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ROLE OF COENZYME Q10 IN CURRENT ONCOLOGY PRACTICE: SUBSTANCE OR SHADOW!

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Abstract Coenzyme Q_{10} (CoQ_{10}) is a naturally occurring, lipid soluble substance. CoQ_{10} acts as an intermediate of the electron transport chain situated in mitochondrial membrane and vital for ATP production. CoQ_{10} also serves as an intercellular antioxidant. These functions make the basis for all the clinical use of CoQ_{10}. CoQ_{10} levels are altered in a number of oncological as well as non-oncological diseases. CoQ_{10} has an impact on the expression of many genes involved in metabolism, cellular transport, transcription control, and cell signaling, making CoQ_{10} a potent gene regulator. CoQ_{10} supplementation is useful in diseases associated with CoQ_{10} deficiency. Oral CoQ_{10} administration can correct CoQ_{10} deficiency since it increases CoQ_{10} tissue levels. CoQ_{10} therapy has no serious side effects in humans and new formulations have been developed that increase CoQ_{10} absorption and tissue distribution. CoQ10 has a role in carcinoma breast, cervix, lung, prostate, melanoma, cancer chemotherapy and cancer related fatigue. Future trends involving CoQ_{10} in many cancers needs more clinical trials for better understanding of CoQ_{10} efficacy.

BACKGROUND

Cancer is one of the most life-threatening diseases and will remain a demanding issue in healthcare. Besides targeting the machinery directly involved in cell death execution, the preceding signaling pathways are attractive targets as these harbor critical upstream mediators with many of them understudied.[1]

Coenzyme Q10 (CoQ10) is a key molecule in all energy requiring processes, including proliferation, apoptosis, angiogenesis, and immune function, suggesting the potential for multiple roles in the initiation and progression of cancer.[2] Despite the critical role of CoQ10 in many cellular functions, its potential relationship with cancer development

and progression has not received appropriate attention. Epidemiological or clinical studies of plasma or tissue CoQ10 are rare in the literature and have involved limited numbers of subjects.[2]

This review intends to critically analyze the role of CoQ10 (if any) in current clinical oncology practice.

INTRODUCTION

CoQ10 is fat-soluble quinine with properties similar to vitamins.[3] Because of its ubiquitous presence in virtually every cell of the human body and its quinine structure, CoQ10 is also known as ubiquinone.[4] It is an antioxidant and a redox coenzyme of the respiratory chain. Its primary role is as an essential intermediate of the electron transport system in the mitochondria. Coenzyme Q, in addition to membrane lipids, protects proteins and DNA.[5]

MECHANISM OF ACTION

Biochemically, CoQ10 works by- (1) having a direct regulatory role on succinyl and the reduced form of nicotinamide adenine dinucleotide (NADH) dehydrogenases, (2) acting as a catalyst and playing an integral role in regulating the cytochrome bc1 complex, and (3) possibly having direct membrane-stabilizing properties that are separate from its role in oxidative phosphorylation.[3]

One of the primary pathways of drug-induced apoptosis is the pathway that involves release of cytochrome c from mitochondria with the concomitant formation of superoxide radicals, hydrogen peroxide and highly toxic hydroxyl radicals via Fenton and Haber-Weiss reactions. Free radical generation is not necessary for a drug to exert its cytotoxic effect on neoplastic cells, because superoxide generation occurs secondarily.[6]

CoQ10 was also recognized to have an effect on genes[4] involved in cell signaling, intermediary metabolism, transport and transcription control, and inflammation. However, the molecular mechanisms whereby CoQ10 induces these pleiotropic effects has yet to be completely understood.[4] Thus, CoQ10 works within human cells to create energy for cell growth and maintenance.[3]

ABSORPTION, TISSUE UPTAKE AND PHARMACOKINETICS

Table 1 shows the different parameters related to CoQ10 absorption and pharmacokinetics. CoQ10 is absorbed slowly from the small intestine, possibly because it has a high molecular weight and is not very water soluble, passes into the lymphatics, and finally to the blood and tissues. Higher plasma CoQ10 concentrations are necessary to facilitate uptake by peripheral tissues. Further studies are needed to elucidate whether age, gender, lipoprotein status, diet, dosage formulation, or other factors may affect the bioavailability of CoQ10 with chronic dosing. Monitoring CoQ10 plasma concentrations may be considered after 3–4 weeks of constant dosing, when steady-state conditions exist, with dosage levels from 5-10 μg/ml.[4]

Cellular and tissue levels of CoQ10 decrease with age, and cellular levels below a critical threshold are incompatible with life. In contrast, plasma levels of CoQ10 are reported by some to rise as a function of age, and are higher in postmenopausal women. Supplemental CoQ10 increases circulating α-T levels in humans, however, the determinants of circulating CoQ10 and its physiological regulation in vivo are unknown.[2]

Table 1 Different parameters related to CoQ10 absorption and pharmacokinetics[1, 10, 11]

CoQ 10 parameter	Remarks
Normal range	0.40-1.91µmol/L (0.34-1.65µg/ml) Males have higher levels than Females Younger have higher level than Adults
Sources	Naturally in diet Heart, chicken leg, herring, trout
Daily intake from food	3-5mg/day
Absorption	3 times faster with food intake Slightly better with oil based forms of CoQ10
Therapeutic Dosage: Adults **Children**	Upto 1200 mg/day Upto 10 mg/kg/day
Peak plasma level	Achieved 5-10 hour after ingestion

TOXICITY, SIDE EFFECTS AND DRUG INTERACTIONS

CoQ10 treatment is safe, even at the highest doses cited in the literature. Most clinical trials have not reported significant adverse effects that necessitated stopping therapy. However, gastrointestinal effects such as abdominal discomfort, nausea, vomiting, diarrhea, and anorexia have occurred. Allergic rash and headache have also been reported.[4]

It's antiplatelet effect may increase the risk of bleeding. It undergoes biotransformation in the liver and is eliminated primarily via the biliary tract, so it can accumulate in patients with hepatic impairment or biliary obstruction.[4]

Side effects of CoQ10 may include insomnia, elevated liver enzymes, dizziness, photophobia, irritability, headache, and heartburn; however, regardless of the dosage used, few untoward effects have been observed.[3]

Beta blockers propranolol and metoprolol, and phenothiazines and tricyclic antidepressants have been shown to inhibit CoQ10 -dependent enzymes. CoQ10 may have an additive antihypertensive effect when given with antihypertensive drugs. It acts like vitamin K, it may counteract the anticoagulant effects of warfarin. Cholesterol-lowering drugs such as lovastatin and pravastatin inhibit the enzyme HMG-CoA reductase, required for synthesis of cholesterol as well as CoQ10, resulting in a decreased serum CoQ10. CoQ10 may improve beta-cell function and enhance insulin sensitivity, which may reduce insulin requirements for diabetic patients.[4]

CoQ10 IN ONCOLOGY

Generally, redox signaling at the mitochondria is a vital pathway relevant to cancer research, as it controls both energy metabolism and regulation of cell death.[1] Table 2 shows the various uses of CoQ10 in addition to cancer.

Free radicals have been implicated in the action of many chemotherapeutic drugs. Camptothecin and other chemotherapeutic drugs, such as etoposide, doxorubicin, and methotrexate, induce an increase in CoQ10 levels as part of the antioxidant defense against free radical production under these anticancer treatments in cancer cell lines. Chemotherapy treatment induced both free radical production and an increase in CoQ10 levels in all the cancer cell lines tested. Reduced CoQ10 form levels were particularly enhanced. CoQ10 increased levels were associated with up-regulation of COQ genes expression, involved in

CoQ10 biosynthesis. At the translational level, COQ7 protein expression levels were also increased. Furthermore, CoQ10 biosynthesis inhibition blocked camptothecin-induced CoQ10 increase, and enhanced camptothecin cytotoxicity. CoQ10 increase is implicated in the cellular defense under chemotherapy treatment and may contribute to cell survival.[7]

Published data suggest that at least 80% of cancer patients who are undergoing treatment, especially multimodality therapy, experience a significant degree of fatigue that may negatively impact their quality of life (QOL), emotional well-being and treatment tolerance. Compared with the fatigue experienced by those without cancer, cancer related fatigue is typically more severe and not reliably relieved by rest. Patients perceive fatigue to be the most distressing symptom associated with their cancer experience, even worse than pain or nausea and vomiting. However, studies suggest that fatigue usually does not exist in isolation, but rather as part of a symptom cluster that often includes depression, difficulty in sleeping and pain.[3] Many clinical trials have addressed correlation between CoQ10 and fatigue.

Table 2

Conditions	
Dietary supplement	
Fatigue	
Inherited defects in CoQ10 biosynthesis	
Cardiovascular conditions	Atherosclerosis Congestive heart failure Hypertrophic cardiomyopathy Cardiac fatigue
Neurodegenerative conditions	Early stage Parkinson's disease
Cancer	Prevent cardiotoxicity in patients receiving anthracycline based Chemotherapy Breast cancer Lung cancer Prostate cancer Melanoma Liver cancer Cancer cervix
Used in CoQ10 deficiency states	Primary CoQ 10 deficiencies Secondary CoQ 10 deficiencies such as mitochondrial diseases Advancing age Encephalomyopathy Severe infantile multisystemic disease Leigh syndrome with growth retardation Isolated myopathy Fibromyalgia Cardiovascular disease Neurodegenerative diseases Diabetes mellitus Male infertility Periodontal disease Down's syndrome Migraine Pregnancy (Pre eclampsia)

BREAST CANCER

Plasma CoQ10 levels were significantly, positively associated with breast cancer risk, especially among women diagnosed at least one year after blood draw, suggesting that inclusion of women with latent breast cancer may have somewhat attenuated the breast cancer-CoQ10 association.[8]

Folkers et al[9] and Jolliet et al[10] reported lower levels of plasma CoQ10 in breast cancer patients. Folkers et al reported that 23% of breast cancer patients compared to 4% of cancer-free women had CoQ10 deficiency (blood CoQ10 levels below 0.5 μg/mL).

Circulating levels of CoQ10 may have been influenced by breast cancer and/or its therapy. It is possible that age or menopausal status may influence the association of breast cancer with levels of CoQ10.[8]

Palan et al[11] reported that serum CoQ10 levels were higher among postmenopausal than among premenopausal women, suggesting that circulating steroid hormone or gonadotropin concentrations may influence plasma levels of CoQ10.

The inverse association of CoQ10 with SHBG might partially explain the relation between CoQ10 and postmenopausal breast cancer, as higher SHBG concentrations are associated with reduced breast cancer risk.[8]

In the Shanghai Women's Health Study (SWHS), a significant inverse association was found for low circulating CoQ10 with subsequent incidence of breast cancer for women whose breast cancer was diagnosed > one year after obtaining blood specimen with the highest risk associated with women in the lowest quintile of circulating CoQ10. Significantly increased risk for breast cancer was observed for the MEC study at CoQ10 levels >1,000 ng/ml. A possible explanation reconciling these opposing results is that women at either extreme of CoQ10 may be at increased risk for breast cancer. Women with circulating CoQ10 levels in the range of 500–800 ng/ml have the lowest risk for developing breast cancer.[2]

Chai et al[8] found that plasma CoQ10 levels were higher among breast cancer cases who were current HRT users compared to non-users. Increased circulating CoQ10 in aging humans may be a response to chronic inflammation and heightened systemic and/or tissue specific oxidation. Clearly, the association of such markers with disease risk is complex and care must be exercised in their interpretation. The observation that CoQ10 was positively associated with breast cancer risk in individuals with low, but not high, γ-tocopherol levels deserves further investigation.

Prospective studies with a larger sample size and longer follow-up periods are needed to determine the potential role of CoQ10 in the etiology of breast cancer, as well as additional research into the physiologic regulation and function of circulating CoQ10.[8]

Doxorubicin (adriamycin), an anthracycline antibiotic is part of standard adjuvant therapy for breast cancer, which significantly improves disease-free and overall survival. Despite these benefits, 3-20% of doxorubicin treated breast cancer patients develop chronic cardiomyopathic changes and congestive heart failure causing deaths, disability, and limiting its use. Effective treatments are needed to prevent this cardiotoxicity while not decreasing the anti-tumor effects of doxorubicin. Currently, no treatments are available to prevent this cardiotoxicity that have been proven to be safe and effective.[6]

During doxorubicin treatment, an acute rise in plasma CoQ10 is followed by a marked

post-treatment decrease in the CoQ10 content of cardiac and skeletal muscle. Damage to the mitochondria of cardiac myocytes is one of the earliest and most prominent histological findings of doxorubicin induced cardiomyopathy. A dose of 300 mg per day (safe limit is 1200mg per day) for 11 days has been shown to raise plasma CoQ10 concentrations by 300-400%. Administering CoQ10 either before or during doxorubicin administration can prevent doxorubicin-induced cardiotoxicity by preventing or slowing the displacement of CoQ10 by doxorubicin metabolites. In addition, CoQ10 allowed for increased doses of doxorubicin to be administered. Despite the potential benefits of CoQ10 in preventing doxorubicin-induced cardiotoxicity, there is concern that CoQ10 may decrease the desired pro-oxidant treatment effects of doxorubicin.[6,12]

Tamoxifen (TAM) is used in adjuvant therapy for all stages of breast carcinomas and in chemoprevention of high-risk group. TAM also has estrogenic activity on liver and endometrium causing severe oxidative stress with various biochemical derangements. Co-administration with CoRN (CoQ 10, Riboflavin and Niacin) with TAM has shown favorable impact on various blood chemistry profiles.[13]

Supplementation of CoRN along with tamoxifen to breast cancer patients reduces the serum tumour marker levels of CEA and CA 15-3, thereby offering better cancer prognosis by reducing the risk of developing cancer recurrence and metastasis, improved quality of life.[13,14]

Tamoxifen therapy is found to cause hypertriglyceridemia by reducing activity of lipolytic enzymes on triglycerides, and thereby increasing the risk of cardiovascular disease. Angiogenesis promotes local tumour progression and invasion and enables tumour cell dissemination and metastasis formation. Study found that co-administration of Coenzyme Q10 (100 mg/d) along with tamoxifen (10 mg, twice a day) to breast cancer patients reduced the level of angiogenesis markers and lipid levels.[15]

LUNG CANCER

CoQ10 is a redox molecule which is found both in oxide forms (Ubikinon-10) and reduced forms (Ubikinol-10) in the mitochondria. Significantly lower erythrocyte CoQ10 levels were seen in patients with lung cancer.[16]

Decreased oxide CoQ10 enzyme level in the lung cancer patients may be a useful parameter for lung cancer risk assessment.[16]

PROSTATE CANCER

Clinical studies have examined the effect of CoQ10 in combination with other antioxidants, in preventive and theapeutic settings.

Chai W et al in a study found no effect of combination of CoQ10, vitamin E, vitamin C, and selenium on PSA or hormonal levels in prostate cancer patients and suggested further studies to assess a possible protective effect of higher circulating CoQ10 levels on the risk of developing prostate cancer.[17]

Hoenjet KM et al found that supplementation of a combination of vitamin E, selenium, vitamin C and coenzyme-Q10 does not affect serum level of PSA or hormone levels in patients with hormonally untreated carcinoma of the prostate.[18]

Quiles JL et al demonstrated role of CoQ10 as modulator of differential gene expression and free radical production in prostate cells. Coenzyme Q supplementation significantly lowered cell growth of the PC3 cancer line of prostate cancer. If these results are confirmed with additional experiments, it could represent a

novel and interesting approach on the biomedical use of coenzyme Q10 in cancer therapy.[19]

LIVER CANCER

Tharappel et al examined the effect of antioxidant phytochemicals on the hepatic tumor promoting activity of 3,3′,4,4′-Tetrachlorobiphenyl (PCB-77) and found that dietary antioxidants were not effective at inhibiting tumor promotion by PCBs.[20]

MELANOMA

Rusciani L et al. in their study on use of recombinant interferon alpha-2b and CoQ10 as a postsurgical adjuvant therapy for stage I & II melanoma found that significantly different rates of disease progression were observed in the interferon+coenzyme Q10 group for both stages. Long-term administration of the CoQ10 combination seemed to induce significantly decreased rates of recurrence and had negligible adverse effects. A survival study could not be undertaken owing to the small patient sample and the short duration of follow-up.[21]

Rusciani L et al, in a study correlating plasma coenzyme Q10 levels as an independent prognostic factor for melanoma progression found that CoQ10 levels were significantly lower in patients who developed metastases than in the metastasis-free subgroup and concluded that baseline plasma CoQ10 levels are a powerful and independent prognostic factor that can be used to estimate the risk for melanoma progression.[22]

CERVICAL CANCER

Palan PR et al assessed plasma concentrations of CoQ10 & tocopherols in cervical intraepithelial neoplasia and cervical cancer. Results showed that mean plasma levels of CoQ10, alpha-tocopherol and gamma-tocopherol were significantly lower, in patients with various grades of CIN and cervical cancer. After controlling for age and smoking, an inverse association between histological grades of epithelial lesions and both plasma CoQ10 and alpha-tocopherol concentrations was observed. The low plasma concentrations of CoQ10 may be due to deficient dietary intake or a decrease in endogenous CoQ10 biosynthesis that may reflect increased utilization as a result of free radical reactive oxygen species induced oxidative stress.[23]

OTHER CANCERS

Hertz et al evaluated the survival of patients with end-stage cancer who received supplements of CoQ10 and a mixture of other antioxidants (e.g. vitamin C, selenium, folic acid and β-carotene). Fourty one patients were included. Primary cancers were located in the breast, brain, lungs, kidneys, pancreas, oesophagus, stomach, colon, prostate, ovaries and skin. Median predicted survival was 12 months (range 3 – 29 months), whereas median actual survival was 17 months, which is > 40% longer than the median predicted survival. Mean actual survival was 28.8 months versus 11.9 months for mean predicted survival. 24% survived for less time than predicted, whereas 76% survived for longer. Treatments were very well tolerated with few adverse effect.[24]

Sieswerda E et al showed that CoQ10 may be used for treating anthracycline-induced symptomatic and asymptomatic cardiotoxicity during and after treatment for childhood cancer.[25]

Forgionne GA et al in their study on bovine cartilage, coenzyme Q10, and wheat grass therapy for primary peritoneal cancer, reported case of an 89-year-old female, who refused chemotherapy but accepted a nutritional alternative. Results after more than 4 years of the

nutritional regime were encouraging with regards to objective and subjective measures.[26]

CONCLUSION

Future research needs to address many unanswered questions regarding the impact of oxidative stress on the therapeutic efficacy of cancer chemotherapy, the role that oxidative stress plays in the development of chemotherapy-induced side effects and the effect of antioxidants on anticancer activity and the development of therapy-induced adverse effects. Fundamental studies that elucidate the impact of oxidative stress, and specifically ROS-generated aldehydes, on cell cycle progression and apoptotic pathways may guide us to interventions that could enhance chemotherapeutic efficacy. Further investigation of GSH for preventing cisplatin toxicity and coenzyme Q10 for preventing doxorubicin cardiotoxicity appears to be indicated based upon existing studies. Finally, clinical studies must be conducted to determine both the short-term and long-term impact of antioxidants, singly and in combination, upon the efficacy of cancer chemotherapy and the development of chemotherapy-induced side effects.

REFERENCES

1. Schweikert EM, Devarajan A, Witte I, Wilgenbus P, Amort J, Forstermann U, et al. PON3 is upregulated in cancer tissues and protects against mitochondrial superoxide-mediated cell death. Cell Death and Differentiation (2012) 19, 1549–60.
2. Cooney RV, Dai Q, Gao YT, Chow WH, Franke AA, Shu XO, et al. Low plasma coenzyme Q10 levels and breast cancer risk in Chinese women. Cancer Epidemiol Biomarkers Prev. 2011 June ; 20(6): 1124–30.
3. Lesser GJ, Case D, Stark N, Williford S, Giguere J, Garino LA, et al. A Randomized Double-Blind, Placebo-Controlled Study of Oral Coenzyme Q10 to Relieve Self-Reported Treatment Related Fatigue in Newly Diagnosed Patients with Breast Cancer Support Oncol. 2013 March ; 11(1): 31–42.
4. Garrido-Maraver J, Cordero MD, Oropesa-Ávila M, Vega AF, Mata M, Pavón AD, et al. Coenzyme Q 10 Therapy. Mol Syndromol 2014;5:187–97.
5. Bahar M, Khaghani S, Pasalar P, Paknejad M, Khorramizadeh MR, Mirmiranpour H, et al. Exogenous coenzyme Q10 modulates MMP-2 activity in MCF-7 cell line as a breast cancer cellular model. Nutrition Journal 2010 9:62.
6. Conklin KA. Cancer Chemotherapy and Antioxidants. American Society for Nutritional Sciences. J. Nutr. 2004; 134: 3201S–3204S.
7. Brea-Calvo G, Rodríguez-Hernández A, Fernández-Ayala DJ, Navas P, Sánchez-Alcázar JA. Chemotherapy induces an increase in coenzyme Q10 levels in cancer cell lines. Free Radic Biol Med. 2006 Apr 15;40(8):1293-302.
8. Chai W, Cooney RV, Franke AA, Shvetsov YB, Caberto CP, Wilkens LR, at al. Plasma Coenzyme Q10 levels and Postmenopausal Breast Cancer Risk: The Multiethnic Cohort Study. Cancer Epidemiol Biomarkers Prev. 2010 September ; 19(9): 2351–6.
9. Folkers K, Osterborg A, Nylander M, Morita M, Mellstedt H. Activities of vitamin Q10 in animal models and a serious deficiency in patients with cancer. Biochem Biophys Res Commun 1997; 234:296–9.
10. Jolliet P, Simon N, Barre J, et al. Plasma coenzyme Q10 concentrations in breast cancer: prognosis and therapeutic consequences. International Journal of Clinical Pharmacology and Therapeutics 1998; 36:506–9.
11. Palan PR, Connell K, Ramirez E, et al. Effects of menopause and hormone replacement therapy on serum levels of coenzyme Q10 and other lipid-soluble antioxidants. Biofactors 2005;25:61–6.
12. Greenlee H, Shaw J, Lau YKI, Naini A, Maurer M. Effect of Coenzyme Q10 on Doxorubicin Cytotoxicity in Breast Cancer Cell CulturesIntegr Cancer Ther. 2012 September ; 11(3): . doi:10.1177/1534735412439749.
13. Yuvaraj S, Premkumar VG, Shanthi P, Vijayasarathy K, Gangadaran SG, Sachdanandam P. Effect of Coenzyme Q(10), Riboflavin and Niacin on Tamoxifen treated postmenopausal breast cancer women with special reference to blood chemistry profiles. Breast Cancer Res Treat. 2009 Mar; 114(2):377-84.

14. Premkumar VG, Yuvaraj S, Vijayasarathy K, Gangadaran SGD, Sachdanandam P. Effect of Coenzyme Q10, Riboflavin and Niacin on Serum CEA and CA 15-3 Levels in Breast Cancer Patients Undergoing Tamoxifen Therapy. Biol. Pharm. Bull. 2007; 30(2): 367-70.
15. Sachdanandam P. Antiangiogenic and hypolipidemic activity of coenzyme Q10 supplementation to breast cancer patients undergoing Tamoxifen therapy. Biofactors. 2008; 32(1-4):151-9.
16. Cobanoglu U, Demir H, Cebi A, Sayır F, Alp HH, Akan Z, et al. Lipid Peroxidation, DNA Damage and CoenzymeQ10 in Lung Cancer Patients - Markers for Risk Assessment? Asian Pacific J Cancer Prev, 12, 1399-1403.
17. Chai W, Cooney RV, Franke AA, Caberto CP, Wilkens LR, Marchand LL, et al. Plasma Coenzyme Q10 Levels and Prostate Cancer Risk: The Multiethnic Cohort Study. Cancer Epidemiol Biomarkers Prev 2011; 20:708-10.
18. Hoenjet KM, Dagnelie PC, Delaere KP, Wijckmans NE, Zambon JV, Oosterhof GO. Effect of a nutritional supplement containing vitamin E, selenium, vitamin c and coenzyme Q10 on serum PSA in patients with hormonally untreated carcinoma of the prostate: a randomised placebo-controlled study. Eur Urol. 2005 Apr; 47(4):433-9.
19. Quiles JL, Farquharson AJ, Ramírez-Tortosa MC, Grant I, Milne L, Huertas JR, Battino M, Mataix J, Wahle KW. Coenzyme Q differentially modulates phospholipid hydroperoxide glutathione peroxidase gene expression and free radicals production in malignant and non-malignant prostate cells. Biofactors. 2003; 18(1-4):265-70.
20. Tharappel JC, Lehmler HJ, Srinivasan C, Robertson LW, Spear BT, Glauert HP. Effect of Antioxidant Phytochemicals on the Hepatic Tumor Promoting Activity of 3,3′,4,4′-Tetrachlorobiphenyl (PCB-77). Food Chem Toxicol. 2008 November ; 46(11): 3467-74.
21. Rusciani L, Proietti I, Paradisi A, Rusciani A, Guerriero G, Mammone A, et al. Recombinant interferon alpha-2b and coenzyme Q10 as a postsurgical adjuvant therapy for melanoma: a 3-year trial with recombinant interferon-alpha and 5-year follow-up. Melanoma Res. 2007 Jun; 17(3):177-83.
22. Rusciani L, Proietti I, Rusciani A, Paradisi A, Sbordoni G, Alfano C, et al. Low plasma coenzyme Q10 levels as an independent prognostic factor for melanoma progression. J Am Acad Dermatol. 2006 Feb; 54(2):234-41.
23. Palan PR, Mikhail MS, Shaban DW, Romney SL. Plasma concentrations of coenzyme Q10 and tocopherols in cervical intraepithelial neoplasia and cervicalcancer. Eur J Cancer Prev. 2003 Aug; 12(4):321-6.
24. N Hertz, RE Lister. Improved survival in patients with end-stage cancer treated with coenzyme Q10 and other antioxidants: a pilot study. J Int Med Res 2009; 37:1961-71.
25. Sieswerda E, van Dalen EC, Postma A, Cheuk DK, Caron HN, Kremer LC. Medical interventions for treating anthracycline-induced symptomatic and asymptomatic cardiotoxicity during and after treatment for childhood cancer. Cochrane Database Syst Rev. 2011 Sep 7; (9):CD008011.
26. Forgionne GA. Hoenjet KM1, Dagnelie PC, Delaere KP, Wijckmans NE, Zambon JV, Oosterhof GO. Bovine cartilage, coenzyme Q10, and wheat grass therapy for primary peritoneal cancer. The Journal of Alternative and Complementary Medicine. February 2005, 11(1): 161-165.

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