. The primary reactive oxygen species (ROS) are the superoxide (O2-), singlet oxygen (O2), hydrogen peroxide (H2O2), hydroxyl radicals (HO-), peroxyl and alkoxyl radicals (ROS- and RO-), and natural peroxides (ROOH). In the event of cellular damage caused by free radicals, for example, involving cellular amino acids, lipids, and DNA, reactive oxygen species (ROS) can activate enzymatic and non-enzymatic cell reactions, with the possibility of tampering with different metabolic processes and interfering with gene expression among other things.

Oxidative stress is an aftereffect of a variation in reactive oxygen species (ROS) and antioxidant resistances. Oxidative stress takes control of the development and function of the cell which can contribute to the pathogenesis of various conditions like neurodegenerative sickness, Parkinson's dementia, diabetes, cancer, immune system ailments, Alzheimer's ailment, cardiovascular diseases, carcinogenesis, asthma [10]. Oxidative stress predisposes cellular harm through oxidation of proteins, nucleic acids, and lipid, structural adjustment of the membranes, the

harm induced may extend to the organs and become systemic [11]. Countering the effect of free radicals can be through a large intake of dietary antioxidants and specific antioxidant supplements as part of the diet. Though, some reports have suggested that combining several antioxidants is more viable in the long-term than single antioxidant substances. Therefore, antioxidants provide a great advantage in improving personal health by hindering several diseases conditions [12].

2.1 Antioxidants

Antioxidants act as scavengers of free radical or reactive oxygen species (ROS) and avert oxidation leading to several disease conditions. An antioxidant hinders the oxidation of lipids, DNA, sugar, and proteins at low concentrations. Antioxidants are found in plants, numerous foods, and some are synthesized in the body [13, 14]. In recent times, there has been increased utilization of natural products and reports have indicated that consumption of vegetables and fruits that contains antioxidants might be related to the decreased frequency of diseases activated by reactive oxygen species (ROS), such as cardiovascular diseases, cancer, etc. Oxidative stress and its damaging effects can be averted through the consumption of naturally occurring antioxidants [15]. Polyphenols and carotenoids (natural antioxidants) reveal natural activities as anti-atherosclerosis, anti-aging, anti-inflammatory, and anticancer [16]. Antioxidants function in the body to promote health and strength, particularly during old age. They ensure protection from damage to the tissues, and skin caused by the production of free radicals. In industries, they help to expand the food shelf-life and are added in the skin-care products for anti-aging purposes [13].

The antioxidant system comprises of enzymatic and non-enzymatic antioxidants. Among the enzymatic antioxidants, are superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT). The non-enzymatic antioxidant also contributes to the cellular redox balance, examples include hormones such as estradiol, melatonin, as well as certain nutrients, for example, vitamins E and C [17].

The antioxidants are grouped into three fundamental classes:

1. The principal line guard antioxidants which involve superoxide dismutase (SOD), glutathione reductase (GR), catalase (CAT), and minerals like Zn, Se, and Cu, etc.

2. The second line safeguard antioxidants which involve glutathione (GSH), flavonoids, carotenoids, vitamin C, vitamin E, etc.

3. The third line safeguards antioxidants which involve a complex combination of chemicals responsible for fixing the damaged DNA, proteins, oxidized lipids, and peroxides. Examples are DNA repair enzymes, methionine sulphoxide reductase, protease, lipase, transferases, and so on [10].

2.2 Dietary antioxidants

Dietary antioxidants are substances found in food and it ensures the protection of cells, tissues, and DNA against oxidative harm of free radicals. Dietary antioxidant supplements involve protein, starch, sodium, fiber, fat as well as minerals and vitamins. Dietary antioxidants having both antioxidant and pro-oxidant impacts involve nutrients (tocopherol, carotenoids, pro-vitamin A, ascorbic acid, basic micronutrients with physiological roles) and also involve phytochemicals and polyphenols. In a review, dietary consumption of anthocyanins (an antioxidant

found in berries) was revealed about 8% decrease in hypertensive condition [18]. Dietary nutrients have also shown significant improvement in bodily functions such as brain health, improved nervous system metabolism, and so on [19].

Since scientific evidence established the role of free radicals in the pathogenesis of diseases such as cardiovascular diseases, cancer among others, there have been considerable studies towards natural antioxidant properties to ameliorate such effects. The dietary antioxidant can have useful impacts on the body by scavenging free radicals and also the redox potential if they are available in tissues at adequate concentrations. For some dietary phytochemicals, direct antioxidants intake for some disease condition might be less significant to health than others as well as its consequences on cell signaling and gene expression [20]. There is a concern that the global consumption of fruits and vegetables is insufficient, leading to a decreased intake of antioxidants and predisposes to degenerative diseases [21].

2.3 Examples of dietary antioxidants and their sources

2.3.1 Vitamin C

Vitamin C (ascorbic acid) is vital to the health of the body by acting as an intense scavenger of radical. Ascorbic acid is a water-soluble vitamin and a huge supplement for quick intestinal absorption. It is needed for the collagen synthesis in the body, essential in regulating norepinephrine from dopamine and function in tyrosine digestion. Insufficient intake of vegetables and fruits, the main sources of vitamin C, can prompt the inadequacy of this crucial nutrient in the body. Ascorbic acid is quickly exhausted and oxidized during oxidative stress. Examples of natural sources rich in vitamin C are grapefruits, pineapple, cherries, citrus fruits, potatoes, pepper, strawberries, gooseberry, broccoli, kiwi fruit, and paprika, etc. [22].

2.3.2 Vitamin D

Vitamin D is a fat-soluble vitamin known to assume an important role in bone and calcium homeostasis and function as an anti-inflammatory agent since it represses invulnerable the expression of cell cytokine and prompts monocyte/macrophage to emit molecules which have a firm antibiotic impact. Its insufficiency can expand the danger of infectious diseases. Almost 95% of vitamin D is gathered in the epidermis of the skin on exposure to the sun, the rest is gotten from different dietary sources. In food, oily fish contains the largest amount of vitamin D, other sources include milk, orange, etc. [22].

2.3.3 Vitamin E

Vitamin E also called tocopherol is a fat-soluble vitamin. Vitamin E has an extremely wide capacity of preserving biological membrane and nucleic acids in the body from the attacks of free radicals. Vitamin E is rich in vegetables, vegetable oil, almonds, walnuts, etc. Vitamin E has been discovered to have repressive capacity on tumors [23].

2.3.4 Flavonoids

Plants have numerous flavonoids essential to mitigate the development of diseases. Basic flavonoids compounds involve anthocyanins, isoflavones, flavones, etc. Flavonoids destroy the free radicals by transforming them into phenolic radicals (inactive) after providing hydrogen to lipid compound radicals. Foods containing a

large number of flavonoids involve herb, onions, blueberries, banana, and all citrus fruits, etc. [23].

2.3.5 Carotenoids

These are dietary antioxidants that have exhibited action of photoprotection. In plants, these compounds are found in the photosynthetic parts where they are classified as extra light-collecting shades and shield from harm caused by sunlight. The photoprotective impacts of carotenoid-rich eating routine have been researched for its capacity to diminish the erythema (skin redness) size upon UV radiation exposure, though an extended period is necessary for a successful mediation. Among carotenoids, beta-carotene, lycopene, and lutein are gotten from various plant sources, for example, tomato, carrots, etc. [24].

2.3.6 Polyphenols

There has been developing interest upheld by various epidemiological tests, on the possible gainful impacts of polyphenols on brain health. Polyphenol is micronutrients abundant in plant-determined nourishment which is also strong antioxidants. Fruits and beverages, for example, coffee, cocoa, and tea, and so on are significant dietary sources of polyphenols. Polyphenols are noted for their neuroprotective activities; protecting neurons against damage induced by neurotoxins, can suppress neuroinflammation, and the possibility to advance memory, learning, and psychological capacity. Recent evidence suggests that their beneficial impact includes a reduction in oxidative stress, an increase in defensive signaling, prompting the expression of genes that encode antioxidant enzymes, neurotrophic factors, and protective protein [7].

3. Cancer

Cancer is a major medical issue globally and is the second leading cause of death in the United States. A century ago, cancer was not all that normal, however, since the last few decades, its frequency has been rising alarmingly, presumably because of our evolving way of life and habits. Cancer is among the most dreaded illnesses of the 20th century and grows forward with the increasing rate in the 21st century. Cancer is the abnormal development of cells. Cancers are made of small cells that have lost the capacity to stop developing and can emerge from any body structure or organ. Caner is not easily detected in its early stages but might be recognized by chance via a laboratory test or radiological routine test [25].

Cancer is a general term used in describing a group of diseases portrayed through independent development and the spread of a somatic clone. In this light, cancer must approach different cell pathways that empower it to disregard the typical requirements on cell development, change the local microenvironment to support its growth, attack through tissue boundaries, spread to different organs, and avoid immune system observation. No single cell program coordinates these behaviors, rather, there is a wide mass of pathogenic abnormalities from which singular cancers draw their combination, the shared traits of macroscopic features across tumors give a false representation of a huge heterogeneous scene of cell abnormalities [1].

Any time a cell divides, errors during the DNA replication process suggest that new mutations are present in the genomes of the daughter cells. Epigenetic marks (e.g. DNA methylation) are also replicated with limited precision. Larger-scope

chromosol or part-chromosome losses or modifications [somatic copy number alternation (SCNAs)] and other structural modifications also occur at a standard frequency in many cancers. It is naturally occurring in the genetic modification that records the history of the cells in the tumor and since tumors are clonally derived; the entire cells in the tumor will carry the mutations in the main cancer cell, thus later-emerging subclones are recognizable by their sharing of a specific arrangement of variants, therefore, the order of clone advancement can be constructed by comparing the arrangement of mutation present in various cell tumor [26]. Cancer cells to meet their energy requirements, they depend on aerobic metabolism and also combined fatty acids, proteins, and nucleotides. Therefore, there is a constant need to expand the glucose supply needed to uphold diseases like diabetic-related hyperglycemia [27].

3.1 Cancer types

3.1.1 Lung cancer

Lung cancer is the most dangerous tumor, and the principal reason for cancer death worldwide in both genders combined. Globally, lung cancer occurrence and mortality on the general populace are essentially dictated by tobacco usage, the fundamental etiological factor in lung carcinogenesis [28]. The hazard factors for lung cancer involve ecological and hereditary hazard factors, all of which have an impact on tumor advancement and additionally influence patients' treatment [29]. Ladies have some unique hazard factors for lung cancer compared to men, and lung tumors in ladies have different pathologic conduct, results, and visualization in comparison to lung cancer growth in men [30]. The viability of lung cancer growth screening, utilizing computed tomography (CT) or chest X-ray (CXR), involving extra aides or not, such as sputum cytology, has been explored in various studies as asymptomatic at-risk populations [31].

3.1.2 Breast cancer

Breast cancer is the commonest cancer analyzed in the female population (excluding skin cancer) and reported the second highest cause of death among ladies after lung cancer [32]. There have been numerous analytic techniques for diagnosing early-stage breast cancer such as biopsy, breast MI, MRI, PET, ultrasonography, and mammography [33]. There are various hazardous factors, for example, sex, maturing, estrogen, family history, gene mutation, and an unhealthy lifestyle, which can contribute to the risk of breast cancer. Most breast cancers occur in ladies and the quantity of cases is multiple times more in ladies than that of men [34]. Various treatments can be utilized, for example, targeted therapy, hormonal therapy, radiation treatment, surgery, and chemotherapy [35].

3.1.3 Prostate cancer

Prostate cancer is another deadly cancer diagnosed in men and the fifth-highest cause of death around the world. Prostate cancer might show no symptoms in the beginning phase, regularly has slow movement, and may require little or even no treatment. Problems with urination have been the most common issue, however, records indicate that it may emerge from prostatic hypertrophy [36]. Screening for prostate cancer is initiated by measuring prostate-specific antigen (PSA) protein levels in the blood. A raised prostate-specific antigen (PSA) level indicates prostate

cancer and other conditions, such as inflammation of the prostate and amplified prostate [37]. Prostate cancer has more victims of older men. Numerous patients with prostate cancer in the beginning stages obtain good results after various treatments involving prostatectomy, radiation therapy, hormonal therapy, etc. [38].

3.1.4 Colon cancer

Colon cancer is the third most commonly diagnosed and second deadliest cancer for all genders joined. Natural affiliations and hereditary are the main risk factors. In patients, screening colonoscopy is required for tissue biopsy neurotic affirmation of colon carcinoma, such as baseline computed tomography (CT) of the chest, mid-region, and pelvis, and carcinoembryonic antigen (CEA) are favored cost-effective [39]. Chemotherapy and Surgery are the fundamental treatment choices for colon cancer, depending on the cancer stages and tumor area, as well as the health qualities of the patients [40].

3.1.5 Pancreatic cancer

Pancreatic cancer is one of the highest causes of cancer deaths in developed nations and one of the deadliest cancers worldwide. The two-fundamental tumors; pancreatic endocrine tumors (less than 5% of cases) and pancreatic cancer are adenocarcinoma (about 85% of cases) [41]. Finding the tumor at a treatable stage is extremely difficult, patients do not usually show symptoms and tumors do not show sensitivity or signals to help in early discovery [42].

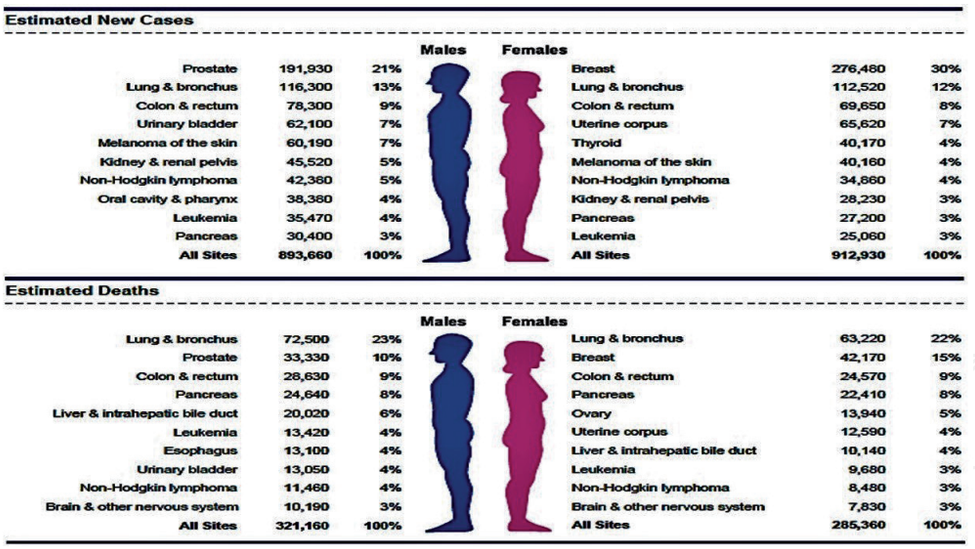
Other types of cancer including skin cancer, kidney cancer, lymphoma, bone cancer, leukemia, liver cancer, etc.

3.2 Causes

Cancer is caused by changes to the DNA within cells which are influenced by factors such as unhealthy diet, alcohol intake, tobacco use, infections, genetic tendency, ionizing radiation, toxins, obesity, inactive lifestyle, and other environmental factors [43] (**Figures 1** and **2**).

3.3 Cancer therapy

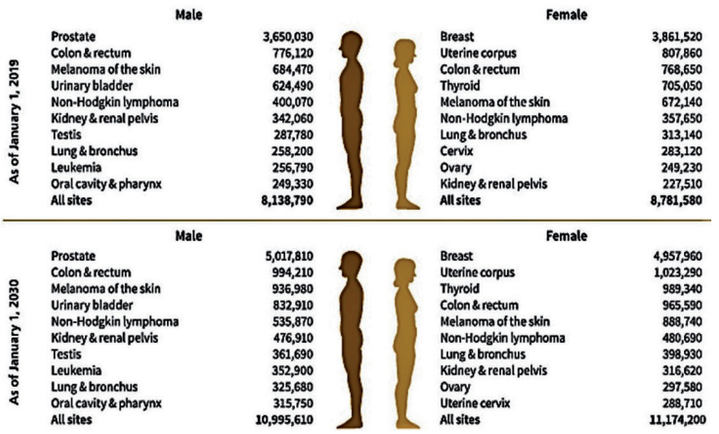
Cancer is among the primary causes of deaths globally, and in the previous years, numerous researches have concentrated on discovering new treatments other than the customary treatments which carry side effects. There are still numerous issues that must be addressed to improve cancer treatment, though much advancement has been accomplished in medication [44]. The number of cancer survivors continues to grow in the United States, notwithstanding the general declining age-normalized rates in men and stable rates in women. This shows an expanding number of new cancer analysis methods coming from the developing population as well as an increase in cancer survival due to advances in early detection and treatment. Many cancer survivors must adapt to the physical impacts of cancer and its treatment, possibly prompting functional and intellectual exhaustion [45]. There are numerous types of cancer treatment techniques based on the type of cancer and stage it has progressed to. There is no specific treatment or procedure rivaling cancer, in some cases, the treatment plan may utilize a mix of the treatment techniques to have a more effective treatment. Every one of the techniques has its side effect on the patient [46].



Estimated New Cases				Males	Females			
Prostate	191,930	21%				Breast	276,480	30%
Lung & bronchus	116,300	13%				Lung & bronchus	112,520	12%
Colon & rectum	78,300	9%				Colon & rectum	69,650	8%
Urinary bladder	62,100	7%				Uterine corpus	65,620	7%
Melanoma of the skin	60,190	7%				Thyroid	40,170	4%
Kidney & renal pelvis	45,520	5%				Melanoma of the skin	40,160	4%
Non-Hodgkin lymphoma	42,360	5%				Non-Hodgkin lymphoma	34,860	4%
Oral cavity & pharynx	38,360	4%				Kidney & renal pelvis	28,230	3%
Leukemia	35,470	4%				Pancreas	27,200	3%
Pancreas	30,400	3%				Leukemia	25,060	3%
All Sites	893,660	100%				All Sites	912,930	100%

Estimated Deaths				Males	Females			
Lung & bronchus	72,500	23%				Lung & bronchus	63,220	22%
Prostate	33,330	10%				Breast	42,170	15%
Colon & rectum	28,630	9%				Colon & rectum	24,570	9%
Pancreas	24,640	8%				Pancreas	22,410	8%
Liver & intrahepatic bile duct	20,020	6%				Ovary	13,940	5%
Leukemia	13,420	4%				Uterine corpus	12,590	4%
Esophagus	13,100	4%				Liver & intrahepatic bile duct	10,140	4%
Urinary bladder	13,050	4%				Leukemia	9,680	3%
Non-Hodgkin lymphoma	11,460	4%				Non-Hodgkin lymphoma	8,480	3%
Brain & other nervous system	10,190	3%				Brain & other nervous system	7,830	3%
All Sites	321,160	100%				All Sites	285,360	100%

Figure 1.
Estimation of new cancer cases and deaths by sex, specifically the ten Main types of cancer in the United States, 2020. Estimates are regulated to the closest 10 and avoid basal cell, squamous cell skin tumors, and cancer which have not undergone metastasis except for urinary bladder [43].



As of January 1, 2019	Male			Female	
	Prostate	3,650,030		Breast	3,861,520
	Colon & rectum	776,120		Uterine corpus	807,860
	Melanoma of the skin	684,470		Colon & rectum	768,650
	Urinary bladder	624,490		Thyroid	705,050
	Non-Hodgkin lymphoma	400,070		Melanoma of the skin	672,140
	Kidney & renal pelvis	342,060		Non-Hodgkin lymphoma	357,650
	Testis	287,780		Lung & bronchus	313,140
	Lung & bronchus	258,200		Cervix	283,120
	Leukemia	256,790		Ovary	249,230
	Oral cavity & pharynx	249,330		Kidney & renal pelvis	227,510
	All sites	8,138,790		All sites	8,781,580

As of January 1, 2030	Male			Female	
	Prostate	5,017,810		Breast	4,957,960
	Colon & rectum	994,210		Uterine corpus	1,023,290
	Melanoma of the skin	936,980		Thyroid	989,340
	Urinary bladder	832,910		Colon & rectum	965,590
	Non-Hodgkin lymphoma	535,870		Melanoma of the skin	888,740
	Kidney & renal pelvis	476,910		Non-Hodgkin lymphoma	480,690
	Testis	361,690		Lung & bronchus	398,930
	Leukemia	352,900		Kidney & renal pelvis	316,620
	Lung & bronchus	325,680		Ovary	297,580
	Oral cavity & pharynx	315,750		Uterine cervix	288,710
	All sites	10,995,610		All sites	11,174,200

Figure 2.
Estimated amount of US cancer survivors. Evaluations exclude cancer which has not undergone metastasis, except for urinary bladder and exclude basal cells or squamous cell skin cancer [45].

3.3.1 Available cancer treatments

3.3.1.1 Surgery

Treatment of cancer by surgery is usually operated on non-hematological cancers. By surgical technique, the specialist expels the cancer tissues from the body. The surgical methodology can give a total or fractional fix for cancer. There might be side effects of the surgery based on the kind of cancer and the patients' health status. If cancer is metastasized to different areas of the body, at that point expelling cancer by the surgical process is impossible. The development of the cancer cells follows the Halstedian model of cancer progression where the tumors begin developing locally and spreading to the lymph nodes and the rest of the body. The treatment of cancer by surgery should be possible to cancers that are limited to an area and the tumor is small in size [47].

3.3.1.2 Chemotherapy

The technique of chemotherapy is done using drugs, generally known as anticancer medications, to destroy or pulverize the cancer cells. These medications

interfere with the development of tumors and even damage the cancer cells. Chemotherapy is commonly considered a powerful technique for the treatment of cancer, though it can cause extreme side effects as it can also damage healthy cells or tissues. The side effects caused by chemotherapy depend on the type of cancer, its areas, and the patients' reaction to the specific kinds of chemotherapy treatment. The side effects on the cancer patient do not represent the viability of the treatment and disappear once the treatment process is finished. For the most part, chemotherapy medicines are recommended to a subject in an estimated amount over a time frame. In some cases, chemotherapy is administered at least two different medications at a time, this method is known as combination chemotherapy [48].

3.3.1.3 Immunotherapy

Immunotherapy is a technique for cancer treatment that causes the immune system to fight cancer. This is otherwise called biologic therapy, which excites the immune system of the patient to fight cancer. Several studies have been conducted on immunotherapy for treating cancer, for example, monoclonal antibodies that block specific protein work by constraining to cancer cells, which train the immune system to perceive and fight the cancer cells. This technique for treatment does not have any significant side effects. Immunotherapy is divided into two principle immunotherapeutic; passive and active. The grouping depends on the component of the therapeutic agent utilized, as well as the status of the patients' immune system. The passive immunotherapeutic is utilized in cancer patients with feeble, unresponsive, or low responsive immune systems. To apply active immunotherapeutic, the patients' immune system should be able to react strongly when opposed, be adequately stimulated, and resolve effector capacities [49].

3.3.1.4 Radiation therapy

Radiation therapy utilizes high portions of ionizing radiation to kill cancer cells and destroy the tumor tissues. This treatment is regularly utilized as a medical procedure to evacuate or lessen the size of the tumors. The radiation treatment is usually administered externally and internally to the target area and can be harmful to ordinary cells and prompt a reaction from ordinary cells because of these ionizing radiations. The radiation treatment utilizes unique equipment to carry estimated portions of radiation to the cancer cells. The radiation treatment destroys tumor cells by damaging their DNA either directly or by harming free radicals inside the cells which can hence damage the DNA. This treatment utilizes high energy ionizing radiation, for example, x-rays. This treatment has significant side effects that have different approaches in both grown-ups and children [50].

3.3.1.5 Hormone therapy

The hormone treatment fights cancer by evolving the number of hormones in the body to treat particular types of cancer that depend on the chemicals to develop and spread. This treatment technique is utilized for treating cancers of the breast, reproductive system, and prostate. The side effects depend on the type of cancer, age, sex, and the sort of medication utilized in the treatment [51].

3.3.1.6 Targeted therapy

The targeted treatment of cancer focuses on the cells that re-empower the cancer cells to develop, separation, and spread. The targeted treatment utilizes specific

agents for the deregulated proteins of cancer cells. The small atoms of targeted therapy medication are inhibitors of enzymatic areas on the change, overexpressed, or critical proteins inside the cancer cells [52].

Other treatments include bone marrow transplant, cryoablation, and radiofrequency ablation.

4. Roles of dietary antioxidants in cancer therapy

Numerous types of cancer have been associated with the relation between free radicals and DNA which can cause harmful impacts on the cell cycle and also prompt dire threats. Antioxidants in suitable portions indicate that they have a generally good effect in making the tumors progressively responsive towards chemotherapy and radiation therapy. They can repress the development of tumors specifically without interfering with typical cells. Antioxidants can ensure protection against the toxicity caused by chemotherapy by hindering cell expansion. Additionally, antioxidants have demonstrated to hold an advantageous ability to decrease harm by oxidative stress, lessening the issues joined with the production of ROS and neurodegenerative issues [53].

ROS are chemically reactive particles containing oxygen, created by cellular metabolism. A moderate amount of ROS assumes a fundamental role in managing cell multiplication and cell survival. Nonetheless, an increase in ROS levels can harm cell components, for example, lipids, proteins, and DNA causing an imbalance between cell reduction–oxidation (redox) conditions and cause disturbance of homeostasis. Constantly, increased reactive oxygen species (ROS) prompt extreme cell harm and lead to carcinogenesis by regulating cell signaling such as cell expansion, angiogenesis, and metastasis [54].

There are two kinds of antioxidant dosages utilized in cancer treatment; a preventive low portion, which restrains typical cells as well as tumor cells from developing, and a remedial high portion, which restrains the development of cancer cells without impacting typical cells. Ongoing tests demonstrated that certain conditions should be met before involving antioxidants in chemotherapy. Moreover, they do not hinder but improve the cytotoxic effect of chemotherapy while protecting the typical tissue which subsequently increases the patients' survival and therapeutic response [55].

Research has indicated that 35% of cancer can be prevented by dietary adjustments. Fruits and vegetables, which are wealthy in antioxidants, act defensively against some types of cancer. Plant nutrients that contain polyphenols have demonstrated to be viable antioxidant agents for the body, they appear to oppose cancer growth in prostate, lung, breast, tongue, gastric, larynx, and colon cancers [56]. Besides, supplements such as nutrients and minerals can lessen the risk of cancer by stimulating antioxidant activity, restraining the multiplication of cancerous cells, tending to DNA methylation, and advancing cell-cycle capture. In patients recently treated for cancer, a healthy eating routine rich in fruits and vegetables can alter biomarkers of cancer growth [57]. Notably, the redox status of the cancer cell which is under stress is not the same as the ordinary cell. Ordinary cells keep up cell homeostasis by the endogenous antioxidant mechanism which perfectly makes redox balance between the beginning and end of an overabundance of reactive oxygen species (ROS). Unfortunately, the remedial technique utilized in cancer treatment could cause an increased ROS level and also increases the endogenous ROS threshold level in cancer cells and may render ordinary cells of certain organs such as the kidney, liver, and heart ineffective against oxidative toxicity caused by oxidative stress. However, current research aims to distinguish the properties which may improve oxidative stress in cancer cells and protect ordinary cells from

oxidative harm. Extensive research conducted in recent years has indicated that plant-based nutrients have a high substance of phytochemicals such as flavonoids and polyphenols with chemopreventive properties that focus on some key factors associated with the improvement of cancer [58].

Some chemo-preventive compounds having antioxidant properties have been noted to have the potential to mitigate the cytotoxic effect of radiation treatment in cancerous cells while reducing its harm to ordinary cells and tissues. In such a manner, different research has demonstrated that phytochemicals soy isoflavones such as glycitein, show anti-carcinogenic properties to an extent using their antioxidant activities, and can be utilized as powerful radio-sensitizers to improve the viability of radiotherapy-mediated suppression of the development and metastatic capacity of tumors. As cancer patients experience treatment some unfavorable side effects may develop such as weight reduction, or loss of appetite, and so on [59].

4.1 The equivocal of dietary antioxidants in cancer therapy

The ability of antioxidants to shield the cells from ROS created the premise of its production in food supplement enterprise, with the increase in the scientific literature on its helpful impacts and wide acknowledgment among the general public. Nonetheless, present research in cancer shows two different aspects of antioxidants. Antioxidants are both helpful as a treatment system for the cancer patient and also involve harmful impacts of expanding the cancer cell growth [60].

DNA protection utilizing antioxidant therapy has been a productive choice for clinical trials. Flavonoids and phenolic acid are being noted as effective agents against the side effects of chemotherapy. A strong antioxidant such as coenzyme Q is mainly applied as a treatment in cancer, inflammation, and maturing. Application of coenzyme Q, for example on human epidermal cells, ensures protection against cell death initiated by reactive oxygen species (ROS) [61]. Supplements of vitamin C, one of the most abundant dietary antioxidants, have been found to ensure protection against oxidative harm caused by tobacco smoking reducing the risk factor of cancer. The relation between reactive oxygen species and cancer initiation is long-established. Other than the significant levels of ROS in environmental carcinogens such as tobacco smoking, reactive oxygen species (ROS) have been demonstrated to be basic for the transformation of cells caused by a gene that can transform a cell into a tumor cell or a loss of tumor suppressors. For instance, the downregulation of the p53 gene (a tumor suppressor) prompts increased reactive oxygen species (ROS) levels and antioxidant-related medications hinder tumor formation in mice lacking this gene. Though every tumor is unique and the role of reactive oxygen species (ROS) and antioxidants can differ depending on hereditary, epigenetic, and environmental variation [62].

Discovery is being made implying that the impact which antioxidants have on cancer patients is truly harmful. It is important to note that a few antioxidants do behave as pro-oxidants under certain conditions. Another study showed that the b-carotene, a likely antioxidant, should be utilized cautiously, clear from its extremely reactive carotenoid radical development during the searching system of free radicals. The investigation indicated that the carotenoid radical structure which is scavenged through vitamin C can have harmful impacts on the initiation of cancer by UV-radiation with altering levels of vitamin C. The research implies that when antioxidants are taken by healthy persons, they present gainful impacts, however, when there is a beginning of tumor development, high portions of antioxidants should be avoided to stop the increase in expansion of tumor cells. It is also important to note that the antioxidants utilized as the cream can turn unstable through the responses related to UV-radiation which can prompt harmful impacts. These facts raise issues concerning antioxidant treatment, a potential solution could be the intake of selected

antioxidants according to the cancer cells movement and utilizing standard eating routine involving such antioxidants instead of the intake of direct supplements [14].

Adequate verification is required to determine the efficacy of different anticancer agents combined with antioxidant supplements. In a recent study, no reports have shown that they cause cancer growth or an increase in mortality rate. However, if antioxidant supplements are to be utilized as aids for cancer patients, more research is required for the combination of cancer therapy and dietary supplement. The use of unauthorized supplements should be avoided [60].

5. Conclusion

There is uncertainty in determining whether antioxidants may have positively affected cancer treatment outcomes or prevent the harmful impacts of chemotherapy and radiotherapy. At first, it is important to consider all options of treatment and some patients are usually in good condition to endure the side effects of antioxidants. On second thought, some patients are not ready to endure the side effects of antioxidants, and to use treatment certain to work to some degree is more advisable. However, to be able to manage the side effects, these conditions should be revised; the dosage and types of antioxidants, the background and condition of the patient, and type of cancer and anticancer therapy. It is advisable to utilize a proof-based technique to choose the most appropriate supplement for cancer patients. Even though there are many opinions on the good and bad of antioxidants, it is difficult to clinically conclude that dietary antioxidants enhance therapeutic toxicities and also, there is no evidence of dietary antioxidant causing harm with cancer treatment, aside from smokers experiencing radiotherapy.

Conflict of interest

The authors declare no conflict of interest.

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