Chapter 8
Food-Based Interventions for Cancer Management: An Ayurvedic Perspective

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8.1 Introduction

Cancer remains a major cause of mortality and morbidity worldwide [1]. There are over 200 different known cancers that afflict humans. The global burden of cancer continues to increase largely because of the aging and growth of the world population alongside an increasing adoption of cancer-causing behaviors. Although overall cancer incidence rates in the developing world are half those seen in the developed world in both sexes, overall cancer mortality rates are generally similar. Cancer survival tends to be poorer in developing countries, most likely because of a combination of a late stage at diagnosis and limited access to timely and standard treatment [2]. Commonly used cancer treatments, including chemotherapy and radiation therapy, often have side effects, and a complete cure is sometimes impossible. Therefore, prevention, suppression, or delaying the onset of the disease is important [3]. The majority of cancers are due to modifiable lifestyle and environmental risk factors and are potentially preventable [4, 5]. Experimental evidence indicates a strong connection between oxidative damage, cancer, and aging. Epidemiological observations suggest that a diet rich in fruits and vegetables is associated with lower incidence of some cancers and longer life expectancy; since fruits and vegetables contain natural antioxidants, considerable effort has been dedicated to understanding their effects in experimental studies and in human trials [6]. There is increased appreciation by the scientific community that dietary phytochemicals can be potential weapons in the fight against cancer. Emerging research has provided new insights into the molecular and cellular framework needed to establish novel mechanism-based strategies for cancer prevention by selective bioactive food

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components [7]. In the future, diet will play an important role in the management of cancer as it will be the major intake source of important functional components [8].

In recent decades, research on various complementary and alternative medicine (CAM) practices that deal with cancer management have received tremendous attention. Ayurveda, a traditional Indian system of medicine, has been successful since ancient times at using many natural drugs in preventing or suppressing a variety of tumors using various lines of treatment [9, 10]. Ayurveda is almost 5,000 years old and deals not only with the body but with the mind and spirit as well. It is designed to promote good health and longevity rather than to fight disease [29]. According to Ayurveda, most diseases connected with psychophysiologic and pathologic changes in the body are caused by imbalances in three different *doshas* (i.e., *Vata*, *Pitta*, and *Kapha*). The fundamental aim of Ayurvedic therapy is to restore the balance between these three major body systems [11–13]. Ayurvedic texts emphasize proper diet (*ahara*) as being vital for promoting health and well-being. The Ayurvedic system of medicine also prescribes more than 700 plant-based medicines that contain spices and food additives to encourage good health [14]. Although this traditional medicine has been around for thousands of years, the scientific community has started to pay serious attention to it only recently. Following Ayurvedic principles a new paradigm for food-based cancer prevention and management can be developed to reduce the burden of this malignant disease.

8.2 Conventional View of Cancer

Cancers are primarily an environmental disease, with 90–95 % of cases attributable to environmental factors and 5–10 % to genetics, i.e., they are inherited genetically [15]. Many things are known to increase the risk of cancer, including tobacco use, certain infections, radiation, lack of physical activity, obesity, and environmental pollutants [5]. Cancer is a highly complex disease whose development may take as many as 20–30 years before it can be detected (Garodia et al. [29]). In general, a given cancer cannot also be blamed entirely on a single event or a single cause. As a rule, the genesis of a cancer requires several independent, rare genetic accidents to occur together in one cell with cumulative effects. The development of cancer generally involves many steps, each governed by multiple factors. There are many intrinsic factors, like oncogenes, tumor suppressor genes, DNA repair genes, angiogenesis, stem cells, and hormones, and extrinsic factors, like infection, contact with (touching, eating, drinking, or breathing) harmful substances, radiation (both ionizing and nonionizing), and environmental pollutants; and, most importantly, diet and lifestyle play a key role in the development of cancer.

Many types of genes are involved in the development of cancer. The first group of genes implicated in the development of cancer are damaged genes, so-called oncogenes. Oncogenes are genes whose presence in certain forms or overactivity can stimulate the development of cancer. When oncogenes arise in normal cells, they can cause the cells to become malignant or cancerous [16]. Oncogenes

contribute to the development of cancer by instructing cells to make proteins that stimulate excessive cell growth and division. A second group of genes implicated in cancer are the tumor suppressor genes. Tumor suppressor genes are normal genes whose absence can lead to cancer. In other words, if a pair of tumor suppressor genes is either lost from a cell or inactivated by mutation, its functional absence can cause cancer [17]. One particular tumor suppressor gene codes for a protein called p53, which can trigger cell suicide (apoptosis). In cells that have undergone DNA damage, the p53 protein acts like a brake pedal and halts cell growth and division. If the damage cannot be repaired, the p53 protein eventually initiates cell suicide, thereby preventing the genetically damaged cell from growing out of control. A third class of genes implicated in cancer are called DNA repair genes. DNA repair genes code for proteins whose normal function is to correct errors that arise when cells duplicate their DNA prior to cell division [18]. Mutations in DNA repair genes can lead to a failure in DNA repair, which in turn allows subsequent mutations in tumor suppressor genes and proto-oncogenes to accumulate.

Angiogenesis is a physiological process through which new blood vessels form from preexisting vessels. This is distinct from vasculogenesis, in which new blood vessel formation of endothelial cells takes place from mesoderm cell precursors [19]. The first vessels in the embryo form through vasculogenesis, after which angiogenesis is responsible for most, if not all, blood vessel growth during development and in disease. Angiogenesis is a normal and vital process in growth and development, as well as in wound healing and in granulation tissue [20]. However, it is also a fundamental step in the transition of tumors from a dormant state to a malignant one. It may be possible at a particular given time our body may contain many malignant micro tumors. However, these tumors cannot grow and become life threatening in the absence of blood supply. However, some tumors can mimic signals for making new blood vessels around them, and as they start securing a reliable food supply, they gradually increase in size and shed cells that can metastasize into other organs.

Stem cells are primal cells common to all multicellular organisms that retain the ability to renew themselves through cell division and can differentiate into a wide range of specialized cell types [21]. Cancer stem cells (CSCs) are cancer cells (found within tumors or hematological cancers) that possess characteristics associated with normal stem cells, specifically the ability to give rise to all cell types found in a particular cancer sample. CSCs are therefore tumorigenic (tumor-forming), perhaps in contrast to other nontumorigenic cancer cells. CSCs may generate tumors through the stem cell processes of self-renewal and differentiation into multiple cell types. Such cells are proposed to persist in tumors as a distinct population and cause relapse and metastasis by giving rise to new tumors [22].

Some hormones play an important role in the development of cancer by promoting cell proliferation. Hormones are important agents in sex-related cancers such as cancer of the breast, endometrium, prostate, ovary, and testis and of thyroid cancer and bone cancer [23].

Substances that cause DNA mutations are known as mutagens, and mutagens that cause cancers are known as carcinogens. Decades of research has led to the identification of many carcinogens [24]. A strong association has been found

between tobacco use and cancer of the lung, larynx, head, neck, stomach, bladder, kidney, esophagus, and pancreas. Tobacco smoking is associated with many forms of cancer, and causes 90 % of lung cancer [25]. Tobacco smoke contains over 50 known carcinogens, including nitrosamines and polycyclic aromatic hydrocarbons. Tobacco is responsible for approximately one in three of all cancer deaths in the developed world, and approximately one in five worldwide. Up to 10 % of invasive cancers are related to radiation exposure, including both ionizing radiation and non-ionizing radiation [5]. Additionally, the vast majority of noninvasive cancers are nonmelanoma skin cancers caused by nonionizing ultraviolet radiation.

8.3 Cancer from an Ayurvedic Perspective

In contrast to the critical analytical approach of modern Western medicine, Ayurveda adopts a holistic approach and propounds a broad-based understanding of the entities of life, health, and disease [26]. Ayurvedic literature defines three body-control systems, viz., the nervous system (*Vata* or air), the venous system (*Pitta* or fire), and the arterial system (*Kapha* or water), which mutually coordinate to perform the normal functions of the body [9]. Any imbalance in these body-control systems can result in a disease state. The fundamental aim of Ayurvedic therapy is to restore the balance between these three major body systems. The therapeutic approach of Ayurveda has been divided into four categories: *Prakritisthapani chikitsa* (health maintenance), *Roganashani chikitsa* (disease cure), *Rasayana chikitsa* (restoration of normal function), and *Naishthiki chikitsa* (spiritual approach) [27]. Finding the cause of an illness is the basic goal of Ayurvedic therapy. It classifies disease development into six stages, including aggravation, accumulation, overflow, relocation, buildup in a new location, and manifestation into a recognizable disease. Ayurvedic physicians can diagnose an illness even at the initial stages of body imbalance, and their therapeutic approach maintains a balance by supplying deficient substances and reducing excessive ones [9].

Ayurveda describes the different stages of tumorigenesis as chronic inflammatory and intractable diseases with the possibility of developing malignancy. Two well-known Ayurvedic classics, *Charaka* samhita [13] and *Sushruta* samhita [12], describe cancer as inflammatory or noninflammatory swelling and mention them as either *granthi* (minor neoplasm) or *arbuda* (major neoplasm).

According to Ayurveda, cancer results from lifestyle errors, such as unhealthy foods, poor hygiene, or poor behavior, or from physical trauma, all leading to imbalances of *Vata*, *Pitta*, and *Kapha*, resulting in injury to the inner layer of the dermis *Rohini* (the sixth layer of the skin) and the formation of abnormal branches of blood vessels [28]. In this stage, early *granthi* or a*rbuda* can develop in the form of bubble-shaped glandular growths; however, both are external and visible growths only. *Granthi* has been described as a round, hard, and bulging swelling produced owing to the aggravation of *Vata* and *Kapha*, vitiating the muscle, blood, and fatty tissues. *Arbuda* has been described as a round, large, muscular, immovable, deeply rooted,

slowly growing swelling produced owing to the aggravation of doshas, vitiating the muscle, blood, and fatty tissues. Both types of swelling can be inflammatory or non-inflammatory, depending on the doshas involved. In benign neoplasm (*Vataja*, *Pittaja*, or *Kaphaja*) one or two of the three bodily systems are out of control which is not too harmful because the body is still trying to coordinate among these systems. Malignant tumors (*Tridosaja*) are very harmful because all three major bodily systems lose mutual coordination and thus cannot prevent tissue damage, resulting in a deadly morbid condition [9]. Internal tumors are represented in the context of different diseases having various symptoms caused by such tumors. In every disease description, the *trodoshaja* presentation gives an opportunity for tumorigenesis to set in. Intra-abdominal tumors may be identified under the head of *Gulma* (abdominal swellings). It is important to state that the Ayurvedic nomenclature of a disease is based only on the similarity of the manifestations and not as per the specific pathophysiology involved therein. The different pathophysiologies leading to the same presentation is dealt with under the subdivisions of the disease where imbalances of various bodily systems like *Vata, Pitta*, or *Kapha* are attributed to the cause of the disease.

Cancer pathogenesis in Ayurveda is explained on the basis of *Tridoshas. Agni* or *Pitta*, which is present in all cells, is responsible for digestion and metabolism in the human body. A decrease in *agni* is inversely proportional to the related tissue, and therefore, in *arbuda*, a decreased state of *dhatwagni* (deranged metabolism) will result in excessive tissue growth. *Vata* can be correlated with the catabolic phase of growth and *kapha* to the anabolic phase. Cancer originates due to a metabolic crisis, i.e., aggravation of *Vata* forces and suppression of *kapha* forces, both interacting with one another, resulting in proliferation of the cancer. However, abnormal cancerous growth in a specific organ (*Eka-desa-vriddhi*) is managed through compensation from other parts of the body (*Anya-sthaniya-kshaya*), e.g., body weight loss (cachexia). Various signs and symptoms, viz., anemia, cachexia, or anorexia, arising due to the progression of the cancer have also been described in detail in the classic Ayurvedic literature [29].

The factors responsible for the vitiation of *doshas* are as follows [9]:

(a) *Vata-aggravating factors*: excessive intake of bitter, pungent, astringent, dry foods and stressful conditions.
(b) *Pitta-aggravating factors*: excessive intake of sour, salty, fried foods and excessive anger.
(c) *Kapha-aggravating factors*: excessive intake of sweet, oily food and a sedentary lifestyle.
(d) *Rakta-aggravating factors*: excessive intake of acid- or alkaline-containing foods, for example, fried or roasted foods, alcoholic beverages, and sour fruits. Excessive anger or severe emotional upset, sunbathing, or working under a scorching sun or near fire and hot conditions are some other causes.
(e) *Mamsa-aggravating factors*: excessive use of exudative foods like meat, fish, yoghurt, milk, and cream. Behaviors leading to exudation, like sleeping during the day and overeating, are some of the causes of pathogen invasions of fatty tissues.
(f) *Medo-aggravating factors*: excessive intake of oily foods, sweets, and alcohol and a lazy attitude.

8.4 Diet and Cancer Prevention

The relationship between diet and health has been recognized throughout recorded history. Dietary habits are one of the major contributory factors for the genesis of cancer. Diet, physical inactivity, and obesity are related to approximately 30–35 % of cancer deaths [30]. Physical inactivity is believed to contribute to cancer risk not only through its effect on body weight but also through negative effects on the immune and endocrine systems. Diets that are low in vegetables, fruits, and whole grains and high in processed or red meats are linked with a number of cancers. A high salt diet is linked to gastric cancer, aflatoxin B_1, a frequent food contaminant, with liver cancer, and betel nut chewing with oral cancer [31].

Surveys conducted in the USA have shown that cancer incidence is above 300 cases per 100,000, whereas in Asian countries it is less than 100 cases per 100,000 (Garodia et al. [29]). Also, although the incidence of cancer of the prostate, lung, breast, and colon is highest in Western countries, it is lowest in Eastern countries [32–34]. The reason for this high incidence of cancer in the USA is unclear; however, lifestyle has been thought to be one of the major contributors to the incidence of cancer. The higher incidence of cancer among immigrants from the East to the West further emphasizes the role of lifestyle [35, 36]. Additionally, diet is considered an important aspect of lifestyle related to cancer development [37]. While many dietary recommendations have been proposed to reduce the risk of cancer, few have significant supporting scientific evidence [38]. The primary dietary factors that increase the risk of cancer are obesity and alcohol consumption, with a diet low in fruits and vegetables and high in red meat being implicated but not confirmed [39]. Consumption of coffee is associated with a reduced risk of liver cancer [40]. Studies have linked the consumption of red or processed meat to an increased risk of breast cancer, colon cancer, and pancreatic cancer, a phenomenon that could be due to the presence of carcinogens in foods cooked at high temperatures [41, 42]. Thus, dietary recommendations for cancer prevention typically include mainly vegetables, fruit, whole grains, and fish and a reduced intake of red meat, animal fat, and refined sugar [38].

Disease prevention through the healthy preparation of foods and eating habits has been discussed in religious and civil writings for thousands of years [14]. Since the nineteenth century, Western scientific methodologies have been applied to the study of diet and disease with the intent of reducing the disease burden from noncommunicable diseases such as cancer, coronary heart disease, and other conditions endemic to societies after the advent of industrialization. Diet in India developed over thousands of years and is based on a mix of religious and secular beliefs. A large percentage of Indians, particularly Hindus, practice vegetarianism and avoid meat and fish products in their diet. Vegetarian diets have been associated with decreased risk of prostate cancer [43]. An impressive body of data exists in support of the concept that Indian food ingredients can be used in preventive strategies aimed at reducing the incidence and mortality of different types of cancers because of their antioxidative, antimutagenic, and anticarcinogenic properties [44]. Case–control studies comparing nonvegetarian and vegetarian diets and alcohol and tobacco use in India have reported that vegetarians have a reduced risk of oral,

esophageal, and breast cancers [14]. Vegetarian diets rely on pulses (e.g., beans, chickpeas, and lentils) as a source of protein, and pulses have been significantly associated with reductions in cancer [45].

Our knowledge of the transformation of a normal cell into a cancer cell has greatly expanded over the past decade. The simplistic, stepwise concept of initiation, promotion, and progression has matured to a better understanding of the serial genotypic changes that ultimately lead to cancer [46]. Chemoprevention inhibits the development of invasive cancer either by blocking the DNA damage that initiates carcinogenesis or by arresting or reversing the progression of premalignant cells in which such damage has already occurred [47]. Many of the chemopreventive agents are antioxidants and might suppress carcinogenesis through (1) inhibiting Phase I enzymes, (2) inducing Phase II enzymes, (3) scavenging DNA reactive agents, (4) suppressing type-2 cell proliferation induced by carcinogens, or (5) inhibiting certain properties of neoplastic cells [48]. The Phase I detoxification system, composed mainly of the cytochrome P450 supergene family of enzymes, is generally the first enzymatic defense against foreign compounds. Most pharmaceuticals are metabolized through Phase I biotransformation. Phase II conjugation reactions generally follow Phase I activation, resulting in a xenobiotic that has been transformed into a water-soluble compound that can be excreted through urine or bile. Several types of conjugation reactions are present in the body, including glucuronidation, sulfation, and glutathione and amino acid conjugation. These reactions require cofactors that must be replenished through dietary sources. The human diet contains a variety of compounds that exhibit chemoprevention effects toward an array of xenobiotics [49]. Epidemiology studies have suggested that some dietary constituents may act as naturally occurring cancer prevention agents and may explain some of the differences in cancer incidence seen in populations with varying dietary intakes [50, 51].

Oxidative stress is one of the main ways in which DNA is damaged from either an exogenous or an endogenous source (e.g., inflammation). Antioxidant micronutrients have been reported to oppose this effect [52]. Thus, food interacts in different ways with the initiation phase, and the protective effect of food is likely to be more important than food's contribution as a mutagen. The promotion step is the clonal proliferation of mutated cells that occurs as a result of genetic alteration and epigenetic modulations and thus achieves tumor growth. Reactive oxygen species (ROSs) are necessary to intracell signaling for the synthesis of growth factor and antioxidants that may interfere in this pathway. Little is known about the effect of food at the invasion step. Food can interfere with genetic and epigenetic alterations in this phase; for example, some experimental work suggests that dietary phenolic compounds can modify angiogenesis [53].

Chemoprevention by natural products has been obtained in several hundred animal studies [52]. Chemopreventive agents can be grouped into three broad categories [54]. The first category is blocking agents. These compounds prevent carcinogenic agents from reaching or reacting with a critical target site; thus, they act by exerting a barrier function. The second category is composed of compounds that decrease the vulnerability of target tissue to carcinogenic stimuli. The third category is suppressing agents. These compounds prevent the evolution of neoplastic processes in tissue that otherwise would become malignant.

8.5 Preventing Cancer by Dietary Modulation: Ayurvedic Viewpoint

Ayurveda promotes health by enlivening the body's inner intelligence to create harmony [55]. Unlike modern nutritional theories, which tend to recommend "one size fits all" guidelines that change with each new wave of research, Ayurvedic physicians maintain there is no one single diet or food that is healthy for all individuals. Ayurveda identifies six major tastes we need in our diet every day – sweet, sour, salty, pungent, bitter, and astringent. Each of these tastes has specific health-giving effects. By including all six, one can be most completely nourished. When we consistently eat only a few of the tastes, it not only causes health problems but also triggers cravings for unhealthy foods. For instance, fast food contains mostly sweet, sour, and salty tastes. If we eat a steady diet of fast food, we can develop a craving for sweets. Adding more pungent, bitter, and astringent tastes can help tame an out-of-control desire for fast foods.

Ayurvedic texts compare the process of digestion to cooking over a flame. Digestive "fires," collectively called *agni*, "cook" food so that nutrients can be optimally utilized. When *agni* is strong, our body fully assimilates nutrients and eliminates what it doesn't need. Ultimately a fully functioning digestive system uses the food we eat to produce a biochemical called *ojas*, a fluid substance that nourishes the body and maintains the balance of all bodily systems. If the digestive fire is weak, the incompletely digested portion of the meal forms a sticky, toxic substance called *ama*. The opposite of *ojas*, *ama* blocks the flow of the body's inner intelligence. It settles in areas of the body that are out of balance, taking on many forms, such as calcium deposits in the joints, plaque in the arteries, and cysts and tumors. A coated tongue, bad breath, dullness of the senses, depression, and unclear thinking can indicate the presence of *ama*. To prevent *ama* from forming, plenty of warm water should be taken and eating late at night should be avoided. Eating freshly prepared meals and cooking with seasonal, organic fruits and vegetables are essential. Strengthen *agni* by "kindling" it with heating foods and spices, such as ginger and black pepper. Every food has its own taste (*rasa*), a heating or cooling energy (*virya*), and a postdigestive effect (*vipaka*). Some also possess *prabhava*, an unexplained effect. So while it is true that an individual's *agni* largely determines how well or poorly food is digested, food combinations are also of great importance. Poor combinations can produce indigestion, fermentation, putrefaction, and gas formation and, if prolonged, can lead to toxemia and disease [56].

Ayurveda recommends strict dietary principles for maintaining healthy life. For example, *Satvika ahara* (fresh food composed of milk, fruits, and vegetables consumed in a congenial environment), as recommended in *Gita*, is considered wholesome compared to *rajas* food (spicy, hot, fast food, acidic food) and *tamas* food and habits (stale food, alcohol, smoking, nonvegetarian food). We can deduce that *rajas* and *tamas* foods may have a greater affinity for developing malignancy compared to *satvika* foods.

8.6 Preventing Cancer with Vegetables, Fruits, Spices, and Herbs: The Contemporary Viewpoint

An interesting finding that has been observed repeatedly is that individuals who consume relatively large amounts of vegetables, fruits, grains, and herbs are at a decreased risk of cancer of many organs [52, 57]. An investigation by Block et al. [58] of 24 epidemiological studies showed that the consumption of a relatively large amount of vegetables and fruits was associated with a decreased incidence of lung cancer. Recent data from 11 cohort and case–control studies showed an inverse relationship between fruit and vegetable consumption and lung cancer [59]. Multiple mechanisms are undoubtedly involved in the protective effect of diets rich in fruits and vegetables [60–62]. However, it is difficult to identify the relative contribution of various components of a plant-based food to overall cancer risk reduction. The issue is further complicated by the recent demonstration of synergism among protectors [63, 64]. Attention has been focused on intercellular signaling as a common molecular target for various chemopreventive phytochemicals [65].

Natural products encompass three main categories of compounds, phenylpropanoids, isoprenoids, and alkaloids, which are widely distributed in plant foods and medicinal herbs. This large array of molecules is crucial to human nutrition and health. Plant-derived foodstuffs and beverages also constitute the so-called functional foods and beverages, which include mainly fruits, vegetables, herbs, and spices [66]. Several plant constituents, including polyphenols, appear to be potent antimutagens and antioxidants [67]. Flavonoids and procyanidins are two major classes of polyphenolic phytochemicals demonstrating a wide range of biochemical and pharmacological effects. The flavonoids, such as apigenin and quercetin, have been shown to inhibit melanoma growth and metastatic potential. When tested for the ability to inhibit lung colonization, these polyphenols decrease the number of B16-BL6 colonies in lung in a dose-dependent manner [68]. Dragsted et al. [69] found that polyphenols in fruits, vegetables, herbs, and spices inhibit tumor formation in experimental animals exposed to carcinogens. The role of dietary plant polyphenol has been emphasized in relation to health maintenance. The various polyphenols have been shown to possess antiatherogenic and anticarcinogenic properties, inhibiting the oxidative destruction of various oxylabel biological structures, inhibiting the processes of bioactivation of carcinogens, blocking LDL oxidation, and stimulating the activity of antioxidant and detoxification enzymes [70].

8.6.1 Vegetables and Cancer Prevention

The consumption of cruciferous vegetables such as cabbage, broccoli, Brussels sprouts, and cauliflower has been shown to have cancer-chemoprevention effects in human and experimental animals [52, 71]. A striking and characteristic chemical property of cruciferous plants is their high content of glucosinolates, which often approaches 1 % or more of their dry weight. Glucosinolates and their isothiocyanate

hydrolysis products are well-known protectors against carcinogenesis [72]. Indole-3-carbinol, found in these cruciferous vegetables, has been shown to have a cancer-chemopreventive effect on liver, skin, colon, and mammary tissue when given before or concurrently with exposure to a carcinogen [71]. The topical application of indole-3-carbinol resulted in a significant protection in 7,12-Dimethylbenz(α) anthracene-initiated and 12-O-tetradecanoylphorbol-13-acetate-promoted mouse skin carcinogenesis [73]. Lycopene, a natural antioxidant found predominantly in tomato, is also reported as a cancer-prevention agent. Serum and dietary lycopene levels have been found to be inversely related to the incidence of cancer. Although the antioxidant properties of lycopene are thought to be primarily responsible for its apparent beneficial affects, other mechanisms may also be involved [74]. Alternative approaches focusing on the development of tomato-based food products for human clinical trials targeting cancer prevention and as an adjunct to therapy have been planned [75]. The consumption of *Phaseolus vulgaris* bean species, such as pinto, black, navy, or kidney, may be beneficial in the prevention and treatment of many chronic diseases including cancer [76].

Soy foods are the major source of isoflavones, which are believed to play important roles in the genesis of breast cancer and its progression. A prospective study conducted in China indicated that soy food intake is associated with longer survival and low recurrence among breast cancer patients [77]. Meta-analyses of epidemiological studies of soy consumption and breast cancer risk have demonstrated modest protective effects. Moreover, concern has been expressed that the estrogenic activity of isoflavones may have adverse effects on breast cancer recurrence. Recent studies on the mechanisms of action of soy in breast cancer provide insights into the epigenetic effects and the interaction of isoflavones with IGF-1 and with a number of polymorphisms of genes associated with breast cancer risk such as MDM2 and CYP1B1. In particular, women who are at increased risk of breast cancer due to gene polymorphisms may benefit from high soy isoflavone intake. Consumption of soy food has also been found to be associated with lower lung cancer risk [78, 79].

From time immemorial, mushrooms have been valued by human beings as a culinary wonder and folk medicine in the East [80]. Mushrooms are considered a natural medicine that is widely used and recommended by Asian physicians and naturopaths for its supporting effects on the immune system. Laboratory research and a handful of preclinical trials have suggested that the nonedible Reishi mushroom (*Ganoderma lucidum*) carries promising anticancer and immunomodulatory properties [81]. Many other commonly consumed edible mushrooms, such as button mushrooms (*Agaricus bisporus*), oyster mushrooms (*Pleurotus ostreatus*), shiitake mushrooms (*Lentinus edodes*), and maitake mushrooms (*Grifola frondosa*) might also play a role in cancer prevention [161].

8.6.2 Fruits and Cancer Prevention

Emblica officinalis Gaertn. or *Phyllanthus emblica* Linn, commonly known as Indian gooseberry or amla, is arguably the most important medicinal plant in

Ayurveda. Various parts of the plant are used to treat a range of diseases, but the most important is the fruit. Experimental studies have shown that amla and some of its phytochemicals, such as gallic acid, ellagic acid, pyrogallol, some norsesquiterpenoids, corilagin, geraniin, elaeocarpusin, and prodelphinidins B1 and B2, also possess antineoplastic effects [82]. Amla is an important component of an Ayurvedic preparation called Triphala, which is made by combining three fruits – *Emblica officinalis* Gaertn, *Terminalia chebula* Retz., and *Terminalia belerica* Retz. It is widely used as a colon cleanser, digestive, diuretic, and laxative. Experimental studies have shown that Triphala possesses antineoplastic, radioprotective, and chemoprotective properties [83, 84]. Triphala has tumor-specific cytotoxicity and does not harm normal cells [85]. A recent study showed that Triphala could induce angiogenesis by suppressing vascular endothelial growth factor receptor-2 phosphorylation and, hence, have tumor-specific activity [86].

Citrus fruits are essential foods in cancer prevention: for their capacity to act directly on cancerous cells as well as their potential for enhancing the anticancer effects of other phytochemical compounds present in diet [87, 88]. A growing body of evidence from human clinical trials has demonstrated that the consumption of grapes, wine, and grape juice exerts many health-promoting and possibly anticancer effects [89]. The resveratrol present in red wine possesses powerful anticancer properties, which may be responsible for the beneficial effects of wine on the prevention of certain cancers. Grape juice and cranberry juice contain resveratrol, but at levels ten times less than red wine. Grape seed polyphenols or procyanides are shown to have anticarcinogenic or antitumor promoting agents [90]. Several lines of evidence suggest that apples and apple products possess a wide range of biological activities that may contribute to beneficial effects on one's health against cardiovascular disease, asthma, and pulmonary dysfunction, diabetes, obesity, and cancer [91]. Apple products have been shown to prevent skin, mammary, and colon carcinogenesis in animal models. Epidemiological observations indicate that regular consumption of one or more apples a day may reduce the risk of lung and colon cancer [92].

The anticancer activity of many other fruits, such as black plum (*Eugenia jambolana* L.) [93], jackfruit (*Artocarpus heterophyllus*) [94], mango (*Mangifera indica* L.) [95], plum (*Prunus domestica*) [96], pineapple (*Ananas comosus*) [97], prickly custard apple (*Annona muricata*) [98], papaya (*Carica papaya*) [99], pomegranate (*Punica granatum*) [100], strawberry [101], watermelon (*Citrullus lanatus* T.) [102], guava (*Psidium guajava* L.) [103], and banana [104], was also verified in in vitro experimental studies.

8.6.3 Spices and Cancer Prevention

Hippocrates is frequently quoted as having said, "Let food be thy medicine and medicine be thy food." Epidemiological, preclinical, and clinical studies continue to provide fundamental insights into the dynamic relationships between nutrients – defined here as any substance in the diet that brings about a physiological effect – and health.

Today, claims about the ability of foods, including spices, to lower disease risk or to enhance the quality of life continue to captivate our attention [105]. Out of the thousands of chemical structures that have been identified in plant foods, many are found in spices. Typically, spices are the dried aromatic parts of plants – generally the seeds, berries, roots, pods, and sometimes leaves – that mainly, but not invariably, grow in hot countries [106]. Spices comprise an important component of our daily diets [107]. Indian spices have been known around the world since ancient times. Spices add aroma and taste to food and possess certain medicinal properties as well. Many spices, like turmeric, red chili, coriander, cumin, and mint, have been shown to cure diseases ranging from the common cold and cough to cancerous tumors [108]. Some spices are rich sources of flavonoids, which can block carcinogenesis. For instance, the potential of turmeric (curcumin), red chilli (capsaicin), cloves (eugenol), ginger (zerumbone), garlic (diallyl sulfide), fennel (anethole), kokum (gambogic acid), fenugreek (diosgenin), and black cumin (thymoquinone) in cancer prevention has been established [109].

When it comes to dealing with cancer, turmeric (Haridra) can be considered the king of spices. Turmeric contains the powerful polyphenol curcumin, or diferuloylmethan, which has been clinically proven to retard the growth of cancer cells causing prostrate cancer, melanoma, breast cancer, brain tumor, pancreatic cancer, and leukemia, among a host of others [110]. Various preclinical cell culture and animal studies suggest that curcumin has potential as an antiproliferative, anti-invasive, and antiangiogenic agent, as a mediator of chemoresistance and radioresistance, and as a chemopreventive agent [111, 112]. Curcumin promotes apoptosis, which safely eliminates cancer breeding cells without posing a threat to the development of other healthy cells. The various cell-signaling pathways inhibited by curcumin include NFκB, AP-1, STAT3, Akt, Bcl-2, Bcl-X(L), caspases, PARP, IKK, EGFR, HER2, JNK, MAPK, COX2, and 5-LOX [113]. Moreover, curcumin was reported to act in synergism with several natural compounds or synthetic agents commonly used in chemotherapy [114]. The results of a small number of clinical pilot studies conducted with curcumin at doses of up to 12 g suggest tentatively that it is safe in humans [115].

The rhizomes of *Zingiber officinale* Roscoe (Zingiberaceae), commonly known as ginger, is one of the most widely used spices and condiments. It is also an integral part of many traditional medicines and has been extensively used since ancient times in Ayurvedic, Chinese, Unani-Tibb, Srilankan, Arabic, and African traditional medicines for many unrelated human ailments [116]. Ginger is an excellent source of several bioactive phenolics, including nonvolatile pungent compounds such as gingerols, paradols, shogaols, and gingerones [117]. A number of preclinical investigations with a wide variety of assay systems and carcinogens have shown that ginger and its compounds possess chemopreventive and antineoplastic effects [118–120]. A number of mechanisms have been observed to be involved in the chemopreventive effects of ginger. The cancer-preventive activities of ginger are supposedly due mainly to free radical scavenging, antioxidant pathways, alterations of gene expression, and induction of apoptosis, all of which contribute to decreases in tumor initiation, promotion, and progression [116].

The medicinal properties of garlic (*Allium sativum* L.) have been widely known and used since ancient times. Garlic enhances immune functions and has antibacterial, antifungal, and antiviral activities [121]. In Ayurveda garlic is used for the treatment of various conditions like asthma, bronchitis, and chest congestion, skin diseases like leprosy, and skin conditions like leucoderma. A few Ayurvedic physicians use garlic in repeated worm infections. Fresh and grounded garlic has been shown to inhibit cancer caused by polycyclic aromatic hydrocarbons and nitrosamines [122]. The protective effect of garlic has been attributed to the presence of organosulfur compounds like diallyl sulfide (DAS), diallyl disulfide (DADS), ajoene, allixine, allyl mercaptans, and allyl methyl sulfides [123]. These compounds in garlic may give rise to its antibacterial properties, which in turn may block the formation of cancer-causing substances, halt the activation of cancer-causing substances, enhance cell repair, reduce cell proliferation, or induce cell death [124]. Several population studies show an association between an increased intake of garlic and a reduced risk of certain cancers, including cancers of the stomach, colon, esophagus, pancreas, and breast. Population studies are multidisciplinary studies of population groups that investigate the cause, incidence, or spread of a disease or examine the effect of health-related interventions, dietary and nutritional intakes, or environmental exposures. An analysis of data from seven population studies showed that the higher the amount of raw and cooked garlic consumed, the lower the risk of stomach and colorectal cancer [125]. A randomized clinical trial was conducted in China to evaluate the effect of synthetic allitridum (an extract of garlic used as a medicine in China for over 3,000 years) and selenium intake on gastric cancer risk involving over 5,000 Chinese men and women at high risk of stomach cancer. The study indicated that the risk for all tumors combined was reduced by 33 % and the risk of stomach cancer was reduced by 52 % in comparison with a group that received only a placebo [126].

Clove (*Syzygium aromaticum*) is one of the most commonly used spices in Indian kitchens [108]. It has been shown to be a potent chemopreventive agent and has been used by the traditional Ayurvedic healers of India since ancient times to treat respiratory and digestive ailments [127]. The major chemical constituents of clove include sesquiterpenes, volatile oil (eugenol), caryophyllene, tannins, and gum. The therapeutic benefits of eugenol are well known. It has been reported to participate in photochemical reactions and to possess insecticidal, antioxidant, and anti-inflammatory activities (162). Recent studies have also identified the promising anticancer properties of clove [108]. Fennel seed (*Foeniculum vulgare*) methanolic extract (FSME), studied in Swiss albino mice, was shown to possess antioxidant, cytotoxic, and antitumor potential. The FSME antitumor effect was due to the lipid peroxidation modulation that augmented the antioxidant defense system in Ehrlich ascites carcinoma-bearing mice with or without exposure to radiation [128]. The chemopreventive potential of fennel seed was also observed against DMBA-induced skin carcinogenesis and benzo[a]pyrene-induced forestomach papillomagenesis in Swiss albino mice [129]. *Nigella sativa* (NS), also known as black cumin, has been used as a traditional medicine for centuries. The crude oil and thymoquinone (TQ) extracted from its seeds and oil are effective against many diseases such

as cardiovascular complications, diabetes, asthma, kidney problems, and cancer [130]. Studies conducted on SiHa human cervical cancer cells indicated that NS induced apoptosis in SiHa cells through both p53 and caspase activation [131]. A lot of research interest has been generated in the last decade on the chemopreventive effects of saffron on neoplastic cells, and experimental evidence indicate anticarcinogenic and antitumor activities of saffron and its compounds in vitro and in vivo platforms [132]. Cinnamon bark (*Cinnamomum cassia*) is another popular herbal ingredient in traditional oriental medicine; it possesses diverse pharmacological activities including antibacterial, antiviral, and anticancer properties [133]. Research studies have suggested that the antitumor effect of cinnamon extracts is directly linked to enhanced proapoptotic activity and to the inhibition of NFκB and AP1 activities and their target genes in vitro and in vivo mouse melanoma models [134]. Cardamom, which belongs to the family Zingiberaceae, is one of the most common ingredients used in Indian cooking and in various parts of Europe [105]. As with many spices, cardamom, especially black cardamom (*Amomum subulatum*), has also been found to have antioxidant properties. The ability of cardamom to inhibit chemical carcinogenesis was shown by Banerjee et al. [135]. It was observed that Swiss albino mice fed cardamom oil (10 μL daily for 2 weeks) experienced a significant decrease in liver CYP content.

8.6.4 Herbs and Cancer Prevention

Medical history since its beginnings is filled with descriptions of persons who used herbs to heal the sick of society. However, parallel to the onset of the industrial revolution was the rise of allopathic medicine. Herbal medicine was also an effective healing method but was viewed less enthusiastically [136]. Botanical and herbal compounds have a substantial place in cancer treatment and palliation globally [137]. Dietary phytochemicals offer nontoxic therapeutic management as well as chemopreventive intervention for slow-growing cancers [118]. Various herbs are mentioned in the classic Ayurvedic texts for possessing potential anticancer properties. Sadabahar or *Catharanthus roseus*, commonly known as Madagascar periwinkle, has been used routinely for centuries in Ayurvedic medicine for the treatment of several diseases, including cancer. The two well-known chemotherapeutic agents vinblastine and vincristine are extracted from this plant, which is now used in the conventional treatment of leukemia and Hodgkin's lymphoma [138, 139]. The benefit of an herbal decoction is that it can nourish the body as a whole by supporting various organ systems [9] as they work on multiple biochemical pathways and are capable of influencing several organ systems simultaneously. Ayurvedic herbs can help in total healing and reduces side effects and cancer-associated complications [140]. Many herbs have been scientifically proven to have anticancer properties. A list of various herbs used for cancer treatment is given in Table 8.1.

Next to water, tea (*Camellia sinensis*) is the cheapest beverage humans consume. Drinking tea has been considered a health-promoting habit since ancient times.

Table 8.1 Herbs and plants used in Ayurvedic anticancer treatment

Scientific name	Sanskrit/Hindi name	English name
Abrus precatorius	Gunja	Coral bead vine
Agati grandiflora	Gaach-munga	Hummingbird tree
Albizzia lebbeck	Sirisha	Rain tree
Allium sativum	Lasuna	Garlic
Aloe vera	Kumari	Aloe
Alstonia scholaries	Sapta parni	Milky pine
Amorphopallus campanulatus	Jimikand	Elephant foot yam
Amura rohitaka	Harinkhana	Rohituka tree
Anacardium occidentale	Kajutaka	Cashew
Anona squamosa	Sitaphala	Custard apple
Annona atemoya		Sugar apple
Aristolochia indica	Ishwari	Birthwort
Asparagus racemosa	Shatawari	Asparagus
Azadiracta indica	Nimba	Margosa tree
Bacopa monnieri	Brahmi	Indian penny wort
Baliospermum montanum	Hastidanti	Wild castor
Barleria prionitis	Kuranta	Porcupine flower
Basella rubra	Pui Ki sag	Ceylon spinach
Bauhinia racemosa	Kanchanara	Mountain ebony
Berberis aristata	Daru haridra	Indian ophthalmic barberry
Berginia ligulata	Prashanbheda	Winter begonia
Boswellia serrata	Shallaki	Indian olibanum
Calotropis gigantean	Arka	Gigantic swallow wort
Caesalpinia sappa	Baka	Sappanwood
Capparis spinosa	Himsra	Caper
Capparis sepiaria	Kanthari	Wild caper bush
Cassia fistula	Bandarlauri	Golden shower tree
Cedrus deodara	Devadaru	Devdar
Centella asiatica	Mandukaparni	Gotu kola
Curcuma longa	Haridra	Turmeric
Cymbopogon citrates	Bhustrina	Lemongrass
Datura metal	Dhattura	Angel's trumpet
Elephantopus scaber	Mayura-shikhaa	Elephant's foot
Euphoria hirta	Dugdhika	Hairy spurge
Euphorbia neriifolia	Sehund	Indian spurge tree
Ficus bengalensis	Bargad	Banyan
Ficus glomerata	Udumbara	Goolar fig
Flacourtia romontchi	Vikankata	Indian plum
Gynandropis pentaphylla	Hurhur	Spider flower
Heliotropium indicum	Hathsura	Indian heliotrope
Holarrhena antidysenterica	Kutaja	Kurchi tree
Hygrophila spinosa	Gokulakanta	Hydrophilia
Inula cappa	Gaaitihaare	Sheep's ear
Ixora undulata	Kukurajihva	West Indian jasmine
Jasminum auriculatum	Juuhi	Jasmine
Juniperus indica	Hapusha	Black juniper

(continued)

Table 8.1 (continued)

Scientific name	Sanskrit/Hindi name	English name
Lagenaria vulgaris	Lauki	Bottle gourd
Leea macrophylla	Hathikana	Dinda
Luffa cylindrical	Ghia torai	Sponge gourds
Madhuca indica	Mahua	Butter tree
Mallotus philippensis	Kamala	Kamala tree
Manilkara hexandra	Khirni	Ceylon iron wood
Melia azadirachta	Maha nimba	Neem tree
Moringa oleifera	Shigru	Horseradish tree
Musa sapientum	Kela	Banana
Nerium indicum	Kara veera	Oleander
Nigella sativa	Krishna jeeraka	Black cumin
Occimum sanctum	Tulasi	Holy basil
Oxoxylum indicum	Bhut-vriksha	Midnight horror
Pandanus odoratissimum	Kevada	Screw pine
Paederia foetida	Gandha prasarani	Chinese fever vine
Phyllantus fraternus	Niruri	Leafflower
Picrorrhiza kurroa	Katuki	Kutki
Piper betle	Nagavalli	Betel leaf pepper
Piper longum	Pippali	Indian long pepper
Pisum sativum	Kalaya	Garden pea
Plumbago zeylanica	Chitraka	Leadwort
Plumbago rosea	Rakta chiktraka	Radix plumbago
Podophyllum hexandrum	Ban kakari	Himalayan mayapple
Pongamia glabra	Karanja	Indian beech
Prosopis cineraria	Khejri/shami	Prosopis
Pterospermum acerifolium	Muchukunda	Maple-leaved bayur tree
Rubia cordifolia	Manjistha	Indian madder
Saussurea lappa	Kustha	Costus root
Saraca indica	Ashoka	Ashoka tree
Semecarpus anacardium	Bhallataka	Varnish tree
Sinapis dichotoma	Serson	Indian rape
Solanum xanthocarpum	Choti Katheri	Yellow-berried nightshade
Soymida febrifuga	Raktarohan	Indian redwood
Syzygium cumini	Jamun	Black plum
Symplocos racemosa	Lodhra	Lodh tree
Taxus buccata	Talispatr	Himalayan yew
Tectona grandis	Sagon	Teak
Tinospora cordifolia	Guduchi	Indian tinospora
Terminalia arjun	Arjun	White marudah
Terminalia chebula	Harra	Chebulic myrobalan
Tylophora asthmatica	Aja dweshi	Indian ipecac
Vernonia species	Sahadevi	Ironweed
Vitis vinifera	Draksha	Grape
Vinca rosea	Sadabahar	Periwinkle
Withania somnifera	Ashwagandha	Indian ginseng
Xantium strumarium	Chota dhatura	Burdock datura

Source: Garodia et al. [29], Balachandran and Govindarajan [9], Smit et al. [140]
Names in *boldface* represent plants whose anticancer activity is supported by experimental research

Encouraging data showing the cancer-preventing effects of green tea from cell cultures and animal and human studies have emerged. Evidence is accumulating that black tea may have similar beneficial effects [141]. The prophylactic and therapeutic properties of tea have been attributed to green tea catechins and black tea theaflavins, besides several other polyphenolic compounds such as thearubigins, epigallocatechin gallate (EGCG), epicatechin (EC), gallic acid (GA), gallocatechin (GC), catechin gallate (CG), gallocatechin gallate (GCG), epicatechin gallate (ECG), and epigallocatechin (EGC), in addition to a certain amount of caffeic acid and proteins [142, 143, 144]. Recent studies show the inhibitory effects of EGCG on the growth of existing tumors, including breast cancer, skin cancer, ovarian, esophageal, and gastrointestinal tract cancers [145–148]. Another mode of action of biologically active compounds in green tea involves inhibiting the neoplastic process (initiation, promotion, and progress). Several independent factors, such as beverage temperature, duration of consumption, amount of tea consumed, and diet intake, have a decisive effect on the final outcome of plant polyphenols in the process of carcinogenesis [145].

For thousands of years, Ayurvedic physicians and laypeople have observed the beneficial effects of using so-called Holy Basil or Tulsi (*Ocimum sanctum*). Modern research and clinical studies have confirmed dozens of Holy Basil's traditional known actions and therapeutic uses including its remarkable adaptogenic and anti-stress activities, as well as its power support for the immune system. Recent studies have also established that Tulsi also has remarkable anticancer activity [149]. Extracts of *O. sanctum* leaves inhibit the proliferation, migration, and invasion and induce the apoptosis of pancreatic cancer cells in vitro [150]. The action of the novel flavonoid vicenin-2 (VCN-2), an active constituent of Tulsi, was studied in prostate carcinoma (CaP) cell lines. It was found that VCN-2 effectively induced antiproliferative, antiangiogenic, and proapoptotic effects in CaP cells (PC-3, DU-145, and LNCaP) irrespective of their androgen responsiveness or p53 status. VCN-2 inhibited the EGFR/Akt/mTOR/p70S6K pathway while decreasing c-Myc, cyclin D1, cyclin B1, CDK4, PCNA, and hTERT in vitro [151].

Azadirachta indica, commonly known as neem, has a wide range of medicinal properties [152]. Because of its tremendous therapeutic, domestic, agricultural, and ethnomedicinal significance and its proximity to human culture and civilization, neem has been called "the wonder tree" and "nature's drugstore." All parts of this tree, particularly the leaves, bark, seed oil, and their purified products, are widely used in the treatment of cancer. Over 60 different types of biochemicals, including terpenoids and steroids, have been purified from this plant. Preclinical research done over the last decade has fine-tuned our understanding of the anticancer properties of the crude and purified products from this plant. The anticancer properties of the plant have been studied largely in terms of its preventive, protective, tumor-suppressive, immunomodulatory, and apoptotic effects against various types of cancer and their molecular mechanisms [153]. Neem extracts and its purified products have been examined for the induction of apoptosis in multiple cancer cell types; however, its underlying mechanisms remain undefined [152]. Thirty-five limonoids, including 15 of the azadiradione type (1–15), 5 of the gedunin type (16–20), 4 of the azadirachtin type (21–24), 9 of the nimbin type (25–33), and 2 degraded limonoids

(34, 35), isolated from Azadirachta indica seed extracts, were evaluated for their cytotoxic activities against 5 human cancer cell lines. Seven compounds (3, 6, 7, 16, 18, 28, and 29) exhibited cytotoxic activity against one or more cell lines. Among these compounds, 7-deacetyl-7-benzoylepoxyazadiradione (7), 7-deacetyl-7-benzoylgeduin (18), and 28-deoxonimbolide (28) exhibited potent cytotoxic activity against HL60 leukemia cells, with IC(50) values in the range 2.7–3.1 μM [154]. Neem leaf preparation (NLP) was found to activate natural killer (NK) cells [CD56(+)CD3(−)] to enhance their cytotoxic ability to kill tumor cells and stimulate the release of interleukin-12 (IL-12) from macrophages from healthy individuals and head-and-neck squamous cell carcinoma patients [155]. The anticancer properties of neem have been reported in many cell lines studies [156–158].

8.7 Conclusions

The ancient Ayurvedic text *Sushrita Samhita* states, "He whose *doshas* are in balance, whose appetite is good…whose body, mind, and senses remain full of bliss, is called a healthy person." By following these simple, time-tested Ayurvedic dietary principles in our daily lives, one can enhance good health and keep cancer away. The disease-preventive and health-promotion approach of Ayurveda takes into consideration the whole body, mind, and spirit while maintaining health, and its approach to promoting health and treating ailments is holistic and is now finding increasing acceptance in many regions of the world. Ancient Ayurvedic physicians developed certain dietary and therapeutic measures to arrest/delay aging and rejuvenate whole functional dynamics of the body [159]. The Ayurvedic system of medicine prescribes more than 700 plant-based medicines, strict dietary principles, and yoga to encourage good health. Hundreds of bioactive chemical compounds have been identified in plant foods. Consuming a diet rich in plant foods will provide a milieu of phytochemicals, nonnutritive substances that possess health-protective benefits [160]. Hence, embracing a cuisine rich in vegetables, fruits, spices, and herbs will enhance the chemopreventive capacity of one's diet. The prevention of cancer through food is a better option than toxic cancer treatment. A proper healthy and balanced diet can definitely prevent or delay the onset of cancer. Urgent attention is thus required to scientifically reevaluate the Ayurvedic concept of food-based cancer prevention and management.

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