



Reversing the Warburg effect to control cancer: a review of diet-based solutions

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Abstract

Warburg effect is a form of cellular metabolism commonly used by cancer cells, in which, consumption of glucose and production of acidic cell metabolic wastes take place at a considerably higher rate. The effect is well described in the literature, however, the applications for cancer prevention and treatment have not been resolved effectively yet. According to the Warburg effect, anaerobic cellular respiration and the resulting acidic cellular environment are linked to the development of cancerous tumors. But an oxygen-rich environment with optimum alkalinity at the cellular level can result in retaining healthy cells and inhibiting cancer cell growth. As an alternative or complementary solution for cancer treatment based on the Warburg effect, a healthy balanced diet with alkalizing (but not alkaline) properties helps maintain acid-base balance in the body and also provides optimum metabolic rate and sufficient hydration for more effective health improvement. This paper presents a review of the key concepts related to links between cancer and dietary and environmental factors, with the main focus on the Warburg effect and energy metabolisms in cancer cells. In addition, some practical diet-based solutions are summarized that may potentially control cancer by utilizing the reversed Warburg effect by which, optimum pH levels and sufficient oxygenation may be provided at the cellular level.

Keywords: The Warburg effect, Cancer prevention, Acid-base disorder, Hypoxia, Balanced diet

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Received: 2022.6.13, Accepted: 2022.8.16



Introduction

Most medical scientists working on fundamental cancer research are familiar with Otto Heinrich Warburg (1883–1970), a German medical scientist and a Nobel Prize winner in Medicine and Physiology, whose contribution to medical science in the field of cancer has been influential and is still stimulating the researchers' views and thoughts in the context of tumor metabolism (1,2).

According to the Warburg studies, the final product of glycolysis in aerobic settings is pyruvate (common in normal cells), which forms water and carbon dioxide as byproducts of the cellular respiration processes. The following equation shows how energy is produced from glucose via aerobic cellular respiration (3):

Glucose (1 C₆H₁₂O₆) + Oxygen (6 O₂) → Energy (32 ATP) + Carbon dioxide (6 CO₂) + Water (6 H₂O)

But in anaerobic conditions due to alterations in the key enzymes, glycolytic pathway produces lactic acid (common in cancer cells), a scientific discovery that was later named as the Warburg effect. Where oxygen cannot reach the cells quickly enough to keep up with demand, glucose is converted into energy via anaerobic respiration and fermentation processes as follows (3):

Glucose (16 C₆H₁₂O₆) → Energy (32 ATP) + Lactic Acid (32 C₃H₆O₃)

In the anaerobic cellular respiration processes utilized by cancer cells, relatively large amounts of glucose as the preferred energy source are consumed, leading to high rates of lactic acid production (lactic acidosis) that makes the blood vessels exiting the tumors to be significantly acidic (3,4). The cancer cells are normally ravenous for glucose and some cancer staging and diagnosis tools also work by addressing where extra glucose is consumed in the body (1,2,4).

The anaerobic glycolysis and the fermentation processes are the main metabolic pathways in most cancer cells, which generally take place in oxygen-deprived cells due to insufficient oxygenation of body tissues, such as those in case of the low partial pressure of oxygen, the impaired ability of hemoglobin to carry oxygen, or the higher than normal rates of oxygen consumption within the cells (5,6, 7,8). There is a

greater risk of cancer initiation/development in poorly oxygenated cells, particularly those that are far from the blood vessels such as hypoxic regions in human breast tissue and prostate gland (9,10,11).

In addition to the effect of oxygen-poor acidic cellular environment, some bad sugars such as artificial sweeteners (such as those in sugary drinks) and sialic acid (found in red meats, particularly pig organs) may increase the risk of cancer progression and tumor formation in humans. But, good sugars such as mannose (found in plant-based foods such as green beans) can interfere with glucose metabolism in cancer cells and impair the growth of cancer tumors (12,13,14).

Warburg believed that healthy nutrition plays an important role in cancer prevention and focused on nutrition-based natural solutions such as including natural products and healthy foods in the diet, and limiting consumption of processed factory food products. Consequently, although he had a family history of cancer, he successfully prevented cancer, until the end of his life when he passed away at age of 87 in 1970 (1,4). This study provides a review of the mechanisms related to cancer and the Warburg effect, and summarizes some practical diet-based solutions accordingly.

Utilizing the Warburg Effect to Resolve Cancer

Based on the Warburg effect, optimal alkalinity and sufficient oxygenation of body tissues at cellular level can retain the healthy cells, and reduce cancer risk (8,10,11). Despite knowing that the Warburg effect is linked to cancer, the applications of the Warburg effect for cancer prevention and treatment have been poorly researched, and the related anticancer strategies have not been well understood yet (3).

For instance, based on the fact that apparently tumor cells depend on large amounts of glucose, some researchers by over-simplifying the energy metabolisms in cancer cells, speculated that cutting down on sugars in the diet can starve and weaken cancer cells to death (2,16). They suggested avoiding any food that contains glucose, even natural fruits, and instead, proposed consuming foods rich in fat and protein. But, later comprehensive studies on the high-fat low-sugar diets showed that not all tumors might

respond positively to that, and therefore as a monotherapy, the diets have largely failed to prove survival prolonging effects (17,18). The sugar-free diets may not starve cancer cells and fail to lower the risk of cancer, because some tumors can also use fat as a source of energy not just sugars (18). Also, stopping sugar getting to cancer cells would also mean that your body's healthy cells get starved of necessary sugars, leading to further cancer progress (19). Moreover, some good sugar sources such as natural sun-ripened fruits have a significant content of antioxidants, vitamins, minerals, and enzymes essential for the health of normal cells and preventing uncontrolled cell mutations, which should not be restricted in the diet (20).

Oxygen therapies and hyperbaric oxygen treatment that were thought to control cancer, have shown only a temporary short effect without much improved benefits in terms of cancer treatment, which may also be associated with some recognized risks related to oxygen toxicity (14,21). Besides, alkaline-water (pH around 8.5-9.0) or baking soda (sodium bicarbonate) that have been advertised as body alkalizer, are just in an alkaline state, but do not have an alkalizing effect inside the human body, because following oral consumption, their alkalinity is immediately neutralized by stomach acid, leading to weakening of stomach acid and some other major health problems consequently (14,22). Even using baking soda for cancer treatment caused the death of a cancer patient (23).

Several studies have shown that artificial supplements in high doses are not effective in preventing or treating cancers, and some also were found to increase cancer risk (24,25). For instance, supplementations with calcium and vitamin-D, high dose vitamin-C or vitamin-D, high-dose beta-carotene, high dose iron, omega-3 fatty acids, folic acid, vitamin-E, or selenium, have shown no significant benefits for cancer prevention, and there are shreds of evidence that some may even increase risk of aggressive cancers or cause

other health problems such as kidney damage (26,27,28,29,30,31). The vitamin/mineral over-dosing is also possible even unknowingly, as sometimes the amount in a supplement can be significantly higher than what the label shows (32). Hence, there is no significant anti-carcinogenic value and health benefits in artificial vitamin/mineral supplements, in an amount greater than those provided just by a healthy balanced diet (24). Some research studies have also found that sufficient intake of nutrients obtained from foods, not supplements, correlate with lower risks of all-cause mortality and cancer (33).

As an effective solution that can potentially utilize the Warburg effect in the favor of normal cells, some healthy balanced diets with alkalizing (but not alkaline) properties have been proposed (22,34). A small pilot study has also shown that the specific alkalizing diet if correctly applied, may effectively increase the venous blood pH and oxygen saturation, towards a condition that according to the Warburg effect, may potentially reduce cancer risk by providing an oxygen-rich environment with optimal alkalinity at the cellular level (14). It has also been proposed to analyze venous blood gas (VBG) test data including pH and oxygen saturation (i.e. the blood parameters related to the Warburg effect) to address metabolic acidosis and acid-base disorders, including for cancer patients (14).

According to the alkalizing diet theory, some foods form alkaline metabolic waste in the body and have an anticancer effect, such as fresh vegetables and on-tree sun-ripened fruits including raw almonds, date fruits, figs, grapes, lemons, olives, apples, red onions, green beans, celery, and sweet oranges. In contrast, some foods form acidic metabolic waste in the body, such as peanuts, pork, processed red meats, dairy products from factory farms, cheesy fast foods, soft drinks, chocolate, coffee, table sugar, frying oil, fried potatoes, sour plums, and salty/acidic pickled vegetables. Table 1 presents a food chart that can be used as a guide for balancing the diet for maintaining optimum alkalinity in the body (14,22,34).

Table 1. Acidifying/Alkalinizing characteristics for certain foods (14,22,34).

Category	Strong Acidifier (least healthy)	Medium Acidifier	Weak Acidifier	Weak Alkalizer	Medium Alkalizer	Strong Alkalizer (healthiest)
Fruits	Canned Fruits, Factory Juices, Unripe fruits	Prunes, Sour Cherry, Sour Plum	Sweet Plums	Oranges, Bananas, Cherries, Peaches, Pomegranates	Grapes, Apples, Pears, Melons, Raisins,	Lemons, Date Fruits, Figs, Mangoes
Vegetables, Beans, Legumes	Fried Potatoes, Chips, Pickled Vegetables	Lima beans, Peas, Lentils, Boiled Potatoes	Kidney beans, Cooked vegetables	Cucumber, Carrots, Tomatoes, Mushrooms, Cabbage, Green Peas	Olives, Green Beans, Okra, Turnip, Celery, Pumpkin, Bell Peppers	Garlic, Onions, Spinach
Nuts and Seeds	Peanuts, Cashews	Walnuts, Pistachios	Seeds of Pumpkin, Sunflower, Sesame	-	-	Natural Raw Almonds
Meats	Pork Meat, Shellfish, Rabbit Meat	Beef, Lamb Turkey, Veall	Fish, Chicken	-	-	-
Eggs and Dairy	Cream, Ice Cream	Homogenized Cow's Milk, Cheese, Store Eggs	Yogurt, Raw Milk, Farm Eggs	-	-	-
Grains and Cereals	Pastries, Pasta, Cereals (corn etc.)	White rice, White flour, Oats, Bread	Whole wheat, Brown rice	-	-	-
Oils	Frying Oils	Sunflower oil, Sesame oil	-	-	-	Pure Olive Oil
Drinks	Liquor, Beer, Soft Drinks, Vitamin C Supplement (1000 mg), Energy Drinks	Green Tea, Dark Black Tea, Coffee, Wine, Alkaline water	Bottled Water	Spring Mineral Water, Ginger Tea, Fresh Quince Tea	Lemon Juice Drink	-
Other foods	Chocolate, Ketchup, Mayonnaise	Jam, Sugar, Vinegar	Processed Honey	Ginger, Natural honey	-	-

In general, excessive consumption of acidifying foods and drinks may increase the risk of developing cancers. But diets that focus on sufficient consumption of natural fruits (on-tree sun-ripened, produced without chemical fertilizers), vegetables (raw and fresh), healthy nuts (such as raw almonds), plant based

proteins (such as legumes), and whole grains (such as wheat and rice) can significantly help improve our overall health (14,22,34). It is noted that food products (such as some breakfast cereals and biscuits) that contain the refined grains and/or the removed brans (not made of the whole grains in their whole forms)

may not be healthy choices, particularly for those who have irritable bowel syndrome (35). The balanced diets including sufficient amounts of alkalizing foods may reverse the Warburg effect by maintaining optimal blood alkalinity, which could particularly be beneficiary for most cancer patients because cancer tumors may cause lactic acidosis that worsens overall health (14). According to some specific studies also, diets rich in acidifying foods (high dietary acid load scores) have been associated with an increased mortality in cancer patients, including some of those who had previously survived the treatments (36).

In addition to the effect of acid-base balance in the body, balancing our metabolism and sufficient hydration are some of the most important aspects of the diet, taking into account the nature and conditions of the body, which the effects are well known in both

traditional and modern systems of medicine. Evidences show that metabolic balance helps the body to produce the required energy more effectively and easier, leading to a balance between energy intake and energy expenditure that is fundamental to health. Moreover, sufficient hydration helps deliver nutrients to cells more effectively, keep organs functioning properly, prevent degenerative disc disease, improve sleep quality, and aid in detoxifying the body from carcinogens (37,38,39,40). Diet type is one of the key factors that can control the metabolic balance and hydration in our body, as some foods or drinks depending on their characteristics, may increase or decrease the metabolic rate (making the metabolism slower or faster), or result in hydration or dehydration. Table 2 presents a food chart that can be used as a guide for balancing the diet for metabolism and hydration (41,42,43).

Table 2. Food characteristics related to metabolic rate and hydration for certain foods (41,42,43).

Category	Metabolic Rate		Hydration	
	Increase Metabolism (Warming effect nature)	Slow down metabolism (Cooling effect nature)	Dehydrate (Drying effect nature)	Hydrate (Wetting effect nature)
Fruits	Grape, Date fruits, Banana, Sweet Apples, Melons	Pomegranate, Lemons, Oranges, Kiwis, Watermelons	Sour Cherries, Sour Plums, Sour Oranges	Cucumber, Watermelon, Sweet Lemons, Peaches, Sweet Oranges
Vegetables	Carrots, Turnips, Onions, Garlic, Peppers	Cucumbers, Celery, Tomato, Lettuce, Potato	Rhubarb	Carrots, Zucchini, Turnip, Celery, Tomatoes
Nuts and Seeds	Almonds, Walnuts, Sunflowers, Sesame seeds	Flixweed	Walnuts, Sunflowers, Sesame seeds	Almonds
Meats	Sheep, Camel, Farm Chickens	Fish, Cow, Goat	Fried Meats (particularly from cows and goats)	Boiled Meats (particularly from sheep)
Eggs and Dairy	Yolk, Farm Butters	Egg White, Milk, Yogurt, White Cheese	Kashk	Farm Milks, Farm Yogurts

Grains, Beans, Legumes	Beans, Green Beans, Peas, Green Peas, Whole wheat	White Rice, Lentils	White Rice, Lentils	Beans, Green Beans, Peas, Green Peas, Whole wheat
Oils	Olive Oil, Sesame Oil, Sunflower Oil	-	-	-
Drinks	Ginger Drink, Ginger Tea, Cinnamon Tea	Coffee, Lemon Juice	Coffee, Instant Coffee, Black Tea, Soft Drinks, Beer, Wine, Energy Drinks	Water, Ginger Tea, Natural Fresh Juices from Fruits or Vegetables
Other foods	Ginger, Black Pepper, Red Pepper, Cinnamon, Turmeric	Terminalia Chebula (Black Halila)	Fried Potatoes, Chips, Biscuits, Cheese Puffs, Chocolate	-

As some examples of balanced diets, olive oil (alkalizes and also increases metabolic rate) can have a balancing effect when added to cooked rice or potatoes (acidifying foods that also make the metabolism slow). Adding olive oil, freshly squeezed juice from lemons and small amounts of pure black pepper powder on fresh vegetable salads can make excellent alkalizing food with a balancing effect on metabolism and hydration (some alkalizing and hydrating vegetables like lemon, cucumber, lettuce and tomato slow down the metabolism, and olive oil, peppers, and carrot increase the metabolic rate, which the mixture is balanced). Eating walnuts (acidifier) with sun-ripened date fruits (alkalizer) make them balanced in the diet in terms of acid-base status. Drinking black tea has an acidifying effect on the body, which with sugar (acidifier) causes a greater acid-base imbalance, but with sun-ripened date fruits (alkalizer) help maintain a healthy balance (14,43).

There are some pieces of evidence that excessive consumption of cooked foods may harm overall health, because some enzymes and vitamins are sensitive to heat and get deactivated or damaged when exposed to high temperatures. Various naturally grown fruits (such as mangoes, oranges, apples, lemons, banana, kiwi, and watermelon), fresh vegetable (such as carrot, tomato, onion, zucchini, garlic, cucumber, lettuce, and ginger),

healthy nuts (such as raw almonds, walnuts, and hazelnut), healthy oils (such as pure unprocessed olive oil), and sprouted grains (like yellow pea sprouts, and sprouted wheat) are all healthy foods that can be consumed raw, in suitable combinations that go well together as a salad, raw soup, or side dish (such as those in Avanesian plant-based raw-live diet). Consuming sufficient amounts of healthy raw-eatable high-fiber foods as a dietary habit can provide the key enzymes and essential nutrients directly from food, which can then lead to better food digestion, increased absorption of vitamins and minerals from the foods, and improved gut bacteria (44,45). In addition, as result of the healthy gut microbiome, the break-down of dietary fiber by the good bacteria in the gut may create significant amounts of Butyric acid, a fatty acid that could reduce the viability of cancer cells, and reduce the risk of developing cancer (46, 47).

There are also some foods or drinks that despite being plant-based and included in vegetarian diets, they may not be as much healthy if excessively consumed. For instance, peanuts increase the risk of cancer spread and promote cancer metastasis (48), excessive consumption of Broccoli may lead to gastric issues, bowel problems and some thyroid gland dysfunctions (49), green tea extract as an herbal supplement contains some harmful compounds that may cause acute liver

failure (50), and processed vegetarian foods such as veggie burgers, deep-fried vegetables, fried potatoes, ketchup, potato chips, frozen pizza, pop corns, instant oatmeal and instant noodles are not healthy choices (51). Hence, even vegetarian diets may not necessarily reduce cancer risk, and a comprehensive look at various properties of each food is needed before including them in the diet regularly.

The Western modern dietary patterns generally have potential adverse effects due to being high in animal proteins, trans or saturated fats, high synthetic sugars, refined carbs, processed cereals and caffeinated artificially sweetened soft drinks. In contrast, healthy traditional diets that are high in fruits, raw vegetables, healthy fats, olive oil, fish, fiber, and unprocessed nuts, seeds, whole grains and legumes are beneficial for reducing the cancer risk (52,53,54). For instance, African-Americans who replaced their fatty meat-heavy diets with rural African foods rich in beans and vegetables showed a significant drop in the biological markers related to colorectal cancer, but the tests in the

African group who were on the Western diet for two weeks indicated that cancer risk dramatically increased. The findings suggest that the risk of cancer may substantially be lowered by taking advantage of healthy-balanced natural diets (55).

The statistical cancer data published by IARC for age-standardized cancer incidence rates (the corrected rates for the effect of age, independent of life expectancy and median age) are shown in Figures 1 and 2 (56). As the data indicate, there are significantly lower cancer incidence rates (in all age groups) where people often eat according to the rules of healthy traditional food cultures and consume sufficient amounts of plant-based alkalizing foods in balanced diets, such as those in African Mediterranean and South Asian diets with long histories of diet evolution based on traditional health science rooted in evidence. But in the Western industrialized countries, significantly higher cancer incidence rates have been reported where people often consume acidifying foods according to the Western dietary habits and practices.

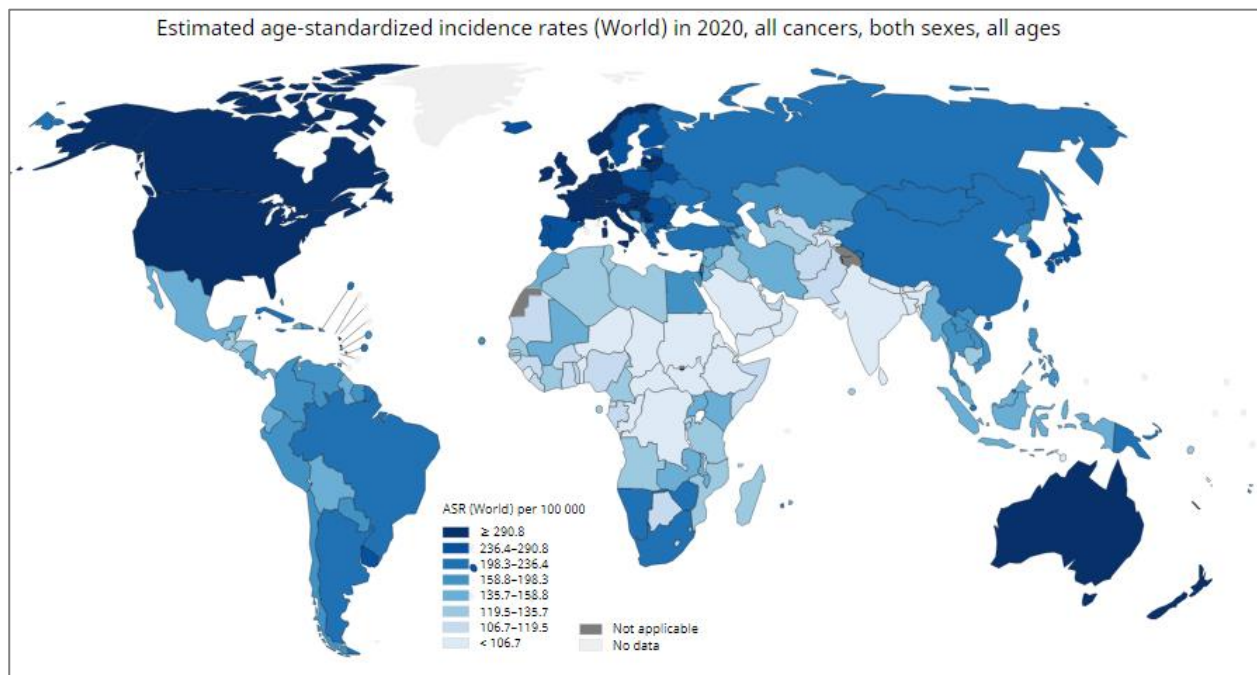


Figure 1. Worldwide statistical data for age-standardized cancer incidence rate, all cancers, all ages (IARC, 2020).

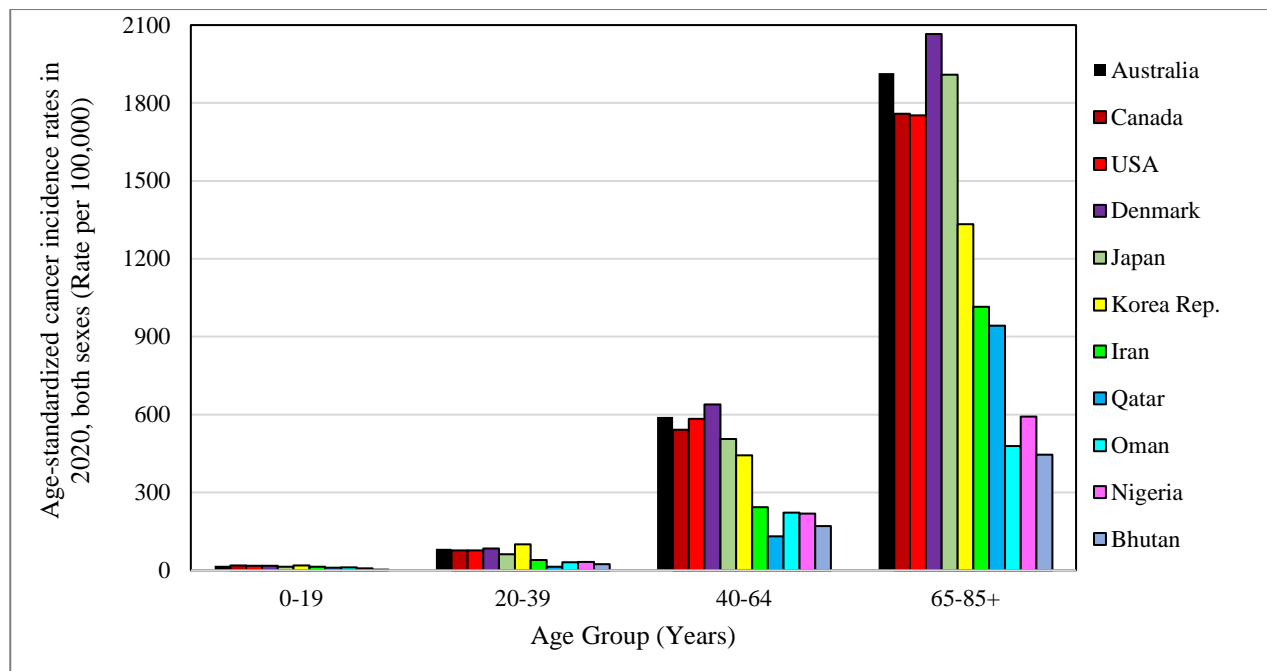


Figure 2. Worldwide cancer statistical data for cancer incidence rate in different age groups (IARC, 2020).

*Note: On the legend, those with * have high data reliability, and the rest are data with moderate reliability*

Carcinogenic Contaminants

Warburg believed that chemicals used in agriculture and artificial additives in foods may lead to the damage of cellular respiration and increase the risk of cancer, as other cancer risk factors such as carcinogens in tobacco and alcohol. Recent studies have also confirmed that the use of chemicals in agriculture, such as nitrate fertilizers, is a major concern about the health aspect of industrial products. A high nitrate intake from the chemical fertilizer residues may shift the body towards increased anaerobic respiration that increases acidic environments at the cellular level. To the extent that nitrates are converted into nitrites, the excessive amounts directly reduce the oxygen-carrying capacity of the blood, changing the body conditions in the favor of cancer cells (14). In addition, chemical fertilizers increase concentration of some heavy metals not only in the soil, but also may contaminate the agricultural products with the carcinogens that increase the risk of cancer, even for foods that are generally included in the vegetarian diets (57).

Considering the health aspect for humans, it is essential to grow some particular fruits naturally and without using any fertilizers, especially raw almonds that contain Amygdalin or Laetrile (commercially named as vitamin B17). Amygdalin releases hydrogen cyanide

(HCN) upon hydrolysis inside the human body, which exposure to small doses may have some potential anticancer effects, and then the body can detoxify and excrete it in the urine. But when large amounts of cyanide are absorbed, then the body's detoxification mechanism may be overwhelmed, leading to cyanide poisoning that can be life-threatening, as it inhibits cellular respiration of all aerobic organisms and prevents oxygen uptake. Almonds grown using chemical nitrate fertilizers are susceptible to an increase in cyanide content due to the absorption of excess nitrates by the plant. Therefore, there is a risk of cyanide poisoning if almonds produced with chemical fertilizers or bitter almonds are excessively consumed (58,59,60). It is noted that taking artificial amygdalin supplements (vitamin B17 in tablet form) is not effective in treating cancers and may even cause cyanide poisoning (61).

The other concern is regarding the excessive use of pesticides and herbicides in food production. Particularly, Glyphosate which is widely used in the production of genetically modified crops (GMO), is linked to cancer and has been classified as probably carcinogenic to humans by the International Agency for Research on Cancer (IARC). Several studies also

have shown associations between pesticide exposure and the development of cancer (62,63).

Another issue in food production is the use of ripening accelerators for fruits, which some have health hazards as a carcinogen, such as calcium carbide (64). In addition, artificial and natural ripening lead to different acidity and alkalizing effect in non-climacteric fruits such as oranges that may not ripen much once removed from the plant, compared to climacteric fruits such as bananas that can still ripen after being picked. Therefore, non-climacteric fruits if picked too-early when still unripen, may be less healthy due to greater acidity (65). Moreover, fruits that are early-picked and then artificially ripened may have lower nutritional value than the on-tree ripened fruits (66), because some elements may further be translocated into the fruits from the leaves and possibly other parts of the plant during ripening on the tree (67).

In modern industrialized farming, even organic-labeled products may not be as healthy as generally thought, because organic-labeled does not mean pesticide-free, rather, it refers to specialized kinds of pesticides that occur in nature and are used instead of synthetic pesticides (68). Moreover, organic-labeled products are often picked early (when still unripen) to make them last longer without chemical additives, and then later, they are artificially ripened with some chemicals (69). The industrial ripening used in the production of organic-labeled fruits, leads to more acidic products, particularly in the case of non-climacteric fruits that remain significantly acidic if picked before sufficient sun-ripening on the plants (14). In addition, even organic-labeled products may contain some natural carcinogens such as heavy toxic elements that increase cancer risk, if farmed in natural or man-made contaminated soil or using water from a contaminated source. But food production standards do not include requirements for measurement of heavy elements and toxic metals concentrations in the agricultural soil, water source, and more importantly in the agricultural products, even for organic labeled foods (70). In other words, some organic-labeled agriculture products may have a significant content of some carcinogens, because there are no requirements for measurement and reporting them as per the standards (71). In a study, they looked at cancer in women who generally consumed organic-labeled foods, and found no

evidence for a decrease in the incidence of cancers associated with usually or always consuming organic-labelled (industrial) foods (72).

Exposure to aflatoxin is associated with an increased risk of cancer, particularly in the liver (73). Aflatoxin is produced by fungal action during production, harvest, storage, and processing of foods for humans and farm animals, which may affect large populations directly or indirectly in some cases (74). For example in Iran, from 2013 onwards, particularly in 2017, large quantities of genetically modified (GMO) corn was imported into the country to be consumed by animals on dairy farms, which were also used for production of some processed foods such as corn-based snacks for human consumption, found to be contaminated with aflatoxin (75, 76). It was later discovered that the animals' consumption of the aflatoxin-contaminated corn at several farms caused the toxin to be transferred to the milk and dairy products they produced, which posed a serious health risk, particularly for infants and children (77). The health concerns that were detailed in reports on the findings, were later disputed, as the average levels of aflatoxins in Iranian products were claimed to be lower than even the averages in the USA and Europe. However, some research studies have shown that some certain food products available for purchase in Iran, including some dairy products, such as milk and ice-cream, may have aflatoxin levels above the maximum recommended tolerance limit for humans. Therefore, effective actions are required from the relevant food and health authorities to ensure about safety of such food products (78, 79).

Some foods may contain carcinogens including excess arsenic, nitrate and other contaminations, which compromise food safety. However, fortunately, it is feasible to partially remove the stored toxic content in some foods (such as carrots, turnips, celeries, green beans, potatoes, wheat and rice), by flushing through with hot water and then cooking in fresh boiling water. In case of consuming raw vegetables, it is suggested to properly wash and then soak in clean water for long enough time (but not too long soaking that spoils the vegetables), throwing out the water and replacing with fresh water for few times, to avoid the removed chemicals to go back into the vegetables again (80,81).

Drinking water can sometimes contain chemical contaminants that may potentially act as carcinogen and cause damage to DNA. These contaminants can include chlorine - present in chlorinated tap water, microplastics and industrial chemicals such as BPA - present in bottled water, nitrates, as well as toxic metals such as arsenic, lead, and fluoride, noting that to humans, fluoride is more toxic than lead, but slightly less toxic than arsenic. All of these in high concentrations may have a significant negative impact on human health (57, 82, 83, 84, 85). Specifically, BPA has hormone-like properties and may bind to estrogen receptors, leading to changes in cell proliferation, apoptosis, or migration and thereby, contributing to cancer development and progression (86,87). Some research studies have revealed that exposure to BPA may promote breast cancer in women, while making men more susceptible to prostate cancer and sexual dysfunctions (88,89,90). Tap water in developed areas is usually safe to drink, but this notwithstanding, drinking water with a lower hardness level is generally healthier for humans. Boiling water for a few minutes is an effective way to release the chlorine from the tap water, as well as partially reducing the hardness level, while lowering the risk of water contamination from bacteria. Therefore, drinking warm or cooled boiled water is considered to be more beneficial to human health, when compared with drinking water straight from the tap. However, boiling water cannot remove nitrate, nitrite, heavy metals and industrial chemicals. Most of these toxins in low concentrations may get filtered through healthy kidneys and then excreted from the body, but if conditions such as chronic kidney diseases or kidney failure are present, the toxins may accumulate in the body and increase the risk of these groups developing cancers (91,92).

Most people truly believe that providing healthy and natural products to the public is beneficial to their health, but some in positions of influence have speculated that genetic modifications and excessive use of chemicals are necessary to feed the world, a claim that is not supported by evidence. According to WHO reports, while an estimated 800 million people do not have enough to eat, around 1.9 billion adults are overweight, and 650 million of them are obese, meaning that some people eat more than their body's need, a self-imposed problem due to over-

consumption. Also, approximately one-third of all food produced globally is lost or goes to waste (93,94,95). All these pieces of evidence indicate that the greater issue with food supply is not food shortage, but food management/strategies. Hence, it is possible to provide healthy natural foods to most of the population, or at least to those who have concerns about food safety and health, and reduce the cancer burden worldwide.

Conclusions

In conclusion, healthy dietary habits and also reducing exposure to carcinogenic contaminants such as chemicals in foods and water, and environmental toxins, may reduce the risk of developing cancer, and may be an important strategy for reducing the burden of cancer.

Moreover, understanding the Warburg effect and the related mechanisms linked to cancer are significantly important, as the Warburg effect is supposed to occur in the majority of cancer cases. As Warburg suggested that acidosis and hypoxia are major root causes of most cancers, maintaining acid-base balance in the body may help reduce cancer risk.

Utilizing the reversed Warburg effect as an alternative or complementary solution for cancer treatment, via healthy balanced diets with alkalizing (but not alkaline) properties, may help maintain the acid-base balance and also provide optimum metabolic rate, sufficient hydration, and detoxification of the body, for more effective health improvement and recovery. Based on this theory, there may be a lower cancer incidence rate among those with balanced alkalizing dietary habits, than those who frequently have imbalanced acidifying diets.

The balanced alkalizing diets may be beneficiary for cancer prevention and treatment, however, large-scale clinical studies regarding the effect of a balanced alkalizing diet on the blood parameters related to the Warburg effect are needed to have certain empirical evidence and proven guidelines to be applicable and beneficiary for cancer patients.

Author contribution

Conceptualization: **HB**. Investigation: **HB, MT** and **SM**. Literature review: **HB, MT**, and **SM**. Multi-

disciplinary research: HB, MT, SM. Methodology: **HB**. Validation: **HB, MT**, and **SM**. Data analysis: **HB** and **SM**. Writing – Original Draft: **HB**. Writing – Review & Editing: **HB, MT**, and **SM**.

Acknowledgments

We would like to acknowledge and show our gratitude to Dr. Ted Greiner (World Nutrition), Thomas Corriher (Health Wyze), Dr. Ali Karami (National Foundation of Healthy Lifestyle), Hanieh Habibfar, Kian Bahrami, Nikan Bahrami, Radin Shouri, Gemma Byfield, Lucas Waters, Sahar Mosaffa, Shiva Bazl and Mohammad Soltani for sharing valuable information that were used in the study.

Conflict of interest

The authors have performed the research study independently, and declare that they have no conflicts of interest. The authors have no affiliations with or involvement in any organization or entity with any financial interest or non-financial in the subject matter or materials discussed in this manuscript.

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