

CONTINUING EDUCATION

Integrative Review of Lycopene and Breast Cancer

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Purpose/Objectives: To perform an integrative research analysis of the literature regarding lycopene, its antioxidant capacity, and its nutritive and physiologic effects on breast cancer.

Data Sources: Articles published from 1990–2004 using PubMed as the primary retrieval base.

Data Synthesis: Forty articles were retrieved and a dimensional analysis was performed based on Fawcett's integrative review process that focused on the following categories: antioxidant, bioavailability, breast cancer risk, and dietary factors.

Conclusions: Noted gaps in the literature included lack of a theoretical model and multiple nutritional variables studied that affected statistical interpretation and application. Findings suggest that additional research is needed to effectively study the specific phytochemical attributes of lycopene with regard to breast cancer.

Implications for Nursing: The emerging area of health-derived benefits from food sources such as lycopene requires additional inquiry into the examination of physiological and nutritional parameters. Nurses should include antioxidant therapy in their base of knowledge when caring for patients with breast cancer.

Lycopene, a phytochemical with antioxidant properties, has been placed in the spotlight by clinical researchers and the general public and has emerged as a separate point of interest from the general category of carotenoids in the areas of cardiovascular disease and cancer. Recognition of its antioxidant ability has been demonstrated consistently in the literature (Agarwal & Rao, 2000). Initial research in this arena focused on evaluation of physiologic parameters of evidence via chemical assays to note relative effects from a biochemical perspective as well as dietary interventions from a behavioral perspective. This review of research focuses on lycopene in the context of its antioxidant capacity and its nutritive and physiologic effects on breast cancer.

Breast cancer is the leading cancer diagnosed and the second leading cause of cancer death among American women and the leading cause of death among African American women (Simmonds, 2003). The number of people living with cancer is estimated to double from 2000–2050 (Simmonds). Because breast cancer is known to be a current international health problem, improving protocols of treatment and preventing recurrence are important. Although many people (both male and female) die from breast cancer, many also live with and after the diagnosis. Any possible scientific trends that could affect prevention as well as treatment of the disease should be explored.

Key Points . . .

- ▶ The majority of studies pertinent to dietary lycopene and breast cancer from 1990–2004 had significant findings related to variable factors such as lycopene bioactivity, chemoprotective effects, and dietary consumption.
- ▶ Continued research specifically in the area of lycopene and incorporation of nutritional therapies in the care and treatment of patients with breast cancer should be included in oncology nurses' plan of care.

Goal for CE Enrollees

To enhance the nurse's knowledge about research regarding lycopene and breast cancer risk

Objectives for CE Enrollees

1. Discuss study findings related to the antioxidant properties of lycopene and breast cancer risk.
2. Discuss study findings related to the relationship between nutritional intake of lycopene and breast cancer risk.
3. Define limitations to the generalization of study findings related to lycopene and breast cancer risk.

Retrieval of Studies

For the integrative research review, an initial search was performed using PubMed as the primary electronic database. The search fields and numbers of articles found included lycopene (1,279 items), antioxidant (111,797 items), nutrition (208,354

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Digital Object Identifier: 10.1188/06.ONF.127-137

items), breast cancer (125,660 items), and randomized clinical trial (RCT) (1,282 items). A combination search was performed focusing on lycopene, antioxidant, and breast cancer that revealed 36 articles. A further restrictive combination search added nutrition to the list and yielded nine. Additionally, a search was run focusing on lycopene and RCT that yielded 13. A dual combination search was run using lycopene and diet (365 items) and lycopene and nutrition (299); however, many of the articles listed did not have lycopene as a focus and therefore were excluded from the main retrieval pool.

Some duplicate items were noted on the searches, and other items were excluded when viewed in the context of the review because of language issues, nonresearch study material, comparative review analysis material, inclusion of other diseases (e.g., cardiovascular problems) as the focus of the research, or use of lycopene in a supplemental form. The final item count yielded 40 studies for consideration. No limit was set with regard to time frame during the search procedure; subsequently, the items chosen were published from 1990–2004. PubMed was chosen as the primary electronic database because of its organizational structure of current publications and its ability to combine search materials and provide abstracts or direct-access links, related articles, and links for further applications.

Inclusion criteria for the integrative review were the combined concept linkage of lycopene, antioxidant, breast cancer, and nutrition. Animal and cell models were included along with male and female human subjects. Bioavailability studies pertaining to lycopene also were included because they contributed to the focus of antioxidant and nutritive effects. Exclusion criteria for the integrative review were foreign language material, primary use of lycopene in a supplementation form, and items found to have a primary focus on disease processes other than breast cancer. Funding status and characteristics of each study (references to department and university listing) were noted but did not influence selection into the retrieval pool.

Classification of Research

One of the most readily apparent gaps was the lack of conceptual models or theoretical frameworks for any of the studies listed in this review. Many of the studies in the review represented a collaborative interdisciplinary approach with their introductions focusing on review of the literature and physiologic evidence.

The examination of study characteristics such as funding status, publication status, and authorship expertise were assessed according to the recommendations of Fawcett's (1999) integrative review process. Of the 40 studies cited in this review, only 4 (10%) had no listed funding sources. Eight studies (20%) had international funding sources, and the remaining 28 studies (70%) had funding sources in the United States; the majority of these had multiple funding sources. Only two of the studies (5%) did not have an identified university listing but were affiliated with a research apprenticeship or a pharmaceutical company. All of the studies were published in journals, the majority of which were peer reviewed. Only one of the studies (La Vecchia, 2002) had a single author. When considering the aspect of the expertise of the authors, the majority had numerous publications as primary and secondary authors. Based on multiple search attempts, each of the authors was found repeatedly in query results; therefore, all were considered "published" experts in the field.

Although conceptual models or theory were not mentioned, aims or purposes were stated for the studies (see Table 1). References to reactive oxidative stress, oxidative damage, and immunologic systems were emphasized in four (10%) of the studies (Hadley, Clinton, & Schwartz, 2003; McMillan et al., 2002; Pellegrini, Riso, & Porrini, 2000; Ringer et al., 1991), whereas the rest of the studies focused on nutrient serum levels and biochemical markers as their basis of comparison. Six of the studies (15%) examined bioavailability issues related to lycopene (Djuric & Powell, 2001; Edwards et al., 2003; Hadley et al.; Ito, Gajalakshmi, Sasaki, Suzuki, & Shanta, 1999; Paetau et al., 1998; Porrini, Riso, & Testolin, 1998; Ronco et al., 1999). Six of the studies (15%) explored the antioxidant role of lycopene (Ching, Ingram, Hahnel, Beilby, & Rossi, 2002; La Vecchia, 2002; McMillan et al.; Pellegrini et al.; Rao & Agarwal, 1998; Ringer et al.). Only one of the studies had a specific focus on ethnicity as a factor in antioxidant levels and breast cancer risk (Simon et al., 2000). Three of the studies (7.5%) focused on cellular models for analysis of the effects of lycopene (Karas et al., 2000; Levy et al., 1995; Prakash, Russell, & Krinsky, 2001). The majority of the studies focused on two main areas: the risk for developing breast cancer or recurrence and the impact of dietary factors. Several of the studies overlapped in both dimensions (see Table 2).

Statistical references to significant and nonsignificant findings were reported, although they were not always easily identifiable in the context of the study. Only 13 of the studies (33%) had lycopene as their primary research focus (Cohen, Zhao, Pittman, & Khachik, 1999; Djuric & Powell, 2001; Edwards et al., 2003; Hadley et al., 2003; Karas et al., 2000; La Vecchia, 2002; Levy et al., 1995; Mayne et al., 1999; Paetau et al., 1998; Pellegrini et al., 2000; Porrini et al., 1998; Rao & Agarwal, 1998), whereas the rest of the studies included the measurement of lycopene levels as part of other selected micronutrient assays.

Regarding examination of scientific data, most of the studies used multiple method approaches with detailing of statistical tests based on group comparison and identification of variables. Several of the studies reflected log transformation of data (Cohen et al., 1999; Edwards et al., 2003; London et al., 1992; McEligot, Rock, Flatt, et al., 1999; Paetau et al., 1998; Pierce et al., 2004; Potischman et al., 1990, 1992), dummy coding (Ching et al., 2002; Dorgan et al., 1998; Hulten et al., 2001), the Cox proportional hazards model (Horn-Ross et al., 2002; Hulten et al.; Jarvinen, Knekt, Seppanen, & Teppo, 1997; Pierce et al., 2002), the Wilcoxon rank test (Mayne et al., 1999; Sato et al., 2002; Simon et al., 2000), and the use of post hoc tests (Djuric & Powell, 2001; Paetau et al.; Rao & Agarwal, 1998). Only two studies specified power analysis (McEligot, Rock, Flatt, et al.; Pierce et al., 2002) in the context of statistical interpretation of data. Levy et al. (1995) used plotted graph summaries to represent scientific data that reflected information regarding specific biochemical assays as the primary method of statistical analysis.

Although reports of significant and nonsignificant statistical findings were found in all of the abstracts, on inspection of the actual studies, some of these findings were not easily apparent on the first read through. Because many of the studies looked at multiple variables of consideration in reference to dietary intake composition, the reporting of individual statistical tests was easy to understand. In addition, variables other than dietary intake were considered in many of the studies, such

Table 1. Stated Aims and Purposes of the Studies

Study	Aims and Purposes	Study	Aims and Purposes
Ching et al., 2002	Comparison of total antioxidant status to individual micronutrient serum level and antioxidant capacity and possible impact on prevention of breast cancer		predictors that might have affected serum measurements during course of study as well as the impact of a high-vegetable diet on breast cancer recurrence
Cohen et al., 1999	Comparison of inhibitory effects of dietary lycopene using an animal model on mammary tumorigenesis	McEligot, Rock, Shanks, et al., 1999	Dietary intervention to decrease risk of recurrence of breast cancer in women previously diagnosed in the Women's Healthy Eating and Living (WHEL) study
Djuric & Powell, 2001	Measurement of total antioxidant capacity of lycopene in different foods	McMillan et al., 2002	Examination of the body's systemic inflammatory response to reduced vitamin antioxidant concentrations in clients with common solid tumors
Dorgan et al., 1998	Prospective evaluation of selected micronutrients (i.e., carotenoids, alpha-tocopherol, selenium, and retinal) and breast cancer risk	Paetau et al., 1998	Comparison of plasma responses from lycopene food sources and lycopene supplements and monitoring oxidation status of lycopene as a result of different concentrations
Edwards et al., 2003	Determination of the bioavailability of watermelon juice in comparison to tomato juice and whether an effective dose response associated with watermelon juice is dependent on measurement; comparison of watermelon with tomato juice in similar dosages	Pellegrini et al., 2000	Comparison of effective concentrations of dietary lycopene intake in a defined geographic area in Italy
Freudenheim et al., 1996	Discussion of the impact of dietary intake of selected micronutrients on cancer risk for premenopausal women	Pierce et al., 2002	Determination of the effectiveness of dietary intervention (high vegetable and low fat) on increasing plasma carotenoid concentrations in relation to reducing significant breast cancer events (recurrence and/or morbidity and mortality) (WHEL study)
Hadley et al., 2003	Exploration of the relationships among different processed tomato products in dietary intervention and as biomarkers of oxidative stress using a three-tiered approach: (a) lycopene-free diet, (b) stable lycopene diet, and (c) assessment of biomarkers following dietary intervention	Pierce et al., 2004	Description of the effect that the telephone-counseling intervention (used in the WHEL study) had on increasing intake of fruits and vegetables (an increase in phytochemicals)
Horn-Ross et al., 2002	Assessment of what role dietary impact may have played in breast cancer risk in the adult population of the California Teachers Study cohort	Porrini et al., 1998	Detection of differences in absorption of lycopene by reporting plasma concentrations in response to two food sources consumed either once a day or twice a day
Hulten et al., 2001	Determination of selected plasma micronutrients (six carotenoids, alpha-tocopherol, and retinal) consumed prior to a diagnosis of breast cancer with comparative evaluation of breast cancer risk	Potischman et al., 1990	Determination of the effectiveness of carotenoids and preformed vitamin A in the diet of patients with breast cancer while controlling for other selected risk factors and nutrients
Ito et al., 1999	Evaluation of serum micronutrient levels in women diagnosed with breast cancer in a defined geographic area of India (Chennai)	Potischman et al., 1992	Understanding of the significance of biochemical indicators of selected plasma nutrient levels on patients with breast cancer
Jarvinen et al., 1997	Examination of the association among dietary interventions (antioxidant vitamins, fiber, and selected foods) on breast cancer risk for a defined geographic population (Finnish women cohort)	Prakash et al., 2001	Use of a cellular model to determine the effects of carotenoids on estrogen-receptor positive and estrogen-receptor negative breast cancer cells
Karas et al., 2000	Study of the inhibitory effects of lycopene on basal and insulin-like growth factor 1-stimulated growth of MCF7 breast cancer cells	Rao & Agarwal, 1998	Identification of the effectiveness of dietary supplementation of healthy individuals with lycopene with regard to bioavailability and antioxidant status activities
La Vecchia, 2002	Determination of relationship between lycopene and selected cancers (digestive and female related) in a defined geographic area of Italy	Ringer et al., 1991	Determination of the effects of beta carotene on specified immunologic indexes in healthy individuals by (a) examining plasma concentrations responding to increased dosages, (b) examining quantitative measurements of immune function using chemical assays, and (c) examining effects of dosages on lipoprotein levels
Levi et al., 2001	Exploration of dietary composition of selected micronutrients related to breast cancer risk in a defined geographic area of Switzerland	Rock et al., 1997	Identification of relative factors associated with serum carotenoid levels in postsurgical patients with breast cancer previously enrolled in a dietary intervention study at 12 months (high-vegetable diet to minimize breast cancer risk) and to identify factors that may account for relative differences in selected micronutrient concentrations
Levy et al., 1995	Examination of the properties of lycopene as a potent inhibitor of cancer cells	Ronco et al., 1999	Determination of whether vegetable and fruit intake has a positive protective effect on breast cancer; if the effect is found, then to determine which micronutrients or substances account for this fact on a select geographic area in Uruguay
London et al., 1992	Assessment of breast cancer risk in relation to serum levels of selected micronutrients (i.e., retinol, carotenoids, and vitamin E)		
Mayne et al., 1999	Assessment of potential effects of selected physiologic and demographic factors on serum lycopene levels in an intervention cancer prevention trial		
McEligot, Rock, Flatt, et al., 1999	Determination of plasma carotenoid levels at baseline and serial measurement intervals on postsurgical patients with breast cancer; examination of potential		

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Table 1. Stated Aims and Purposes of the Studies (Continued)

Study	Aims and Purposes
Sato et al., 2002	Evaluation of effective concentrations of selected micronutrients (i.e., carotenoids, tocopherol, and retinoid) on risk of breast cancer development
Simon et al., 2000	Pilot study that (a) looked at the relationship between ethnicity (African American versus Caucasian) as a factor in plasma antioxidant levels and risk of breast cancer and (b) obtained preliminary data regarding selected micronutrient levels and risk of developing breast cancer
Terry et al., 2002	Determination of the effects of dietary intakes of selected carotenoids on breast cancer risk in a selected population (Canadian women cohort)
Thomson et al., 2003	Comparison of change in dietary interventions using the Arizona Food Frequency Questionnaire and repeat 24-hour telephone recalls as a subset of the WHEL study
Toniolo et al., 2001	Determination of whether dietary consumption of carotenoids (fruits and vegetables) had an etiologic impact on the development of breast cancer by looking at serum biochemical markers
van Kappel et al., 2001	Examination of the effectiveness of serum carotenoids as a biochemical marker of fruit and vegetable consumption as a part of the New York Women's Health Study cohort
Yeum et al., 1998	Comparative analysis of carotenoid concentrations in tissue samples of healthy patients with benign tumors or breast cancer looking at possible risk factor determination of breast cancer
Zhang et al., 1997	Examination of the relationship between adipose retinoid and carotenoid concentrations on risk of developing breast cancer by using a case control study approach

as demographic variables that were factored in as covariates in multivariate analyses. Fifteen of the studies (33%) reported nonsignificant findings specifically related to lycopene (Ching et al., 2002; Freudenheim et al., 1996; Horn-Ross et al., 2002; Jarvinen et al., 1997; London et al., 1992; McEligot, Rock, Shanks, et al., 1999; Pellegrini et al., 2000; Potischman et al., 1990; Ringer et al., 1991; Rock et al., 1997; Terry, Jain, Miller, Howe, & Rohan, 2002; Toniolo et al., 2001; Yeum et al., 1998; Zhang et al., 1997).

When assessing the magnitude of the findings presented in the selected studies, consideration was given to the fact that several of the studies were subsets of other larger RCTs (Horn-Ross et al., 2002; McEligot, Rock, Flatt, et al., 1999; McEligot, Rock, Shanks, et al., 1999; Pierce et al., 2004; Thomson et al., 2003; van Kappel et al., 2001); thus, the extent of the sample population and the timeframe duration of the study led to the possibility of improved generalizations concerning documented findings. One of the studies, the Women's Healthy Eating and Living (WHEL) study, still is ongoing (Pierce et al., 2002), and data collection is scheduled to end in 2006. Results published during the course of this prospective study are early yet reveal some interesting applications regarding this collective effort to implement a detailed intervention program looking at the impact of diet on breast cancer.

Integration of Research Findings

Because no conceptual model or theoretical framework exist to provide a cohesive structure for a qualitative integration of research findings, antioxidant, bioavailability, nutrition, and risk factors related to breast cancer will serve as the basis for discussion. Using this dimensional framework, the selected studies will be discussed in terms of clinical significance and general applications to real-world populations.

Research consistently has demonstrated that lycopene has a significant antioxidant capacity (Pellegrini et al., 2000), but it is just one component of human diets that include many other micronutrients with phytochemical activity. Although the effects of lycopene may be easier to isolate in an experimental setting, the real world of nutrition and diet is not as easily separated. Additionally, other concurrent or contributory factors such as age, gender, and general health status can act as potential confounders and therefore require the use of covariate analysis to determine relative influences on the dependent variables of interest.

Ching et al. (2002) reported that an increase in total antioxidant levels was correlated with a decreased risk with regard to the development of breast cancer but cited that no significant association with lycopene was noted. La Vecchia (2002) identified that the antioxidant effects of lycopene had an inverse relationship with digestive neoplasms, but no significant association was found between the antioxidant effects of lycopene and breast cancer. Although a large sample size (N = 6,572 for intervention group and N > 5,000 for control group) was used, the results of the study were directed at a specific geographic area in Italy and may have only limited generalizability to that population. McMillan et al. (2002) used a biochemical approach to studying the antioxidant capacity of lycopene, noting its potential effect on the systemic inflammatory response system. An inverse relationship was found to exist between adequate levels of lycopene and the presence of C-reactive protein as an oxidative stress marker. The sample size was 71 and included healthy subjects as well as those diagnosed with several different types of cancer. In another study by Pellegrini et al. (2000), a dietary intervention was used to determine potential differences in the antioxidant capacity of plasma resulting from varying methods of lycopene administration and found no statistically significant differences. The sample size was limited (N = 11) and consisted of only healthy female subjects, which may have contributed to the overall nonsignificant findings. Another small study by Rao and Agarwal (1998) that used healthy male and female subjects (N = 19) examined differences in absorption relative to multiple tomato products. Results found increased antioxidant effects. Ringer et al. (1991) also used healthy subjects (N = 50) but focused on the impact of lycopene on immunologic indexes in the human body. Although no effects were noted on immunologic indexes, lycopene was found to be the most prevalent carotenoid in the study. Again, the authors speculated whether the use of only healthy subjects with intact immune responses could appreciably show the projected effects of lycopene. Additionally, subjects were given differing levels of beta carotene and not specifically lycopene during the course of the study. Simon et al. (2000) also looked at the plasma antioxidant level of lycopene (as

Table 2. Dimensional Analysis of Studies

Study	Antioxidant	Bioavailability	Breast Cancer Risk	Dietary Factors	Overlap
Ching et al., 2002	X		X		X
Cohen et al., 1999		X	X		X
Djuric & Powell, 2001	X	X			X
Dorgan et al., 1998			X		
Edwards et al., 2003		X			
Freudenheim et al., 1996			X	X	X
Hadley et al., 2003		X		X	X
Horn-Ross et al., 2002			X	X	X
Hulten et al., 2001			X		
Ito et al., 1999			X	X	X
Jarvinen et al., 1997			X	X	X
Karas et al., 2000	X				
La Vecchia, 2002	X		X		X
Levi et al., 2001			X	X	X
Levy et al., 1995	X				
London et al., 1992			X	X	
Mayne et al., 1999				X	
McEligot, Rock, Flatt, et al., 1999				X	
McEligot, Rock, Shanks, et al., 1999				X	
McMillan et al., 2002	X				
Paetau et al., 1998		X			
Pellegrini et al., 2000	X				
Pierce et al., 2002			X	X	X
Pierce et al., 2004				X	
Porrini et al., 1998		X			
Potischman et al., 1990			X	X	X
Potischman et al., 1992			X	X	X
Prakash et al., 2001	X				
Rao & Agarwal, 1998	X				
Ringer et al., 1991	X				
Rock et al., 1997			X	X	X
Ronco et al., 1999			X	X	X
Sato et al., 2002			X		
Simon et al., 2000			X		
Terry et al., 2002			X		
Thomson et al., 2003				X	
Toniolo et al., 2001			X		
van Kappel et al., 2001			X	X	X
Yeum et al., 1998			X	X	X
Zhang et al., 1997			X		

well as other micronutrients), but those researchers were interested in determining whether an ethnic component was not being addressed with regard to differences between African American and Caucasian women. Findings of this pilot study revealed a significant interaction effect between race and lycopene when comparing the two groups of women ($p = 0.048$).

Cellular model studies also were included in the antioxidant dimension (Karas et al., 2000; Levy et al., 1995; Prakash et al., 2001) with each examining the effects of lycopene on large numbers of breast cancer cells. Karas et al. noted inhibitory effects of lycopene on MCF7 breast cancer cells caused by interference in insulin-like growth factor 1 receptor signaling and cycle progression. Levy et al. noted that lycopene exhibited greater potency than alpha and beta carotene in multiple cancer lines because of its effects on the autocrine and paracrine systems. Prakash et al. noted that lycopene had an inhibitory effect on estrogen-negative and estrogen-positive breast cancer cells. Although the cellular model studies are more physiologically driven, they serve as an important basis for examining

biochemical explanations and for future direction in applicable clinical research.

Considering the dimension of bioavailability, one of the studies focused specifically on food as the sample and used Trolox-equivalent antioxidant capacity assay to measure lycopene content and correlate it with antioxidant capacity (Djuric & Powell, 2001). Although this study did not have human subjects or a cellular model, the results revealed significant findings concerning high levels of total antioxidants but not specifically foods that had the highest individual concentrations of lycopene. Three of the studies focusing on bioavailability involved washout periods during the dietary intervention (Edwards et al., 2003; Hadley et al., 2003; Paetau et al., 1998; Porrini et al., 1998) in an attempt to prevent overlap effects resulting from group treatment. Edwards et al. found no difference in bioavailability of lycopene between watermelon and tomato juice in a small sample ($N = 22$) of men and women. Hadley et al. noted an increase in the bioavailability of lycopene in its isomeric form ($N = 60$). Paetau et al. found no difference in bioavailability of lycopene in a

small sample (N = 15) of healthy men and women. Porrini et al. noted that daily intake of a tomato puree led to increased bioavailability as a result of food processing in a small sample (N = 10) of healthy women. Ronco et al. (1999) used a larger sample size (N = 805) of women with case control comparison between healthy participants and those who had a diagnosis of cancer and found increased bioavailability in cooked tomato products that correlated with a significant reduction in breast cancer risk.

When examining the dimension of nutrition (diet) and breast cancer risk, many of the studies had overlapping elements. More than half of the studies (53%) used questionnaires as part of their research method of data collection (Freudenheim et al., 1996; Horn-Ross et al., 2002; Hulten et al., 2001; La Vecchia, 2002; Levi, Pasche, Lucchini, & La Vecchia, 2001; London et al., 1992; Mayne et al., 1999; McEligot, Rock, Flatt, et al., 1999; McEligot, Rock, Shanks, et al., 1999; Pierce et al., 2002; Potischman et al., 1990, 1992; Ronco et al., 1999; Sato et al., 2002; Simon et al., 2000; Terry et al., 2002; Thomson et al., 2003; Toniolo et al., 2001; van Kappel et al., 2001; Zhang et al., 1997), but only three of the studies provided some information relative to reliability or validity of the instrument (Horn-Ross et al.; La Vecchia; Mayne et al.).

Several of the studies examined selected factors as covariates in analysis ranging from other micronutrients, physical data calculations (e.g., anthropometrics, weight and body mass index), and demographic factors (Dorgan et al., 1998; Hulten et al., 2001; Ito et al., 1999; Jarvinen et al., 1997; La Vecchia, 2002; Levi et al., 2001; London et al., 1992; Rock et al., 1997; Sato et al., 2002; Terry et al., 2002; Toniolo et al., 2001; van Kappel et al., 2001; Zhang et al., 1997). Eleven of the studies (28%) included nutrient database calculations as part of their data collection based on dietary reference allowances defined by the U.S. Food and Drug Administration (Edwards et al., 2003; Freudenheim et al., 1996; Horn-Ross et al., 2002; Jarvinen et al.; Levi et al.; Mayne et al., 1999; McEligot, Rock, Flatt, et al., 1999; McEligot, Rock, Shanks, et al., 1999; Pierce et al., 2002, 2004; Rock et al.; Thomson et al., 2003).

An observed significant inverse relationship between adequate levels of lycopene and decreased risk of breast cancer or recurrence was noted in 5 (13%) of the studies (Dorgan et al., 1998; Hulten et al., 2001; Levi et al., 2001; Ronco et al., 1999; Sato et al., 2002). Simon et al. (2000) noted a significant interaction effect between race and lycopene ($p = 0.048$) when comparing African American and Caucasian women. Only one study focused specifically on ethnicity as a factor in serum lycopene levels. Horn-Ross et al. (2002) found no significant findings related to lycopene levels and breast cancer risk but found that alcohol consumption was a significant risk factor.

Considering nutritional and dietary factor, Hadley et al. (2003) noted that changes in dietary intake patterns affected plasma lycopene concentrations. Mayne et al. (1999) identified plasma cholesterol, selected demographics, and dietary intake of lycopene as significant determinants of plasma lycopene levels. Lycopene plasma concentrations were shown to have a marginal inverse relationship with body mass index ($p < 0.09$) and an independent relationship with baseline measures of lycopene ($p < 0.05$) (McEligot, Rock, Flatt, et al., 1999). The ongoing WHEL study is examining whether

the consumption of a high-vegetable and low-fat diet will have a positive effect on raising carotenoid levels in patients with breast cancer (Pierce et al., 2002) using a comprehensive intervention program. Ronco et al. (1999) noted the significant effects of dietary lycopene intake in decreasing the risk of breast cancer. Thomson et al. (2003) noted significant results using a multimethod dietary intervention approach with regard to serum lycopene levels. Van Kappel et al. (2001) noted that vegetable consumption was positively correlated with increased lycopene levels.

Many of the studies focusing on nutritional aspects used a group design to examine comparisons between individuals diagnosed with cancer and those in the control group (Dorgan et al., 1998; Hulten et al., 2001; Ito et al., 1999; La Vecchia, 2002; London et al., 1992; Potischman et al., 1990; Ronco et al., 1999; Terry et al., 2002; Toniolo et al., 2001; Yeum et al., 1998; Zhang et al., 1997). Hulten et al. noted that adequate lycopene levels were associated with a decrease in the risk of developing breast cancer in postmenopausal women. Ito et al. noted a significant decrease in beta carotene levels in postmenopausal women. Yeum et al. did not find any significant differences in lycopene concentrations between a two-group comparison of women diagnosed with breast cancer and those diagnosed with benign breast tissue.


Conclusions

Although many research studies are available through individual database searches, the body of knowledge specifically addressing the individual aspects of lycopene's role as a phytochemical is limited. Most dietary intake is in a composite form, so isolating individual effects of phytochemicals such as lycopene is difficult because substances in nature exist in group arrangements. Lycopene is also a component part of serum carotenoids and therefore has been studied indirectly in various clinical research studies. Cancer is a multicomponent diagnosis; even though it may be located in one specific area of the body, treatment interventions often have whole body effects. Research has been aimed at many different types of cancer, and information about the protective effects of lycopene is continuing to emerge. The antioxidant capacity of lycopene also has been explored from biochemical as well as cellular aspects and has been studied with regard to oxidative stress mechanisms as well as immune response indicators. The bioavailability of lycopene has been studied extensively in the food service industry and now is being evaluated for its potential health benefits in recognition of the antioxidant effects of lycopene. Finally, the broad issue of lycopene and nutrition is affected not only by dietary intake but also by a client's entire contributory history (medical, family, social, environmental, and genetic factors) that helps to define the individual's response. The recognition of factors related to lycopene, namely antioxidant status, bioavailability, breast cancer, and nutrition, depict a complex process of integration in the area of research. More research is needed to fully explore this domain of knowledge, particularly in disease processes in cancer.

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