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Review Article

ROLE OF MICRONUTRIENTS IN BREAST CANCER: A REVIEW

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ABSTRACT
In women, cancer of the breast is the most common incident of cancer and cause of death from cancer. Epidemiological studies tentatively and inconsistently suggest that among individual women, high intake of vitamin A, caroteniods, vitamin E, selenium and vitamin C may be protective against breast cancer. They are potent antioxidants, and thus may provide a cellular defence against reactive oxygen species which damage Deoxyribonucleic acid. The improper balance between reactive oxygen molecules production and antioxidant defences results in oxidative stress, which deregulates the cellular functions leading to cancer. The association of these micro-nutrients with breast cancer has been discussed in this review article.

Key Words: *Breast Cancer, Micronutrients, Nutrition*

INTRODUCTION

In women, cancer of the breast is the most common incident cancer and cause of death from cancer (Parkin, 1989). It is the third most common cancer overall, throughout the world (Potter, 1997). High risk area includes Europe and North America, which together accounted for 400,000 cases of breast cancer in 1996. The lowest rates are reported from Africa and Asia (Potter, 1997). The breast cancer rates are however increasing in most countries, particularly in areas which had previously low rates (Doll *et al.,* 1994). Globally, a wide variation in the incidence of breast cancer ranging from 1657 per 1,00,000 (in developed countries) and 1153 per 1,00,000 (in developing countries) has been reported (WHO 1995). In India, the Age adjusted rate of breast cancer has been reported to range between 8.8 to 28.6 per 1,00,000 population in six different regions of the country (ICMR 2001). Epidemiological studies tentatively and inconsistently suggest that among individual women, high intake of vitamin A, caroteniods, vitamin E, selenium and vitamin C may be protective against breast cancer (Brinton, 1994). They are potent antioxidants, and thus may provide a cellular defense against reactive oxygen species which damage Deoxyribonucleic acid (DNA). The improper balance between reactive oxygen molecules (ROMs) production and antioxidant defenses results in oxidative stress, which deregulates the cellular functions leading to cancer (Ray and Husain, 2001). The association of these micro-nutrients with breast cancer has been discussed in this review article.

Vitamin A and Breast Cancer

Vitamin A consists of preformed vitamin A (retinol, retinyl esters and related compounds) from animal sources and certain carotenoids- found primarily in fruits and vegetables – which are partially converted to retinol in the intestinal epithelium (carotenoid vitamin A). Many carotenoids are potent antioxidants, and thus may provide a cellular defense against reactive oxygen species which damage DNA and initiate actions such as lipid peroxidation and may have implications not only in the initiation and promotion of breast cancer but also in its spread (Peto, 1983, Hunter and Willett, 1993). Carotenoids have retinoid like effects on cellular differentiation and apoptosis and also exhibit inhibitory effects on mammary cell growth (Micozzi *et al.,* 1990; Dawson *et al.,* 1995; Prakash *et al.,* 2000). Vitamin A also regulates cellular differentiation and may prevent the emergence of malignant cells (Hunter and Willett, 1993; Peto *et al.,* 1981; Sporn and Roberts, 1993). B-carotene might reduce cancer risk either as a result of its conversion to retinol or through its action as an antioxidant and free radical scavenger (Mayne and Parker, 1989, Zeigler, 1991). Statistically significant inverse association of intake of carotene has been observed with

breast cancer risk (Graham *et al.,* 1991 and Yuan *et al.,* 1995). In a case- control study conducted in Switzerland, the odds ratio (OR) tended to decline with increasing tertile of intake, with significant inverse trends in risk for total carotenoids (OR for the highest tertile = 0.42) (Levi *et al.,* 2001).

In another large nested case-control study conducted in USA, there was an evident increase in the risk of breast cancer for decreasing concentrations of beta carotene, lutein, alpha- carotene and beta-cryproxanthin. The risk of breast cancer approximately doubled amongst subjects with blood levels of beta-carotene at the lowest quartile, as compared with those at the highest quartile (OR=2.21; 95% CI: 1.29-3.79). The OR for the lowest quartile of total carotenoids was 2.31 (95% CI: 1.35-3.96) (Toniolo *et al.,* 2001). A case- control study conducted in Italy also revealed a significant inverse association of beta-carotene with breast cancer, the estimated OR for the highest quintile compared to the lowest one was 0.84(Francheschi *et al.,* 1999).

In a case- control study conducted in Greece, it was observed that among pre-menopausal women, β-carotene was inversely associated with the risk of breast cancer. The OR for the highest quintile of β-carotene intake relative to the lowest quintile was 0.36 (95% CI: 0.21-0.61). The effect of β- carotene remained significant after mutual adjustment, the OR for a one quintile increase in intake was 0.84 (95% CI: 0.73-0.97) (Bohlke *et al.,* 1999). Results of another case- control study conducted in six regions of Italy, revealed that the estimated OR of the 5^{th} quintile compared to the lowest ones for β- carotene was found to be 0.84 (Negri *et al.,* 1996). Other studies have also shown similar results, OR for the highest versus the lowest tertile of beta- carotene intake was (0.73; 95% CI: 0.38-1.38); (Van't Veer *et al.,* 1990) (OR=0.09; 95% CI: 0.02-0.49); (Zaridze *et al.,* 1991) (0.61; 95% CI: 0.39-0.96); (Holmberg *et al.,* 1994) (0.84); (Francheschi, 1997) (1.24; 95% CI: 0.83-1.83); (Verhoeven *et al.,* 1997) (1.24; 95% CI: 1.05-1.47); (Mezzetti *et al.,* 1998) (0.82 (95% CI: 0.76-0.91); (Gandini *et al.,* 2000) (0.47; 95% CI: 0.24-0.91); (Jakovljevic *et al.,* 2002) (0.46; 95% CI: 0.27-0.80) (Adzersen *et al.,* 2003).

Graham et al observed an inverse dose response relationship between consumption of foods containing vitamin A and risk of breast cancer. The relative risk was 0.8 between the highest quartile of vitamin A consumption and the lowest, with a significant increase trend with increasing vitamin A consumption (Graham *et al.,* 1982).

A case- control study conducted in Greece found that the cases reported significantly less frequent consumption of vitamin A. The odds ratio estimated for consumption of vitamin A equal to the value of the 90^{th} centile versus consumption equal to the value of 10^{th} centile was 0.46 with 90% CI of 0.26-0.82 (Katsouyanni *et al.,* 1988). In another case- control study conducted in USA, a relatively low level intake of vitamin A was associated with a 53% increase in risk compared with the highest reported levels of ingestion of dietary sources of this nutrient (Mettlin, 1984).

Studies have revealed that the mean dietary intake of retinol is lower in cases as compared to controls (Wald *et al.,* 1984 andPotischman *et al.,* 1990). In India, the serum carotenoid levels were found to be significantly lower in breast cancer patients (125.2 µg/dl) as compared to controls (141.5 µg/dl). Similarly, the vitamin A levels were also significantly lower in breast cancer patients (35.1 µg/dl) as compared to controls (39.8 µg/dl). The serum levels of both vitamin A and carotenoids decreased with increasing stage of the disease (Ramaswamy *et al.,* 1996).A case- control study conducted in India revealed that the serum levels of total carotenes and total carotenoids were significantly lower amongst breast cancer cases compared to healthy controls. Serum β- carotene levels tended to be lower among breast cancer cases than among controls in pre-menopausal women. This may be possibly due to a low intake of Green Leafy Vegetables rich in fiber and carotenoids such as Beta carotene (Ito *et al.,* 1999).

A nested case- control study was conducted in USA and it was found that β- carotene, lycopene and total carotene were significantly lower in cases compared with controls. The risk of developing breast cancer in the highest fifth was approximately half of that of women in the lowest fifth for β- carotene (OR= 0.41; 95% CI: 0.22-0.79), lycopene (OR=0.55; 95% CI: 0.29-1.06) and total carotene (OR==0.55; 95% CI: 0.29-1.03) (Sato *et al.,* 2002).

A prospective study conducted amongst cohort of women participating in the Nurses' health study, USA found that intakes of β- carotene from food and supplements and vitamin A from foods were weakly inversely associated with breast cancer risk in pre-menopausal women. Strong inverse associations were found for increasing quintiles of α –carotene, β- carotene from food and total vitamin A among pre-menopausal women with a positive family history of breast cancer. An inverse association was also found for increasing quintiles of β- carotene among pre-menopausal women who consumed 15 g or more of alcohol per day. Women in the highest quintile of intakes of lutein/zeaxanthin and preformed vitamin A from food and supplements had statistically significant 21% and 22% reductions in risk of breast cancer as compared with those in the lowest quintile (Zhang *et al.,* 1999). In another prospective analysis of women in the Nurses Health Survey in USA, a highly significant inverse trend was observed, with a 20-30% reduction in risk with higher intake of vitamin A. Women in the highest quintile of intake had a relative risk of 0.78 (95% CI, 0.66-0.93) compared with those in the lowest quintile of intake (Hunter *et al.,* 1993). A significant dose response relationship was also observed amongst women in the highest quartiles of beta carotene intake (Hazard Ratio = 0.48; 95% CI: 0.28-0.99), during the National Breast Screening Study conducted in Canada. The risk dropped by 15% for each additional 1000 IU of beta carotene (Jain *et al.,* 1994).

The Iowa women's health study conducted in USA amongst postmenopausal women revealed that from the lowest to highest total vitamin A intake categorised by quintiles, the age adjusted RRs of breast cancer were 1.0, 0.95, 1.17, 1.20 and 0.90 (p trend = 0.92). Women who consumed more than 10,000 IU/day of vitamin A had a corresponding RR of 0.73 (Kushi *et al.,* 1996).

In a meta analysis of 9 case-control studies, Howe et al reported a weak but statistically significant inverse association for beta-carotene intake, with a collective odds ratio of 0.85 (p=0.007) for the uppermost quintile, compared to the lowermost (Howe *et al.,* 1990). However, in a case- cohort analysis, undertaken amongst women enrolled for the Canadian national breast screening study, no association was found between dietary intakes of β- carotene, α- carotene, β- cryptoxanthin, lycopene, and lutein + zeaxanthin were not associated with breast cancer risk. The multivariate adjusted incidence rate ratios (95% CI) for increasing quartiles of the index, compared with the lowest, were 1.12 (0.94, 1.34); 1.10 (0.89, 1.36) and 1.10 (0.72, 1.65); P for trend = 0.34 (Terry *et al.,* 2002).

Vitamin C and Breast Cancer

Vitamin C is possibly a marker of vegetable and fruit intake. The action of vitamin C may be related to its function as an antioxidant and has been shown to inhibit the formation of nitrosamines. It also acts on the immune system, thereby reducing the risk of breast cancer (Ramaswamy and Krishnamoorthy, 1996, Watternberg, 1985, Freudenheim *et al.,* 1996). Vitamin C can neutralise reactive oxygen species, may reduce oxidative DNA damage, genetic mutations and also enhance host immunological functions. These reactions may help to protect against breast carcinogenesis (Frei, 1994). Vitamin C also plays an important role in the hydroxylation of lysine and proline, in the synthesis of connective tissue proteins such as collagen. Deficiency of vitamin C therefore, may affect the integrity of intercellular matrices and thus may promote tumour growth or inhibit tumor encapsulation (Steinmetz and Potter, 1991).

Significant inverse associations have been observed with vitamin C intake (Zaridze *et al.,* 1991; Holmberg *et al.,* 1994; Verhoeven *et al.,* 1997; Gandini *et al.,* 2000; Adzersen *et al.,* 2003; Graham *et al.,* 1982). In a case- control study conducted in USA, it was observed that with the lowest quartile of intake for vitamin C as the reference adjusted OR for the highest quartile of intake was 0.53 (95% CI: 0.33-0.86) (Freudenheim *et al.,* 1996). A case- control study conducted in Greece revealed significant inverse association of vitamin C with breast cancer risk. It was observed that among pre-menopausal women, the OR for the highest quintile relative to the lowest quintile was 0.80 (95% CI, 0.70-0.92) for Vitamin C (Bohlke *et al.,* 1999).

The results of a case- control study conducted in Switzerland, revealed that the OR tended to decline with increasing tertile of intake, with significant inverse trends in risk for vitamin C (OR for the highest tertile

=0.19; 95% CI: 0.12-0.30). The results of the multivariate analysis revealed a significant inverse relation for Vitamin C (OR =0.23) (Levi *et al.*, 2001). In another case- control study conducted in Spain, cases reported significantly less frequent consumption of vitamin C. The RR after controlling for total calories intake was 0.40; 95% CI: 0.2-0.9 (Landa *et al.*, 1994).

A matched case- control study conducted in USA revealed that the controls had a significantly higher intake of vitamin C (193± 94 mg/day) as compared to the breast cancer cases (180± 82 mg/day), p=0.02. The risk of breast cancer was highest amongst those eating the smallest amounts of Vitamin C (Graham *et al.*, 1991). In another case- control study conducted in India the vitamin C levels were found to be significantly lower in breast cancer patients (1.10 mg/dl) as compared to controls (1.98 mg/dl). The sera levels of vitamin C decreased with increasing stage of the disease (Ramaswamy and Krishnamoorthy, 1996). Results of a case- control study conducted in India revealed that the vitamin C levels were significantly decreased in breast cancer patients (155.0 µmol/l) than in controls (186.3 µmol/l) ($P<0.01$) (Ray and Husain, 2001).

In the National Breast Screening Study conducted in Canada, a significant dose response relationship was observed with vitamin C. There was a lower risk of dying of breast cancer in the highest quartiles of vitamin C intake (Hazard Ratio (HR) = 0.43; 95% CI: 0.21-0.86). The risk of breast cancer dropped by 33% for each 100 mg intake of vitamin C (Jain *et al.*, 1994). In a prospective study, the Iowa women's health study conducted in USA amongst postmenopausal women revealed that women who reported consuming at least 500 mg/day of supplemental vitamin C had a RR of breast cancer of 0.79 (95% CI: 0.60-1.05) compared with women who did not take supplemental vitamin C. Those whose daily dose was greater than 1000 mg/day had an age adjusted RR of 0.77 (95% CI: 0.51-1.16) (Kushi *et al.*, 1996).

In the Swedish Mammography Screening Cohort, it was observed that high intake of ascorbic acid was inversely related to breast cancer incidence among overweight women (HR=0.61; 95% CI: 0.45-0.82, for highest quintile of intake among women with BMI more than 25 kg/m^2) (Michels *et al.*, 2001). In a cohort of women followed in USA, it was observed that women with greater intakes of vitamin C were at a lower risk of dying from breast cancer: OR=0.4 (0.2-0.9) for the highest versus the lowest intakes (approximately more than 210-230 mg/day in the study) (Rohan *et al.*, 1993).

However, in the Nurses' health study population in USA, no relationship was found between intake of vitamin C and reduced risk of breast cancer. There was no evidence of lower risk of breast cancer amongst women in the top quintile, consisting of subjects who consumed mega doses of ≥ 500 mg/d, and those who had supplements for ≥ 10 years (Hunter *et al.*, 1993).

Results of a Meta analysis of 9 cases – control studies revealed a statistically significant decrease in risk with increasing consumption of vitamin C. The RR was 0.69 for each 300 mg/day increase in vitamin C. The results further revealed that if all postmenopausal women in the population, were to increase the fruit and vegetable intake to reach an average daily consumption of vitamin C totaling 380 mg/day, the risk of breast cancer in the population would be reduced by 16% (Howe *et al.*, 1990).

Vitamin E and Breast Cancer

Vitamin E has a role in inhibiting cancer via its action as an antioxidant, as well as its potential effects on selenium. It reduces nitrite, thereby inhibiting the production of carcinogenic nitrosamines and nitrosoamides and expression of certain oncogenes (Freudenheim *et al.*, 1996; Kimmick *et al.*, 1997). Vitamin E can neutralise reactive oxygen species, may reduce oxidative DNA damage, genetic mutations and also enhance host immunological functions. These reactions may help to protect against breast carcinogenesis (Frei, 1994). Vitamin E is effective against both tumor initiation and promoters. It also enhances body's immune response and it may regulate the gene expression in mammalian cells (Boutwell, 1974; Dorgan and Schatzkin, 1991; Knekt, 1991; Packer, 1991; Garland *et al.*, 1993).

Vitamin E is the major antioxidant in cell membranes. Out of the eight naturally occurring forms (saturated and unsaturated side chains) of vitamin E, D- A-tocopherol is the most active and the most common. Vitamin E reacts with oxyradicals and singlet oxygen to prevent peroxidation of polyunsaturated lipids in membranes. Many other effects have also been described like

physiochemical stabilistaion of membranes, protection of cytochrome P450 metabolism, stimulation of immune parameters, induction of differentiation and intercellular gap junction communication, inhibition of prolifertaion, arachidonic acid metabolism and nitrosamine formation which have role in anticarcinogenic process (Kelloff *et al.,* 1996 and Riboli *et al.,* 1996).

Studies in animals have demonstrated that animals fed vitamin E develop fewer or later appearing tumors after exposure to carcinogenic compounds or ultraviolet radiations than animals that do not receive the vitamin (Wang *et al.,* 1989).

Vitamin E has been found to be significantly associated with breast cancer (Franceschi *et al.,* 1999; Negri *et al.,* 1996; Franceschi, 1997; Mezzetti *et al.,* 1998; Gerber *et al.,* 1988). In a case- control study conducted in Uruguay, vitamin E intake was found to be significantly associated with a reduction in risk of breast cancer (4^{th} quartile OR for vitamin E intake = 0.40, 95% CI=0.3-0.6, p<0.001) (Ronco *et al.,* 1999). In another case- control study conducted in Switzerland, the OR tended to decline with increasing tertile of intake, with significant inverse trends in risk for vitamin E (OR for the highest tertile =0.97; 95% CI: 0.23-0.59) (Levi *et al.,* 2001).

A case- control study conducted in USA revealed that the risk of breast cancer was decreased among women in the highest quintile of intake of vitamin E from food sources only (OR for the highest quintile = 0.4; 95% CI: 0.2-0.9), but less so for total vitamin E intake including supplements (OR = 0.7; 95% CI: 0.4-1.3) (London *et al.,* 1992). In another case – control study conducted in Mexico, a protective effect against breast cancer was observed due to a high intake of vitamin E (OR=0.10; 95% CI: 0.02-0.44, P for trend = 0.003) among postmenopausal women (Bonilla-Fernandez *et al.,* 2003). Results of a case- control study conducted in USA, revealed that the risk of breast cancer was highest amongst those eating the smallest amounts of Vitamin E (Graham *et al.,* 1991). In another case control study conducted in Greece, the OR for the highest versus the lowest quintile was 0.84 (95% CI, 0.72-0.98) for Vitamin E (Bohlke *et al.,* 1999).

A case- control study conducted in Finland analysed vitamin E concentration in breast adipose tissue. It was observed that in postmenopausal women, lower dietary intake (P=0.006) and a smaller concentration of vitamin E in breast adipose tissue (P=0.024) were observed in breast cancer patients than in subjects with benign breast disease. Partial correlation showed that the vitamin E concentration in the breast adipose tissue correlated positively with the dietary intake of vitamin E (r=0.25, P=0.023), indicating that the vitamin E concentration in breast adipose tissue reflects the dietary intake of vitamin E (Zhu *et al.,* 1996). In a case- control study conducted in India the vitamin E levels were observed to be significantly decreased in breast cancer patients (24.87 µmol/l) than in controls (28.3 µmol/l) (P<0.01) (Ray and Husain, 2001). Two case-control studies that have examined levels of vitamin E in blood have reported OR of 0.8 and 4.2 for the highest quintile levels. Two other studies have found marginally to significantly higher levels of vitamin E in plasma, erythrocytes and leucocytes in cases, as compared to controls (Garland *et al.,* 1993).

A prospective case- control study was conducted in UK and a statistically significant inverses association was found between plasma vitamin E and risk of breast cancer. The mean vitamin E levels were significantly lower among cases (4.7 mg/l) compared with controls (9.0 mg/l). The risk of breast cancer in women with the lowest quintile was about 8 times higher than the risk for women with levels in the highest quintile (P<0.01) (Wald *et al.,* 1984).

A cohort analysis of the National Breast Screening Survey in Canada reported that women with greater premorbid intakes of vitamin E were at lower risk of dying from their breast cancer (OR=0.6, 0.3-1.2, for more than 24 vs less than 14 mg/day) (Jain *et al.,* 1994).

Contrary to the evidence stated above, in the Nurses' health study population in USA, no relationship was found between intake of vitamin E and reduced risk of breast cancer. There was no evidence of lower risk of breast cancer amongst women in the top quintile, consisting of subjects who consumed mega doses of ≥ 400 IU/day (Hunter *et al.,* 1993).

Selenium and Breast Cancer

Selenium is an essential trace element in human nutrition and is a co-factor for enzyme glutathione peroxidase. The metabolic function of this enzyme is vital for cells, as it is a part of the mechanism responsible for the metabolism and detoxification of oxygen. It is assumed that glutathione peroxidase can protect the DNA from oxidative damage and consequently from mutation leading to neoplastic transformation of cells (Watternberg, 1985, Biesalski, 2002).

Animal studies have shown that selenium can lower the tumor promoting effect of fatty acids (Brinton, 1994). In in vitro and in vivo studies, organic and inorganic selenium has been demonstrated to inhibit proliferation of normal and malignant cells and inhibit tumor growth (Griffin, 1982). Selenium decreases the mutagenic activity of several known carcinogens, altering the patterns of degradation to produce less toxic metabolites (Willett *et al.,* 1983).

Case- control studies have shown serum selenium to be lower in breast cancer cases as compared to controls (McConnell *et al.,* 1980; Chaitchik *et al.,* 1988; Basu *et al.,* 1989). A longitudinal case- control study conducted in Finland revealed that the breast cancer patients had lower mean selenium levels (65.2 µg/l) as compared to controls (66.4 µg/l) (Knekt *et al.,* 1990). In another case- control study conducted amongst postmenopausal women residing in Ireland, the toenail selenium concentrations tended to be lower in cases (584 µg/g) than in controls (603 µg/g), but the difference did not reach statistical significance (Strain *et al.,* 1997). A case- control study conducted in Spain revealed that the mean serum concentrations of selenium was 61.1 µg/l in women with breast cancer and 98.5 µg/l in women with non tumoral disease ($p<0.001$) (Lopez-Saezz *et al.,* 2003).

A case - control study conducted amongst Japanese and American women, revealed that low blood selenium concentrations may be indicative of increased breast cancer risk. The mean blood selenium concentrations of healthy Japanese women were significantly higher (0.285 µg/ml) than those of women with newly diagnosed breast cancer (0.195 µg/ml). Similarly, healthy American women had higher selenium concentrations (0.191 µg/ml) as compared to women with newly diagnosed breast cancer (0.167 µg/ml) (Schrauzer *et al.,* 1985). Results of a case- control study conducted in Finland, revealed that the mean toenail selenium concentration was 0.80 mg/kg in pre-menopausal breast cancer cases and 0.84 mg/kg in pre-menopausal controls. It was 0.77 mg/kg in postmenopausal cases and 0.80 mg/kg in postmenopausal controls. The OR comparing the highest with the lowest quintiles of toenail selenium concentration was 1.1 (95% CI: 0.4-3.2) in pre-menopausal women and 0.7 (95% CI: 0.3-1.5) in postmenopausal women (Mannisto *et al.,* 2000).

Results of a case- control study conducted in Netherlands revealed lower mean plasma selenium concentrations in cases (89 µg/l) as compared to the controls (93 µg/l). However, there was no substantial association between selenium and breast cancer. The multivariate adjusted OR of breast cancer for subjects in the lowest compared with the highest quartile were 1.6 (95% CI: 0.8-3.4) for dietary selenium, 2.0 (95% CI: 0.9-4.4) for plasma selenium, 0.9 (95% CI: 0.4-1.9) for erythrocyte selenium and 1.1 (95% CI: 0.6-2.1) for toenail selenium (Van't Veer *et al.,* 1990).

However, in a case- referent study conducted in Netherlands (the DOM project), no relationship was observed between nail selenium levels up to two years before diagnosis and breast cancer risk in pre-menopausal women (Van Noord *et al.,* 1987).

The results of the Nurses' health study cohort conducted in USA revealed that the mean selenium levels in toenails in the cases (0.823 µg/g) were almost identical to that of the controls (0.821 µg/g). After controlling for known breast cancer risk factors, the RR for women in the highest quintile of selenium as compared with the lowest quintile was 8.10 (95% CI: 0.70-1.72) (Hunter *et al.,* 1990).

CONCLUSION

A vast amount of epidemiological evidence suggests that a relatively high fruit and vegetable intake is associated with a reduced risk of breast cancer (Potter, 1997). A wide variety of compounds are contained in fruits and vegetables which have potential anticarcionogenic activity in vitro. These include carotenes,

dithiolthiones, indoles, isothiocyanides, selenium, folic acid, dietary fiber, vitamins C and E, certain diphenolic lignans and isoflavonoid, phytoestrogens, glucosinolate, indoles, phenols and others. Epidemiological studies tentatively and inconsistently suggest that high intake of vitamin A, caroteniods, vitamin E, selenium and vitamin C may decrease the risk of breast cancer, but the data on this aspect is, as yet, insufficient (Brinton, 1994; Watternberg, 1985; Ronco *et al.*, 1999).There is a need to undertake studies in this area in our country as nutrition and diet are certainly among the priorities for epidemiological research on breast cancer, not only from an etiological viewpoint, but also from a preventive one.

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