

## **SUMMARY AND CONCLUSIONS**

Breast cancer is by far the most common cancer among women worldwide. It is also the leading cause of cancer death in females since annually, 400,000 women die from this disease. In Egypt, breast cancer is estimated to be the most common cancer among females accounting for 37.7% of their total 12,621 with new cases in 2008. It is also the leading cause of cancer related mortality accounting for 29.1% of their total with 6546 deaths. The incidence to mortality ratio is poor (1.9:1). The etiology of breast cancer is multifactorial and several risk factors associated with breast cancer may exert their effects via generation of an oxidative stress status.

Most patients with breast cancer are treated with a combination of the anticancer chemotherapy drugs of 5-fluorouracil, doxorubicin, and cyclophosphamide (FAC). Chemotherapy agents act through various oxidative stress mechanisms to produce free radicals that damage tumor cells. Oxidative stress during cancer therapy also harms healthy tissue. It is possible that taking antioxidant supplements during treatment can protect normal tissues from the damaging of side effects of treatments, and may improve tumor response and patient survival. However, antioxidant supplementation during conventional chemotherapy and radiation therapy is a controversial subject. Some studies suggest taking antioxidants supplements during treatment may be beneficial; however, there are just as many studies that tell us this may be harmful. The scientific evidence on this topic is not strongly for or against taking antioxidant supplements during cancer treatment.

Accordingly the present study is undertaking to explore whether vitamin A and E supplementation during 5-fluorouracil, doxorubicin, and cyclophosphamide (FAC) therapy will have its impact on chemotherapy-induced oxidative stress.

This study is carried out, after the approval of Ethics Committee – Medical Research Institute, on 45 breast cancer patients who were divided into two groups; group (I) which was subjected only to chemotherapy (20 patients) and group (II) which was subjected to chemotherapy plus supplementation with vitamin A and E(25 patients). Markers of oxidative stress including serum MDA,  $\beta$ -carbonyl protein ( $\beta$ -CP) and total antioxidant capacity (TAOC) are measured in patients of those two groups before and after chemotherapy with or without vitamins supplement.

In group (I), vitamins supplemented -ve, the results showed that chemotherapy with FAC resulted in a significant elevation in MDA and  $\beta$ -CP accompanied by a significant decrease in TAOC. These results may indicate that breast cancer patients are subjected to oxidative stress which is manifested by elevation in free radicals production and decreased antioxidant capacity. The developed oxidative stress may have its impact on the breast cancer patients render them subjected to different side effects including chronic fatigue which is the most common side effects.

In group II, vitamins supplemented +ve, and after chemotherapy, while, the mean concentration levels of MDA and  $\beta$ -CP were significantly reduced, the mean total antioxidant capacity level was significantly elevated. Moreover, in group II after chemotherapy and vitamin supplementation, the mean concentration levels of MDA and  $\beta$ -CP were significantly reduced when compared to those in group I after chemotherapy. The observed reduction in free radical production and the interesting increase in total

antioxidant capacity level could be attributed to the antioxidant properties of both vitamins A and E. The improvement in oxidative status in those patients may reduce side effects of chemotherapy agents and might result in an improved quality of life for the patient, and possibly better survival rates.

In conclusion; the present study is an attempt to through more lights on the beneficial effects of providing breast cancer patients with antioxidant vitamins as vitamin A and vitamin E during chemotherapy. Thus, as shown in the present study, the ability of these vitamins to reduce oxidative stress in breast cancer patients during chemotherapy and its subsequent impacts may lead to recommend supplementation of breast cancer patients with antioxidant vitamins as vitamin A and vitamin E during chemotherapy. Also, it is recommended to evaluate the levels of these vitamins in sera of breast cancer patients before and during chemotherapy.

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## REFERENCES

1. Dozier JM, Anderson WF, Devesa SS, Brinton LA. Global trends in breast cancer incidence and mortality 1973-1997. *Int J Epidemiol* 2005; 34:405-12.
2. Yang L, Parkin DM, Ferlay J, Li L, Chen Y. Estimates of cancer incidence in China for 2000 and projections for 2005. *Cancer Epidemiol Biomarkers Prev* 2005; 14:243-50.
3. Parkin DM, Bray F, Ferlay J, Pisani P. *Global Cancer Statistics, 2002*. *CA Cancer J Clin* 2005; 55: 74-108.
4. World Health Organization. *The World Health Report*. Geneva: WHO; 1997.
5. Elatar I, Cancer Registration, NCI Egypt 2001; National Cancer Institute: Cairo, Egypt, 2002. Available online at: <http://www.nci.edu.eg/Journal/nci2001%20.pdf> (accessed on 26 September 2010).
6. Annual report. Alexandria, Cancer Registry Department of Bioinformatics and Medical Statistic .Medical Research Institute ,Alexandria University ,Egypt 2008.
7. Martin AM, Weber BL. Genetic and hormonal risk factors in breast cancer. *J Natl Cancer Inst* 2000; 92:1126-35.
8. Eshre C.Workshop Group. Hormones and breast cancer. *Hu prod Update* 2004; 10:281-93.
9. Ronckers CM, Erdmann CA, Land CE. Radiation and breast cancer: a review of current evidence. *Breast Cancer Res* 2005; 7:21-32.
10. Carmichael A, Sami AS, Dixon JM. Breast cancer risk among the survivors of atomic bomb and patients exposed to therapeutic ionizing radiation. *Eur J Surg Oncol* 2003; 29:475-79.
11. Albrektsen G, Heuch I, Hansen S, Kvale G. Breast cancer risk by age at birth, time since birth and time intervals between births: exploring interaction effects. *Br J Cancer* 2005; 92:167-75.
12. Lipworth L, Bailey LR, Trichopoulos D. History of breast-feeding in relation to breast cancer risk: a review of the epidemiologic literature. *J Natl Cancer Inst* 2000; 92:302-12.
13. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. *Lancet* 2002; 360:187-95.

14. Beral V, Bull D, Doll R, Peto R, Reeves G, Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and abortion: collaborative reanalysis of data from 53 epidemiological studies, including 83,000 women with breast cancer from 16 countries. *Lancet* 2004; 363:1007-16.
15. Beral V. Million Women Study Collaborators. Breast cancer and hormonereplacement therapy in the Million Women Study. *Lancet* 2003; 362:419-27.
16. Bergkvist L, Adami HO, Persson I, Hoover R, Schairer C. The risk of breast cancer after estrogen and estrogen-progestin replacement. *N Engl J Med* 1989; 321:293-97.
17. Hulley S, Furberg +C, Barrett-Connor E, Cauley J, Grady D, Haskell W, et al. Noncardiovascular disease outcomes during 6.8 years of hormone therapy: Heart and Estrogen/progestin Replacement Study follow-up (HERS II). *JAMA* 2002; 288:58-66.
18. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. *Lancet* 1996; 347:1713-27.
19. Gauthier E, Paoletti X, Clavel-Chapelon F. Breast cancer risk associated with being treated for infertility: results from the French E3N cohort study. *Hum Reprod* 2004; 19:2216-21.
20. Burkman RT, Tang MT, Malone KE, Marchbanks PA, McDonald JA, Folger SG, et al. Infertility drugs and the risk of breast cancer: findings from the National Institute of Child Health and Human Development Women's Contraceptive and Reproductive Experiences Study. *Fertil Steril* 2003; 79:844-51.
21. Wang J, Costantino JP, Tan-Chiu E, Wickerham DL, Paik S, Wolmark N. Lower-category benign breast disease and the risk of invasive breast cancer. *J Natl Cancer Inst* 2004; 96:616-20.
22. Vogel VG. Atypia in the assessment of breast cancer risk: implications for management. *Diagn Cytopathol* 2004; 30:151-57.
23. Cho E, Spiegelman D, Hunter DJ, Chen WY, Stampfer MJ, Colditz GA, et al. Premenopausal fat intake and risk of breast cancer. *J Natl Cancer Inst* 2003; 95:1079-85.
24. Velie E, Kulldorff M, Schairer C, Block G, Albanes D, Schatzkin A. Dietary fat, fat subtypes, and breast cancer in postmenopausal women: a prospective cohort study. *J Natl Cancer Inst* 2000; 92:833-39.

25. Key TJ, Appleby PN, Reeves GK, Roddam A, Dorgan JF, Longcope C, et al. Body mass index, serum sex hormones, and breast cancer risk in postmenopausal women. *J Natl Cancer Inst* 2003; 95:1218-26.
26. Harvie M, Howell A, Vierkant RA, Kumar N, Cerhan JR, Kelemen LE, et al. Association of gain and loss of weight before and after menopause with risk of postmenopausal breast cancer in the Iowa women's health study. *Cancer Epidemiol Biomarkers Prev* 2005; 14:656-61.
27. Patel AV, Calle EE, Bernstein L, Wu AH, Thun MJ. Recreational physical activity and risk of postmenopausal breast cancer in a large cohort of US women. *Cancer Causes Control* 2003; 14:519-29.
28. Zhang S, Hunter DJ, Forman MR, Rosner BA, Speizer FE, Colditz GA, et al. Dietary carotenoids and vitamins A, C, and E and risk of breast cancer. *J Natl Cancer Inst* 1999; 91:547-56.
29. Fares FA, Ge X, Yannai S, Rennert G. Dietary indole derivatives induce apoptosis in human breast cancer cells. *Adv Exp Med Biol* 1998; 451:153- 57.
30. Donald JA, Mandel MG, Marchbanks PA, Folger SG, Daling JR, Ursin G, et al. Alcohol exposure and breast cancer: results of the women's contraceptive and reproductive experiences study. *Cancer Epidemiol Biomarkers Prev* 2004; 13:2106-16.
31. Collaborative Group on Hormonal Factors in Breast Cancer. Alcohol, tobacco and breast cancer—collaborative reanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease. *Br J Cancer* 2002; 87:1234-45.
32. Reynolds P, Hurley S, Goldberg DE, Anton-Culver H, Bernstein L, Deapen D, et al. Active smoking, household passive smoking, and breast cancer: evidence from the California Teachers Study. *J Natl Cancer Inst* 2004; 96:29-37.
33. Coyle YM. The effect of environment on breast cancer risk. *Breast Cancer Res Treat* 2004; 84: 273-88.
34. Calle EE, Frumkin H, Henley SJ, Savitz DA, Thun MJ. Organochlorines and breast cancer risk. *CA Cancer J Clin* 2002; 52: 301-9.
35. Kerlikowske K, Shepherd J, Creasman J, Tice JA, Ziv E, Cummings SR. Are breast density and bone mineral density independent risk factors for breast cancer? *J Natl Cancer Inst* 2005; 97:368-74.
36. Szabo CI, King MC. Population genetics of BRCA1 and BRCA2. *Am J Hum Genet* 1997; 60:1013-20.

37. Struewing JP, Hartge P, Wacholder S, Baker SM, Berlin M, McAdams M, et al. The risk of cancer associated with specific mutations of BRCA1 and BRCA2 among Ashkenazi Jews. *N Engl J Med* 1997; 336:1401-8.
38. Anglian Breast Cancer Study Group. Prevalence and penetrance of BRCA1 and BRCA2 mutations in a population-based series of breast cancer cases. *Br J Cancer* 2000; 83:1301-8.
39. Hopper JL, Southey MC, Dite GS, Jolley DJ, Giles GG, McCredie MR, et al. Population-based estimate of the average age-specific cumulative risk of breast cancer for a defined set of protein-truncating mutations in BRCA1 and BRCA2. Australian Breast Cancer Family Study. *Cancer Epidemiol Biomarkers Prev* 1999; 8:741-47.
40. Ford D, Easton DF, Stratton M, Narod S, Goldgar D, Devilee P, et al. Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families. *Am J Hum Genet* 1998; 62:676-89.
41. Rennert G, Dishon S, Rennert HS, Fares F. Phenotypic characteristics of families with BRCA1 and BRCA2 mutations in Israel. *Eur J Cancer Prev* 2005;14:357-61.
42. American Society of Clinical Oncology policy statement update: Genetic testing for cancer susceptibility. *J Clin Oncol* 2003; 21:2397-406.
43. Ji J, Forsti A, Sundquist J, Hemminki K. Risks of breast among older women. *Breast Cancer Res Trat*, 2007; 102:365-74.
44. King MC, Marks JH, Mandell JB; New York Breast Cancer Study: Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2. *Science* 2003; 302:643-46.
45. Fawzy S, Sallam M, Awad NM .Detection of Epstein –Barr virus in breast carcinoma in Egyptian women .*Clin Biochem* 2008; 41:486-92.
46. Dupont WD, Parl FF, Hartmann WH, Brinton LA, Winfield AC, Worrell JA, Schuyler PA, Plummer WD . Breast cancer risk associated with proliferative breast disease and atypical hyperplasia. *Cancer* 1993; 71:1256-58.
47. Schnitt, SJ, Guidi, AJ. Pathology of invasive breast cancer. In: *Diseases of the Breast*, Harris JR, Lippman ME, Morrow M, Osborne CK, (Eds), 3rd ed, Lippincott, Williams , Wilkins, Philadelphia 2004. p.393.
48. Burstein HJ, Harris JR , Monica M. In Vincent T. Devita Jr, Hellman S, Rosenberg SA 8<sup>th</sup> ed Philadelphia, Pa, Lippincott Williams, Wilkins .*Cancer Principles and Practice of Oncology*. *JAMA* 2005; 294: 1615-40.

49. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, Jeong JH , Wolmark N. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002; 347:1233-41.
50. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, Aguilar M , Marubini E. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* 2002; 347: 1227-32.
51. Mauri D, Pavlidis N, Ioannidis JP. Neoadjuvant versus adjuvant systemic treatment in breast cancer: a meta-analysis. *J Natl Cancer Inst* 2005; 97: 188-94.
52. El-Awady RA, Saleh EM, Dahm-Daphi J. Targeting DNA double-strand break repair: is it the right way for sensitizing cells to 5-fluorouracil? *Anticancer Drugs* 2010; 21:277-87.
53. Johnston A, Gudjonsson JE, Sigmundsdottir H, Ludviksson BR, Valdimarsson H. The anti-inflammatory action of methotrexate is not mediated by lymphocyte apoptosis, but by the suppression of activation and adhesion molecule. *Clin Immunol* 2005; 114: 154–63.
54. Hirata S, Matsubara T, Saura R, Tateishi H, Hirohata K. Inhibition of in vitro vascular endothelial cell proliferation and in vivo neovascularisation by low-dose methotrexate. *Arthritis Rheum* 1989; 32: 1065–73.
55. Wang J, Gregory J, Lohman S, and Stubbe J. Enhanced subunit interactions with gemcitabine-5'-diphosphate inhibit ribonucleotide reductases. *PNAS* 2007; 104: 14324-9.
56. El Serafi MM, El Khodary AI, El Zawahry HR, Mansour OM, Gaballa HE. Gemcitabine plus doxorubicin as first-line treatment in advanced or metastatic breast cancer (MBC), a phase II study. *J Egypt Natl Canc Inst* 2006; 18: 209-15.
57. Fornari FA, Randolph JK, Yalowich JC, Ritke MK and Gewirtz DA. Interference by doxorubicin with DNA unwinding in MCF-7 breast tumor cells. *Mol Pharmacol* 1994; 45: 649–56.
58. Meschino JP. *How Chemotherapy Drugs Work. A Practical Guide for Complementary Health Care Practitioners* Dynamic Chiropractic Canada 2010; 03, Issue 05
59. Lyseng-Williamson KA, Fenton C. Docetaxel: a review of its use in metastatic breast cancer. *Drugs* 2005; 65: 2513-31.
60. Zhukov NV and Tjulandin SA. "Targeted therapy in the treatment of solid tumors: practice contradicts theory". *Biochemistry Mosc* 2008; 73: 605–18.
61. Howell A, Howell SJ, Clarke R and Anderson E. Where do selective estrogen receptor modulators (SERMs) and aromatase inhibitors (AIs) now fit into breast cancer treatment algorithms? *J Steroid Biochem Mol Biol* 2001; 79: 227-37.
62. Buchholz TA. Radiation therapy for early-stage breast cancer after breast-conserving surgery. *N Engl J Med* 2009; 360: 63-70.

63. Vishal RT, Sharma S, Mahajan A, Bardi, GH. Oxidative Stress: A Novel Strategy in Cancer Treatment. *JK Sci* 2005; 7: 1–3.
64. Chandra J, Samali A, Orrenius S. Triggering and modulation of apoptosis by stress. *Free Rad Med Biol* 2000, 29:323–33.
65. Poli G, Biasi F, Chiarpotto E. Oxidative stress and cell signaling. *Curr. Med. Chem* 2004, 11: 1163–82.
66. Pillai C.K, Pillai KS. Antioxidants in health. *Int. J. Physiol. Pharmacol* 2002; 46: 1 – 5.
67. Sohal RS. Oxidative stress, caloric restriction, and aging. *Science* 1996, 273:59–63.
68. Sikka S C. Relative impact of oxidative stress on male reproductive function. *Med Chem* 2001; 8: 851.
69. Darley-Usmar V, Wiseman H , Halliwell B, Nitric oxide and oxygen radicals: A question of balance, *FEBS Len* 1995; 369: 131.
70. Björnström L, Sjöberg M. Mechanisms of Estrogen Receptor Signaling: Convergence of Genomic and Nongenomic Actions on Target Genes. *Mo Endocrinology* 2005; 19: 833-42.
71. Weroha SJ, Li SA, Tawfik O and Li JJ. Overexpression of cyclins D1 and D3 during estrogen-induced breast oncogenesis in female ACI rats. *Carcinogenesis* 2006; 27: 491-98.
72. Schutze N, Vollmer G, Tiemann I, Geiger M and Knuppen R. Catecholestrogens are MCF-7 cell estrogen receptor agonists. *J Steroid Biochem Mol Biol* 1993; 46: 781–89.
73. Zahid M, Gaikwad NW, Rogan EG and Cavalieri EL. Inhibition of Depurinating Estrogen–DNA Adduct Formation by Natural Compounds. *Chem Res Toxicol* 2007; 20: 1947–53.
74. Jezek P, Hlavatá L. Mitochondria in homeostasis of reactive oxygen species in cell, tissues, and organism. *Int J Biochem Cell Biol* 2005; 37: 2478-83.
75. Federico A, Morgillo F, Tuccillo C, Ciardiello F , Loguercio C. Chronic inflammation and oxidative stress in human carcinogenesis. *Int. J. Cancer* 2007; 121: 2381–86.
76. Portakal O, Ozkaya O, Erden Inal M, Bozan B, Kosan M , Sayek I. Coenzyme Q10 concentrations and antioxidant status in tissues of breast cancer patients. *Clin Biochem* 2000; 33: 279–84.

77. Park JE, Yang JH, Yoon SJ, Lee JH, Yang ES, Park JW. Lipid peroxidation-mediated cytotoxicity and DNA damage in U937 cells. *Biochimie* 2002; 84: 1199-205.
78. Akbulut H, Akbulutb KG, Iclia F, Büyükcelika A. Daily variations of plasma malondialdehyde levels in patients with early breast cancer. *Cancer Detection and Prevention* 2003; 32: 27-32.
79. Cebrian A, Pharoah PD, Ahmed S, Smith PL, Luccarini C, Luben R, Redman K, Munday H and Douglas F. Easton DF, Dunning AD, Ponder BAJ. Tagging Single-Nucleotide Polymorphisms in Antioxidant Defense Enzymes and Susceptibility to Breast Cancer. *Cancer Research* 2006; 66: 1225-33.
80. Tas F, Hansel H, Belce A, Ilvan S, Argon A, Camlica H, Topuz E. Oxidative stress in breast cancer. *Med Oncol* 2005; 22:11-15.
81. Aghvami T, Djalali M, Keshavarz A, Sadeghi MR, Zeraati H, Yeganeh HS and Negahdar M. Plasma Level of Antioxidant Vitamins and Lipid Peroxidation in Breast Cancer Patients. *Iranian J Publ Health* 2006; 35:42-47.
82. Bendicha A. Antioxidant Vitamins and Human Immune Responses. *Vitamins & Hormones* 1996; 52: 35-62.
83. Brown NS, Bicknell R. Hypoxia and oxidative stress in breast cancer: Oxidative stress: its effects on the growth, metastatic potential and response to therapy of breast cancer. *Breast Cancer Res* 2001; 3: 323-27.
84. Davies KJA. Protein damage and degradation by oxygen radicals. I. General aspects. *J Biol Chem* 1987; 262: 9895-901.
85. Dalle-Donne I, Rossi R, Colombo R, Giustarini D, Milzani A. Biomarkers of oxidative damage in human disease. *Clin Chem* 2006; 52: 601-23.
86. Packer L, Cadenas E. Oxidants and antioxidants revisited. New concepts of oxidative stress. *Free Radic Res* 2007; 41: 951-52.
87. Ogino K, Wang DH. Biomarkers of oxidative/nitrosative stress: an approach to disease prevention. *Acta Med Okayama* 2007; 61: 181-89.
88. Breimer LH. Molecular mechanisms of oxygen radical carcinogenesis mutagenesis: the role of DNA base damage. *Mol Carcinogenesis* 1990; 3:188-97.
89. Chaudhary AK, Nokubo M, Marnett LJ, Blair IA. Analysis of the -2'-deoxyguanosine adduct in rat liver DNA by gas chromatography negative chemical ionization mass spectrometry. *Biol Mass Spectrom* 1994; 23:457-64.

90. Feig DI, Reid TM, Loeb LA. Reactive oxygen species in tumorigenesis. *Cancer Res* 1990; 54:1890-94
91. Floyd RA. 8-Hydroxy-2'-deoxyguanosine in carcinogenesis. *Carcinogenesis* 1990; 11:1447- 50.
92. Rice-Evans C, Burdon R. Free radical-lipid interactions and their patho . *Prog Lipid Res* 1993;32:71-110 .
93. Grotto D, Santa Maria LD, Boeira S, Valentini J, Charão M F, Moro A M, Pomblum V J, Nascimento P C, Garcia S C . *Pharm. Biomed. Anal* 2007; 43:619.
94. Rosenblum E R ,Gavaler J S , Van Thiel D H, Free Radical Biol. Med 1989; 7: 569.
95. Dahle L K , Hill E G , Holman R T .*Arch. Biochem. Biophys* 1962; 98: 253.
96. Gillham B ,Papachristodoulou D K , Thomas J H , Will's . *Biochemical basis of medicine*, 3rd ed., Butterworth- Heinemann: Oxford, 1997.
97. Alessio H M. In *Handbook of Oxidants and Antioxidants in Exercise*; Hanninen O.;Packer, L.; Sen, C. K., eds.; Elsevier: Amsterdam. White AAKM, PattCS, Lad PJ. Activation of soluble guanylate cylase from rat lung by incubation or by hydrogen peroxide. *J Biol Chem* 2000; 275:7304-12.
98. Seto H , Akiyama K , Okuda T, Hashimoto T , Takesue T , Ikemura T , *Chem. Lett* 1981; 52: 707.
99. Bellomo G, Mirabelli F, Richelmi P, Orrenius S. Critical role of sulfhydryl (s) in the ATP-dependent Ca<sup>2+</sup> sequestration by the plasma fraction from rat liver. *FEB letters* 1983; 163:136-39.
100. Kerr LD, Inoue J, Verm IM. Signal transduction: the nuclear target. *Curr Opin Biol* 1992; 4:496-501.
101. Davies KJA. Intracellular proteolytic systems may function as secondary defence an hypothesis. *J Free Radic Biol Medicine* 1986; 9:155-73.
102. Stadtman ER , Berlett BS. Reactive oxygen-mediated protein oxidation in aging and disease. *Chem. Res. Toxicol* 1997; 10, 485-94.
103. Berlet BS , Stman ER . Protein oxidation in aging, disease, and oxidative stress. *J.Biol. Chem* 1997; 272: 2313-16.
104. Dalle-Donne I, Rossi R, Giustarini D, Milzani A, Colombo R. Protein carbonyl groups as biomarkers of oxidative stress. *Clin Chim Acta* 2003; 329: 23-38.

105. Halliwell B, Gutteridge J. Free radicals in biology and medicine. NY: Oxford Univ. Press; 1999.
106. Dean RT, Fu S, Stocker R, Davies MJ. Biochemistry and pathology of radical-mediated protein oxidation. *Biochem J* 1997; 324:1–18.
107. Uchida K. Role of reactive aldehyde in cardiovascular diseases. *Free Radic Bio Med* 2000; 28:1685–96.
108. Yilmaz IA, Akcay T, Cakatay U, Telci A, Ataus S, Yalcin V. Relation between bladder cancer and protein oxidation. *Int Urol Nephrol* 2003; 35: 345-50.
109. Morabito F, Cristani M, Saija A, Stelitano C, Callea V, Tomaino A, Minciullo PL, S. Lipid peroxidation and protein oxidation in patients affected Hodgkin's lymphoma. *Mediators Inflamm* 2004; 13: 381-83.
110. Rossner P, Terry MB, Gammon MD, Agrawal M, Zhang F, Ferris JS, Teitelbaum SL, Eng SM, Gaudet MM, Neugut AI, Santella RM. Plasma protein levels and breast cancer risk. *J Cellular Molecular Med* 2007; 11:1138-48.
111. Pignatelli B, Li CQ, Boffetta P, Chen Q, Ahrens W, Nyberg F, Mukeria A, Bruske-Hohlfeld I, Fortes C, Constantinescu V, Ischiropoulos H, Ohshima H. Nitrated and oxidized plasma proteins in smokers and lung cancer patients. *Cancer Res* 2001; 61: 778-84.
112. Floyd RA, Watson JJ, Wong PK, Altmiller DH, RecKard RD. Hydroxyl free radical adduct of deoxyguanosine: sensitive detection and mechanisms of formation. *Free Radic Res Commun* 1986; 1: 163–72.
113. Mates JM, Perez-Gomez, C. and Nunez de Castro, I. Antioxidant enzymes and Human disease. *Clin Biochem* 1999; 32:595-603.
114. Arrigo AP. Gene expression and the thiol redox state. *Free Radic Biol Med* 1999; 27: 936–44.
115. Yoshikawa T, Naito Y, Kondo M: Free radical involvement in the aging process 1990; 16:603-12.
116. Naito Y: How to choose the anti-oxidative supplement. *Modern Physician* 2006; 26: 547- 50. (in Japanese) .
117. D,Andrea GM. Use of antioxidants during chemotherapy and radiotherapy should be avoided. *Cancer Journal of Clinician* 2005; 55 :319-21.
118. D,Agostini F, Izzotti, B, Bennicelli C, De Flora S. Modulation of apoptosis by cancer chemopreventive agents. *Mutation Res* 2005; 59:173-86.
119. National Institutes of Health Office of Dietary Supplements. Dietary supplements fact sheets. [http://ods.od.nih.gov/Health Information/Information about Individual Dietary Supplements .aspx](http://ods.od.nih.gov/Health%20Information/Information%20about%20Individual%20Dietary%20Supplements.aspx) [accessed April 19, 2010].

120. Mignone LI, Giovannucci E, Newcomb PA, et al. Dietary carotenoids and the risk of invasive breast cancer. *Int J Cancer* 2009; 124(12): 2929-37.
121. Dennnehy C, Tsourounis C. A review of select vitamins and minerals used by postmenopausal women. *Maturitas* 2010; 66:370-80.
122. Goodman DS, Blaner WS. Biosynthesis, absorption, and hepatic metabolism of retinol. In *The Retinoids*; Sporn, M.B., Roberts, A.B., Goodman, D.S., Eds.; Academic Press: New York, NY, USA 1984; Volume 2, pp. 1-39.
123. Blomhoff R, Green MH, Green J.B, Berg T, Norum KR. Vitamin A metabolism: new perspectives on absorption, transport, and storage. *Rev. Physiol* 1991, 71, 951-90.
124. Blaner WS, Olson J.A. Retinol and retinoic acid metabolism. In *The Retinoids: Biology, Chemistry, and Medicine*, 2nd ed.; Sporn, M.B., Roberts, A.B., Goodman, D.S., Eds.; Raven Press: New York, NY, USA 1994; pp. 229-56.
125. Vogel S, Gamble M.V, Blaner WS. Retinoid uptake, metabolism and transport. In *The Handbook of Experimental Pharmacology, The Retinoids*; Nau, H., Blaner, W.S., Eds.; Springer: Verlag Heidelberg Germany 1999; pp. 31-96.
126. Kirschner R, Rother K, Muller GA, Engeland K. Regulation of vitamin by p 35 and 133. P63 in development and cancer. *Cell Cycle* 2010; 9: 2177 - 88.
127. Simoni D, Tolomeo M. Retinoids, apoptosis and cancer. *Curr Pharm Des* 2001; 7:1823-37.
128. Zang D, Holmes WF, Wu S, Soprano DR, Soprano KJ. Retinoids and ovarian cancer. *J Cell Physiol* 2000; 18: 1-20.
129. Fontana JA, Rishi AK. Classical and novel retinoids: their targets in cancer therapy. *Leukemia* 2002; 18:1-20.
130. Dorjgochoo T, Gu K, Kallianpur A, et al. Menopausal symptoms among breast cancer patients 6 months after diagnosis: a report from the Shanghai Breast Cancer Survival Study. *Menopause* 2009; 16 (6): 1205 -12.
131. Wang C, Baumgartner RN, Yang D, et al. No evidence of association between and dietary carotenoids, retinols, vitamin C and tocopherols in Southwestern Hispanic and non Hispanic white women. *Breast Cancer Treat* 2009; 114(1): 137-45. [Epub August 1, 2008].
132. Epplein M, Shvetsov YB, Wilkens LR, et al. Plasma carotenoids, retinol, and tocopherols and postmenopausal breast cancer risk in the Multiethnic Cohort Study: aKabat GC, Kim M, Adams-Campbell LL, et al. Longitudinal study of serum

- carotenoid, retinol, and tocopherol concentrations in relation to breast cancer risk among postmenopausal women. *Am J Clin Nutr* 2009; 90(1):162–9 [Epub May 27, 2009].
133. Formelli F, Meneghini E, Cavadini E, et al. Plasma retinol and prognosis of postmenopausal breast cancer patients. *Cancer Epidemiol Biomarkers Prev* 2009; 18(1):42-48.
134. Hultén K, Van Kappel AL, Winkvist A, Kaaks R, Hallmans G, Lenner P, Reboli E. Carotenoids, alpha-tocopherols, and retinol in plasma and breast cancer risk in northern Sweden. *Cancer Causes Control* 2001;12(6):529-37.
135. Cui Y, Shikany JM, Liu S, Shagufta Y, Rohan TE. Selected antioxidants and risk hormone receptor-defined invasive breast cancers among postmenopausal women in Health Initiative Observational Study. *Am J Clin Nutr* 2008; 87:1009-18.
136. Epping MT, Wang L, Edel MJ, Carless L, Hernandez R. The human tumor antigen PRAME is a dominant repressor of retinoic acid receptor signaling. *Cell* 2005;122:835-47.
137. Kogai T, Kanamoto Y, Che LH, Taki K, Moatamed F, Schultz F, Schultz JJ, ETAL. Systemic retinoic acid treatment induces sodium/iodine symporter expression and radioiodide uptake in mouse breast cancer models. *Cancer Res* 2004; 64:415-22.
138. Lim SJ, Paeng JC, Kim SJY, Lee H, Moon DH. Enhanced expression of adenovirus-mediated sodium iodide symporter gene in MCF-7 breast cancer cells with retinoic acid treatment. *J Nucl Med* 2007, 48: 398-404.
139. Pazdro R, Burgess RJ. The role of vitamin E and oxidative stress in diabetes complications. *Mechanisms of Aging and Development* 2010;131:276-86.
140. Zingg JM. Modulation of signal transduction by vitamin E. *Mol Aspects Med* 2007; 28:5-6.
141. Sen CK, Khanna S, Roy S. Tocotrienols in health and disease: the other half of the natural vitamin E family. *Mol Aspects Med* 2007;28:692-728.
142. Porta EA. Dietary factors in lipofuscinogenesis and ceroidogenesis. *Arch Gerontol Geriatr* 2002;34:319-27.
143. Ezaki Y, Nishihara E, Shibata Y, Matsuo T, Kitagawa N, Negata I, et al. Vitamin E prevents neuronal cell death by repressing cyclooxygenase-2 activity. *Neuroreport* 2005; 16:1163-67.

144. Htland S, Muller D, Hayton S, Stoeckli E, Barrella L. Cortical gene expression in the vitamin E –deficient rat : possible mechanism for the electrophysiological abnormalities of visual and neural function .*Ann Nutr Metab* 2006;50:433-41.
145. Stolzing A, Widmer R, Jung T, Voss P, Grune T .Tocopherol-mediated modulation of age-related changes in microglial cells : Turnover of extracellular oxidizing protein material .*Free Radic Bio Med* 2006;40:2126-35.
146. Cecchini T, Ciaroni S, Ferri P , Ambrogini P , Cuppini R, Santi S, et al .  $\alpha$ -Tocopherol, an exogenous factor of adult hippocampal neurogenesis regulation . *J Neurosci Res* 2003;73:447-55.
147. Taber MG, Atkinson J, Vitamin E, antioxidant and nothing more ,*Free Radic Biol* 2007 ; 43:4-15.
148. Azzi A. Molecular mechanism of  $\alpha$  –tocopherol action. *Free Radic Biol Med* 2007; 43: 16-21.
149. Zingg JM .Vitamin E :An review of Major research direction .*Molecular Aspect of medicine* 2007;28:400-22.
150. Papas AM. Vitamin E : A new Prospective .*NUTRI News* 2008:1-8.
151. Constantinou C, Papas A, Constantinou A. Vitamin E and cancer: An insight into the anticancer activities of vitamin E isomers and analogs. *Int J Cancer* 2008; 123:739-52.
152. Sylvester PW, Theriault A .A role of tocopherols in the prevention of cardiovascular disease and breast cancer .*Curr Top Nutraceutical Res* 2003; 121-36.
153. Friderich MJ .To“E”, vitamin E, its role in health and disease in the question . *JAMA* 2004; 292:671-73.
154. Chang PN, Yap WN, Lee DT , Ling MT , Wong YC, Yap YL .Evidence of gamma tocotrienol as an apoptosis –inducing , invasion –suppressing and chemotherapy drug sensitizing agent in human melanoma CELLS . *Nutr Cancer* 2009; 1:357-66.
155. Hussin D, Mo H .d-Delta –tocotrienol –mediated suppression of proliferation of human PANC-1 , MIA pa Ca-2 and BxpC-3 pancreatic carcinoma cells .*pancreas* 2009;38:124-36.
156. Weng –Yew W ,Selvandy KR, Ming CH , Nesaretnam K. Suppression of tumor growth by plam tocotrienols via the attenuation of angiogenesis .*Nutr Cancer* 2009,61,367-73.

157. Kashiwagi K, Harada K, Yano Y, Kumadaki I , et al . A redox –silent analogue of tocotreinol inhibits hypoxic adaptation of lung cancer cells. *Biochem Biophys Res Commun* 2008; 365:875-81.
158. Kashiwagi K , Virgona N, Harada K , Kido W ,et al. A redox silent analogue of tocotretol acts as a potential cytotoxic agent against human methothelioma cells. *Life Sci* 2009; 84:650-56.
159. Nesaretnam K. Multitargeted therapy of cancer by tocotretinols: mini review .*Cancer Letters* 2008; 269:388-95.
160. Weij NL , Elsendoorn TJ, Lentjes EG ,Hopman GD , Wipkink –Bakker A, Zropean AH, Cleton FJ ,Osanto S. Supplementation with antioxidant micronutrients and chemotherapy- induced toxicity in cancer patients treated with cisplatin based chemotherapy : arandomised , doubleblinded , placebo- controlled study .*European Journal of Cancer* 2004; 40: 1713-23.
161. Bairati I, Meyer F, Jobin E, Gelinias M, Fortin A, Nabid A, et al. Antioxidant vitamins supplementation and mortality: a randomized trial in head and neck cancer patients. *Int J Cancer* 2006; 119:2221–24.
162. Armstrong, D.; Browne, R. *Free Rad. Diag. Med* 1994; 366: 43-58.
163. Levin RL, Willam JA., Stadetman ER, et al. Carbonyl assay for determination of oxidatively modified protein .*Method Enzymol* 1994; 233:346-57.
164. prieto P, Pineda M and AGUILAR m. Spectrophotometric quantization of antioxidant capacity through the formation of phosphomolybdenum complex: Specific application to the determination of vitamin E, *Analytical Biochemistry* 1999; 269: 337-41.
165. Pendyala G, Thomas B and Kumari S, The challenge of antioxidants to free radicals in periodontitis . *J Indian Soc Periodontol* 2008. ; 12: 79 – 83.
166. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 10. Lyon, France: International Agency for Research on Cancer [online], <<http://www.globocan.iarc.fr/factsheets/cancers/breast.asp>>; 2010 [accessed on 24.09.2012].
167. The National Cancer Registry Program of Egypt (NCRPE). Reports and Statistics: Aswan, Damietta & El-Minia [online], <<http://www.cancerregistry.gov.eg/reports.aspx>> [accessed 5.09.2012].

- 
168. The Gharbiah Population-based Cancer Registry (GPCR). Cancer in Egypt, Gharbiah [online], <[http://www.emro.who.int/ncd/pdf/cancer\\_registry\\_Egypt.pdf](http://www.emro.who.int/ncd/pdf/cancer_registry_Egypt.pdf)>; 2007 [accessed 5.09.2012].\
  169. Ali-eldin N. Cancer statistics 2002–2007: Preliminary report [online], <[http://www.nci.cu.edu.eg/lectures/Cancer\\_statistics\\_002-2007.pdf](http://www.nci.cu.edu.eg/lectures/Cancer_statistics_002-2007.pdf)> [accessed 5.09.2012].
  170. Sies H. Biochemistry of oxidative stress. *Angew Chem Int Ed Engl* 1986; 25: 1058-71.
  171. Gago-Domínguez M, Jiang X, Castelao JE. Lipid peroxidation, oxidative stress genes and dietary factors in breast cancer protection: a hypothesis. *Breast Cancer Res* 2007; 9: 201-11.
  172. Ray G, Batra S, Shukla NK, Deo S, Raina V, Ashok S et al. Lipid peroxidation, free radical production and antioxidant status in breast cancer. *Breast Cancer Res Treat* 2000; 59: 163-70.
  173. Trevisan M, Browne R, Ram M, Muti P, Freudenheim J, Carosella AM et al. Correlates of markers of oxidative status in the general population. *Am J Epidemiol* 2001; 154: 348-56.
  174. Shacter E. Quantification and significance of protein oxidation in biological samples. *Drug Metab Rev* 2000; 32: 306-7.
  175. Levine RL, Garland D, Oliver CN, Amici A, Climent I, Lenz AG, et al. Determination of carbonyl content in oxidatively modified proteins. *Methods Enzymol* 1990; 186: 464-78.
  176. Lawenda BD, Kelly KM, Ladas EJ, Sagar SM, Vickers A, Blumberg JB. Should supplemental antioxidant administration be avoided during chemotherapy and radiation therapy? *J Natl Cancer Inst* 2008; 100: 773–83.
  177. Ladas EJ, Jacobson JS, Kennedy DD, Teel K, Fleischauer A, Kelly KM. Antioxidants and cancer therapy: a systematic review. *J Clin Oncol* 2004; 22: 517–28.
  178. Greenlee H, Hershman DL, Jacobson JS. Use of antioxidant supplements during breast cancer treatment: a comprehensive review. *Breast Cancer Res Treat* 2009; 115: 437–52.
  179. Velicer CM, Ulrich CM. Vitamin and mineral supplement use among US adults after cancer diagnosis: a systematic review. *J Clin Oncol* 2008; 26: 665–73.
-

180. Lamson DW, Brignall MS. Antioxidants in cancer therapy; their actions and interactions with oncologic therapies. *Altern Med Rev* 1999; 4: 304–29.
181. Fantappie O, Lodovici M, Fabrizio P, Marchettia S, Fabbroni V, Solazzo M, et al. Vitamin E protects DNA from oxidative damage in human hepatocellular carcinoma cell lines. *Free Radic Res* 2004; 38:751–59.
182. Sakamoto K, Sakka M. Reduced effect of irradiation on normal and malignant cells irradiated in vivo in mice pretreated with vitamin E. *Br J Radiol* 1973;46:538–40.
183. Witenberg B, Kletter Y, Kalir HH, Raviv Z, Fenig E, Nagler A, et al. Ascorbic acid inhibits apoptosis induced by X irradiation in HL60 myeloid leukemia cells. *Radiat Res* 1999; 152:468–78.
184. Bairati I, Meyer F, Jobin E, Gelinas M, Fortin A, Nabid A, et al. Antioxidant vitamins supplementation and mortality: a randomized trial in head and neck cancer patients. *Int J Cancer* 2006;119:2221–24.
185. Bairati I, Meyer F, Gelinas M, Fortin A, Nabid A, Brochet F, et al. A randomized trial of antioxidant vitamins to prevent second primary cancers in head and neck cancer patients. *J Natl Cancer Inst* 2005;97:481–88.
186. D’Andrea GM. Use of antioxidants during chemotherapy and radiotherapy should be avoided. *CA Cancer J Clin* 2005;55:319–21.
187. Doyle C, Kushi LH, Byers T, Courneya KS, Demark-Wahnefried W, Grant B, et al. Nutrition and physical activity during and after cancer treatment: an American Cancer Society guide for informed choices. *CA Cancer J Clin* 2006; 56:323–53.
188. Hardy ML. Dietary supplement use in cancer care: help or harm. *Hematol Oncol Clin N Am* 2008; 22: 581–617.
189. Newman V, Rock CL, Faerber S, Flatt SW, Wright FA, Pierce JP, et al. Dietary supplement use by women at risk for breast cancer recurrence. *J Am Diet Assoc* 1998; 98:285–92.
190. Boon HS, Olatunde F, Zick SM. Trends in complementary/alternative medicine use by breast cancer survivors: comparing survey data from 1998 and 2005. *BMC Womens Health* 2007; 7:4.
191. Chen Z, Gu K, Zheng Y, Zheng W, Lu W, Shu XO. The use of complementary and alternative medicine among Chinese women with breast cancer. *J Altern Complement Med* 2008; 14:1049–55.
192. Greenlee H, Gammon MD, Abrahamson PE, Gaudet MM, Terry MB, Hershman DL, et al. Prevalence and predictors of antioxidant supplement use during breast

- cancer treatment: the Long Island Breast Cancer Study Project. *Cancer* 2009; 115:3271–82.
193. Weiss RB. The anthracyclines: will we ever find a better doxorubicin? *Semin Oncol* 1992; 19: 670-86.
194. Conklin KA. Chemotherapy-associated oxidative stress: impact on chemotherapeutic effectiveness. *Integr Cancer Ther* 2004; 3: 294-300.
195. Nohl H. Demonstration of the existence of an organo-specific NADH dehydrogenase in heart mitochondria. *Eur J Biochem* 1987; 169:585-91.
196. Kono Y, Fridovich I. Superoxide radical inhibits catalase. *J Biol Chem* 1982; 257:5751-54.
197. Amin KA, Mohamed BM, El-wakil MAM and Ibrahim SO. Impact of Breast Cancer and Combination Chemotherapy on Oxidative Stress, Hepatic and Cardiac Markers. *J Breast Cancer* 2012; 15(3): 306–12.
198. Alshabanah OA, Hafez MM, Al-Harbi MM, Hassan ZK, Al Rejaie SS, Asiri YA, et al. Doxorubicin toxicity can be ameliorated during antioxidant L-carnitine supplementation. *Oxid Med Cell Longev* 2010; 3: 428- 33.
199. Shacter E, Williamss JA, Lim M, Levine RL. Differential susceptibility of plasma proteins to oxidative modification: examination by western blot immunoassay. *Free Radic Biol Med* 1994; 17: 429–37.
200. Davies KJ. Degradation of oxidized proteins by the 20S proteasome. *Biochimie* 2001; 83: 301–10.
201. Cardona F, Tunez I, Tasset I, Montilla P, Collantes E, Tinahones FJ. Fat overload aggravates oxidative stress in patients with the metabolic syndrome. *Eur J Clin Invest* 2008; 38: 510– 15.
202. Lamprecht M, Greilberger JF, Schwabegger G, Hofmann P, Oettl K. Single bouts of exercise affect albumin redox state and carbonyl groups on plasma protein of trained men in a workload-dependent manner. *J Appl Physiol* 2008; 104: 1611–17.
203. Gulbahar O, Adisen H, Koca C, Aricioglu A, Gulekon A. Changes in serum carbonyl and malondialdehyde levels following colchicine and vitamin E treatment in Behcet's disease. *Methods Find Exp Clin Pharmacol* 2007; 29:521–24.
204. Uzun H, Konukoglu D, Gelisgen R, Zengin K, Taskin M. Plasma protein carbonyl and thiol stress before and after laparoscopic gastric banding in morbidly obese patients. *Obes Surg* 2007; 17: 1367–73.

- 
205. Il'yasova D, Mixon G, Wang F, Marcom PK, Marks J, Spasojevich I, Craft N, Arredondo F, DiGiulio R. Markers of oxidative status in a clinical model of oxidative assault: a pilot study in human blood following doxorubicin administration. *Biomarker* 2009; 14(5): 321-25.
  206. Timur M, Akbas SH, Ozben T. The effect of Topotecan on oxidative stress in MCF-7 human breast cancer cell line. *Acta Biochim Pol* 2005;52(4):897-902.
  207. Conklin KA. Dietary antioxidants during cancer chemotherapy: impact on chemotherapeutic effectiveness and development of side effects. *Nutr Cancer* 2000; 37: 1-18.
  208. Conklin KA. Chemotherapy-associated oxidative stress: impact on chemotherapeutic effectiveness. *Integr Cancer Ther* 2004; 3: 294-300.
  209. Conklin KA, Nicolson GL. Molecular replacement in cancer therapy: reversing cancer metabolic and mitochondrial dysfunction, fatigue and the adverse effects of therapy. *Curr Cancer Ther Rev* 2008; 4: 66-76.
  210. Nicolson GL, Conklin KA. Reversing mitochondrial dysfunction, fatigue and the adverse effects of chemotherapy of metastatic disease by Molecular Replacement Therapy. *Clin Expl Metastasis* 2008; 25: 161-69.
  211. Nicolson GL. Lipid replacement/antioxidant therapy as an adjunct supplement to reduce the adverse effects of cancer therapy and restore mitochondrial function. *Pathol Oncol Res* 2005; 11: 139-44.
  212. Britton G. Structure and properties of Carotenoids in relation to function. *FASEB J* 1995; 9: 1551-58.
  213. Krinsky NI. The biological properties of carotenoids. *Pure Appl Chem* 1994; 66: 1003-10.
  214. Foote CS, Chang YC, Denny RW. Chemistry of singlet oxygen X. Carotenoid quenching parallels biological protection. *J Am Chem Soc* 1970; 92: 5216-18.
  215. Handelman GJ. Carotenoids as scavengers of active oxygen species. In: *Handbook of antioxidants*, E Cadenas, L Packer (eds). Marcel Dekker, Inc, New York 1996. pp. 259-314.
  216. Kamal-Eldin A, Appelqvist LA. The chemistry and antioxidant properties of tocopherols and tocotrienols, *Lipids* 1996; 31: 671-701.
  217. Machlin LJ, Vitamin E, in: L.J. Machlin (Ed.), *Handbook of Vitamins*, Dekker, New York, 1991; pp. 99-144.
-

218. A. Bast, G.R.M.M. Haenen, The toxicity of antioxidants and their metabolites, *Environ. Toxicol. Pharmacol* 2002 ; 11: 251–58.

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## Appendix (1)

Serum malondialdehyde (MDA) concentrations (nmol/ml) in all different studies groups

Number of cases	Control Group (Group I)		Vitamin-treated Group (Group II)	
	Before chemotherapy (n=20)	After chemotherapy (n=20)	Before chemotherapy (n=25)	After chemotherapy (n=25)
1	8.819	12.673	11.448	6.551
2	12.67	14.714	12.714	8.795
3	7.979	11.653	9.612	4.285
4	5.122	10.632	10.69	7.979
5	10.836	15.0	6.714	3.714
6	9.612	14.918	10.87	6.142
7	10.857	14.102	12.67	8.367
8	13.0	14.918	8.816	4.285
9	10.408	13.734	12.673	12.285
10	14.408	16.183	7.571	3.897
11	14.489	12.857	10.877	6.551
12	12.489	16.142	12.265	8.367
13	8.102	14.06	12.897	8.918
14	10.04	12.061	11.653	8.163
15	12.673	10.285	9.224	5.938
16	14.489	12.653	9.408	7.183
17	12.061	12.865	10.632	5.938
18	9.653	12.011	10.02	7.979
19	8.102	10.523	11.32	8.698
20	8.795	9.92	9.225	6.836
21			11.874	9.6122
22			10.0	7.265
23			12.045	9.224
24			11.5	9.15
25			12.3	8.71

## Appendix (2)

Serum carbonyl protein (CP) concentration ( $\mu\text{M}^{-1}\text{cm}^{-1}$ ) in all different studies groups

Number of cases	Control Group (Group I)		Vitamin-treated Group (Group II)	
	Before chemotherapy (n=20)	After chemotherapy (n=20)	Before chemotherapy (n=25)	After chemotherapy (n=25)
1	16.745	5.836	15.927	9.854
2	15.836	19.65	16.927	11.29
3	17.545	25.127	16.309	9.618
4	14.381	34.909	16.381	11.49
5	16.018	31.29	14.4	7.454
6	13.781	33.672	16.545	9.472
7	14.963	19.636	15.872	13.29
8	13.29	26.036	13.472	9.472
9	16.927	27.654	15.49	10.909
10	14.49	31.29	16.945	14.58
11	13.4	24.018	15.854	9.654
12	15.618	24.127	13.818	8.48
13	17.109	28.49	16.781	13.29
14	15.963	31.54	17.145	13.472
15	16.8	27.654	15.909	9.836
16	16.8	24.381	14.145	9.145
17	15.872	28.381	16.727	13.49
18	14.52	27.12	6.745	13.09
19	12.021	25.012	15.924	9.836
20	10.3	16.9	16.2	11.272
21			14.145	8.181
22			16.745	11.436
23			15.7	12.4
24			16.3	13.9
25			13.8	9.7

## Appendix (3)

The total antioxidant capacity (ug/ml) in different studies groups

Number of cases	Control Group (Group I)		Vitamin-treated Group (Group II)	
	Before chemotherapy (Group Ia) (n=20)	After chemotherapy (n=20)	Before chemotherapy (n=25)	After chemotherapy (n=25)
1	0.98	0.854	0.933	1.918
2	0.985	0.856	1.72	2.5
3	1.002	0.654	1.81	2.76
4	1.2	0.632	1.23	1.429
5	0.985	0.521	1.43	2.105
6	0.935	0.785	1.373	2.364
7	1.325	0.846	1.302	2.075
8	1.523	0.528	2.137	2.804
9	1.231	0.698	1.92	1.431
10	1.256	0.541	1.2	2.364
11	0.854	0.879	1.21	1.702
12	1.652	1.002	0.973	1.644
13	1.023	0.658	1.017	2.364
14	1.654	0.209	1.0172	2.102
15	0.254	1.589	0.182	2.768
16	0.897	0.98	1.381	1.871
17	1.987	1.003	1.973	2.831
18	1.532	0.589	2.275	3.426
19	0.954	0.79	1.918	1.918
20	0.97	0.73	1.05	1.12
21			1.11	1.91
22			0.76	1.77
23			0.809	1.34
24			1.25	2.12
25			1.03	2.56

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دور الامداد بفيتامينات أ وهـ فى التوازن الأوكسىدى فى مريضات سرطان الثدى

رسالة مقدمة

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الماجستير

فى

الكيمياء الطبية التطبيقية

من

فردوس خميس مصطفى

بكالوريوس علوم ٢٠٠٤

معهد البحوث الطبية

جامعة الإسكندرية

٢٠١٤

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