

**Plant-Based Approaches to Cancer Prevention and Treatment: A Holistic Perspective**

Daigo Hirao<sup>1</sup>, Adil Maqbool<sup>3</sup>, Takehito Sugasawa<sup>2</sup>, AKM Shaharul Islam<sup>4</sup>, Abdullah Al Mamun<sup>3</sup>, Arifur Rahman<sup>3</sup>, Farzana Sohael<sup>3</sup>, Nobutake Shimojo<sup>2</sup>, Chishimba Nathan Mowa<sup>5</sup>, Subrina Jesmin<sup>1,2,3</sup>

<sup>1</sup> Hirao Cardiovascular Clinic, Chiba, Japan

<sup>2</sup> Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

<sup>3</sup> Health and Disease Research Center (HDRCRP), Bogra, Bangladesh

<sup>4</sup> TMSS Medical College and Hospital in Bogra, Bangladesh

<sup>5</sup> Climate-Smart Agriculture Commodities, 1890 Research & Extension, South Carolina State University, Orangeburg, SC, USA

\*Correspondence: Daigo Hirao

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**Abstract**

*Cancer is a leading cause of mortality worldwide, significantly impacted by lifestyle choices and environmental factors. Conventional cancer treatments, while effective in many cases, often come with substantial side effects, emphasizing the need for alternative or complementary approaches. This review explores plant-based therapies as a holistic alternative, focusing on bioactive compounds such as polyphenols and phytochemicals for their anticancer properties. Challenges like bioavailability and limited clinical translation of these compounds are also discussed. The review underscores the potential of integrating plant-based strategies to enhance cancer prevention and treatment, advocating for further research to address existing limitations and optimize their application in clinical settings.*

**Keywords:** Cancer, Phytochemicals, Bioactive Compounds, Anti-inflammatory, Polyphenols, Holistic Therapy.

**Introduction**

Cancer is one of the diseases that spread in every part of the world. There is no country where cancer has not taken lives. Every year, it claims lives. In fact, according to the reports made by the World Health Organization, one out of six deaths is caused by cancer. In a country as developed as the United States of America (USA), it is the second leading cause of death [1]. The disease has existed for centuries while being intractable. With time and advancements in modern technology, the gaps in knowledge about cancer is rapidly being filled. According to many researchers, at least half of the cases, if not more are preventable [2]. Nowadays, it is critical to understand the disease's mechanisms at a molecular as well as

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metabolic level [3]. Within cancer, there is the issue of plasticity along with heterogeneity surrounding the disease, giving it uniqueness. The disease will evolve at a genetic level while equally evolving at the pathological level. While there is the matter of decoding a genetic fingerprint, it is vital to also keep the systematic tumor environment in mind [4].

At some point during the cancer journey, patients may opt for alternative or complementary therapies. Surely there is an underlying cause for choosing this route. The cause may vary from one patient to the other. To some, it can ease the stress of cancer treatment [5]. There is still little to suggest that these alternative therapeutic approaches can help to cure cancer. In some cases, patients may also doubt the safety of these approaches. As of now, there has been no excessive side effects in patients taking complementary therapies with conventional treatment.

Some of the complementary therapies depend on taking antioxidants like, vitamins A, C as well as E. There is a minor concern in this regard. The concern is that the cancer cells could be protected by the complementary therapies. Concerns of this nature have to be supported by strong evidence. Evidence for such concerns can be derived from high impact research work in this field. However, there is insufficient research to support the concern so far. Even so, patients may ask their doctors before seeking out these therapeutic approaches. After all, there is always a possibility of these therapies consisting of side effects [6].

On the topic of seeking alternative therapeutic approaches, it will be beneficial to remember the value of having a healthy diet. Plant-based food is the

purest source of fiber in a person's diet [7]. Food such as, nuts, seeds and cereal, all contain bioactive compounds. Bioactive compounds play a vital role in keeping a human body healthy. In fact, plant bioactives comprise of carotenoids, polyphenols along with sulfur compounds which are known for anti-carcinogenic properties [8]. Experimental studies into the matter reveal positive outcome meaning that there is a reduction in the cancer mortality risk [9]. There is actually a two-tier mechanism to explain here regarding the incidence of cancer. Firstly, soluble fibers are capable of modulating the composition for gut microbiota. As a result, there is improvement in the functionalities of the colonic barriers. Secondly, there are substrates that can be metabolized into the active ones (metabolites). With the formation of the metabolites, there is an increase in anti-cancer effects [10].

### **Epidemiology of Cancer**

Cancer is a disease with very little answer for the past several decades. With the advancements in healthcare related technology, it is now possible to determine some of the causes of cancer. Looking at cancer with a simple view, it can be said that the abnormal division of cell is a key factor [11]. What makes cancer so lethal and a cause for great headache is that it can start in any place in the human body. The cells in our body grow and multiply for the formation of new cells in normal order. With the death or damage to old cells, new cells are supposed to take their place. However, on occasions the system will break down and cause the damaged cells to multiply at an abnormal rate [12]. It is an event that would not happen under normal circumstances. As such, these damaged cells may form tumors. The tumors are known as lumps of tissue which can either be cancerous or benign.

Cancerous tumors have the ability to affect nearby tissues. At the same time, they may travel great distances within the human body. As a part of this travelling, these tumors will form other new tumors and this process is termed as metastasis [13].

The possible causes of cancer are many and there have been great many studies conducted on the issue. Several studies find a connection between vitamin D deficiency and the increase in cancer risk [14]. In other studies, it has been confirmed that cancer is a genetic disease due to the changes caused in the genes. The reasons behind these genetic changes are:

- Randomized errors occurring in the DNA during cell multiplication
- Changes in DNA due to carcinogens present in environment
- Inherited from the previous generation

When people hear that it can be inherited, this may strike fear. So, to break it down, cancer cannot be passed from parent to children. At the same time, the tumor cells that experience genetic changes may also not be passed from one generation to the next. However, the genetic changes which increase the risk of having cancer may get passed down if it is available in the egg or sperm cells of a parent. For this reason, experts may say that cancer can run in families. There is quite a bit of truth to it as 10% of all the cancer cases may be caused by the genetic changes that were inherited. Meanwhile, some of the carcinogens mentioned above are present in UV rays from the sun, chemicals present in tobacco smoke as well as the human papillomavirus (HPV) [15].

The IARC has been collecting data on cancer patients to decipher the underlying causes. So far, ac-

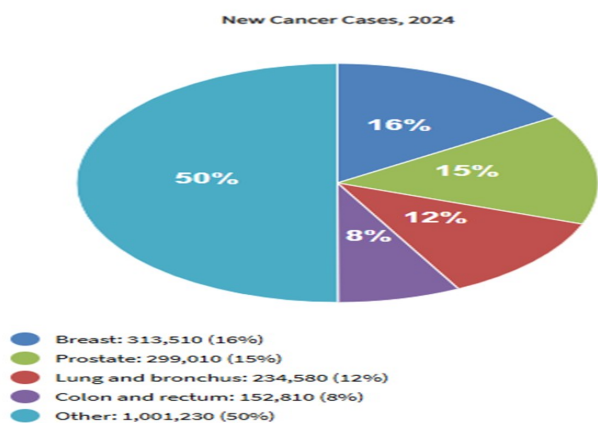
ording to this organization, the top three most frequent cancers are lung, breast and colorectal cancer. There is one drawback to this report and it is that they are based around 2022. Even so, lung cancer contributing to 12.4% of all cases around 2022 has to be taken seriously and develop more preventive measures. With that said, here is a look at the global cancer incidence for both sexes in 2022 and the table constitutes of age-standardized rates (ASR):

**Table 1: Global Cancer Incidence**

Both Sexes	Number of Cases	ASR (World)
World	19,976,499	196.9
China	4,824,703	201.6
United States of America	2,380,189	367.0
Japan	1,005,157	267.1
Germany	605,805	274.2
United Kingdom	454,954	307.2
Pakistan	185,748	105.6
Vietnam	180,480	150.8
Ukraine	155,239	199.9

It is imperative to note that the table does not represent the number of cases from all the countries globally as there are some limitations. In addition, the list of cases consist of non-melanoma skin cancer cases as well [16].

There are different types of cancer occurring in the human body every year. Of them, the most common cases in developed countries such as, the United States of America (USA) is breast cancer, lung cancer and prostate cancer. Other types of cancer with notable frequencies are pancreatic and colorectal cancer. Here is a diagram of a chart representing the new cases of 2024 inside the USA:



There are close 2.0 million cancer cases in 2024 from the USA alone. So, it provides a look into the prevalence of the many different types of cancer which attack the human body. In light of these cases, the National Cancer Institute made a prediction for all the types of cancer which may spread in 2024. The following table has been prepared on the basis of statistical insights and a rough estimation of the current trends in cancer cases:

**Figure 1:** Cancer cases within the USA (2024) so far, image sourced from the [National Cancer Institute](https://www.nationalcancerinstitute.gov)

**Table 2: Estimated New Cases of Cancer**

Site	Estimated New Case in 2024	Rate of New Cases (2017-2021)	Estimated deaths (2024)	Death Rate (2018-2022)	Relative Survival % (2014-2020)
Anus	10,540	1.9	2,190	0.4	70.6
Bladder	83,190	18.2	16,840	4.1	78.4
Breast	313,510	68.4	42,780	10.6	91.1
Colon and Rectum	152,810	36.5	53,010	12.9	65.0
Larynx	12,650	2.6	3,880	0.9	61.5
Leukemia	62,770	14.1	23,670	5.9	67.0
Lung and Bronchus	234,580	49.0	125,070	32.4	26.7
Ovary	19,680	10.2	12,740	6.0	50.9
Stomach	26,890	7.0	10,880	2.7	36.4

This table was prepared with assist taken from the National Cancer Institute. There is many cancer related statistics covered through the platform itself [17].

Underlying factors in the rise of cancer cases can be lifestyle choices since cancer is a non-communicable disease (NCD). In addition, the environmental factors are known to play an influential role. On lifestyle choices, the World Health Organization (WHO) made a statement indicating the continued usage of tobacco as a contributing factor. With the current consumption rate of tobacco and

alcohol, WHO suggests that cancer cases will increase each year. Obesity has also been linked with these new cases alongside physical inactivity [18]. As for environmental factors, experts state that the exposure to air pollution has a lot to do with the lung cancer cases. As things stand, WHO made a prediction that by 2050, the number of active cancer cases will rise to 50 million worldwide [19].

A lot of research has been conducted over the years to identify the causes of cancer. As everyone knows by now, cancer can affect any part of the human body. There are some infectious organisms which

may be at the root of certain types of cancers. For majority of the cancers, there are some risk factors which can be highlighted through a table:

**Table 3: Cancer risk factors**

Exposure variable		Theoretical-minimum-risk exposure distribution	Cancer sites affected
Diet and physical activity			
Overweight and obesity	BMI (kg/m <sup>2</sup> )	21 SD 1 kg/m <sup>2</sup>	Corpus uteri cancer, colorectal cancer (≥30 years), post-menopausal breast cancer (45 years)
Low fruit and vegetable intake	Fruit and vegetable intake per day	600 SD 50g intake per day for adults	Colorectal cancer, stomach cancer, lung cancer, esophageal cancer (>15 years)
Physical inactivity	Three categories: inactive, insufficiently active (<2.5hrs per week of moderate-intensity activity), and sufficiently active. Active in spare time, work and transport considered	>2.5hrs per week of moderate-intensity activity or equivalent (4,000 KJ per week)	Breast cancer, colorectal cancer (>15 years), prostate cancer
Addictive substance			
Smoking	Current levels of smoking impact ratio (indirect indicator of accumulated smoking risk based on excess lung cancer mortality)	No smoking	Lung cancer, mouth as well as oropharynx cancer, esophageal cancer, pancreatic cancer, bladder cancer, leukemia (>30 years)
Environmental risks			
Urban air pollution	Estimated yearly average particulate matter concentration for particles with aerodynamic diameters <2.5μ or 10μ	7.5 μg/m <sup>3</sup> for PM2.5, 15 μg/m <sup>3</sup> for PM10	Lung cancer (>30 years)
Other selected risks			
Contaminated injections in healthcare environment	Exposure to ≥1 contaminated injection	No contaminated injections	Liver cancer (all ages)

This table has been compiled with the help of thorough studies into the risk factors behind different cancers by authors Ansari and Jha in 2022. Of all the cancer types, it can be stated that the cervix-uterine, lung as well as esophageal cancers are quite common in multiple countries across continents. Experts suggest that a mix of factors can play a strong role in their spread and these factors are: poor intake of fruits and vegetables, smoking, alcohol consumption as well as the sexual transmission of the HPV which leads to an infection of the oncogenic viruses [20].

Other than these factors, there are a few other causes which can be attributed to cancer:

- **Exposure to toxic compounds:** Studies show that exposure for long duration to toxic compounds such as, benzene, asbestos, cadmium as well as vinyl chloride may lead to cancer.
- **Ionizing radiations:** Exposure to Uranium, Radon, and radiations such as, alpha, beta and gamma

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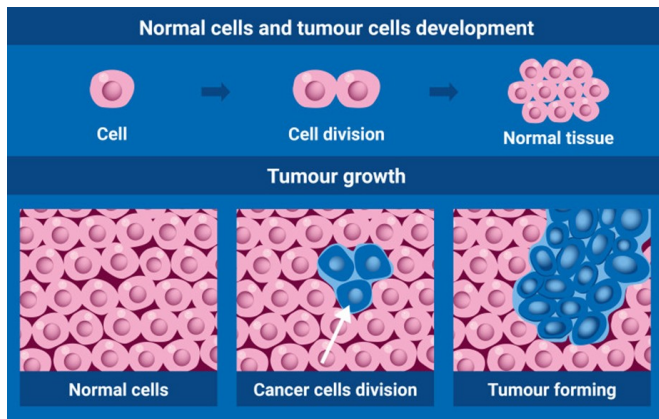
ray sources.

In recent times, some new risk factors have been added to the list. It has been stated by the IARC that red meat like lamb and pork as well as beef may consist of substances which make them high-risk agents that lead to cancer. Moreover, the organization also considers processed meat as to elements which put it on the carcinogenic list [21].

### Conventional Cancer Therapies

Every year, experts try to develop approaches to cancer treatment. The target each year is the early detection of cancer. At present, the conventional approaches to cancer treatment are surgeries, radiotherapies, chemotherapies and lastly targeted therapies. Studies were conducted in 2015 among cancer survivor women and it shows that there has been stability in the incidence rate. Conventional approaches to cancer treatment and its diagnosis incur a great cost on families. On average, the care cost of cancer at the state-level in the USA ranges from \$227 million to a staggering \$13.6 billion. Here is a look at the conventional cancer therapies:

- **Surgeries:** Of all conventional treatment known to combat cancer, surgery is one of the oldest. Cancer patients can be cured with surgery from the non-metastatic tumors [22]. There is a catch though and it's that, early diagnosis is a necessity for the process to succeed. In addition, there is a combination of other treatments which have to go in the patient's favor. The difficulty lies in the fact that the tumor has to be assessed thoroughly. Only by assessing thoroughly will physicians know about the existence of cancerous tissue in the tumor. Usually, physicians recommend patients to undergo biopsy as well as tumor imaging. Physicians also advise patients to opt for a complete surgical resection when dealing with local primary tumor [23].
- **Chemotherapy:** If the tumor is benign, then physicians suggest using chemotherapeutic drugs. So far, there exists three stages to chemotherapy: preoperative (before undergoing surgery), intraoperative (at the time of surgery) and postoperative (after completing surgery). There is specific use of each chemotherapy. The work of chemotherapeutic drugs is to target the cells that divide rapidly [24]. Chemotherapy can work with other forms of treatment as well. In fact, the right combination helps to reduce the tumor's size before the patient enters surgery. Moreover, the drugs will terminate any remaining cancer cell after the surgery is complete. There are different methods of providing the chemotherapeutic drugs, such as, oral, injection, intravenous and topical being the common ones. Chemotherapy also depends on the stage of cancer and its specific type. Healthcare providers cannot advise patients to take any form of chemotherapeutic drug without knowing how advanced it is [25].
- **Radiotherapy:** The working principle of radiotherapy is to treat the patient with strong energy beams. There is no confirmation yet that the energy may come from X-rays, protons and more. Health discrepancies occur when patients look to get treatment for cancer. As previously mentioned, radiotherapy target the patient's body and will eradicate the cancerous cells. It is done through exposure to ionizing radiations. When done correctly, radiotherapy is all about patiently selecting the radiation doses. These doses are responsible for damaging the cancer cells. It is up to the DNA to control cell division.



**Figure 2: Process of radiotherapy, image sourced from IAEA.org**

Radiotherapy has been in use for well over a century. It is possible to use it separately or with other forms of treatment. At present, there are two types of radiotherapy in use and they are teletherapy and brachytherapy. In order to administer any one form of radiotherapy, it is imperative to consult with an expert team. The team needs to comprise of a medical physicist, radiation oncologist as well as radiotherapy technologist. As for its effectiveness, radiotherapy does not yield visible results right away. It will take time for its impact to show, sometimes it may take days. In other cases it will be weeks or months [26].

The concept of surgical resection was the only viable mode of treatment at the start of the 20th century. On the other hand, radiotherapy became an option during 1900. There was one problem with radiotherapy and that it was unsuccessful in saving the lives of many. All of that began to change with the advent of chemotherapy as the cure rates increased. At first, nitrogen mustard was used alongside chemotherapy in terms of treatment modality to cure lymphomas. The first incident occurred just after the end of the Second World War. A lot of time has passed since then and it is only natural for there to be improvements to treatment modalities.

Nowadays, the treatment schedules are taken into consideration before trying different combinations of chemotherapeutic drugs. More importantly, physicians have to first take the genetic landscape into consideration before anything else.

With that said, there is no way to forget that treatment of that level is sure to have side-effects. During much of the 20th century and early parts of the 21st century, there were cases of therapy-related toxicities. It is common for anti-cancer treatment to be the cause of secondary malignancies along with hepatotoxicity, neurotoxicity and cardiotoxicity [27]. The primary objective of chemo as well as radiotherapy is to terminate tumor cells. In order to reach that objective, they target the DNA and in turn heighten the damage done to the healthy tissue. Numerous studies into the issue reveal accelerated aging to be one of the side effects [28].

Given the rate at which medical technology is improving every year, the life expectancy is higher than before. The same can be said in a different way for cancer survivors. To be more specific, children who survive cancer have to live a lower quality life than before. The drug tolerance level in children far exceed that of adults. There are quite a few reasons behind that. It may be mere speculation but children's organs, kidneys and livers should be better at detoxifying than adults. Some of the side-effects of chemotherapy are listed below:

- **Nephrotoxiety:** The kidneys are responsible for clearing out all the wastes in the body and that includes chemotherapeutic drugs. Kidneys clear out the drugs through glomerular filtration as well as tubular secretion [29]. Subtypes of chemotherapy that are almost always on use are the alkylating agents. The common alkylating agents are platinum agents, ifosfamide along

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with cyclophosphamide. It is well known that platinum agents cause injury to the proximal tubule cells [30].

- **Hepatotoxicity:** During and after chemotherapy, the liver takes on the responsibility of detoxifying the body. As such, certain chemotherapeutic drugs possess a threat to the liver's well-being. There is no definite proof as to which drugs directly damage the liver but, the connection exists. Alkylating agents are often brought up in studies as posing a threat. One alkylating agent in particular has shown signs of hepatotoxicity and it is cyclophosphamide. The liver is responsible for activating and degrading the agent. It does so with the help of P450 microsomal oxidative activities. The series of activities generates by-products such as, cytotoxic acrolein as well as phosphoramide mustard. When it combines with irradiation, there is visible rise in cyclophosphamide toxicity [31].
- **Neurotoxicity:** Treatment that involves the use of antimetabolites result in PNS neurotoxicity as well as in CNS. Methotrexate is one compound that crosses the barrier between blood and brain. Once it crosses the barrier, this chemotherapeutic creates subacute as well as delayed neurotoxicity. In addition, vinca alkaloids cause neurotoxicity for having a strong tubulin binding affinity [32].

Now, here are some of the discoveries about the side-effects of radiotherapy:

- **Permanent dry mouth:** Radiotherapy has often led to cell damages in the salivary gland. In many cases, the effect is irreversible. The salivary glands have high sensitivity regarding radiation. In addition, radiotherapy can cause denture stomatitis as well as changes in pH and salivary stones.

- **Burning Mouth Syndrome:** Radiation leads to reoccurring feelings of mouth burning. In this condition, the patient's gum, tongue as well as lips may experience a burning sensation. As such, patients will experience a loss of taste.
- **Osteoradionecrosis:** Another side-effect of radiotherapy is osteoradionecrosis which may require surgical interventions. The common symptoms are pain, numbness, and mastication as well as systemic infections. If it is a mild one then antibiotics and even ultrasound may do the trick. However, severe form of necrosis will definitely require radical resection [33].

Understanding the pathogenesis properly is beneficial to curing the body of any disease. Unfortunately, there is still a long way to go in terms of understanding the causes and natural history for different cancers. The positive aspect in this scenario is that, a high number of tumors can now be detected during the earlier stage lesions. When it is found, there is still no way to tell with conventional techniques whether the lesions are going to stay indolent. A high number of prostate cancers seem to be asymptomatic upon early detection. However, there is always a chance that some slow growing lesions exist in the human body. In such cases, the primary course of action will be active surveillance. It is not always possible to do so and this inability leads to a drop in the quality of life. Despite the recent advancements in medical technology, the challenge lies in developing evidence-based tools for early screening [34].

## **Plant-Based Approaches to Cancer Prevention and Treatment**

### **Nutritional Intervention**

Disease management is a necessary step when going up against any disease and especially cancer.



Since cancer can be classified as multifactorial disease, it is natural for many factors to play a role in its advancement. At the same time, the disease can also be contained by controlling certain lifestyle factors. There is possible link between a person's diet and cancer's development. Food that contain high-fat are known to cause breast cancer. On the other hand, diet consisting of red meat can be associated with a risk of colon cancer development. At this point, it is also well known that lifestyle factors like alcohol consumption and smoking can play an anchoring role.

Diet that comprise of whole grain products can be beneficial to eliminate cancer risks [35]. One study on colon cancer reveals that daily consumption of fermented dairy products protects the body from such risks. This is done by the lactobacillales in the fermented dairy products. Lactobacillales is responsible for reducing the pro-carcinogen load in an intestine.

Studies suggest the consumption of different fruits and vegetables along with whole grains to inhibit

carcinogenic progress. This will halt the progress of bladder cancer. Another simple activity like drinking fluids can lessen the chances of bladder cancer ever developing in the body. The issue surrounding the development of bladder cancer is the presence of carcinogens within the urothelium. If the amount is low then, the chances of bladder cancer occurring is also low. Proper fluid intake ensures that the urothelium does not have enough contact with carcinogens [36].

For several years, researchers have discussed the idea of therapeutic food. On the basis of this idea, clinical studies were conducted. The goal of these studies was to find out whether the bioactive compounds found in certain food can mitigate cancer risk. A certain number of fruits and vegetables consist of bioactive compounds like amino acid residues. These residues have shown antioxidant properties as well as antithrombotic ones. In recent times, the American Institute for Cancer Research (AICR) has made a list of foods that exhibit anti-cancer properties. The following table will list most of them:

**Table 4: List of foods that fight cancer**

Natural product	Compounds present	Strong evidence	Limited evidence
Apples	Dietary fibers, flavonols and triterpenoid compounds	Colorectal cancer	Lung cancer
Asparagus	Flavonols, inulin, folate		Estrogen receptor-negative (ER-) breast cancer
Broccoli and cruciferous vegetables	Glucosinolates, carotenoids	Colorectal cancer	Lung cancer, ER-breast cancer
Carrots	Carotenoids, phenolic acids		Lung cancer, ER-breast cancer
Cauliflower	Vitamin C, folate		Lung cancer
Cranberries	Anthocyanins, tannins, flavonols		Lung cancer
Kale	Dietary fiber, flavonols, folate, glucosinolates	Colorectal cancer	ER-breast cancer, lung cancer
Oranges	Dietary fiber, flavanones, vitamin C	Colorectal cancer	Lung cancer, stomach cancer
Raspberries	Vitamin C, dietary fiber, anthocyanins	Colorectal cancer	Lung cancer
Spinach	Carotenoids, flavonols, folate	Colorectal cancer	ER-breast cancer, lung cancer

The bioactive compounds present in the food mentioned above are second metabolites. Not only do they possess nutritional value but also provide health protection. Some of the bioactive compounds along with their anticancer effects are demonstrated in the following table:

**Table 5: Bioactive compounds with probable anticancer effect**

Bioactive compounds	Examples	Probable anticancer effect
Polyphenolic compounds	Quercetin, resveratrol, catechin	Carcinogen detoxification, inhibits tumor initiating
Carotenoids	Lycopene, lutein	Antimutagen
Terpenoid	Perillic acid, d-limonene	Carcinogen detoxification

There is a great potential of bioactive compounds in the treatment of cancer [37]. When mentioning plant-based approach, it is imperative to mention successful cases for cancer treatment. Grapes and berries are great sources of resveratrol which contains anticancer properties. In one particular study by Xiao-Min Yu and his colleagues, resveratrol demonstrated its ability to slow the progression of Anaplastic Thyroid Carcinoma (ATC) cells. Resveratrol has the potential of stopping cell cycle progression of ATC cells [38].

**Table 6: Phytomedicine-based treatment**

Plant source	Bioactive compound	Cancer Cell Type	Type of Study	Action	Reference
Aconitum sinomontanum	Lappaconitine	Liver	In vitro	Downregulation of Bcl-2 and Bax expression	Song, et al. (2021)
Artemisia annua	Artemisin	Breast	In vitro	G2/M (cell cycle) arrest, autophagy	Guan & Guan (2020)
Cannabis sativa	Cannabinoids	Liver	In vivo	Anti-apoptotic	Hussein, et al. (2014)

Curcumin is a polyphenolic compound that turns naturally. This compound exhibits antibacterial, antioxidant as well as antiangiogenic characteristics. Studies into its effectiveness at the University Of Ulsan College Of Medicine reveals curcumin's ability for improving ATC cells sensitivity towards docetaxel. Docetaxel itself contains growth-inhibitory properties which are enhanced in the presence of curcumin. Meanwhile, grapefruits along with other citrus fruits are rich in naringin. Naringin is classified as a flavonoid that exhibits properties against tumor progression as well as oxidative stress. The compound will activate MAPK pathways while also obstructing the PI3K/Akt/mTOR cascade. Studies into the matter showed these activities to hinder the tumor cell development [39].

### Herbal and Phytomedicine-based Treatments

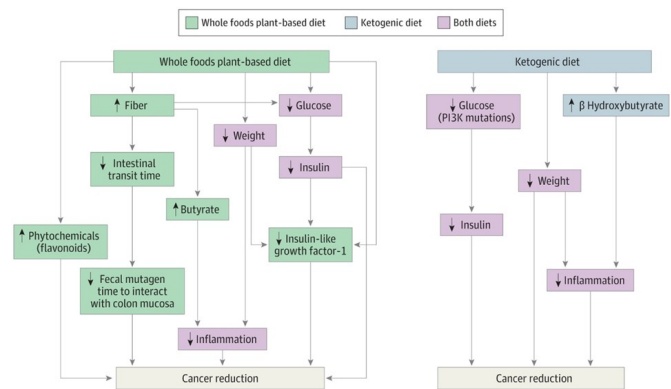
As already mentioned, plants contain several bioactive compounds. Now, these bioactive compounds showcase ethnomedicinal characteristics. For this reason, several researchers investigated this characteristic along with other ethnopharmacological properties in plants. In order to find out their usefulness in the fight against cancer, researchers opted for in vitro as well as in vivo approach. The following table comprises of some findings on that note:

Carica papaya	Benzyl isothiocyanate	Pancreatic	In vitro, in vivo	FOXO/PI3K/AKT pathways-arbitrated tumor apoptosis	Boreddy, Pramanik & Srivastava (2011)
Eclipta alba	Luteolin	Breast	In vitro, in vivo	Activates intrinsic apoptotic pathway	Arya, et al. (2015)
Polygonum cuspidatum	Pterostilbene	Colon	In vitro, in vivo	DNA repairing by Top1/Tdp1 pathway	Zhang, et al. (2021)

Plants have been used in studies to investigate the anticancer agents in various ways. In a particular study, a couple of alkaloids' solution, namely vincristine along with vinblastine were used to derive the outcome. The plants used for this study were *Madagascar periwinkle* and *Catharanthus roseus*. These drugs have been in use for oncology cases for the last 5 decades. Meanwhile, a study with *Hy-lomecon japonica* was conducted regarding MCF-7 breast cancer cells. As part of the study, the researcher extracted a total of 13 isoquinoline alkaloids to investigate anticancer properties. A high number of those alkaloids demonstrated anticancer properties [40].

### Dietary Pattern

In the field of oncology, whole foods plant-based diet (WFPBD) is quite popular already. Recently, other forms of food intake is gaining traction as well for fighting cancer and that is non-plant based diet. The non-plant based diet to gain the widespread popularity is ketogenic diet (KD). There are a few differences between both diets at a nutrient level. Studies show that KD is capable of increasing the levels of  $\beta$  hydroxybutyrate which itself can exert anticancer properties. While there are nutrient-related differences between the two diets, there is similarity in the mechanisms in some aspect.



**Figure 3:** Cancer suppressing by WFPBD and KD, image sourced from [PubMed Central](#)

Both of the diets are capable of eradicating refined carbohydrates which has long been linked to weight gain. Moreover, the redefined carbohydrates are connected to an increase in mortality rate. When following a WFPBD, there are enough low-calorie fiber-rich food to satiety early. Meanwhile, KD is known to suppress the appetite which has a similar effect to reduced caloric intake. The issue surrounding KD is the adverse impact it will put long term. Side-effects may exist for KD such as its density of lipoprotein (LDL) being on the high. There is also a matter of fatigue-inertia scores to deal with in case of having KD. Another study on the phytochemical components of both diets reveal WFPBD to have a larger amount. All in all, KD is less helpful to the human body than WFPBD as per multiple epidemiological studies [41].

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## Mechanisms of Action

The whole concept of eating healthy is to derive sufficient nutrition from the plant sources. When talking about plant-based diet, the conversation includes a number of fruits and vegetables to go with nuts, oils, legumes etc. There is an interest among researchers regarding the plant-based diets ability to be reduced biomarkers for inflammation. Many studies can confirm the positive influence of vegetarian diets on metabolic health and the management of Crohn's disease. The WFPBD consist of bioactive components, such as, phytonutrients along with fiber. Phytonutrients are known to play a supporting role in immunomodulatory procedures.

Plant-based diet helps the body to deal with inflammation by addressing the oxidative stress. A natural process occurring in the body is the metabolic process. There are a few byproducts of metabolic processes and those are reactive oxygen species (ROS) along with reactive nitrogen species. Now, these byproducts can be harmful to the tissues. If they cannot be neutralized then they will also cause inflammation. The role of plant-based diet is to supply the body with enough antioxidants to neutralize the ill effects. Meanwhile, the fiber in WFPBD assists the body by keeping the bowels regular. Additionally, they feed healthy microbes inside the gut, thereby managing inflammation [42].

Protein is found abundantly in plant-based diet in the form of foods like lentils and quinoa. There is growing interest in the plant-based diet's role to modulate the gut microbiome. Primarily, these type of foods are natural and less likely to undergo any processing. There is a small dose of saturated fat and high dose of fiber with phytochemicals. The combination is able to lower the concentration lev-

els for blood low-density lipoprotein cholesterol [43]. Experts suggest maintaining a plant-based diet as it decreases the risk for developing diabetes, hypertension along with some non-communicable diseases.

There is bacteria, archaea along with microscopic eukaryotic organisms inside the human gut microbiota. The human body contains several microorganisms that are also a part of the gut microbiota. These tiny elements are responsible for the wellbeing. It is imperative to keep in mind that environmental factors combined with dietary habits have an impact on the gut microbiota. The dietary habits will vary from one person to another. With that said, there are plenty of studies confirming the positive impact of maintaining a vegan diet on the gut microbiota. In addition, the studies suggested that the positive link exists between the gut microbiota and metabolic syndromes due to the vegan diet [44].

A vegan diet can go a long way to reduce the chances of developing cancer. There are other ways to do so as well. One such way is to consume a specialized diet that contains anti-angiogenic molecules. The process of tumor progression starts by activating the angiogenic switch. This switch can be kept under control by consuming food rich in anti-angiogenic molecules. Of all the cancer types, this approach shows the most favorable results in studies conducted on urological cancer. Food that are rich in phytochemicals comprise of disease prevention characteristics. There is proof of that in multiple human studies. In those studies, the test subjects had a history of cruciferous vegetable consumption that lowered the risk of different cancers. Cruciferous vegetables are mainly cabbage, kale, cauliflowers etc.

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All of these vegetables consist of bioactive indoles along with isothiocyanates. Epidemiological studies about the consumption of broccoli and its related health benefits reveal its ability to reduce bladder cancer risk. Moreover, the cruciferous vegetables are one of the biggest sources of glucosinolates. Glucosinolates have the ability to produce chemopreventive phytochemicals. As mentioned above, there are indoles in cruciferous vegetables. For that matter, the Indole-3-carbinol along with 3,3'-diindolymethane present in these vegetables will suppress the angiogenesis through in vivo alongside in vitro [45].

### Case Studies and Clinical Trials

#### Turmeric

Turmeric is scientifically known as *Curcuma longa* and as a herbaceous plant. This plant is a rich source of secondary metabolites. From the top, it produces metabolites like alkaloids, flavonoids, phenolic acids along with tannins [46]. The key derivative of turmeric is curcumin, a hydrophobic polyphenol diferuloylmethane known for its active role in treating several diseases. On the list of diseases are metabolic syndrome, inflammatory disease and liver disorders.

The human body is host to a wide variety of chemical processes. Lifestyle factors may contribute to the onset of infectious diseases in the body that may disrupt these processes. Some of the infectious disease along with chronic inflammatory disorders upset the genomic stability. It is a telltale sign of cancer development. The inflammatory process is responsible for producing ROS, cytokines and NF- $\kappa$ B among many other pro-inflammatory molecules. These aforementioned molecules play active role in the growth phase of tumor. Curcumin has shown its capability to bind with ROS scavengers in several

studies. Due to this binding, curcumin suppresses the growth of cancers. Evidence-based studies highlight curcumin's anti-inflammatory properties as it downregulates NLRP3 inflammation [47].

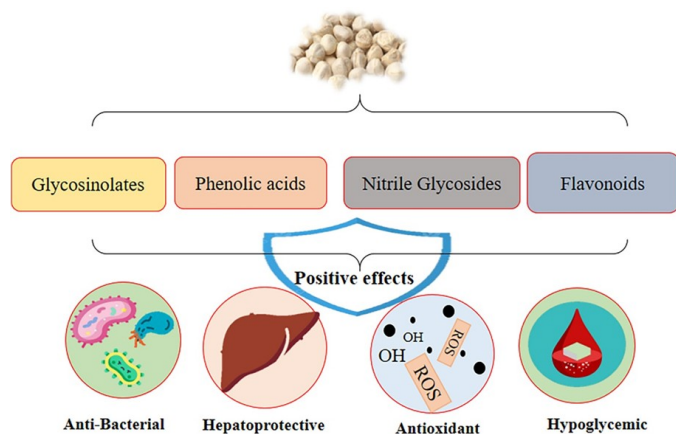
#### Garlic

Garlic comprises of organic sulfur compounds that play anchoring role in the production of antitumor effect. Those compounds are namely, diallyl disulfide (DADS), diallyl trisulfide (DATS), S-allylmercaptocysteine (SAMC) alongside allicin. The primary activity of these compounds is cell cycle regulation. To start off, DADS along with DATS play the role of initiator for the P53/P21 pathway. Additionally, DADS is an inhibitor for the expression for cyclin B1, cdc2 as well as cdc25c proteins. All of these activities are essential for G2/M phase arrest in the case of tumor cells [48]. Afterwards, DADS coupled with SAMC take on the role of inhibitor for tubulin's polymerization process. On the other hand, allicin prompts the arrest of cell cycle during the S phase. All in all, these compounds present in garlic can essentially lead to apoptosis through various activities in tumor cells [49].

#### Moringa oleifera

*Moringa oleifera* is a medicinal plant with a number of benefits. Each part of the plant's body can be caused with varying health benefits. There is high presence of anticancer properties in them as they have bioactive components. *Moringa oleifera* seeds comprise of cytotoxic properties that have been used in experiments on cancer cells. The seed extracts are made up of methionine and cysteine, which exhibit antioxidant properties. Seeds are also high on ascorbic acid, phenolic content as well as isothiocyanate derivatives. It is already well known

that the aforementioned components can prevent inflammatory disorders.



**Figure 4:** Benefits of *Moringa oleifera* seed consumption, image sourced from [Wiley Online Library](#)

Extracts from *Moringa oleifera* seeds can modulate the biotransformation enzymes. At the same time, they can enhance the detoxification properties to fend off cancer. Time and again, the seed extracts have displayed a strong hepatoprotective property. There are a number of bioactive compounds available as well, such as, linoleic acid, oleic acid along with essential amino acids. The biomolecules present in the seed extracts are also beneficial for the human body. A study was conducted on the seed flour by defatting it. The purpose of the study was to investigate about the existence and mechanism related to antioxidant and antibacterial properties. There were high levels of antioxidant and antibacterial activities in the findings of a bound phenolic extract. Given their level of antioxidant and antibacterial properties, the study concluded that moringa seeds are suitable for use in pharmaceutical industries [50].

### Green Tea

*Camellia sinensis* is the source of all tea. Due to a difference in processing, there are varieties of tea available. Experts opine that tea is the mixture of

high number of bioactive compounds. The usual scenario dictates that tea is made up of catechins, flavonols as well as phenolic acids. Multiple studies were conducted with the help of animal models which displayed green tea extracts to possess inhibitory activities when countering tumorigenesis.

There are several risk factors associated with each cancer type. Out of all them, cigarette smoking along with alcohol consumption have a direct link with esophageal cancer. For that reason, tea consumption and esophageal cancer is by perceived to have a complex relationship. In many countries of Asia, a high number of people who consume tea are also historically cigarette smokers. Some also happen to consume large volumes of alcohol. With that said, population-based case-control studies in China showed that lesser risk of esophageal cancer development among green tea consumers. There is one exception to this. Only those consumers of green tea who do not consume alcohol or smoke cigarettes have fewer risks.

As previously mentioned, green tea comprise of catechins. A strong case can be made for the benefits of green tea consumption to reduce the risk of gastric cancer. The tea catechins along with metabolites found in urine samples of patients before developing gastric cancer were studied in China. According to an analysis of the samples, the tea catechins play a protective role against the development of gastric cancer. The same metabolites and tea catechins have proven to be beneficial against colon cancer development [51].

### Grapes

The notable active compound in grapes is resveratrol which is polyphenolic. Resveratrol is known to possess multiple biological effects like anticancer,

antioxidant as well as anti-inflammatory properties. **Aloe**

One of the many activities of this compound is providing protection for hepatic cells against oxidative stress. Multiple studies show resveratrol to change the gene expression and increase the antioxidant enzyme activity. By doing so, it can protect the hepatic cells [52]. The same studies also confirm its role in enhancing urine protein excretion. Resveratrol can have an impact on tumor suppressors like p53. The role of p53 is that of a proapoptotic mediator such that it activates the transcription for proapoptotic genes. So, resveratrol will make a target of p-53 mediated pathway that induces apoptosis. Researchers also found resveratrol to inhibit cell viability within colorectal cancer cells. As such, it is highly effective to reduce colorectal cancer risk [53].

There exists 420 species of Aloe. The most popular of them all is Aloe Barbadensis Miller and is commonly called Aloe Vera. Aloe contains a plethora of therapeutic characteristics like, anti-viral, anti-cancer as well as anti-inflammatory. In one study conducted on rats that had pleural tumor, Aloe Vera played a significant role to inhibit tumor growth. The leaf extracts from Aloe arborescens are capable of exhibiting anti-proliferative properties. In order to investigate these properties, the murine myeloma cells were experimented with and showed favorable results [54].

**Other Noteworthy Plants**

Quite a few noteworthy plants other than the ones mentioned above are beneficial to fight cancer. The following table will demonstrate their phytochemical compounds with anti-colorectal cancer effects:

**Table 7: Other Noteworthy Plants with anti-colorectal cancer effect**

Plant species	Family	Phytochemicals available	Anti-colorectal cancer effect	Reference
<i>Zingiber officinale</i> Roscoe	Zingiberaceae	Polysaccharides, 6-gingerol, 10-gingerol, quercetin, zingerone, dehydrogingerdione, hexahydrocurcumin	Antitumor effects, apoptotic effects, antioxidative along with anti-inflammatory effects	Mao et al., (2019)
<i>W.somnifera</i> (L.)	Solanaceae	Polyphenolic compounds, saponins, alkaloids, glycosides	Anti-peroxidative, anti-tumor, anti-stress, apoptotic effects	Pant et al., (2021)
<i>Azadirachta indica</i> A. juss	Meliaceae	Limonoids, polysaccharides, nimbidin, nimbin, quercetin, terpenoids	Inhibits proliferation, metastasis, nimbolinin, sodium nimbinate, sitosterol	Srivastava et al., (2020)

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Several studies have documented the anticancer properties of the plants above. Ginger in particular consists of numerous active metabolites hindering proliferation of colorectal cancer cell lines. One of the causes of colorectal cancer is the growth of the HCT116 cells. So, researchers took extracts of 6-gingerol found in ginger bulbs to check the growth of these cells. The outcome is that this chemical component can successfully inhibit the growth of these cancer cells [55].

### Challenges and Limitations

There is no way to have total control over the proliferation of cancer cells. The underlying reasons are many. It is impossible to determine just one reason for the unusual cell behavior. In the above section, an attempt has been made to demonstrate the beneficial impact of phytochemical compounds. All of the compounds have an abundance of anticancer properties. Even so, limitations exist and there is still some ways to go before clinical application. Some studies on the phytochemical agents revealed below par aqueous solubility. Other studies found there to be an issue of poor penetration meaning that the phytochemical agents could not enter the targeted cells. Another concern is the limitation in therapeutic potential of some phytochemical agents [56].

Compounds such as, colchicine, podophyllotoxin derivatives alongside camptothecin have limitations caused by side effects. Vinca alkaloids are also limited in their impact. They have been used in combination with other agents during the experiments. Other noteworthy compounds present the issue of low availability. Thus, it is one of the primary reasons behind the limited effect of the phytochemicals. Some experts in the past have used a singular target chemical agent to treat cancer. This approach

is less than ideal as one chemical agent alone cannot provide optimal levels of cytotoxic effects. Another condition is that the agents undergo fast molecular adaptations. In that regard, combining similar compounds is an avenue that can be explored more. With time, experts have come to the decision to improve the bioavailability of chemotherapeutic drugs. If the bioavailability issue is resolved, then there will be more opportunities to combine the drugs. They can then be tested for their effectiveness [57].

In the case of elderly cancer patients, studies reveal the important issue of polypharmacy. Meanwhile, patients of younger ages have frequently used complementary and alternative medicines (CAM). One study conducted in 2019 on cancer patients revealed the existence of drug-drug interactions. The treatment and patient's health were affected due to one case of clinically relevant drug-drug interaction. Even now, there are data limitations on the drug-drug interaction and side-effects between CAM substances and conventional therapies. The sooner this aspect is thoroughly checked for potential harm, the better [58].

### Future Directions

Studies have been going on for a short while on the human interleukin-29 (IL29). The primary reason being the gene's antiproliferative and antiviral impact. These characteristics are beneficial to innate immunity. In one study, IL29 had been used for the expression system regarding *E.coli* and encountered a significant drawback. The problem here is the lack of post-translational modification. In recent times, IL29 is being produced more often as it demonstrates the ability of algal chloroplast to produce this gene to serve therapeutic needs. Meanwhile, plant molecular farming is an ongoing con-



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cept with continued research for the past decade. The existence of *Chlamydomonas reinhardtii* is convenient for researchers. It provides the right platform to produce recombinant protein. As such, it is possible to produce IL29 in a cost-effective way [59]. It is a cytokine that possesses the characteristics needed to induce tumor promoting effects. research should prioritize the optimization of bioactive compound formulations, comprehensive clinical evaluations, and the integration of these therapies into holistic cancer care models. Bridging these gaps can lead to cost-effective, minimally invasive, and accessible solutions for cancer prevention and treatment globally.

Another highly sought out approach in modern times is the use of synthetic biology in cancer therapy. The aim of synthetic biologists has been to control the cellular behaviors. This approach allows them to execute a number of functions in the design. Use of CAR-T cells have been met with positivity in cancer therapy. At the moment, a high number of gene circuits are being developed that result in the safety of CAR-T cells. Soon enough, the gene circuits will increase the trafficking of T-cells and then accumulate at the tumor site. With more research work, it will be possible for gene circuits to prevent the T-cells from becoming exhausted. In addition, enhancing the longevity of T-cells will be pivotal in cancer treatment [60].

## Conclusion

Cancer continues to be a global health challenge, driven by multifactorial causes, including genetic predisposition, lifestyle habits, and environmental exposures. Conventional therapies remain the mainstay of treatment but are often associated with high costs and adverse effects, prompting interest in alternative approaches. This paper highlights the promising role of plant-based therapies in cancer management, emphasizing the potential of bioactive compounds such as polyphenols and phytochemicals. While preliminary evidence suggests their efficacy in reducing cancer risks and supporting treatment, the lack of robust clinical trials and issues like bioavailability pose significant hurdles. Future

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