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Food systems approach to cancer prevention

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ABSTRACT

New cancer cases are expected to surge 57% worldwide in the next two decades. The greatest burden will be in low- and middle-income countries that are ill equipped to face this epidemic. Similarly, in the United States, low-income populations are at greater risk for cancer. As most cancers contain over 50 genetic alterations, and as these alterations define dysregulation of over 10 different critical cellular signaling pathways, a "silver bullet" treatment is not effective against most cancers. Instead, the latest World Cancer Report (2012) suggests a research shift toward developing prevention strategies for cancer. Accumulating evidence suggests that a diet high in plant-based foods is preventive of a variety of chronic diseases, including cancer. A plethora of bioactive compounds—such as polyphenols, glucosinolates and carotenoids in fruits, vegetables, grains, and legumes—are shown to suppress a variety of biological capabilities required for tumor growth. While much research has shown that plant bioactive compounds can suppress sustained proliferative signaling, angiogenesis, and metastasis, as well as promote cancer stem cell apoptosis, public health campaigns to increase fruit and vegetable consumption have, overall, been less effective than desired. Thus, there is a need for innovative strategies to support increased consumption of bioactive compounds for cancer prevention particularly in vulnerable populations. Many practices of the farm-to-fork continuum, including preharvest practices, postharvest storage, and processing and consumer practices, affect a food's bioactive compound content, composition, and chemopreventive bioactivity. Food system practices may be adjusted to reduce the toxic compound levels (e.g., glycoalkaloids in potatoes) and improve the bioactive compound profile, thus, elevate the cancer fighting properties of fruits, vegetables, and other food products. This review presents current scientific evidence outlining farm-to-fork effects on fruit and vegetable bioactive compounds in order to aid the development of new and reasonable strategies for cancer prevention.

KEYWORDS
Food systems; cancer prevention; cancer stem cells; flavonoids; carotenoids; glucosinolates; polyphenols; processing

Introduction

Though the concept of food for disease prevention was eclipsed by the rapidly expanding modern drug industry during the 1900s, there has been a resurgence of interest in this area, especially in regard to cancer. Despite rapid technological developments, effective drug treatments remain elusive and cancer rates continue to rise worldwide. Much is still unknown about the pathobiology of cancer, yet theory and evidence suggest that a healthy diet and lifestyle may be successful for both aiding prevention and in treatment.

In addition, only 5–10% of cancers are attributable to inherited changes in the genes involved in growth, development, or tissue function; the majority of cancers, particularly colon cancer, appear to be due to environmental factors such as food and lifestyle (Palli et al., 2001; Balder et al., 2005; Fung et al., 2005; Calton et al., 2006). A recent explosion of evidence suggests that diet can affect gene expression via epigenetic mechanisms, which can modify cancer risk and tumor behavior (Ross et al., 2008; Hughes et al., 2009; Duthie, 2010; Link et al., 2010; Paluszczak et al., 2010). Furthermore, observations of cancer incidence amongst migrant populations demonstrate the connection between cancer, diet, and lifestyle. Evidence suggests populations migrating from countries with healthy lifestyles, including fresh food consumption and physical activity, to countries with unhealthy lifestyles, including processed food consumption and sedentary routines, take on the higher cancer incidence of their new country (Shimizu et al., 1991).

Cancer is a multifactorial and multifaceted disease, characterized by the presence of heterogeneous cancer cell types including cancer stem cells (CSCs), endothelial cells, fibroblasts, mesenchymal stem cells, hematopoietic cells, and infiltrating macrophages (Catalano et al., 2013), that interact with each other and are nested within complex niches. Over a decade ago, Weinberg and Hanahan defined the six hallmark traits of cancer: sustaining proliferative signaling, evading growth suppressors, activating invasion and metastasis, enabling replicative immortality, inducing angiogenesis, and resisting cell death (Hanahan and Weinberg, 2000). In 2011, the same authors suggested two additional hallmarks—reprogramming energy metabolism and evading immune destruction to be important for the malignant phenotype. Fostering these hallmark

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Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/bfsn functions are genome instability, and inflammation, which have been explained in detail in their manuscript (Hanahan and Weinberg, 2011). These acquired capabilities, which are shared by nearly all cancer cells, are regulated by highly complex protein signaling networks. The discovery of cancer stem cell subpopulations within the majority of human tumors, have also increased the knowledge relative to cancer etiology (i.e., the CSC hypothesis). The CSC theory suggests that most, if not all, cancerous tumors are driven by CSCs probably through dysregulation of self-renewal pathways. This leads to an expansion of this cell population that may further undergo genetic or epigenetic changes to become fully transformed (Wicha et al., 2006). CSCs are capable of self-renewal, cellular differentiation, and maintain their SC-like characteristics even after invasion and metastasis (Yu et al., 2009). There is a need for new therapeutic strategies to effectively target CSCs that are currently considered responsible for tumor resistance to therapy and cancer relapse (Zhou et al., 2009).

Many scientists hypothesize that the health benefits, including anticancer properties, associated with fruits, vegetables, and even plants used in ancient medicinal practices may be due to the presence of bioactive compounds, which are extranutritional constituents occurring in small quantities. Dietary bioactive compounds differ in composition from various fruits, vegetables, and whole grains, and often have complementary mechanisms to one another. These compounds have been linked to anticancer activities by regulating protein-signaling cascades in each of the hallmarks mentioned above (Kris-Etherton et al., 2002; Liu, 2003; Liu, 2004a; Vanamala et al., 2008; Gullett et al., 2010; Kim et al., 2012; Cerella et al., 2013; Liu, 2013; Pistollato et al., 2015; Kasdagly et al., 2014). Conventional chemotherapies can significantly reduce tumor size, but they mostly fail to eliminate CSCs and can have serious side effects (Yu et al., 2009). The search for a nontoxic chemotherapeutic regimen is fueled by epidemiological studies that show correlation between plant-based diets and the reduced risk of various cancers (Li et al., 2011a). Targeting CSCs could be achieved by several strategies including sensitizing them to chemotherapeutic agents, induction of differentiation and inhibition of self-renewal signaling (Kawasaki et al., 2008; Zhou et al., 2009). Accumulating recent research evidence suggests that plant-based bioactive compounds are promising chemopreventive agents against cancer cells including CSCs. Figure 1 demonstrates a few of the bioactive components from plant-based foods reported in the scientific literature with the potential to target CSCs. These plant-derived bioactive compounds have been proven effective in counteracting CSC growth, their metabolism, self-renewal pathways, and their microenvironment.

Curcumin, soy isoflavones such as genistein, sulforaphane found in cruciferous vegetables, quercetin, epigallocatechin-3-gallate (EGCG), resveratrol, piperine, present in black and long peppers have shown to either directly or indirectly target CSC growth (Li et al., 2011b). Yu et al. observed that curcumin, an active ingredient in turmeric, either alone or together with FOLFOX, a main anticolon cancer drug, was effective in eliminating colon CSCs that had elevated expression of CD133, CD44, and/or CD166, putative colon CSC markers (Yu et al., 2009). Genistein-treated adipocytes conditioned medium treated on MCF-7 breast cancer cells was shown to generate a lower number of mammospheres, characteristic of cancer stem cells (Montales et al., 2013). Sulforaphane was shown to decrease the CSC fraction in human breast cancer cells, as shown by decrease of aldehyde dehydrogenase $(ALDH)^+$ cells and reduction of primary mammospheres in vitro (Li et al., 2010). Further, in a xenografted murine model for breast cancer, daily injection of sulforaphane for two weeks resulted in over 50% reduction of $ALDH^+$ cells and abrogation of breast cancer growth after reimplantation of primary tumor cells into secondary mice recipients. Sulforaphane effects were related to the downregulation of the Wnt/β-catenin self-renewal pathway (Li et al., 2010). The antiproliferative effects of sulforaphane have been reported in vitro on pancreatic CSCs, which strongly depend on the activation of sonic hedgehog pathway for their

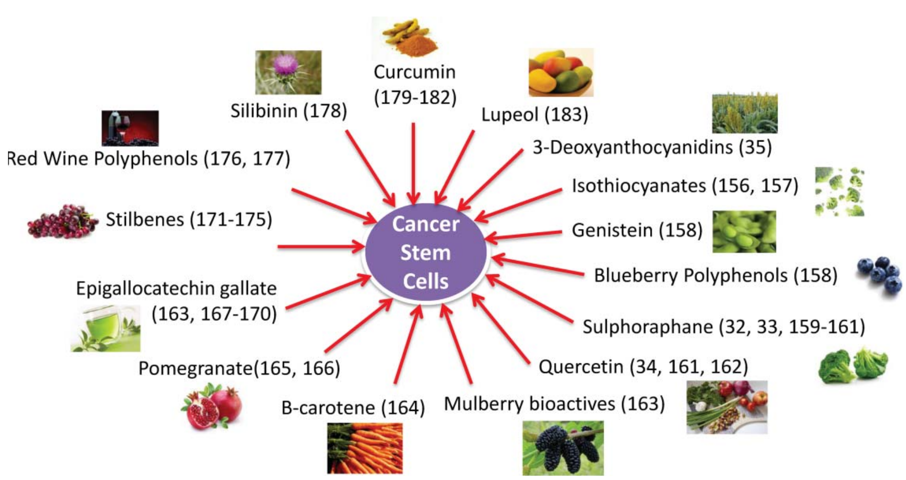

Figure 1. Bioactive compounds from different sources have shown anticancer activity by directly targeting cancer stem cells. Citations for each bioactive compound are presented in parenthesis next to the name of the plant/compounds. Isothiocyanates: (Kim et al., 2013; Wang et al., 2014)/Genistein: (Montales et al., 2012)/Sulphoraphane: (Li et al., 2010; Rodova et al., 2012; Li and Zhang, 2013; Li et al., 2013; Srivastava et al.;)/Quercetin: (Zhou et al., 2010; Srivastava et al., 2011; Tang et al., 2010)/Mulberry bioactives: (Park et al., 2012)/B-carotene: (Lee et al., 2013b)/Pomegranate bioactives: (Nair et al., 2011; Dai et al., 2010)/Epigallocatechin gallate: (Tang et al., 2010; Chen et al., 2012; Asano et al., 1997; Mineva et al., 2013; Lee et al., 2013a)/Stilbenes: (Shankar et al., 2011; Pandey et al., 2011; Mak et al., 2013; Shen et al., 2013; Lee et al., 2013c)/Red Wine Polyphenols: (Sharif et al., 2011b; Sharif et al., 2011a)/Silibinin: (Wang et al., 2012)/Curcumin: (Kakarala et al., 2010; Patel et al., 2010a; Fong et al., 2010; Lim et al., 2011) Blueberry Polyphenols: (Montales et al., 2012)/Lupeol: (Lee et al., 2011)/3-Deoxyanthocyanidins: (Massey et al., 2014).

self-renewal (Rodova et al., 2012). Quercetin decreased ALDH1 activity, induced apoptosis and reduced the expression of proteins implicated in epithelial to mesenchymal transition in vitro, and it inhibited CSC-derived xenografts in vivo, while reducing the expression of proliferation, stemness and angiogenesis related genes (Zhou et al., 2010). Studies from our lab demonstrated that the dermal layer extract of sweet sorghum, rich in 3-deoxyanthocyanidins, apigeninidin, and luteolinidin, suppressed colon CSC proliferation and induced apoptosis (Massey et al., 2014). Our recent studies revealed that anthocyanins from purple-fleshed potato also suppressed colon CSC proliferation and induced apoptosis in vitro and in a azoxymethane-induced colon cancer mice model, and these properties were linked to suppression of CSC self-renewal Wnt/β-catenin signaling pathway. The inhibitory effect of bioactive compounds on self-renewal pathways may contribute to the preferential inhibition of CSCs (Kawasaki et al., 2008). For this reason, their natural inclusion in the diet should be encouraged in order to lower the risk of developing or recurrence of cancer. However, current medical management often does not go beyond basic recommendation on total calories, macronutrients, and a few select food groups.

It should be noted that in many in vitro and animal studies, dietary compounds are supplemented at levels that would be high for a normal diet if extrapolated to humans. For example, a supplementation level of 10 mg/g diet per day (diet = 25 g/day) for a rat roughly corresponds to about 4.5 g per day (diet = 450 g/day) for a 70 kg human (Vanamala et al., 2008). However, these amounts are becoming more achievable (Walton et al., 2006) as, for example, a number of beverages with high levels of bioactive compounds such as anthocyanins are rapidly becoming more available (Weisel et al., 2006; Santhakumar et al., 2015). It is also important to bear in mind that these high doses demonstrate effects within a relatively short time period. It is possible that much lower levels of supplementation taken over a span of many years would demonstrate similar effects. Moreover, bioactive compounds may demonstrate pleiotropic effects and thus demonstrate synergistic effects in combination. Therefore, dietary consumption of a wide variety of plant-based foods may protect against cancer in humans (Liu, 2003; Liu, 2004a).

Increased fruit and vegetable consumption has been a major focus of research and public health efforts surrounding the food for cancer prevention concept. The National Cancer Institute (NCI) started the 5-A-Day program (Fruits and Veggies Matter, 2013) in 1991 to encourage people to consume five or more servings of fruits and vegetables every day. This recommendation was based on the outcomes of case-control studies that showed up to 50% reduction in cancer incidence with increased consumption of fruits and vegetables. Since then, epidemiological studies have continued to associate increased fruit and vegetable intakes with cancer prevention, though the strength of results has varied. For example, the European Prospective Investigation into Cancer and Nutrition (EPIC; 1992–2000) (Boffetta et al., 2010), which included approximately 400,000 men and women followed for $\sim$8 years, showed only a 4% reduction in the incidence of cancer for those consuming two additional servings (200 g) of total fruits and vegetables per day. On the other hand, a recent study by Buchner et al. (Buchner et al., 2010) reported a decrease in lung cancer incidence with an increased *variety* of vegetable subgroups in the diet (hazard ratios (HR); an estimate of relative risk, 0.77; 95% confidence interval (CI)) as well as lowered risk for squamous cell carcinomas when more variety in fruit and vegetable products were combined (HR, 0.88; 95% CI, (Buchner et al., 2010)).

Current evidence suggests humans can gain a spectrum of health benefits from consumption of many different plant bioactive compounds. Some bioactive compounds (e.g., phytosterols) have been shown to lower cholesterol (Clifton, 2009; Marangoni and Poli, 2010), and others (e.g., flavonoids, limonoids) have demonstrated chemopreventive properties in in vivo models (Vanamala et al., 2006; Miller et al., 2008). Recent in vivo and in vitro studies reported that two types of bioactive compounds, resveratrol and isothiocyanates, possess cancer preventive/protective activity (Clinton, 2005; Adhami et al., 2009; Gullett et al., 2010; Patel et al., 2010b; Venkateswaran and Klotz, 2010). These two compounds are present in many whole foods, such as grapes, broccoli, and others. However, no studies were conducted to using farm-to-fork-function continuum on whole foods even though pre- and postharvest practices were shown to alter the content and composition of bioactive compounds. During the late 20th century, advancements in analytical techniques allowed for the improved isolation, quantification, and characterization of bioactive compounds in food matrices, which then led to the study of single compounds in relation to cancer prevention (Kris-Etherton et al., 2002; Patil et al., 2009). However, this silver-bullet approach could provide relatively few successes in terms of cancer prevention strategies or treatments and, in some cases, actually increased cancer risk (CPSG, 1994; Omenn et al., 1996; Heinonen et al., 1998; Lonn et al., 2005). As studies searching for an anticancer, pharmacologic effect from a single, individual bioactive compound have proved largely unsuccessful, the study of whole foods, of many functional groups working in concert, is more promising. Whole foods are complex mixtures of many bioactive compounds and other constituents, the synergy of which expresses "polypharmacologic" effects. Thus, in the 21st century, research is focused on whole foods approaches/strategies to cancer prevention and treatment. In this approach, whole foods are understood to contain a plethora of bioactive compounds, functional carbohydrates, healthy fats, vitamins, minerals, and a correct energy balance, all acting in concert to prevent and treat cancer from multiple dimensions and molecular pathways.

As researchers continue to investigate the role of fruit and vegetable bioactive compounds in cancer prevention, many factors related to consumption should be considered. There are more elements affecting intake levels of bioactive compounds and their associated health benefits than the sheer volume of produce consumed. Fruits and vegetables contain varying amounts and combinations of the approximate 5000 that have been isolated and identified (still a large percent remains unknown) different bioactive compounds, which each have different physicochemical properties and biological effects. Bioactive compounds can be classified based on their chemical structures as well as their functional characteristics including anti-inflammatory, antioxidant, detoxifying, protease inhibiting, anticancer, or antiangiogenic properties. Phenolic compounds are one of the major classes of bioactive compounds and include phenolic acids, flavonoids, stilbenoids, lignans, and more. Wine (from grapes), onions, apples, and berries are rich in flavonoids; tea and coffee are rich sources of phenolic acids; and red grapes are rich in stilbenoids like resveratrol. Carotenoids, another major class of bioactive compounds, are found in many fruits and vegetables including carrots, sweet potatoes, mangoes, and papaya. Members of the *Brassicaceae* family contain an abundance of glucosinolates (GLS), yet another unique class of bioactive compounds.

Aside from the varying bioactive compound profiles of fruits and vegetables, the content and composition of their bioactive compounds may be greatly affected by practices throughout the farm-to-fork continuum including preharvest and postharvest factors, processing events, and/or consumer handling. For example, studies (Reddivari et al., 2007a; Verkerk et al., 2009) have shown that climactic conditions, such as altitude, temperature, light intensity, and soil conditions, alter bioactive compound content in foods (Reddivari et al., 2007a; Verkerk et al., 2009). Reddivari et al. previously demonstrated that preharvest factors not only alter the content and composition but also affect the antiproliferative and pro-apoptotic properties of bioactive compounds from color-fleshed potatoes (Reddivari et al., 2007b). We also demonstrated that postharvest irradiation suppressed the chemopreventive properties of whole grapefruit (Vanamala et al., 2006). Thus, the changes in fruit and vegetable bioactive compound profile due to farm-to-fork practices could have significant implications for public health and cancer prevention.

This relatively new area of research focusing on systems based-integrative thinking on farm-to-fork operations and how they affect the bioactive compound profile could lead to many novel applications and developments in cancer prevention and treatment. Over the last few decades, public health campaigns have been largely ineffective in raising fruit and vegetable intakes in the population. Thus, there is a need for complementary strategies to elevate the consumption of bioactive compounds for cancer prevention. Critical evaluation of the current delivery of bioactive compounds from our food system is a practical next step. Investigating effects throughout the farm-to-fork continuum on bioactive compounds in fruits, vegetables, and related food products could enable valuable, strategic improvements to the food supply. Adjusting food system processes to increase delivery of bioactive compounds could be one important aspect of an effective strategy for cancer prevention/therapy in the future. This is particularly important because the burden of cancer continues to grow although extensive resources are dedicated to the development and study of pharmacologic agents. This review presents current scientific evidence outlining farm-to-fork effects on fruit and vegetable bioactive compounds—the knowledge of which could aid the development of new and reasonable approaches/strategies for cancer prevention.

Farm-to-fork processes alter bioactive compounds: Agri-industrial practices

Practices throughout the farm-to-fork continuum can influence the content, composition, and chemopreventive/chemoprotective properties of bioactive compounds in whole foods. Figure 2 shows the stages throughout the continuum along with examples of practices within each stage that may affect bioactive compounds. The consumer represents the "fork" end of the continuum, and the stages preceding the consumer can be considered "agri-industrial practices." These agri-industrial practices include preharvest factors as well as postharvest storage and processing. Furthermore, these resulting changes in bioactive compounds accumulate throughout the farm-to-fork continuum, potentially leading to significant reduction in their anti-cancer properties (Madiwale et al., 2011; Madiwale et al., 2012).

Preharvest

Due to mechanization and a food system focus on "distance and durability" (Friedmann, 1992), modern plant-breeding programs have concentrated on developing cultivars with similar morphological characteristics and uniform maturity. Over a few decades, this process has forced producers to cultivate just a few cultivars of each type of fruit or vegetable (Khoury et al., 2014). Now only about 4–6 cultivars of each crop type occupy ~95% of production, thus leading to a biodiversity crisis (Altieri, 1995; Modern Agriculture, 2011). Moreover, contemporary breeding strategies focused primarily on improving yield, appearance, and taste, and disease/pest resistance, but have generally overlooked the possibility of

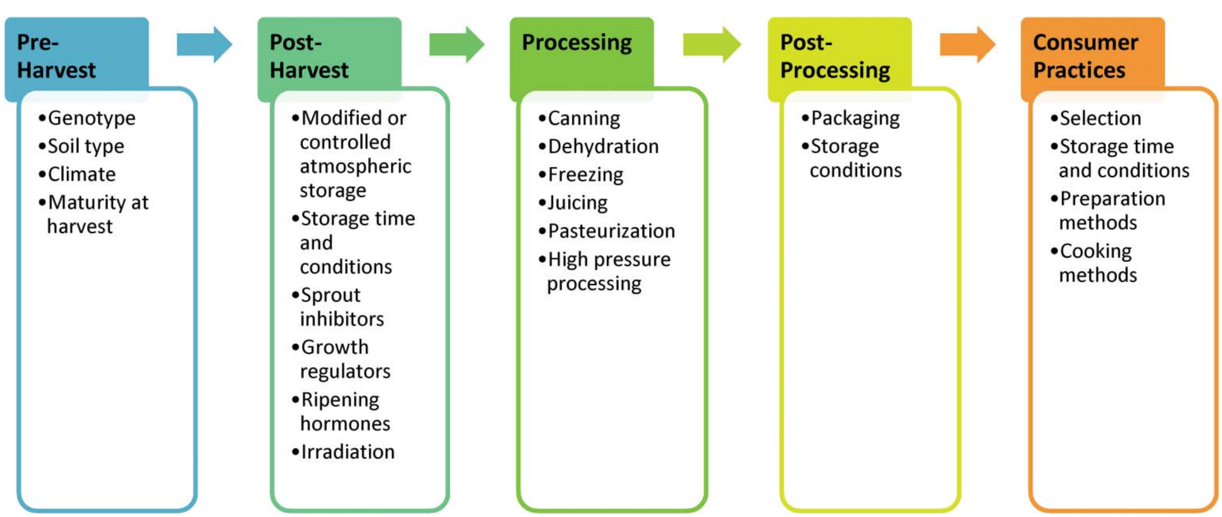

Figure 2. Stages of the farm-to-fork continuum.

improving the health benefiting properties of specific cultivars. Recent evidence linking genotype to bioactive compound content and composition reveals the serious implications modern plant breeding may have on public health. However, if harnessed properly it also provides an opportunity to improve public health.

Irrespective of the crop (or cultivar) and class of bioactive compounds, genotype accounts for 40–92% of the variation in bioactive compounds (Wang and Lewers, 2007). Reddivari et al. (Reddivari et al., 2007a) and others (Gatto et al., 2008; Jeffery et al., 2003) showed that genotype influences the content and composition of phenolic compounds, carotenoids, stilbenoids, and glucosinolates with putative chemopreventive properties. The variation not accounted for by genotype can be attributed to environmental factors such as soil type, altitude, temperature, rainfall, and/or light. However, the contribution of environmental factors to the total variation in bioactive compounds is minimal (Reddivari et al., 2007a), thus making genotype the major preharvest contributor.

Potato is the world's 4th largest food crop and the leading vegetable crop in the United States with per capita consumption of about 126 lbs annually (Potato Statistical Yearbook, 2008; Lee et al., 2009). Potatoes contain a variety of polyphenolic compounds. Reddivari et al. observed a wide variation in total phenolics in more than 320 cultivars, ranging from 41 mg to 155 mg of chlorogenic acid equivalents per 100 g fresh weight (gfw, (Reddivari et al., 2007a)). We also reported that a baked purple-fleshed potato variety contained 3.5 times more phenolics than a baked yellow colored variety (Figure 3, (Madiwale et al., 2011)). Given the popularity of potatoes, selecting the right cultivar could greatly improve the population's consumption of dietary phenolics.

Wide variation in phenolic content can also be found in other crops. Total phenolic content in different apple cultivars ranged from 105 mg to 269 mg gallic acid equivalents/100 gfw. Anthocyanin content in the cultivars tested ranged from 4.8 to 42.0 mg/100 gfw (Vieira et al., 2009). In another study, the total phenolic content in persimmons, ranged from 16 to 42 mg of gallic acid equivalents per gram of dry weight (gfd, (Ercisli et al., 2008)). Furthermore, wild type strawberries and blueberries contained significantly more phenolics than cultivated varieties (Wang and Lewers, 2007; Giovanelli and Buratti, 2009), supporting the claim that modern breeding programs have, whether intentionally or not, selected against bioactive compounds.

Stilbenoids, a class of polyphenols, are present in only a few crops including grapes, peanuts, and strawberries (Vanamala et al., 2010). Widely consumed white, pink, and red grapes vary in the content of the stilbenoid, resveratrol. Up to 26 times variation in resveratrol content was observed in white and pink cultivars, and there was a 30-fold variation observed even amongst the resveratrol-rich red cultivars (Gatto et al., 2008). Given these wide variations in resveratrol content, increased grape consumption may not necessarily lead to greater resveratrol intake unless the cultivar type is taken into account. Results have been similar for strawberries, where variation in resveratrol content was also observed (Wang and Lewers, 2007).

Carotenoids, another class of bioactive compounds, are found in a variety of common fruits and vegetables (Voutilainen et al., 2006), also vary in content and composition according to genotype. Previously, Reddivari et al. reported that total carotenoid content of 320 potato selections ranged from 96 to 930 μg of lutein equivalents/100 gfw. Potatoes contained over seven types of carotenoids such as lutein, zeaxanthin, violaxanthin, neoxanthin, and their composition varied depending on cultivar (Reddivari et al., 2007a). Commonly consumed white-fleshed potato cultivars are very low in carotenoids. Thus, even a marginal increase in carotenoid content via conventional breeding will result in significant increases in the consumption of carotenoids (and anthocyanins), potentially having a major impact on public health. This is because the popularity of potatoes across the world makes potato and potato products an attractive "delivery system" for bioactive compounds.

Glucosinolates (GLS) are a class of bioactive compounds most prevalent in cruciferous vegetables, and their GLS content and composition vary across cultivars. Broccoli contains both aliphatic and indolyl forms of GLS. Approximately, a 20-fold (1.7–38.6 μmol/gdw) variation in GLS content was observed among 50 cultivars (Kushad et al., 1999). However, variation is not similar for both forms of GLS. Cultivars showed greater variation for aliphatic compared to indolyl GLS Kushad et al., 1999; (Verkerk et al., 2009). Genotype accounted for 60% of the variation in aliphatic GLS, but only 12% of the variation in indolyl GLS (Brown et al., 2002). The content and composition of GLS also vary substantially depending on the type of cruciferous crop. In broccoli, the predominant GLS is glucoraphanin (Jeffery et al., 2003), while cauliflower contains sinigrin, and most cruciferous vegetables contain glucobrassicin. These results suggest that to obtain a complex mixture of GLS in a diet for chemoprotection, it is essential to consume a variety of cruciferous vegetables.

Apart from health benefitting compounds, foods may also contain toxicant compounds. For example, potatoes contain toxicants such as glycoalkaloids. Higher concentrations of glycoalkaloids disrupt cholesterol-containing membranes in the intestinal epithelium, thus promoting colonic inflammation (Iablokov et al., 2010). Preharvest factors also greatly affect the composition of these toxicants. Valcarcel et al. (2014) assessed the glycoalkaloid content in 60 varieties of potatoes planted in two different locations and found that potato glycoalkaloid

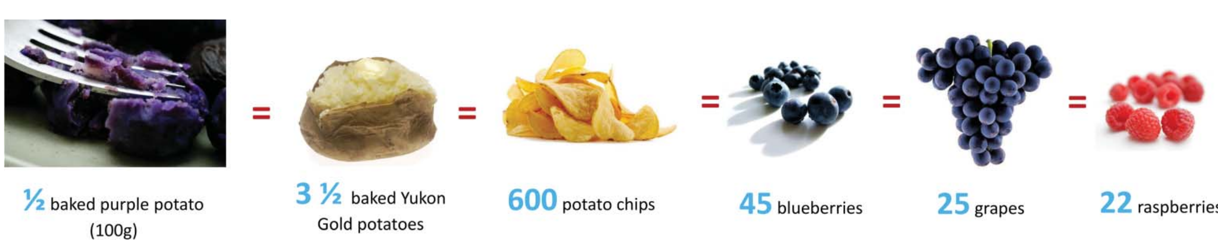

Figure 3. Examples of foods with comparable phenolic contents.

content ranged from 4 to 957 mg/kg of dry weight in the flesh, and from 150 to 8133 mg/kg in the potato skin (Valcarcel et al., 2014). Another study by Deusser et al., 2012 demonstrated that total glycoalkaloid content ranged from 585 to 5342 μg gdw in peel, and from 7 to 466 μg gdw in the flesh. Thus, it is critical to track the levels of toxic compound levels in plant foods throughout the farm-to-fork operations.

Postharvest storage

At the beginning of the 20th century, our food system was less international and more local, and accordingly seasonal. In order to meet growing food requirements, especially for perishable fruits and vegetables, advanced storage methods were developed. Recent advancements in cold storage as well as controlled and modified atmospheric conditions ensure supply of quality fruits and vegetables from around the world and different parts within the country to different markets and processing plants throughout the year. However, technological developments in storage and distribution are focused mainly on the preservation of superficial characteristics, such as crop appearance, color, and other sensory characteristics; content and composition of bioactive compounds in the crop is not a consideration. For example, ionizing radiation is used to destroy microorganisms, bacteria, viruses, or insects and/or for sprout inhibition and delay of ripening of fruits and vegetables with no regard as to its effect on bioactive compounds. Irradiation is likely to induce oxidative stress, which could alter the content and composition of bioactive compounds as well as their chemopreventive activity (Vanamala et al., 2005). Although recent studies have made efforts to determine the effect of prolonged storage/techniques (e.g., hot water treatment, irradiation, steam treatment, modified atmospheric packaging, controlled atmospheric packaging) on the content of bioactive compounds in crops; however, it is important to note that the "net effect" on chemopreventive/protective properties of fruits and vegetables has received little attention (Bergquist et al., 2007; Chirinos et al., 2007; Bunea et al., 2008; Granito et al., 2008; Bottino et al., 2009). Modification of storage or postharvest preservation techniques may significantly improve bioactive content in crops, and maximize the health benefiting potential of fruits and vegetables (Hsu, 2008; Patras et al., 2009).

In some cases, prolonged storage of certain crops was associated with significant decreases in phenolic compound content. Four months storage of potatoes subjected to gamma irradiation (3 kGy) to inhibit sprouting resulted in a decrease of chlorogenic acid, the major hydroxy-cinnamic acid in potatoes (Bergers, 1980). Spinach, a good source of phenolic acids such as orthocoumaric acid, ferulic acid, and paracoumaric acid, stored at 4°C or −18°C for one month showed ~ 20% reduction in total phenolic content (Bunea et al., 2008). Storage of litchi (*Litchi sinensis*), a subtropical fruit, at both ambient temperature (20–25°C) for up to 7 d or at 4°C for up to 35 d resulted in degradation of polyphenols (Zhang et al., 2000). These results suggest that storage of fruits and vegetables results in degradation of phenolic compounds. Since most fruits and vegetables consumed in developed countries are subjected to prolonged storage, many crops are likely to lose some bioactive compounds before reaching the consumer. As a result, there is substantial potential in our food supply system to reduce loss and degradation of bioactive compounds. When coupled with informed cultivar selection, a significant opportunity exists to improve human health through the delivery of chemopreventive/chemoprotective bioactive compounds.

Interestingly, in certain fruits and vegetables, storage did not alter the phenolic content. For example, no significant effect on total phenolics and flavonols was observed in curly kale when stored at 1°C for 6 weeks (Hagen et al., 2009). Whole oranges stored at 4°C for 12 d had increased flavonones (Plaza et al., 2011). Plums stored for 35 d at 2°C showed an increase in total phenolics and anthocyanins compared to fresh plums (Diaz-Mula et al., 2009). For blackberries, the effect of storage was dependent on cultivar. The evergreen cultivar showed significant reduction in total phenolics and anthocyanins after 7 d of storage at 2°C, whereas the Marion cultivar showed no significant fluctuations in total phenolics or anthocyanins (Wu et al., 2010).

As mentioned earlier, the focus of modern postharvest storage techniques is on preserving favorable sensory attributes of food and not on the retention of bioactive compounds. Thus, although sensory attributes are maintained, the bioactive compounds may be significantly affected in the process. For example, stilbenoids showed an inverse association with quality parameters during marketing simulation. Table grapes treated with high levels of CO_2 (20 kPa) for 3 days before storage retained better appearance, quality and moisture content, as compared with control grapes, even after 33 days at 0°C. However, control untreated fruits had greater levels of trans-resveratrol (Sanchez-Ballesta et al., 2006). Conversely, some postharvest practices elevate levels of bioactive compounds. Short-time UV exposure elevated resveratrol content in grapes almost 11 times, but the exact mechanism for this beneficial action is not clear (Cantos et al., 2001). UV-C pre-exposure resulted in greater increase of resveratrol content while maintaining anthocyanin levels compared to UV-B. In addition, storage and low doses of irradiation increased flavonoids in grapefruit. However, content of limonoids, compounds that induce detoxifying enzymes in rodent models of carcinogenesis, were decreased (Vanamala et al., 2006; Perez et al., 2009; Perez et al., 2010).

Carotenoid content of crops may also be influenced by postharvest storage techniques. Gac (*Mimordica colchichinensis*), a common fruit in Vietnam, is a rich source of both lycopene (2.4–3.7 mg/gfw) and β-carotene (0.26 to 0.38 mg/gfw) (Nhung et al., 2010). Carotenoids from Gac were stable during the first week of storage, but declined sharply after two weeks (Nhung et al., 2010). This is important to note as some tropical fruits are commonly stored at ambient temperature for a week or two after purchase by the consumer. Many tropical fruits exported to Western countries are harvested at the hard mature green stage to prolong shelf life. Mangoes stored for 3–5 weeks under 2% O_2 and 5% CO_2 (balance N_2) at 13 ± 0.5°C and 85 ± 3% relative humidity had poor color development, and poststorage application of ethylene had little effect on fruit color and quality (Dang et al., 2008). However, following controlled atmosphere storage, fruit harvested at sprung maturity stage exhibited better color development and carotenoid content than fruit harvested at the hard mature green stage, irrespective of ethylene treatments (Dang et al., 2008). Therefore, the stage of crops at harvest as well as storage time and conditions may significantly affect carotenoid content.

Assessing the overall effects of farm-to-fork processes on fruit and vegetable bioactive compound content, composition, and/or chemoprotective properties can be difficult using analytical techniques alone. For example, different subclasses of bioactive compounds within a food may respond differently to postharvest treatments. A recent study (Liu et al., 2009b) explored the effects of sunlight on the carotenoid content and physical quality of tomatoes during postharvest storage up to 21 days. Sunlight elevated lycopene but decreased β-carotene content (Liu et al., 2009b). In another study, "Spring belle" peach fruits stored at 20°C showed decreased violaxanthin and β-carotene, but beta-cryptoxanthin levels were elevated (Caprioli et al., 2009). Carrots, a good source of carotenoids such as β-carotene, α-carotene, and lutein, retained carotene when stored for 6 months at 0°C and 85–90% RH, but lutein declined significantly (37.5%) (Koca and Karadeniz, 2008). Since bioactive compounds are found as complex mixtures in fruits and vegetables and can work synergistically, loss of some compounds might suppress overall biological activity (Koca and Karadeniz, 2008; Liu et al., 2009a).

Storage time, temperature and relative humidity play a critical role in retention of glucosinolates (GLS) as well (Verkerk et al., 2009). In broccoli florets, the aliphatic GLS, glucoraphanin, was reduced by 82% after 5 days at 2°C, but it was decreased by only 31% at 4°C (Rodrigues, Rosa 1999). Broccoli stored at 1°C for 7 d and at 15°C for 3 d showed a 50% and 65% reduction in glucoraphanin content, respectively (Vallejo et al., 2003a; Jones et al., 2006). In contrast, concentration of glucobrassicin, an indole GLS, increased during 9 d of storage at 10°C. Even after chopping and storing at ambient temperature for two days, glucobrassicin content increased with marked reduction in other GLS (Verkerk et al., 2001). These results further suggest that even within the same class of bioactive compounds, different sub-classes respond differently to postharvest treatments.

Postharvest factors also affect the toxic compounds that are naturally present (for e.g., glycoalkaloids in potato) or formed during processing (acrylamide in potatoes). Storage at low (below 5°C) or high temperatures (above 10°C) or presence of light induces an increase of glycoalkaloid levels in potato tubers. Acrylamide is formed from the reaction of reducing sugars (free glucose, fructose, and hydrolyzed starch) with asparagine, an amino acid, via the Maillard reaction. Acrylamide formation occurs during processing at temperature above 120°C (Tareke et al., 2002). In order to lower AL formation, potatoes used for processing should contain reducing sugar levels below 3 mg/kg fresh weight (www.fda.gov). We and others have shown that the reducing sugar accumulation is dependent upon the initial levels, and storage conditions such as storage temperature and time (Amer et al., 2014).

On the whole, postharvest storage/techniques can play a critical role in the levels of health-benefitting bioactive compounds (and toxicants). It is important to note that most studies that looked at postharvest effects on bioactive compounds only used analytical techniques to assess the effects. As fruits and vegetables contain over 5000 bioactive compounds, it is difficult to assess the net effect of storage on actual chemopreventive properties with analytical techniques alone, and results can be unintentionally misleading. For example, several reports (Oufedjikh et al., 1998; Girennavar et al., 2008; Harbaum-Piayda et al., 2010) suggested that flavonoid levels are elevated with low doses of radiation. The fruit/plant perceives low dose radiation as pathogen attack, and responds with de novo synthesis of secondary metabolites/bioactive compounds. In our study on grapefruit bioactive compounds, low doses of radiation did elevate flavonoid content in the grapefruit pulp. However, we reported that grapefruit exposed to low doses of radiation (300 Gy; Cs^{137}) failed to suppress high multiplicity aberrant crypt foci (HMACF), a biomarker for colon cancer induced by azoxymethane, a colon specific carcinogen, in rodent models, while non-irradiated natural grapefruit significantly suppressed the HMACF (Vanamala et al., 2006). Despite elevation of flavonoid content in these grapefruits, irradiation reduced another class of bioactive compounds, limonoids, which induce detoxifying enzymes (Vanamala et al., 2006). We also reported that storage elevated phenolic content and antioxidant activity but suppressed antiproliferative and pro-apoptotic properties of colored-flesh potatoes against human colon cancer cell lines (Madiwale et al., 2011). These results suggest it is critical to use relevant in vivo (or in vitro) biomarkers in assessing the net effect of postharvest storage/techniques on chemopreventive properties of fruits and vegetables.

Processing

Research into the effect of processing on fruit and vegetable bioactive compounds is timely considering the high demand for convenient, ready-to-eat foods as well as increased awareness of the health benefits of fruits and vegetables. The popularity of fresh-cut, canned, frozen, juiced, freeze-dried, hot air-dried, and other forms of processed fruits and vegetables is increasing (Verkerk et al., 2009). Growing consumer demands and the development of a great number of processing techniques have increased the types of food products available in the supermarket today. Processing includes traditional methods (e.g., cleaning, trimming, and peeling, cooking, canning, drying or freezing) and/or new techniques (e.g., ohmic processing, high pressure processing, and microwave processing) that are becoming more popular. It is important to recognize these processing methods vary in their effects on bioactive constituents. Similar to storage, processing also degrades some bioactive compounds while increasing levels of others depending on the techniques applied and the foods involved.

Phenolics are water-soluble bioactive compounds, and thus processing that either uses water (e.g., boiling, steaming, and blanching) or removes water (e.g., drying, dehydration, baking) will typcally decrease phenolic content. Several common vegetables, for example, spinach, carrots, peas, potatoes, cabbage, broccoli, and cauliflower, are blanched to inactivate enzymes responsible for browning. Puupponen-Pimiä et al. (Puupponen-Pimia et al., 2003) studied the effect of blanching (95–99°C; 2–4 minutes) on the phenolics of the aforementioned vegetables and reported varying results. Blanching resulted in a slight reduction in phenolic content of cauliflower, a 20–30%

reduction in peas, and a 30% reduction in spinach. Conversely, blanching did not significantly affect the phenolic content of potatoes or carrots (Puuponen-Pimia et al., 2003). It is important to note that increased blanching time may result in greater loss of phenolic content due to increased leaching of phenolics into the blanching water bath.

Peanuts and peanut butter are commonly consumed around the world, and many peanut products undergo a variety of processing techniques (e.g., peeling, blanching, and roasting) before consumption. Compared to direct peeling, roasting yielded a 39.5% higher concentration of phenolics irrespective of extraction solvent (water or ethanol). Blanching lowered phenolic concentration compared to direct peeling (Yu et al., 2005). Peanut skins, a waste product of the peanut butter industry, are also a rich source of phenolic compounds. Therefore, leaving peanut skins intact and incorporating roasting in peanut butter processing may be a sensible approach to increase polyphenol content. However, roasting increases the allergenicity of peanuts (Chung et al., 2003; Kopper et al., 2005; Mondoulet et al., 2005). Thus, many aspects should be considered when developing approaches to maximize bioactive compound content in processed foods.

Citrus fruit juice is another example of a commonly consumed food item whose production may involve several processing techniques. Juicing can include squeezing, freezing, mild pasteurization, standard pasteurization, and/or concentration. Gil-Izquierdo et al. (Gil-Izquierdo et al., 2002; Gil-Izquierdo et al., 2003) evaluated the effect of different processes on the phenolic content, solubility, and metabolism of citrus fruit juice flavonoids. Industrial squeezing yielded a 22% higher phenolic content than hand squeezing. However, hand squeezing yielded a higher concentration of soluble flavonones and slightly less transformation to chalcones compared to industrially squeezed juice. Freezing resulted in significantly reduced phenolics. Pasteurization of pulp (mild and standard) resulted in significant losses (~30%) of caffeic acid derivatives, vicenin 2 and narirutin, whereas no significant effects of pasteurization were observed in the juice. Juice made from frozen concentrate yielded less flavonones and chalcones, and concentration increased precipitation of phenolic compounds into the cloud fraction. Because citrus juice consumption is so common, more information of this kind should be used to develop standard processes for manufacturers that maximize retention of health-promoting compounds while maintaining good sensory attributes.

Resveratrol is a well-known and one of the most studied bioactive compound found in red and purple grape skins, peanuts and berries, which has demonstrated "polypharmacologic" effects. Because of health benefits associated with resveratrol, the food industry is interested in increasing resveratrol content in food products, particularly wine. Grape skin fermentation, heat mashing, or a combination of both were explored to elevate the antioxidant content of red wine. The combination of skin fermentation and heat mashing resulted in greater concentration of stilbenes, anthocyanins, flavan-3-ols, and flavanols (Netzel et al., 2003). Resveratrol content in blueberries and bilberries has also been explored, as these berries are widely used in baked products. It was reported that baking (18 min; 190°C) induced 17–46% loss in resveratrol content depending on species of berries tested (Lyons et al., 2003). This clearly demonstrates that processing effects on bioactive compounds also vary with genotype.

Since carotenoids are fat soluble, processing techniques that use water may not readily degrade them. However, evidence does suggest that some processing techniques, including those that involve water, can alter carotenoid content. Spinach, a rich source of β-carotene, is often preserved by drying. Compared to raw spinach, dried samples retained only 72% and 43% of β-carotene content when oven-dried (10 h, 65°C) or sun-dried (10 hours), respectively (Yadav and Sehgal, 1995). The difference was attributed to exposure of sun-dried samples to UV-radiation and oxygen. Blanching spinach leaves for 5 minutes resulted in minimal loss of β-carotene, whereas 15 minutes caused a 26% reduction (Yadav and Sehgal, 1995). These results demonstrate that even though carotenoids are lipid-soluble, prolonged exposure to water may result in some losses.

Processing which results in the disruption of the food matrix tends to increase the bioavailability of carotenoids. Tomatoes are the major dietary source of lycopene, a carotenoid that occurs predominantly in the all-*trans* form, however, *cis*-lycopene has higher bioavailability (Schierle et al., 1997). Although common thermal methods employed in tomato processing do not alter the isomer profile of lycopene (Nguyen and Schwartz, 1998), high temperature and longer processing (e.g., cooking in olive oil at 200°C for 45 minutes) resulted in some isomerization of lycopene, possibly increasing its bioavailability from tomatoes (Nguyen and Schwartz, 1998). This implies that, in general, processing methods should be designed to disrupt the food matrix while minimizing degradation of carotenoids. Nevertheless, it is evident the properties of fruits and vegetables vary greatly, and this principle may not apply to all cases. For example, carotenoids from certain food matrices are readily bioavailable, even without disruption. Lycopene from watermelon is readily bioavailable without prolonged processing because of a low-density and nonfibrous cell wall (Edwards et al., 2003; Jeffery et al., 2012). The effect of high temperature cooking on bioactive compounds other than lycopene was not addressed in the tomato study (Nguyen and Schwartz, 1998) and is important to consider.

Glucosinolates (GLS) are converted to a number of biologically active compounds via hydrolysis catalyzed by the enzyme myrosinase. Myrosinase and GLS are stored in different cellular compartments. Chopping GLS-rich vegetables enables myrosinase to come into contact with and chemically transform GLS (Verkerk et al., 1997). GLS and their biotransformed products are water-soluble, so processing that uses water as the cooking medium will result in losses. Myrosinase is also heat-sensitive, and thus thermal processing diminishes its activity on GLS (Volden et al., 2008). This is particularly important as broccoli, known for its chemopreventive properties, usually is consumed after cooking, as are many other GLS rich vegetables. Canning, the most severe heat treatment, will result in significant thermal degradation (73%) of the total amount of glucosinolates in red cabbage, suggesting that cumulative farm-fork effects on GLS would be much more pronounced (Volden et al., 2008).

Processing also impacts the levels of toxicants in potatoes. Heating temperatures utilized during the production of potato products have small effect on the content of potato glycoalkaloids due to their thermostable nature (Finotti et al., 2006), and the distribution in the tuber; thus, they remain at high levels even after being cooked at the desired frying, and baking temperature. However, potato glycoalkaloids can be reduced by one or more pretreatments of raw potato such as peeling and blanching (Rytel, 2012; Friedman et al., 2003). Acrylamide is mainly a processing-induced toxin. The major strategy to reduce the acrylamide in potato products is to reduce the precursor levels (reducing sugars and asparagine) in raw potato materials by blanching or by addition of exogenous additives. Goal of processing methods should be to retain maximum levels of bioactive compounds while reducing levels of toxicants.

Farm-to-fork processes alter bioactive compounds: Consumer practices

The consumer represents the "fork" in the farm-to-fork continuum and plays an important role in the delivery of bioactive compounds through their own diet. Simple decisions like the means of storage (e.g., exposure to light, temperature abuse, moisture, and oxygen), cooking methods (e.g., frying, baking, steaming), and food selection impacts the quantity, variety, and integrity of bioactive compounds consumed. Understanding the effects of consumer practices on fruit and vegetable bioactive compounds completes the story of farm-to-fork continuum effects on bioactive compounds.

Consumer storage

The same principles discussed involving storage practices at the industrial level are also true at the consumer level. Temperature abuse, excessive light or oxygen exposure, and storage time can affect the content and bioactivity of consumer produce. Freezing and refrigeration are common ways consumers store fruits and vegetables. These forms of cold storage impact bioactive content both positively and negatively by reducing the rate of reactions, changing fruit or vegetable physiology, and/or damaging cell walls. For example, cold storage of citrus fruits elevated phenolics including anthocyanins (e.g.,, blood red orange) (Rapisarda et al., 2008), an effect attributed to elevation of phenylalanine ammonia lyase, a rate-limiting enzyme in polyphenol biosynthesis. Freezing fruits and vegetables also typically preserves bioactive components, though results may vary with different factors and types of produce.

Freezing fresh strawberries and raspberries at -20°C for 6 months reduced ellagic acid content by 24% (Hkkinen et al., 2000). Türkben and colleagues investigated the effects of freezing and frozen storage on phenolic compounds in five varieties of raspberries and four varieties of blackberries. On an average, a 48.2% and 28.4% reduction of total phenolics were found in frozen raspberries and blackberries, respectively (Trkben et al., 2010). Refrigeration of spinach for 72 hours (4°C) resulted in significant increases for the phenolic acids, *p*-coumaric acid, *o*-coumaric acid, and ferulic acid; however, total phenolics were significantly reduced by 11.2% (Bunea et al., 2008). Furthermore, refrigeration reduced the spinach carotenoids β-carotene, lutein, neoxanthin, and violaxanthin, (Bunea et al., 2008). In carrots refrigerated for 6 months, lutein was the only measured carotenoid negatively affected by cold storage (37% reduction) (Koca and Karadeniz, 2008). It seems different compounds respond differently to refrigeration and freezing. In certain cases, frozen storage can break cell walls, releasing enzymes that allow for degradation of bioactive compounds in fruits and vegetables. In the case of cruciferous vegetables, this process releases the enzyme myrosinase. Indeed, freezing and thawing of vegetables rich in GLS resulted in almost complete isothiocyanate conversion as a result of myrosinase activity (Verkerk and Dekker, 2008).

Consumer food preparation

Domestic processing techniques like juicing, peeling, chopping and crushing also affect bioactive content of fruits and vegetables. These processes can release enzymes from cellular compartments, which can negatively or positively influence the bioactive composition of food. For example, garlic is a source of bioactive sulfur compounds that are biotransformed during crushing and chopping. Crushing and chopping releases alliinase, which lyses cysteine sulfoxides, ultimately forming other bioactive constituents (Amagase et al., 2001). However, cooking before crushing, as in the case of smoked garlic, inactivates alliinase and prevents the formation of these bioactive compounds. Preparation techniques like peeling and juicing remove plant tissues. Peels tend to be rich in phytochemicals and bioactives, so excluding peels from a whole food will inevitably lead to a loss of bioactive content. In the case of potatoes, peeling also removes the toxic glycoalkaloids. Most often, juicing excludes the peel, and sometimes the pulp from fruit and vegetable juices. Considering that many bioactive compounds are bound in some form in pulp and peel, excluding these from juice reduces the bioactive potential of fruits and vegetables. Furthermore, these techniques increase the surface area exposed to degrading environmental factors like ultraviolet light, visible light, and oxygen. Domestic juicing of lingonberry reduced quercetin and myricetin levels by 85% and 70%, respectively (Hkkinen et al., 2000). Similar results were found in the bioactive compound content of commercially produced cranberry juices, the losses in phytochemical content were attributed to the exclusion of skin and seeds (White et al., 2011). In another study (Aaby et al., 2007), juicing resulted in up to 61% loss in anthocyanins, compared to only a 15% loss in anthocyanins from whole, intact strawberry puree.

Other common home preparation techniques can also affect bioactive compounds. In a study that mimicked domestic processing, Green Oak Leaf and Red Oak leaf lettuces were shredded and exposed for 48 hours to fluorescent light. This treatment resulted in 94% and 43% losses of quercetin glycosides, respectively (DuPont et al., 2000). Berries and other fruits are often processed domestically in jams and jellies. Domestic jam production resulted in a loss in the flavonoids quercetin (18%) and kaempferol (15%) as compared to in the respective whole fruits (Hkkinen et al., 2000). As mentioned earlier, phenolics are particularly susceptible to degradation via food preparation involving water. On average, blanching reduced total phenolics and DPPH radical scavenging activity by 20–30% in peas, spinach and swede (i.e., rutabaga) (Reddivari et al., 2007a). In a similar study, total phenolics of several cabbage varieties decreased by 55% after 15 minutes of blanching (Amin and Lee, 2005). Bilberries boiled for 10 minutes to mimic the preparation of a common local dessert resulted in a 40% reduction of quercetin (Hkkinen et al., 2000). Furthermore, this study reported an 88% reduction of conjugated quercetin in boiled tomatoes. Microwaving seemed to have the most dramatic effect on the reduction of phenolic compounds in broccoli when compared to high pressure boiling, boiling, or steaming (Vallejo et al., 2003b).

Choosing processing techniques that minimize exposure to light, heat, and oxygen can positively influence carotenoid content in domestically processed foods. For example, shredding of raw carrots led to a 28.5% reduction in β-carotene, most likely a result of increased surface exposure to air and light (Stringheta et al., 998). Blanching spinach for 2 minutes at 100°C resulted in significant decreases of total carotenoid content (Bunea et al., 2008). Interestingly, comparing different cooking techniques of colored peppers, carotenoids were well maintained after microwaving, stir-frying and boiling (Chuah et al., 2008). This evidence suggests that gentler processing methods like stir-frying and steaming better maintain carotenoids in cooked foods.

Glucosinolates (GLS) are also be affected by cooking methods that use water. Turnip greens and tops are often steamed or boiled before consumption. Francisco et al. evaluated the effect of various cooking methods on turnip GLS. Compared to fresh turnips, conventional and high-pressure boiling caused a 64% reduction in GLS in turnip greens and tops. Steaming reduced GLS only 9% and 21% for greens and tops, respectively (Francisco et al., 2010). Unlike steaming, boiling process extracts more GLS into the cooking liquid, which explains greater loss due to boiling. Indeed, a study on red cabbage demonstrated that reduction in GLS is lower with steaming (19%) than with boiling (64%) or blanching (38%) (Volden et al., 2008). Similar results were reported in boiled and steamed cauliflower where total GLS were significantly reduced by boiling but not by steaming (Song and Thornalley, 2007). Microwaving and stir-frying also had little effect on GLS levels in broccoli, Brussel sprouts, cauliflower, and green cabbage (Song and Thornalley, 2007). Thus, boiling may not be a good method for cooking GLS rich vegetables; steaming and stir-frying are better alternatives for maintaining the GLS content.

Though many studies simply report changes in the quantity of bioactive compounds, some studies have looked further into changes in bioavailability or bioactivity as a result of farm-to-fork processes. Cooking usually results in the thermal degradation of bioactive compounds. Even though this may negatively impact the total bioactive content, gentler cooking practices (e.g., steaming and stir frying) may actually enhance bioavailability, and therefore improve the bioactivity of cooked fruits and vegetables. Cooking of tomatoes was found to significantly reduce their carotenoid content (Elizalde-Gonzlez and Hernndez-Ogarca, 2007). However, cooking tomatoes was also shown to increase the bioavailability of chalconaringen and chlorogenic acid, as indicated by increased plasma levels in healthy adults (Bugianesi et al., 2004). These results suggest cooking affects content and bioavailability of food bioactive compounds in a dynamic and differential way. Various cooking methods may also affect the chemopreventive potential of bioactive compounds differently. Whole cooked lentils demonstrated greater chemoprevention than raw whole lentils in rodent models of carcinogen-induced colon carcinogenesis (Faris et al., 2009). We also investigated the effects of baking vs. frying of color-fleshed potatoes and found that baking retained more phenolics and bioactivity than frying (Madiwale et al., 2012). Further understanding the role of processing for optimization of bioactive content could help consumers choose the right cooking methods to maximize potential health benefits of the fruits and vegetables they consume.

Consumer selection

The consumer ultimately controls the content and variation of bioactive compounds in their diet by selecting the fruits and vegetables they wish to consume. As discussed, large variation exists within and across fruits, vegetables, and related products in terms of bioactive content. Accumulating evidence suggests that variety, not just the total amount of fruits and vegetables, is important for cancer risk reduction. Choosing whole foods also seems to be more beneficial than focusing on individual nutrients or singular bioactive constituents. In the end, the choice to improve health through diet is left up to the consumer. Scientific research has only just begun providing information that can help point consumers towards maximizing consumption of bioactive compounds.

Choose a variety of foods. Individual fruits and vegetables may contain bioactive compounds from several different classes, but some bioactive compounds are found only in certain fruits and vegetables. Citrus fruits contain limonoids, bioactive compounds which impart slight bitterness to citrus juices and are known to induce detoxifying enzymes (Perez et al., 2010). Other examples of bioactive compound specificity include capsanthin in chili peppers, glucosinolates in cruciferous vegetables, and stilbenoids in grapes, peanuts, and strawberries. A wide variety of bioactive compounds act synergistically to provide health benefits against chronic diseases, making it more important to eat a wide variety of fruits and vegetables instead of focusing on a single food or an individual bioactive compound. For example, lycopene, a phytonutrient from tomatoes could not significantly suppress prostate tumor weight at 23 or 224 nmol/g of diet in rodent models of carcinogenesis; however, a 34% reduction in tumor weight was associated with a diet of 10% tomato powder. Furthermore, the combination of tomato and broccoli (10:10) caused a 52% decrease in tumor weight (Canene-Adams et al., 2007). Thus, the combination of foods was more effective at slowing tumor growth than lycopene, tomato, or broccoli alone. Consumers who lack variation in their diet may not receive the complete anticancer synergistic effects of fruit and vegetable bioactive constituents (Liu, 2004b; Canene-Adams et al., 2007; Jacobs et al., 2009).

Choose whole foods. Food synergy is a concept that also explains the enhanced benefits of consuming whole foods and foodstuffs in combinations, which are not seen in individual plant constituents or compounds. For example, grapes contain complex mixtures of bioactive compounds, including the compound resveratrol. Grape seed extract is commonly consumed as a supplement, but it lacks resveratrol (Radhakrishnan et al., 2011). Consumers may be missing the full benefit of the whole grape by consuming a grape seed extract supplement in its place. In fact, we found that resveratrol potentiated grape seed extract's ability to induce apoptosis in human colon cancer cells when compared to grape seed extract alone (Radhakrishnan et al., 2011). Another study found the combination of apple peel and apple flesh demonstrated more antiproliferative activity against colon cancer cells than apple flesh alone (Eberhardt et al., 2000). The attempt to establish a relationship between individual dietary compounds and cancer prevention has proved ineffective and, in some cases, detrimental (CPSG, 1994; Omenn et al., 1996; Heinonen et al., 1998). In a commentary by Meyskens and Szabo (Meyskens and Szabo, 2005), it was recommended to stop trials of single compounds and to reconsider clinical trials incorporating whole food supplementation and changes in dietary patterns.

Conclusion

It is evident, operations throughout the farm-to-fork continuum alter the content and composition and bioactivity of bioactive compounds in fruits and vegetables. Further assessment of chemopreventive/protective bioactivity is essential for a complete understanding of effects throughout the farm-to-fork continuum. Methodical documentation of farm-to-fork effects will best be accomplished through the use of well-established in vivo (and in vitro) carcinogen models in conjunction with appropriate analytical techniques such as foodomics. This approach will allow investigators to determine not only the presence of major bioactive compounds (content and composition), but also their concentrations and chemopreventive/other biological activities. Such studies should be conducted with transdisciplinary cooperation because the experiments demand knowledge from a broad range of disciplines (e.g., plant breeding, food science, nutrition, analytical chemistry, animal science, medicine, etc.). Ultimately, more systematic study of farm-to-fork effects on bioactive compounds will allow greater understanding of the role of food in cancer prevention and will provide valuable information for use in many applications.

More detailed research into how different farm-to-fork operations affect bioactive compounds could allow for strategic food system reform aimed at increasing delivery of bioactive compounds and decreasing cancer incidence. For example, modern breeding methods seem to have contributed to the loss of certain genetic material essential for the preservation of bioactive compounds, which has serious implications on public health and epidemiology given the wide variation of bioactive compounds across crop cultivars. Despite these detrimental losses of biodiversity, the gene banks in many countries around the world have preserved genetic material for a variety of major crops. These resources could be utilized in the future for developing cultivars with better health promoting/disease preventing properties. It is essential that more concentrated efforts be made by using modern genetic breeding techniques, not only to enhance the yield, sensory properties and safety of crops but also to augment their content of bioactive compounds. This is especially critical as the number of servings of fruits increased only by 0.3 and vegetables by only 0.8 per capita during the last 30 years (Krebs-Smith and Kantor, 2001). Given the ineffectiveness of public health campaigns to increase fruit and vegetable consumption, selection of cultivars with greater bioactive compound content may be a more effective means of improving the overall health of the population. It is also important to note that cultivar/genotype selection is the first stage in the farm-to-fork continuum. Foods may be subject to many other practices that alter their bioactive compound content throughout the rest of the continuum, so it is important to maximize health-benefiting components by starting our focused efforts at the first stage.

The same idea can apply to postharvest and industrial operations as well. Though storage and processing techniques have focused on improving sensory characteristics and food safety up to this point, thoughtful strategies to retain bioactive compounds may be possible with more research. Modeling/designing/adjusting storage conditions and processing techniques to maximize the bioactive compound content and biological activity of foods sold to consumers could have significant, positive effects on health. A better understanding of how farm-to-fork processes affect fruit and vegetable bioactive compounds may also be useful in other areas of research. For example, contemporary nutritional/epidemiological studies do not take farm-to-fork effects into consideration due to insufficient data. This may be the cause for the modest reduction in cancer incidence weakly associated with fruit and vegetable intake reported in the EPIC study (Boffetta et al., 2010). It will be important for future epidemiological research to establish definite associations between fruit and vegetable consumption and cancer. More comprehensive data on changes in bioactive compounds throughout the farm-to-fork continuum would enable development of more accurate tools for assessing intakes. Food frequency questionnaires could take into account storage, processing, variety, cultivar type, food preparation, and other factors when assessing and comparing dietary intakes. This detailed dietary assessment strategy would provide better data on actual chemopreventive compounds consumed, possibly strengthening the association between cancer incidence and intakes of certain fruits and vegetables.

More research in this area would also enable development of evidence-based educational materials and public health programs for consumers. After determining changes in bioactive compounds due to common consumer storage and preparation practices, tips could be developed for consumers to maximize the health benefits gained from their foods. Consumer selection also has a great impact on overall dietary intake of bioactive compounds. Though crop biodiversity has decreased, consumers still have the ability to choose foods with more bioactive compounds in many situations. Choosing red onions, purple-fleshed potatoes, or even blue corn chips instead of their respective white alternatives could lead to increased bioactive compound intakes. By selecting a wide variety of whole foods (consuming a rainbow of foods), consumers can maximize the health benefits gained from fruit and vegetable bioactive compounds. However, consumers at this time may not know how or why this is important. Evidence-based education could be provided to consumers on how to shop, and make a meal plan for maximizing bioactive compound intakes and the associated health benefits.

Lastly, information on the content and composition of at least the major classes of bioactive compounds should be included in national and international food composition databases. Currently, these databases contain information on food macronutrient and micronutrient compositions. With more data available, databases could provide information on bioactive compounds for future use by nutrition professionals and others.

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References

Aaby, K., Wrolstad, R. E., Ekeberg, D. and Skrede, G. (2007). Polyphenol composition and antioxidant activity in strawberry purees; impact of achene level and storage. *J. Agric. Food Chem.* **55**:5156–5166.

Adhami, V. M., Khan, N. and Mukhtar, H. (2009). Cancer chemoprevention by pomegranate: Laboratory and clinical evidence. *Nutr. Cancer.* **61**(6):811–815.

Altieri, M. A. (1995). Crop production strategies for subsistence farmers (Vol 19, Pg 279, 1995). *Disasters.* **9**(4):Cp2–Cp2.

Amagase, H., Petesch, B. L., Matsuura, H., Kasuga, S. and Itakura, Y. (2001). Intake of garlic and its bioactive components. *J. Nutr.* **131**:955S.

Amer, F., Reddivari, L., Madiwale, G., Stone, M., Holm, D. and Vanamala, J. (2014). Effect of genotype and storage on glycoalkaloid and acrylamide content and sensory attributes of potato chips. *Am. J. Potato Res.* **91**(6):632–641.

Amin, I. and Lee, W. Y. (2005). Effect of different blanching times on antioxidant properties in selected cruciferous vegetables. *J. Sci. Food Agr.* **85**:2314–2320.

Asano, Y., Okamura, S., Ogo, T., Eto, T., Otsuka, T. and Niho, Y. (1997). Effect of (−)-epigallocatechin gallate on leukemic blast cells from patients with acute myeloblastic leukemia. *Life Sci.* **60**(2):135–142.

Balder, H. F., Goldbohm, R. A. and van den Brandt, P. A. (2005). Dietary patterns associated with male lung cancer risk in the Netherlands Cohort Study. *Cancer Epidem. Biomar.* **14**(2):483–490.

Bergers, W. W. A. (1980). On the colour reactions of potato glycoalkaloids in strong acids in the presence of paraformaldehyde. *Food. Chem.* **6** (2):123–131.

Bergquist, S. A. M., Gertsson, U. E., Nordmark, L. Y. G. and Olsson, M. E. (2007). Ascorbic acid, carotenoids, and visual quality of baby spinach as affected by shade netting and postharvest storage. *J. Agric. Food Chem.* **55**(21):8444–8451.

Boffetta, P., Couto, E., Wichmann, J., Ferrari, P., Trichopoulos, D., Bueno-de-Mesquita, H. B., van Duijnhoven, F. J., Buchner, F. L., Key, T., Boeing, H. et al. (2010). Fruit and vegetable intake and overall cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). *J. Natl. Cancer Inst.* **102**(8):529–537.

Bottino, A., Degl'Innocenti, E., Guidi, L., Graziani, G. and Fogliano, V. (2009). Bioactive compounds during storage of fresh-cut spinach: The role of endogenous ascorbic acid in the improvement of product quality. *J. Agric. Food Chem.* **57**(7):2925–2931.

Brown, A. F., Yousef, G. G., Jeffrey, E. H., Klein, B. P., Wallig, M. A., Kushad, M. M. and Juvik, J. A. (2002). Glucosinolate profiles in broccoli: Variation in levels and implications in breeding for cancer chemoprotection. *J. Am. Soc. Hortic. Sci.* **127**(5):807–813.

Buchner, F. L., Bueno-de-Mesquita, H. B., Ros, M. M., Overvad, K., Dahm, C. C., Hansen, L., Tjonneland, A., Clavel-Chapelon, F., Boutron-Ruault, M. C., Touillaud, M. et al. (2010). Variety in fruit and vegetable consumption and the risk of lung cancer in the European prospective investigation into cancer and nutrition. *Cancer Epidemiol. Biomarkers Prev.* **19**(9):2278–2286.

Bugianesi, R., Salucci, M., Leonardi, C., Ferracane, R., Catasta, G., Azzini, E. and Maiani, G. (2004). Effect of domestic cooking on human bioavailability of naringenin, chlorogenic acid, lycopene and beta-carotene in cherry tomatoes. *Eur. J. Nutr.* **43**:360–366.

Bunea, A., Andjelkovic, M., Socaciu, C., Bobis, O., Neacsu, M., Verhe, R. and Van Camp, J. (2008). Total and individual carotenoids and phenolic acids content in fresh, refrigerated and processed spinach (*Spinacia oleracea* L.). *Food Chem.* **108**(2):649–656.

Calton, B. A., Lacey, J. V., Schatzkin, A., Schairer, C., Colbert, L. H., Albanes, D. and Leitzmann, M. F. (2006). Physical activity and the risk of colon cancer among women: A prospective cohort study (United States). *Int. J. Cancer.* **119**(2):385–391.

Canene-Adams, K., Lindshield, B. L., Wang, S., Jeffery, E. H., Clinton, S. K., Erdman, J. W., Jr. (2007). Combinations of tomato and broccoli enhance antitumor activity in dunning r3327-h prostate adenocarcinomas. *Cancer Res.* **67**(2):836–843.

Cantos, E., Espin, J. C. and Tomas-Barberan, F. A. (2001). Postharvest induction modeling method using UV irradiation pulses for obtaining resveratrol-enriched table grapes: A new "functional" fruit? *J. Agric. Food Chem.* **49**(10):5052–5058.

Caprioli, I., Lafuente, M. T., Rodrigo, M. J. and Mencarelli, F. (2009). Influence of postharvest treatments on quality, carotenoids, and abscisic acid content of stored "Spring Belle" peach (*Prunus persica*) fruit. *J. Agric. Food Chem.* **57**(15):7056–7063.

Catalano, V., Turdo, A., Di Franco, S., Dieli, F., Todaro, M. and Stassi, G. (2013). Tumor and its microenvironment: A synergistic interplay. *Semin. Cancer Biol.* **23**(6 Pt B):522–532.

Cerella, C., Radogna, F., Dicato, M., Diederich, M. (2013). Natural compounds as regulators of the cancer cell metabolism. *Int. J. Cell Biol.* **2013**:16.

Chen, D., Pamu, S., Cui, Q., Chan, T. H. and Dou, Q. P. (2012). Novel epigallocatechin gallate (EGCG) analogs activate AMP-activated protein kinase pathway and target cancer stem cells. *Bioorganic. Med. Chem.* **20**(9):3031–3037.

Chirinos, R., Campos, D., Arbizu, C., Rogez, H., Rees, J. F., Larondelle, Y., Noratto, G. and Cisneros-Zevallos, L. (2007). Effect of genotype, maturity stage and post-harvest storage on phenolic compounds, carotenoid content and antioxidant capacity, of Andean mashua tubers (*Tropaeolum tuberosum* Ruiz & Pavon). *J. Sci. Food Agr.* **87**(3):437–446.

Chuah, A. M., Lee, Y-C, Yamaguchi, T., Takamura, H., Yin, L.-J. and Matoba, T. (2008). Effect of cooking on the antioxidant properties of coloured peppers. *Food Chem.* **111**:20–28.

Chung, S. Y., Butts, C. L., Maleki, S. J. and Champagne, E. T. (2003). Linking peanut allergenicity to the processes of maturation, curing, and roasting. *J. Agric. Food Chem.* **51**(15):4273–4277.

Clifton, P. (2009). Lowering cholesterol—A review on the role of plant sterols. *Aust. Fam. Physician.* **38**(4):218–221.

Clinton, S. K. (2005). Tomatoes or lycopene: A role in prostate carcinogenesis? *J. Nutr.* **135**(8):2057S–2059S.

CPSG. (1994). The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. The alpha-tocopherol, beta carotene cancer prevention study group. *NEJM.* **330** (15):1029–1035.

Dai, Z., Nair, V., Khan, M. and Ciolino, H. P. (2010). Pomegranate extract inhibits the proliferation and viability of MMTV-Wnt-1 mouse mammary cancer stem cells in vitro. *Oncology Rep.* **24**(4):1087–1091.

Dang, K., Singh, Z. and Tan, S. (2008). Influence of maturity stage at harvest and ethylene application on color and quality of controlled atmosphere-stored mango fruit. In: *XXVII International Horticultural Congress: 2008; Seoul, S Korea*: International Society Horticultural Science; 209–216.

Deusser, H., Guignard, C., Hoffmann, L. and Evers, D. (2012). Polyphenol and glycoalkaloid contents in potato cultivars grown in Luxembourg. *Food Chem.* **135**(4):2814–2824.

Diaz-Mula, H. M., Zapata, P. J., Guillen, F., Martinez-Romero, D., Castillo, S., Serrano, M. and Valero, D. (2009). Changes in hydrophilic and lipophilic antioxidant activity and related bioactive compounds during postharvest storage of yellow and purple plum cultivars. *Postharvest. Biol. Tec.* **51**(3):354–363.

DuPont, M. S., Mondin, Z., Williamson, G. and Price, K. R. (2000). Effect of variety, processing, and storage on the flavonoid glycoside content and composition of lettuce and endive. *J. Agric. Food Chem.* **48**(9):3957–3964.

Duthie, S. J. (2010). Folate and cancer: How DNA damage, repair and methylation impact on colon carcinogenesis. *J. Inherit. Metab. Dis.* **34** (1):101–109.

Eberhardt, M. V., Lee, C. Y. and Liu, R. H. (2000). Antioxidant activity of fresh apples. *Nature.* **405**:903–904.

Edwards, A. J., Vinyard, B. T., Wiley, E. R., Brown, E. D., Collins, J. K., Perkins-Veazie, P., Baker, R. A. and Clevidence, B. A. (2003). Consumption of watermelon juice increases plasma concentrations of lycopene and beta-carotene in humans. *J. Nutr.* **133**(4):1043–1050.

Elizalde-González, M. P. and Hernández-Ogarcía, S. G. (2007). Effect of cooking processes on the contents of two bioactive carotenoids in *Solanum lycopersicum* tomatoes and *Physalis ixocarpa* and *Physalis philadelphica* tomatillos. *Molecules.* **12**:1829–1835.

Ercisli, S., Akbulut, M., Ozdemir, O., Sengul, M. and Orhan, E. (2008). Phenolic and antioxidant diversity among persimmon (*Diospyrus kaki* L.) genotypes in Turkey. *Int. J. Food Sci. Nutr.* **59**(6):477–482.

Faris, MeA-IE, Takruri, H. R., Shomaf, M. S. and Bustanji, Y. K. (2009). Chemopreventive effect of raw and cooked lentils (*Lens culinaris* L) and soybeans (Glycine max) against azoxymethane-induced aberrant crypt foci. *Nutr. Res.* **29**:355–362.

Finotti, E., Bertone, A. and Vivanti, V. (2006). Balance between nutrients and anti-nutrients in nine Italian potato cultivars. *Food Chem.* **99** (4):698–701.

Fong, D., Yeh, A., Naftalovich, R., Choi, T. H. and Chan, M. M. (2010). Curcumin inhibits the side population (SP) phenotype of the rat C6 glioma cell line: Towards targeting of cancer stem cells with phytochemicals. *Cancer Lett.* **293**(1):65–72.

Francisco, M., Velasco, P., Moreno, D. A., Garcia-Viguera, C. and Cartea, M. E. (2010). Cooking methods of *Brassica rapa* affect the preservation of glucosinolates, phenolics and vitamin C. *Food Res. Int.* **43**(5):1455–1463.

Friedmann, H. (1992). Distance and durability: Shaky foundations of the world food economy. *Third World Quarterly.* **13**(2):371–383.

Friedman, M., Roitman, J. N. and Kozukue, N. (2003). Glycoalkaloid and calystegine contents of eight potato cultivars. *J. Agric. Food Chem.* **51** (10):2964–2973.

Fruits and Veggies Matter. (2013). Fruits and veggies matter (www.fruitsandveggiesmatter.gov; http://www.fns.usda.gov/5-day).

Fung, T. T., Hu, F. B., Holmes, M. D., Rosner, B. A., Hunter, D. J., Colditz, G. A. and Willett, W. C. (2005). Dietary patterns and the risk of postmenopausal breast cancer. *Int. J. Cancer.* **116**(1):116–121.

Gatto, P., Vrhovsek, U., Muth, J., Segala, C., Romualdi, C., Fontana, P., Pruefer, D., Stefanini, M., Moser, C., Mattivi, F. et al. (2008). Ripening and genotype control stilbene accumulation in healthy grapes. *J. Agric. Food Chem.* **56**(24):11773–11785.

Gil-Izquierdo, A., Gil, M. I. and Ferreres, F. (2002). Effect of processing techniques at industrial scale on orange juice antioxidant and beneficial health compounds. *J. Agric. Food Chem.* **50**(18):5107–5114.

Gil-Izquierdo, A., Gil, M. I., Tomas-Barberan, F. A. and Ferreres, F. (2003). Influence of industrial processing on orange juice flavanone solubility and transformation to chalcones under gastrointestinal conditions. *J. Agric. Food Chem.* **51**(10):3024–3028.

Giovanelli, G. and Buratti, S. (2009). Comparison of polyphenolic composition and antioxidant activity of wild Italian blueberries and some cultivated varieties. *Food Chem.* **112**(4):903–908.

Girennavar, B., Jayaprakasha, G. K., Mclin, S. E., Maxim, J., Yoo, K. S. and Patil, B. S. (2008). Influence of electron-beam irradiation on bioactive compounds in grapefruits (*Citrus paradisi* Macf.). *J. Agric. Food Chem.* **56**(22):10941–10946.

Granito, M., Paolini, M. and Perez, S. (2008). Polyphenols and antioxidant capacity of Phaseolus vulgaris stored under extreme conditions and processed. *Lwt. Food Sci. Technol.* **41**(6):994–999.

Gullett, N. P., Ruhul Amin, A. R., Bayraktar, S., Pezzuto, J. M., Shin, D. M., Khuri, F. R., Aggarwal, B. B., Surh, Y. J. and Kucuk, O. (2010). Cancer prevention with natural compounds. *Semin. Oncol.* **37**(3):258–281.

Hagen, S. F., Borge, G. I. A., Solhaug, K. A. and Bengtsson, G. B. (2009). Effect of cold storage and harvest date on bioactive compounds in curly kale (*Brassica oleracea* L. var. acephala). *Postharvest. Biol. Tec.* **51** (1):36–42.

Hanahan, D. and Weinberg, R. A. (2000). The hallmarks of cancer. *Cell.* **100**(1):57–70.

Hanahan, D. and Weinberg, R. A. (2011). Hallmarks of cancer: The next generation. *Cell.* **144**(5):646–674.

Harbaum-Piayda, B., Walter, B., Bengtsson, G. B., Hubbermann, E. M., Bilger, W. and Schwarz, K. (2010). Influence of pre-harvest UV-B irradiation and normal or controlled atmosphere storage on flavonoid and hydroxycinnamic acid contents of pak choi (*Brassica campestris* L. ssp chinensis var. communis). *Postharvest. Biol. Tec.* **56**(3):202–208.

Heinonen, O. P., Albanes, D., Virtamo, J., Taylor, P. R., Huttunen, J. K., Hartman, a. M., Haapakoski, J., Malila, N., Rautalahti, M., Ripatti, S. et al. (1998). Prostate cancer and supplementation with alpha-tocopherol and beta-carotene: Incidence and mortality in a controlled trial. *J. Natl. Cancer Institute.* **90**:440–446.

Hsu, K.-C. (2008). Evaluation of processing qualities of tomato juice induced by thermal and pressure processing. *LWT - Food Science and Technology.* **41**(3):450–459.

Hughes, L. A., van den Brandt, P. A., de Bruine, A. P., Wouters, K. A., Hulsmans, S., Spiertz, A., Goldbohm, R. A., de Goeij, A. F., Herman, J. G., Weijenberg, M. P. et al. (2009). Early life exposure to famine and colorectal cancer risk: A role for epigenetic mechanisms. *Plos One.* **4** (11):e7951.

Häkkinen, S. H., Kärenlampi, S. O., Mykkänen, H. M., Heinonen, I. M. and Törrönen, A. R. (2000). Ellagic acid content in berries: Influence of domestic processing and storage. *Eur. Food Res. Technol.* **22**:75–80.

Häkkinen, S. H., Kärenlampi, S. O., Mykkänen, H. M. and Törrönen, a. R. (2000). Influence of domestic processing and storage on flavonol contents in berries. *J. Agric. Food Chem.* **48**:2960–2965.

Iablokov, V., Sydora, B. C., Foshaug, R., Meddings, J., Driedger, D., Churchill, T. and Fedorak, R. N. (2010). Naturally occurring glycoalkaloids in potatoes aggravate intestinal inflammation in two mouse models of inflammatory bowel disease. *Dig. Dis. Sci.* **55**(11):3078–3085.

Jacobs, D. R., Gross, M. D. and Tapsell, L. C. (2009). Food synergy: An operational concept for understanding nutrition. *Am. J. Clin. Nutr.* **89**:1543S.

Jeffery, E. H., Brown, A. F., Kurilich, A. C., Keck, A. S., Matusheski, N., Klein, B. P. and Juvik, J. A. (2003). Variation in content of bioactive components in broccoli. *J. Food Compos. Anal.* **16**(3):323–330.

Jeffery, J. L., Turner, N. D. and King, S. R. (2012). Carotenoid bioaccessibility from nine raw carotenoid-storing fruits and vegetables using an in vitro model. *J. Sci. Food Agric.* **92**(13):2603–2610.

Jones, R. B., Faragher, J. D. and Winkler, S. (2006). A review of the influence of postharvest treatments on quality and glucosinolate content in broccoli (Brassica oleracea var. italica) heads. *Postharvest. Biol. Tec.* **41** (1):1–8.

Kakarala, M., Brenner, D. E., Korkaya, H., Cheng, C., Tazi, K., Ginestier, C., Liu, S., Dontu, G. and Wicha, M. S. (2010). Targeting breast stem cells with the cancer preventive compounds curcumin and piperine. *Breast Cancer Res. Treatment.* **122**(3):777–785.

Kasdagly, M., Radhakrishnan, S., Reddivari, L., Veeramachaneni, D. N. R. and Vanamala, J. (2014). Colon carcinogenesis: Influence of Western diet-induced obesity and targeting stem cells using dietary bioactive compounds. *Nutrition.* **30**(11):1242–1256.

Kawasaki, B. T., Hurt, E. M., Mistree, T. and Farrar, W. L. (2008). Targeting cancer stem cells with phytochemicals. *Mol. Int.* **8**(4):174.

Khoury, C. K., Bjorkman, A. D., Dempewolf, H., Ramirez-Villegas, J., Guarino, L., Jarvis, A., Rieseberg, L. H. and Struik, P. C. (2014). Increasing homogeneity in global food supplies and the implications for food security. *Proc. Natl. Acad. Sci.* **111**(11):4001–4006.

Kim, Y. S., Farrar, W., Colburn, N. H. and Milner, J. A. (2012). Cancer stem cells: Potential target for bioactive food components. *J. Nutr. Biochem.* **23**(7):691–698.

Kim, S. H., Sehrawat, A. and Singh, S. V. (2013). Dietary chemopreventative benzyl isothiocyanate inhibits breast cancer stem cells in vitro and in vivo. *Cancer Prev. Res.* **6**(8):782–790.

Koca, N. and Karadeniz, F. (2008). Changes of bioactive compounds and anti-oxidant activity during cold storage of carrots. *Int. J. Food Sci. Tech.* **43**(11):2019–2025.

Kopper, R. A., Odum, N. J., Sen, M., Helm, R. M., Stanley, J. S. and Burks, A. W. (2005). Peanut protein allergens: The effect of roasting on solubility and allergenicity. *Int. Arch. Allergy Immunol.* **136**(1):16–22.

Krebs-Smith, S. M. and Kantor, L. S. (2001). Choose a variety of fruits and vegetables daily: Understanding the complexities. *J. Nutr.* **131**(2S–1):487S–501S.

Kris-Etherton, P. M., Hecker, K. D., Bonanome, A., Coval, S. M., Binkoski, A. E., Hilpert, K. F., Griel, A. E. and Etherton, T. D. (2002). Bioactive compounds in foods: Their role in the prevention of cardiovascular disease and cancer. *Am. J. Med.* **113**:71–88.

Kushad, M. M., Brown, A. F., Kurilich, A. C., Juvik, J. A., Klein, B. P., Wallig, M. A. and Jeffery, E. H. (1999). Variation of glucosinolates in vegetable crops of Brassica oleracea. *J. Agric. Food Chem.* **47**(4):1541–1548.

Lee, T. K., Castilho, A., Cheung, V. C., Tang, K. H., Ma, S. and Ng, I. O. (2011). Lupeol targets liver tumor-initiating cells through phosphatase and tensin homolog modulation. *Hepatology (Baltimore, Md).* **53** (1):160–170.

Lee, M., Kovacs-Nolan, J., Yang, C., Archbold, T., Fan, M. Z. and Mine, Y. (2009). Hen egg lysozyme attenuates inflammation and modulates local gene expression in a porcine model of dextran sodium sulfate (DSS)-induced colitis. *J. Agric. Food Chem.* **57**(6):2233–2240.

Lee, S. H., Nam, H. J., Kang, H. J., Kwon, H. W. and Lim, Y. C. (2013a). Epigallocatechin-3-gallate attenuates head and neck cancer stem cell traits through suppression of Notch pathway. *Eur. J. Cancer.* **49** (15):3210–3218.

Lee, H. A., Park, S. and Kim, Y. (2013b). Effect of beta-carotene on cancer cell stemness and differentiation in SK-N-BE(2)C neuroblastoma cells. *Oncology Rep.* **30**(4):1869–1877.

Lee, C. M., Su, Y. H., Huynh, T. T., Lee, W. H., Chiou, J. F., Lin, Y. K., Hsiao, M., Wu, C. H., Lin, Y. F., Wu, A. T. et al. (2013c). Blue berry isolate, pterostilbene, functions as a potential anticancer stem cell agent in suppressing irradiation-mediated enrichment of hepatoma stem cells. *Evidence-Based Comp. Alt. Med.* **2013**:258425.

Li, S. H., Fu, J., Watkins, D. N., Srivastava, R. K. and Shankar, S. (2013). Sulforaphane regulates self-renewal of pancreatic cancer stem cells through the modulation of Sonic hedgehog-GLI pathway. *Mol. Cell Biochem.* **373**(1–2):217–227.

Lim, K. J., Bisht, S., Bar, E. E., Maitra, A. and Eberhart, C. G. (2011). A polymeric nanoparticle formulation of curcumin inhibits growth, clonogenicity and stem-like fraction in malignant brain tumors. *Cancer Biol. Ther.* **11**(5):464–473.

Link, A., Balaguer, F. and Goel, A. (2010). Cancer chemoprevention by dietary polyphenols: Promising role for epigenetics. *Biochem. Pharmacol.* **80**(12):1771–1792.

Liu, R. H. (2003). Health benefits of fruit and vegetables are from additive and synergistic combinations of phytochemicals. *Am. J. Clin. Nutr.* **78** (3 Suppl):517S–520S.

Liu, R. H. (2004a). Potential synergy of phytochemicals in cancer prevention: Mechanism of action. *J Nutr.* **134**(12 Suppl):3479S–3485S.

Liu, R. H. (2004b). Potential synergy of phytochemicals in cancer prevention: Mechanism of action 1. *J. Nutr.* 3479–3485.

Liu, R. H. (2013). Dietary bioactive compounds and their health implications. *J. Food Sci.* **78**(s1):A18–A25.

Liu, A. G., Volker, S. E., Jeffery, E. H. and Erdman, J. W., Jr. (2009a). Feeding tomato and broccoli powders enriched with bioactives improves bioactivity markers in rats. *J. Agric. Food Chem.* **57**(16):7304–7310.

Liu, L. H., Zabaras, D., Bennett, L. E., Aguas, P. and Woonton, B. W. (2009b). Effects of UV-C, red light and sun light on the carotenoid content and physical qualities of tomatoes during post-harvest storage. *Food Chem.* **115**(2):495–500.

Li, Y. Y., Wicha, M. S., Schwart, S. J. and Sun, D. X. (2011a). Implications of cancer stem cell theory for cancer chemoprevention by natural dietary compounds. *J. Nutr. Biochem.* **22**(9):799–806.

Li, Y., Wicha, M. S., Schwartz, S. J. and Sun, D. (2011b). Implications of cancer stem cell theory for cancer chemoprevention by natural dietary compounds. *J. Nutr. Biochem.* **22**(9):799–806.

Li, Y. and Zhang, T. (2013). Targeting cancer stem cells with sulforaphane, a dietary component from broccoli and broccoli sprouts. *Future Oncol.* **9**(8):1097–1103.

Li, Y., Zhang, T., Korkaya, H., Liu, S., Lee, H. F., Newman, B., Yu, Y., Clouthier, S. G., Schwartz, S. J., Wicha, M. S. et al. (2010). Sulforaphane, a dietary component of broccoli/broccoli sprouts, inhibits breast cancer stem cells. *Clin. Cancer Res.* **16**(9):2580–2590.

Lonn, E., Bosch, J., Yusuf, S., Sheridan, P., Pogue, J., Arnold, J., Ross, C., Arnold, A., Sleight, P., Probstfield, J. et al. (2005). Effects of long-term vitamin E supplementation on cardiovascular events and cancer: A randomized controlled trial. *JAMA.* **293**:1338.

Lyons, M. M., Yu, C., Toma, R. B., Cho, S. Y., Reiboldt, W., Lee, J. and van Breemen, R. B. (2003). Resveratrol in raw and baked blueberries and bilberries. *J. Agric. Food Chem.* **51**(20):5867–5870.

Madiwale, G. P., Reddivari, L., Holm, D. G. and Vanamala, J. (2011). Storage elevates phenolic content and antioxidant activity but suppresses antiproliferative and pro-apoptotic properties of colored-flesh potatoes against human colon cancer cell lines. *J. Agr. Food Chem.* **59**:8155–8166.

Madiwale, G. P., Reddivari, L., Stone, M., Holm, D. G. and Vanamala, J. (2012). Combined effects of storage and processing on the bioactive compounds and pro-apoptotic properties of color-fleshed potatoes in human colon cancer cells. *J. Agric. Food Chem.* **60**(44):11088–11096.

Mak, K. K., Wu, A. T., Lee, W. H., Chang, T. C., Chiou, J. F., Wang, L. S., Wu, C. H., Huang, C. Y., Shieh, Y. S., Chao, TY et al. (2013). Pterostilbene, a bioactive component of blueberries, suppresses the generation of breast cancer stem cells within tumor microenvironment and metastasis via modulating NF-kappaB/microRNA 448 circuit. *Mol. Nutr. Food Res.* **57**(7):1123–1134.

Marangoni, F. and Poli, A. (2010). Phytosterols and cardiovascular health. *Pharmacol. Res.* **61**(3):193–199.

Massey, A. R., Reddivari, L. and Vanamala, J. (2014). The dermal layer of sweet sorghum (sorghum bicolor) stalk, a byproduct of biofuel production and source of unique 3-deoxyanthocyanidins, has more antiproliferative and proapoptotic activity than the pith in p53 variants of HCT116 and colon cancer stem cells. *J. Agric. Food Chem.*

Meyskens, F. L. and Szabo, E. (2005). Diet and cancer: The disconnect between epidemiology and randomized clinical trials. *Cancer Epidemiol. Biomarkers. Prev.* **14**:1366–1369.

Miller, E. G., Peacock, J. J., Bourland, T. C., Taylor, S. E., Wright, J. M. and Patil, B. S. (2008). Inhibition of oral carcinogenesis by citrus flavonoids. *Nutr. Cancer.* **60**(1):69–74.

Mineva, N. D., Paulson, K. E., Naber, S. P., Yee, A. S. and Sonenshein, G. E. (2013). Epigallocatechin-3-gallate inhibits stem-like inflammatory breast cancer cells. *PLoS One.* **8**(9):e73464.

Modern Agriculture. (2011). Ecological impacts and the possibilities for truly sustainable farming (Modern Agriculture: Ecological impacts and the possibilities for truly sustainable farming). http://agroeco.org/wp-content/uploads/2011/02/ecol_impact_modern_ag.pdf

Mondoulet, L., Paty, E., Drumare, M. F., Ah-Leung, S., Scheinmann, P., Willemot, R. M., Wal, J. M. and Bernard, H. (2005). Influence of thermal processing on the allergenicity of peanut proteins. *J. Agric. Food Chem.* **53**(11):4547–4553.

Montales, M. T., Rahal, O. M., Kang, J., Rogers, T. J., Prior, R. L., Wu, X. and Simmen, R. C. (2012). Repression of mammosphere formation of human breast cancer cells by soy isoflavone genistein and blueberry polyphenolic acids suggests diet-mediated targeting of cancer stem-like/progenitor cells. *Carcinogenesis.* **33**(3):652–660.

Montales, M. T., Rahal, O. M., Nakatani, H., Matsuda, T. and Simmen, R. C. (2013). Repression of mammary adipogenesis by genistein limits mammosphere formation of human MCF-7 cells. *J. Endocrinol.* **218** (1):135–149.

Nair, V., Dai, Z., Khan, M. and Ciolino, H. P. (2011). Pomegranate extract induces cell cycle arrest and alters cellular phenotype of human pancreatic cancer cells. *Anticancer Res.* **31**(9):2699–2704.

Netzel, A., Strass, G., Bitsch, I., Konitz, R., Christmann, M. and Bitsch, R. (2003). Effect of grape processing on selected antioxidant phenolics in red wine. *J. Food Eng.* **56**(2–3):223–228.

Nguyen, M. L. and Schwartz, S. J. (1998). Lycopene stability during food processing. *P Soc. Exp. Biol. Med.* **218**(2):101–105.

Nhung, D. T. T., Bung, P. N., Ha, N. T. and Phong, T. K. (2010). Changes in lycopene and beta carotene contents in aril and oil of gac fruit during storage. *Food Chem.* **121**(2):326–331.

Omenn, G. S., Goodman, G. E., Thornquist, M. D., Balmes, J., Cullen, M. R., Glass, A., Keogh, J. P., Meyskens, F. L., Valanis, B., Williams, J. H. et al. (1996). Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. *NEJM.* **334**:1150–1155.

Oufedjikh, H., Mahrouz, M., Lacroix, M., Amiot, M. J. and Taccini, M. (1998). The influence of gamma irradiation on flavonoids content during storage of irradiated clementina. *Radiat. Phys. Chem.* **52**(1–6):107–112.

Palli, D., Russo, A. and Decarli, A. (2001). Dietary patterns, nutrient intake and gastric cancer in a high-risk area of Italy. *Cancer Cause Control.* **12**(2):163–172.

Paluszczak, J., Krajka-Kuzniak, V., Baer-Dubowska, W. (2010). The effect of dietary polyphenols on the epigenetic regulation of gene expression in MCF7 breast cancer cells. *Toxicol. Lett.* **192**(2):119–125.

Pandey, P. R., Okuda, H., Watabe, M., Pai, S. K., Liu, W., Kobayashi, A., Xing, F., Fukuda, K., Hirota, S., Sugai, T. et al (2011). Resveratrol suppresses growth of cancer stem-like cells by inhibiting fatty acid synthase. *Breast Cancer Res. Treatment.* **130**(2):387–398.

Park, S., Kim, J. and Kim, Y. (2012). Mulberry leaf extract inhibits cancer cell stemness in neuroblastoma. *Nutr. Cancer.* **64**(6):889–898.

Patel, B. B., Gupta, D., Elliott, A. A., Sengupta, V., Yu, Y. and Majumdar, A. P. (2010a). Curcumin targets FOLFOX-surviving colon cancer cells via inhibition of EGFRs and IGF-1R. *Anticancer Res.* **30**(2):319–325.

Patel, V. B., Misra, S., Patel, B. B. and Majumdar, A. P. (2010b). Colorectal cancer: Chemopreventive role of curcumin and resveratrol. *Nutr. Cancer.* **62**(7):958–967.

Patil, B. S., Jayaprakasha, G. K., Chidambara Murthy, K. N. and Vikram, A. (2009). Bioactive compounds: Historical perspectives, opportunities, and challenges. *J. Agric. Food Chem.* **57**(18):8142–8160.

Patras, A., Brunton, N. P., Da Pieve, S. and Butler, F. (2009). Impact of high pressure processing on total antioxidant activity, phenolic, ascorbic acid, anthocyanin content and colour of strawberry and blackberry purées. *Inn. Food Sci. Emerging Tech.* **10**(3):308–313.

Perez, J. L., Jayaprakasha, G. K., Cadena, A., Martinez, E., Ahmad, H. and Patil, B. S. (2010). In vivo induction of phase II detoxifying enzymes, glutathione transferase and quinone reductase by citrus triterpenoids. *BMC Complement Altern. Med.* **10**:51.

Perez, J. L., Jayaprakasha, G. K., Valdivia, V., Munoz, D., Dandekar, D. V., Ahmad, H. and Patil, B. S. (2009). Limonin methoxylation influences the induction of glutathione S-transferase and quinone reductase. *J. Agric. Food Chem.* **57**(12):5279–5286.

Pistollato, F., Giampieri, F. and Battino, M. (2015). The use of plant-derived bioactive compounds to target cancer stem cells and modulate tumor microenvironment. *Food Chem. Toxicol.* **75**(0):58–70.

Plaza, L., Crespoa, I., Pascual-Teresaa, S., De Ancos, B., Sánchez-Morenoa, M., Muñoza, M. and Cano, M. P. (2011). Impact of minimal processing on orange bioactive compounds during refrigerated storage. *Food Chem.* **124**(2):646–651.

Potato Statistical Yearbook. (2008). In.: National Potato Council (NPC); 2008.

Puuponen-Pimia, R., Hakkinen, S. T., Aarni, M., Suortti, T., Lampi, A. M., Eurola, M., Piironen, V., Nuutila, A. M. and Oksman-Caldentey, K. M. (2003). Blanching and long-term freezing affect various bioactive compounds of vegetables in different ways. *J. Sci. Food Agr.* **83**(14):1389–1402.

Radhakrishnan, S., Reddivari, L., Sclafani, R., Das, U. N. and Vanamala, J. (2011). Resveratrol potentiates grape seed extract induced human colon cancer cell apoptosis. *Front. Biosci.* **3**:1509–1523.

Rapisarda, P., Bianco, M. L., Pannuzzo, P. and Timpanaro, N. (2008). Effect of cold storage on vitamin C, phenolics and antioxidant activity of five orange genotypes (Citrus sinensis (L.) Osbeck). *Postharvest. Biol. Tec.* **49**(3):348–354.

Reddivari, L., Hale, A. L. and Miller, J. C., Jr. (2007a). Genotype, location, and year influence antioxidant activity, carotenoid content, phenolic content, and composition in specialty potatoes. *J. Agric. Food Chem.* **55**(20):8073–8079.

Reddivari, L., Vanamala, J., Chintharlapalli, S., Safe, S. H., Miller, J. C., Jr. (2007b). Anthocyanin fraction from potato extracts is cytotoxic to prostate cancer cells through activation of caspase-dependent and caspase-independent pathways. *Carcinogenesis.* **28**(10):2227–2235.

Rodova, M., Fu, J., Watkins, D. N., Srivastava, R. K. and Shankar, S. (2012). Sonic hedgehog signaling inhibition provides opportunities for targeted therapy by sulforaphane in regulating pancreatic cancer stem cell self-renewal. *PLoS One.* **7**(9):e46083.

Rodrigues, A. S. and Rosa, E. A. S. (1999). Effect of post-harvest treatments on the level of glucosinolates in broccoli. *J. Sci. Food Agr.* **79**(7):1028–1032.

Ross, S. A., Dwyer, J., Umar, A., Kagan, J., Verma, M., Van Bemmel, D. M. and Dunn, B. K. (2008). Introduction: Diet, epigenetic events and cancer prevention. *Nutrition. Rev.* **66**(Suppl 1):S1–S6.

Rytel, E. (2012). Changes in the levels of glycoalkaloids and nitrates after the dehydration of cooked potatoes. *Am. J. Potato Res.* **89**(6):501–507.

Sanchez-Ballesta, M. T., Jimenez, J. B., Romero, I., Orea, J. M., Maldonado, R., Urena, A. G., Escribano, M. I. and Merodio, C. (2006). Effect of high CO_2 pretreatment on quality, fungal decay and molecular regulation of stilbene phytoalexin biosynthesis in stored table grapes. *Postharvest. Biol. Tec.* **42**(3):209–216.

Santhakumar, A. B., Kundur, A. R., Fanning, K., Netzel, M., Stanley, R. and Singh, I. (2015). Consumption of anthocyanin-rich Queen Garnet plum juice reduces platelet activation related thrombogenesis in healthy volunteers. *J. Func. Foods.* **12**(0):11–22.

Schierle, J., Bretzel, W., Buhler, I., Faccin, N., Hess, D., Steiner, K. and Schuep, W. (1997). Content and isomeric ratio of lycopene in food and human blood plasma. *Food Chem.* **59**(3):459–465.

Shankar, S., Nall, D., Tang, S. N., Meeker, D., Passarini, J., Sharma, J. and Srivastava, R. K. (2011). Resveratrol inhibits pancreatic cancer stem cell characteristics in human and KrasG12D transgenic mice by inhibiting pluripotency maintaining factors and epithelial-mesenchymal transition. *PLoS One.* **6**(1):e16530.

Sharif, T., Auger, C., Bronner, C., Alhosin, M., Klein, T., Etienne-Selloum, N., Schini-Kerth, V. and Fuhrmann, G. (2011a). Selective proapoptotic activity of polyphenols from red wine on teratocarcinoma cell, a model of cancer stem-like cell. *Investigational New Drugs.* **29**(2):239–247.

Sharif, T., Auger, C., Bronner, C., Alhosin, M., Klein, T., Etienne-Selloum, N., Schini-Kerth, V. B. and Fuhrmann, G. (2011b). Selective proapoptotic activity of polyphenols from red wine on teratocarcinoma cell, a model of cancer stem-like cell. *Investigational New Drugs.* **29**(2):239–247.

Shen, Y.-A., Lin, C.-H., Chi, W.-H., Wang, C.-Y., Hsieh, Y.-T., Wei, Y.-H. and Chen, Y-J (2013). Resveratrol impedes the stemness, epithelial-mesenchymal transition, and metabolic reprogramming of cancer stem cells in nasopharyngeal carcinoma through p53 activation. *Evidence-Based Comp. Alt. Med.* **2013**:13.

Shimizu, H., Ross, R. K., Bernstein, L., Yatani, R., Henderson, B. E. and Mack, T. M. (1991). Cancers of the prostate and breast among Japanese and white immigrants in Los Angeles County. *British. J. Cancer.* **63**(6):963–966.

Song, L. and Thornalley, P. J. (2007). Effect of storage, processing and cooking on glucosinolate content of Brassica vegetables. *Food Chem. Toxicol.* **45**:216–224.

Srivastava, R. K., Tang, S. N., Zhu, W., Meeker, D. and Shankar, S. (2011). Sulforaphane synergizes with quercetin to inhibit self-renewal capacity of pancreatic cancer stem cells. *Front. Biosci.* **3**:515–528.

Stringheta, Â., Branda, Â. C., Maria, H., Sant, P. and Ce, P. (1998). Carotenoid retention and vitamin a value in carrot (Daucus carota L.) prepared by food service. *Science.* 61.

Tang, S. N., Singh, C., Nall, D., Meeker, D., Shankar, S. and Srivastava, R. K. (2010). The dietary bioflavonoid quercetin synergizes with epigallocathechin gallate (EGCG) to inhibit prostate cancer stem cell characteristics, invasion, migration and epithelial-mesenchymal transition. *J. Mol. Signaling.* **5**:14.

Tareke, E., Rydberg, P., Karlsson, P., Eriksson, S. and Tornqvist, M. (2002). Analysis of acrylamide, a carcinogen formed in heated foodstuffs. *J. Agric. Food Chem.* **50**(17):4998–5006.

Türkben, C., Sarıburun, E. and Demir, C. (2010). Effect of freezing and frozen storage on phenolic compounds of raspberry and blackberry cultivars. *Methods.* 144–153.

Valcarcel, J., Reilly, K., Gaffney, M. and O'Brien, N. (2014). Effect of genotype and environment on the glycoalkaloid content of rare, heritage, and commercial potato varieties. *J. Food Sci.* **79**(5):T1039–T1048.

Vallejo, F., Tomas-Barberan, F. and Garcia-Viguera, C. (2003a). Health-promoting compounds in broccoli as influenced by refrigerated transport and retail sale period. *J. Agr. Food Chem.* **51**(10):3029–3034.

Vallejo, F., Tomás-Barberán, F. A. and García-Viguera, C. (2003b). Phenolic compound contents in edible parts of broccoli inflorescences after domestic cooking. *J. Sci. Food Agr.* **83**:1511–1516.

Vanamala, J., Cobb, G., Turner, N. D., Lupton, J. R., Yoo, K. S., Pike, L. M. and Patil, B. S. (2005). Bioactive compounds of grapefruit (Citrus paradisi Cv. Rio red) respond differently to postharvest irradiation, storage, and freeze drying. *J. Agric. Food Chem.* **53**(10):3980–3985.

Vanamala, J., Leonardi, T., Patil, B. S., Taddeo, S. S., Murphy, M. E., Pike, L. M., Chapkin, R. S., Lupton, J. R. and Turner, N. D. (2006). Suppression of colon carcinogenesis by bioactive compounds in grapefruit. *Carcinogenesis.* **27**(6):1257–1265.

Vanamala, J., Reddivari, L., Radhakrishnan, S. and Tarver, C. (2010). Resveratrol suppresses IGF-1 induced human colon cancer cell proliferation and elevates apoptosis via suppression of IGF-1R/Wnt and activation of p53 signaling pathways. *BMC Cancer.* **10**:238.

Vanamala, J., Tarver, C. C. and Murano, P. S. (2008). Obesity-enhanced colon cancer: Functional food compounds and their mechanisms of action. *Curr. Cancer Drug Targets.* **8**(7):611–633.

Venkateswaran, V. and Klotz, L. H. (2010). Diet and prostate cancer: Mechanisms of action and implications for chemoprevention. *Nat. Rev. Urol.* **7**(8):442–453.

Verkerk, R. and Dekker, M. (2008). Glucosinolates. In: *Bioactive Compounds in Foods*. edn. Edited by Gilbert, J. and Senyuva, H. Z. Oxford, UK: Blackwell Publishing; 31–47.

Verkerk, R., Dekker, M. and Jongen, W. M. F. (2001). Post-harvest increase of indolyl glucosinolates in response to chopping and storage of Brassica vegetables. *J. Sci. Food Agr.* **81**(9):953–958.

Verkerk, R., Schreiner, M., Krumbein, A., Ciska, E., Holst, B., Rowland, I., De Schrijver, R., Hansen, M., Gerhauser, C., Mithen, R. et al. (2009). Glucosinolates in Brassica vegetables: The influence of the food supply chain on intake, bioavailability and human health. *Mol. Nutr. Food Res.* **53**(Suppl 2):S219.

Verkerk, R., vander Gaag, M. S., Dekker, M. and Jongen, W. M. F. (1997). Effects of processing conditions on glucosinolates in cruciferous vegetables. *Cancer Lett.* **114**(1–2):193–194.

Vieira, F. G. K., Borges, G. D. C., Copetti, C., Amboni, R. D. D. C., Denardi, F. and Fett, R. (2009). Physico-chemical and antioxidant properties of six apple cultivars (Malus domestica Borkh) grown in southern Brazil. *Sci. Hortic. Amsterdam.* **122**(3):421–425.

Volden, J., Borge, G. I. A., Bengtsson, G. B., Hansen, M., Thygesen, I. E. and Wicklund, T. (2008). Effect of thermal treatment on glucosinolates and antioxidant-related parameters in red cabbage (Brassica oleracea L. ssp capitata f. rubra). *Food Chem.* **109**(3):595–605.

Voutilainen, S., Nurmi, T., Mursu, J. and Rissanen, T. H. (2006). Carotenoids and cardiovascular health. *Am. J. Clin. Nutr.* **83**(6):1265–1271.

Walton, M. C., Lentle, R. G., Reynolds, G. W., Kruger, M. C. and McGhie, T. K. (2006). Anthocyanin absorption and antioxidant status in pigs. *J. Agric. Food Chem.* **54**(20):7940–7946.

Wang, J.-Y., Chang, C.-C., Chiang, C.-C., Chen, W.-M. and Hung, S.-C. (2012). Silibinin suppresses the maintenance of colorectal cancer stem-like cells by inhibiting PP2A/AKT/mTOR pathways. *J. Cell Biochem.* **113**(5):1733–1743.

Wang, S. Y. and Lewers, K. S. (2007). Antioxidant capacity and flavonoid content in wild strawberries. *J. Am. Soc. Hortic. Sci.* **132**(5):629–637.

Wang, D., Upadhyaya, B., Liu, Y., Knudsen, D. and Dey, M. (2014). Phenethyl isothiocyanate upregulates death receptors 4 and 5 and inhibits proliferation in human cancer stem-like cells. *BMC Cancer.* **14**:591.

Weisel, T., Baum, M., Eisenbrand, G., Dietrich, H., Will, F., Stockis, J. P., Kulling, S., Rufer, C., Johannes, C. and Janzowski, C. (2006). An anthocyanin/polyphenolic-rich fruit juice reduces oxidative DNA damage and increases glutathione level in healthy probands. *Biotechnol. J.* **1** (4):388–397.

White, B. L., Howard, L. R. and Prior, R. L. (2011). Impact of different stages of juice processing on the anthocyanin, flavonol, and procyanidin contents of cranberries. *J. Agric. Food Chem.* **59**:4692–4698.

Wicha, M. S., Liu, S. L. and Dontu, G. (2006). Cancer stem cells: An old idea—A paradigm shift. *Cancer Res.* **66**(4):1883–1890.

Wu, R. Y., Frei, B., Kennedy, J. A. and Zhao, Y. Y. (2010). Effects of refrigerated storage and processing technologies on the bioactive compounds and antioxidant capacities of 'Marion' and 'Evergreen' blackberries. *Lwt-Food Sci. Technol.* **43**(8):1253–1264.

Yadav, S. K. and Sehgal, S. (1995). Effect of home processing on ascorbic acid and beta-carotene content of spinach (*Spinacia oleracia*) and amaranth (*Amaranthus tricolor*) leaves. *Plant Foods Hum. Nutr.* **47**(2):125–131.

Yu, J. M., Ahmedna, M. and Goktepe, P. (2005). Effects of processing methods and extraction solvents on concentration and antioxidant activity of peanut skin phenolics. *Food Chem.* **90**(1–2):199–206.

Yu, Y., Kanwar, S. S., Patel, B. B., Nautiyal, J., Sarkar, F. H. and Majumdar, A. P. N. (2009). Elimination of colon cancer stem-like cells by the combination of curcumin and FOLFOX. *Translational. Oncol.* **2**(4):321–328.

Zhang, D. L., Quantick, P. C. and Grigor, J. M. (2000). Changes in phenolic compounds in Litchi (*Litchi chinensis* Sonn.) fruit during postharvest storage. *Postharvest. Biol. Tec.* **19**(2):165–172.

Zhou, W., Kallifatidis, G., Baumann, B., Rausch, V., Mattern, J., Gladkich, J., Giese, N., Moldenhauer, G., Wirth, T., Buchler, M. W. et al. (2010). Dietary polyphenol quercetin targets pancreatic cancer stem cells. *Int. J. Oncol.* **37**(3):551–561.

Zhou, B. B. S., Zhang, H., Damelin, M., Geles, K. G., Grindley, J. C. and Dirks, P. B. (2009). Tumour-initiating cells: Challenges and opportunities for anticancer drug discovery. *Nat. Rev. Drug Dis.* **8**(10):806–823.