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Breast cancer treatment with coenzyme Q10 (CoQ10)

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Abstract Coenzyme Q10 (CoQ10) was identified in the late 1950s, and its potential role in cancer therapy appeared in the early 1960s when decreasing CoQ10 levels were found in some cancer patients. Breast cancer is a serious global health issue, and novel treatments are being developed. Its treatment is being investigated. CoQ10 has shown immune-boosting effects in clinical studies, encouraging researchers to look into its possible influence on breast cancer. Several research have looked at the link between CoQ10 and breast cancer, focusing on its biological effects such as cytochrome c release and subsequent radical production. CoQ10 supplementation is commonly used by cancer patients to alleviate a perceived CoQ10 deficit associated with treatment-related toxicity. Notably, evidence shows that CoQ10 may be connected to lower tocopherol levels increasing the risk of breast cancer. However, bigger sample sizes, longer follow-up periods, and a better knowledge of the physiological role of circulating CoQ10 are required for a thorough assessment of CoQ10's possible role in breast cancer etiology. Antibacterial medications, therapy-induced adverse effects, and oxidative stress all have an impact on chemotherapy-related problems. Although CoQ10 has shown potential as an alternative breast cancer treatment, it is crucial to highlight that existing standard therapies, such as chemotherapy, radiation therapy, and hormone therapy, are not without their limitations. and targeted therapies are all options. Remain the cornerstone of breast cancer care. Always seek the most current and trustworthy information about breast cancer therapy from medical specialists.

Keywords: coenzyme Q10, apoptosis, mitochondria, mechanism of action, breast cancer

1. Introduction and Background

In 1957 Chemotherapy, radiation treatment, hormone therapy, and targeted therapies were all options. Coenzyme Q10 (CoQ10) was first studied as a potential cancer therapy in 1961 when it was found that certain patients with cancer had lower-than-normal levels of the substance in their blood. In patients with myeloma, lymphoma, and malignancies it has been demonstrated that low blood levels of CoQ10 occur in the breast, lung, prostate, pancreas, colon, kidney, and head and neck regions. Trials have demonstrated that CoQ10 improves immune system performance. CoQ10 is utilized as an adjuvant treatment for cancer as a result. Analogs of CoQ10 have been proven to stop the development of cancer cells in research conducted on animals and in laboratories. Adjuvant therapy is a type of treatment that is used to increase the chances of a successful recovery after primary therapy. Research in labs and in animals has demonstrated that CoQ10 analogues may stop cancer cells from growing (Faloon, 2006).Cancer is one of the most fatal illnesses and will continue to be a difficult issue in health services. Aside from aiming for the equipment immediately engaged in the execution of cell death, the previous indicating networks are appealing because they contain essential upstream mediators, many of which are unknown (Schweikert et al., 2012). Ubiquinone, often known as coenzyme Q10, is a natural component of food and is also synthesized internally. Although it is a natural part of human milk, preterm women's breast milk has somewhat lower milk levels than average. There are no known applications of coenzyme Q10 that are specifically connected to breastfeeding, and there is no information on the effectiveness or safety of supplementation for nursing mothers or babies. Supplements containing CoQ10 are often well tolerated and only sometimes cause mild adverse effects (Faloon, 2006). Although CoQ10 has a vital role in numerous cellular activities, its possible relevance to cancer formation and advancement has gotten little study. Clinical or epidemiological studies on plasma or cell CoQ10 are uncommon and present a small number of participants (Cooney et al., 2011). CoQ10, often referred to as ubiquinone, this quinone molecule has the chemical formula 2, 3-dimethoxy-5- methyl-6, 1-and 4-benzoquinone decaprenyl (Figure 1) (Greenberg & Frishman, 1990). As a cofactor in the production of (adenosine triphosphate) ATP by oxidative phosphorylation, CoQ10 is an essential part of the mitochondria's electron transport chain (Hyun et al., 2006). All energy-consuming activities, including angiogenesis, apoptosis, immunological function, and proliferation, depend on CoQ10. (the process of programmed cell death), indicating the possibility of numerous roles in the development and spread of cancer (Cooney et al., 2011).

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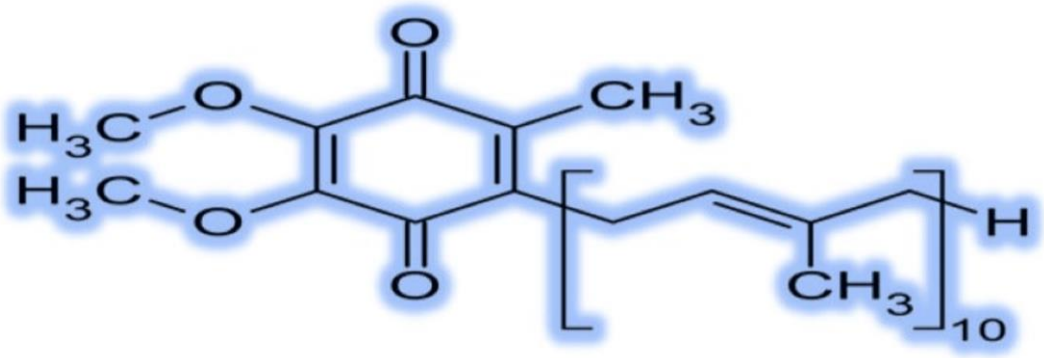

Figure 1 Structure of coenzyme Q10 (CoQ10).
(CH3- Methyl O- Oxygen H- Hydrogen The chemical structure of Coenzyme Q10 is 1,4-benzoquinone 2,3-dimethoxy-5-methyl-6-decaprenyl)

Humans who receive CoQ10 treatment don't experience any severe adverse effects, and novel formulations have been created to improve tissue absorption and diffusion. Melanoma, lung, prostate, breast, cervix, cancer treatment, and lethargy associated with cancer are all affected by CoQ10 (Soni et al., 2015). The impact of CoQ10 on people when dealing with breast cancer has been examined in several clinical investigations (Thapa & Dallmann, 2020). According to the World Health Organisation, breast cancer is the most common cancer among women worldwide. Affecting nations at all levels of civilization, taking the lives of women every year. As a result, new methods for managing breast cancer must be created (Aponte, 2015). Hormone replacement therapy (HRT) may have an impact on CoQ10 plasma levels, so it is important to examine the levels of CoQ10 in female users of HRT. Therefore, some research links low levels to a higher probability of breast cancer, while other studies link high levels of CoQ10 to a Breast cancer risk is reduced.

2. Review

2.1. Coenzyme Q10 (CoQ10) biochemical purposes

Coenzyme Q is widely acknowledged to be crucial to the process of mitochondrial oxidative phosphorylation, which produces ATP from the energy found in carbs and fatty acids to power cellular machinery. Coenzyme Q is just now beginning to be understood in new ways in relation to other cellular processes. CoQ10 can be subjected to reduction/oxidation processes in plasma membranes, Golgi apparatus, and lysosomes, among other cell membranes, which has led to the development of unique properties. Coenzyme Q passes through reduction/oxidation cycles in lysosomes and mitochondria, transferring and generating a proton gradient by moving protons across the membrane. All membranes contain large levels of quinol, which provides a foundation for antioxidant activity by either a direct interaction with radicals or through the regeneration of tocopherol and ascorbate. Coenzyme Q appears to have research on its promotion of cell growth suggests that it may have a role in the redox regulation of gene expression and cell signaling. Inhibition of apoptosis, regulation of thiol groups, generation of hydrogen peroxide, and control of membrane channels. According to biosynthesis suppression brought on by Human menopausal gonadotropin (HMG) Coarctation of the aorta (CoA) reductive inhibitors (statins), biosynthesis failure brought on by gene mutation, or undiscovered reasons of aging and cancer, coenzyme Q shortage has been established. To make up for a shortfall in coenzyme Q, higher levels must be added to the diet (Crane, 2001).

2.2. CoQ10 mechanism of action in breast cancer

CoQ10 exerts its biological effects. (a) Directly controlling succinyl and nicotinamide adenine dinucleotide (NADH) dehydrogenases in their reduced forms, (b) serving as an active catalyst and regulator of the compound of cytochrome bc1, and (c) perhaps having direct qualities that stabilize membranes independent of its function in oxidative phosphorylation (Lesser et al., 2013). One of the key mechanisms the release of cytochrome c from mitochondria and the concurrent production of superoxide radicals, hydrogen peroxide, and very deadly hydroxyl radicals via the Fenton and Haber-Weiss reactions. Because superoxide generation happens incidentally, for a medication to have the intended cytotoxic effect on cancer cells, free radical production is not necessary (Conklin, 2004). CoQ10's impact on Deoxyribonucleic acid (DNA) has also been acknowledged (Garrido-Maraver et al., 2014). Essential in transcription regulation, transport, intermediary metabolism, and inflammation. The chemical processes by which CoQ10 produces these pleiotropic effects are still not fully known. Therefore, CoQ10 produces energy for cell development and repair inside human cells (Lesser et al., 2013). CoQ10 occurs in the human body naturally. CoQ10 dosages are generally well tolerated, resulting in relatively mild and rare side effects such as stomach discomfort, feeling sick, throwing up, and diarrhea (Bonakdar & Guarneri, 2005; Baggio et al., 1994). Dietary supplementation has been demonstrated to be safe, even at doses as high as 1200 mg/day (Garrido-Maraver et al., 2014). Dizziness, photophobia, irritability, migraines, heartburn, elevated spontaneous motions, and weariness have all been reported as uncommon side effects (Bonakdar & Guarneri, 2005; Feigin et al., 1996). The multi-step process of developing breast cancer

involves hormones and genes, including tumour suppressor genes, oncogenes, and, more recently, developmental genes (Yang et al., 2004). Oestrogen is a hormone that promotes the growth of cancer cells. Similarly, genes involved in embryo development are subsequently shown to be implicated in cancer growth. The "twist" gene, which is crucial in the embryonic developmental period, is one such gene that has attracted a lot of interest recently. A similar process is in action in cancer metastasis, when E-Cadherin is down-regulated, promoting cell movement and invasion. Twist protein is a Basic helix-loop-helix proteins (bHLH) transcription agent that binds to the E-box responsive element (CANNTG) and, depending on the biological environment, acts as an activator or repressor of transcription (Hamamori et al., 1999; Gong & Li, 2002; Pan et al., 2009).

Twist is overexpressed in several tumour types, such as those of the breast, uterus, lung, and liver, hepatocellular, prostate, gastric carcinoma, and melanomas (Kwok et al., 2005; Kyo et al., 2006; Puisieux et al., 2006; Yuen et al., 2007). Natural medications are becoming increasingly important as cancer cells develop resistance and decrease susceptibility to current chemotherapeutic treatments. Although contemporary chemotherapeutics can suppress or kill tumors, concerns about toxicity and side effects continue to limit their clinical utility. For cancer therapy techniques, any natural substance that may be effective in destroying cancer cells while barely affecting healthy cells is evaluated.

2.3. CoQ10 and breast cancer and treatment

India's breast cancer burden has nearly doubled that of the United States. And it is rapidly growing. It's believed that there are 1.5-2 million cancer cases in India. India has a rather high fatality rate (Yang et al., 2004). There is a clear and positive correlation between plasma CoQ10 levels and the risk of breast cancer, especially in women who received a diagnosis at least a year after blood collection, suggesting that those with latent breast cancer may have lessened the correlation between breast cancer and CoQ10 (Chai et al., 2010). (Folkers et al., 1997) and (Jolliet et al., 1998) found reduced plasma CoQ10 levels in individuals with breast cancer. Folkers et al. state that 23% of individuals with breast cancer were deficient in CoQ10 (since blood CoQ10 levels were less than 0.5 g/mL). 4% of women are cancer-free, in contrast. Breast cancer and/or its treatment may have altered CoQ10 levels in the blood. Age or menopausal state likely alters the link between CoQ10 levels and breast cancer (Chai et al., 2010). According to Palan et al, plasma CoQ10 levels are substantially greater in women who have gone through menopause than in premenopausal women, suggesting that gonadotropin or circulating steroid hormone concentrations may affect plasma CoQ10 levels (Palan et al., 2005). Since higher concentrations of sex hormonebinding globulin (SHBG) are associated with a lower risk of breast cancer, the negative correlation between CoQ10 and SHBG may help to explain the association between CoQ10 and postmenopausal breast cancer risk (Chai et al., 2010).

In the Shanghai Women's Health Study (SWHS), it was discovered that women whose breast cancer was diagnosed more than a year after blood samples were taken had a significant inverse correlation between low circulating CoQ10 levels and subsequent cases of the disease, with the highest risk being connected to those in the lowest quintile of circulating CoQ10. CoQ10 levels greater than 1,000 mg/ml were the (MEC) Medical Examiner's Certificate study, it was linked to a considerably increased incidence of breast cancer. One possible reason for these contradictory findings is that women with CoQ10 levels have an increased chance of breast cancer at either extreme. Women with circulating CoQ10 levels in the 500-800 mg/ml range are at the lowest risk of getting breast cancer (Cooney et al., 2011). Patients with breast cancer were shown to have higher plasma CoQ10 levels using HRT compared to those who weren't by Chai et al. Chronic inflammation elevated systemic or tissue-specific oxidation, or all three may contribute to elevated circulating CoQ10 levels in the elderly. The association between such indications and sickness risk is obviously convoluted, and they must be read with caution (Chai et al., 2010).

2.4. CoQ10 reducing toxicity of anti-cancer agentes

The finding that CoQ10 was related to a lower risk of breast cancer in those whose levels of -tocopherol are modest but not high warrants additional research. Future investigations with a bigger sample size and longer follow-up periods, as well as a greater investigation into the function of circulating CoQ10 and its physiological regulation, are required to assess the possible role of CoQ10 in the etiology of breast cancer (Chai et al., 2010). Anthracycline antibiotic Doxorubicin (Adriamycin) has been utilized as adjuvant therapy as a part of breast cancer treatment. And it increases free of illnesses and long-term survival considerably. Despite these advantages, Doxorubicin-treated breast cancer people experience persistent cardiomyopathy alterations and congestive heart failure, resulting in fatalities, illness, and restrictions on its usage. To avoid cardiotoxicity while maintaining Doxorubicin's antitumor benefits, effective therapies are required. There at present, no known safe and effective therapies are available to avoid this cardiotoxicity (Conklin, 2004). An early increase in plasma CoQ10 during Doxorubicin therapy is followed by a significant post-treatment drop in cardiac and skeletal muscle CoQ10 levels. One of the earliest and most visible histopathological results for Doxorubicin-induced cardiomyopathy is mitochondrial damage in cardiac myocytes. Plasma CoQ10 concentrations were demonstrated to increase by 300-400% after 11 days of taking a daily dosage of 300 mg (safe limit is 1200 mg). By avoiding or reducing CoQ10 displacement by Doxorubicin metabolites, CoQ10 treatment administered before to or concurrently with Doxorubicin administration may lessen the cardiotoxicity caused by this drug. Furthermore, CoQ10 enabled the administration of higher Doxorubicin dosages. Although CoQ10 may help prevent

cardiotoxicity caused by doxorubicin, there is the worry that CoQ10 may reduce Doxorubicin's desirable pro-oxidant beneficial effects (Conklin, 2004; Greenlee et al., 2012).

2.5. CoQ10 reducing toxicity of Tamoxifen (TAM)

Tamoxifen (TAM) is utilized as a chemoprevention in high-risk patients as well as adjuvant therapy for breast cancers at all stages. TAM causes significant oxidative stress by acting estrogenically on the liver and endometrial and disorders of metabolism. Combined administration of CoRN (CoQ 10, Niacin, and Riboflavin) combined with TAM has been demonstrated to improve blood chemical characteristics (Yuvaraj et al., 2009). CoRN supplementation combined with TAM decreases blood tumor marker levels such as (CEA) carcinoembryonic antigen and (cancer and carcinoma) By reducing the risk of cancer recurrence, CA 15-3 improves cancer prognosis and metastatic disease, as well as enhancing the quality of life (Yuvaraj et al., 2009; Premkumar et al., 2007). TAM has been proven to raise cholesterol levels by raising the risk of cardiovascular disease by preventing triglyceride lipolytic enzyme activity. Angiogenesis encourages regional cancer growth and invasion, as well as the dissemination and metastasis of tumor cells. The study discovered that giving TAM (10 mg twice a day) combined with CoQ10 (100 mg/d) for people with breast cancer lowered the levels of the formation of vessel indicators and cholesterol levels (Sachdanandam, 2008). CoQ10 is an antioxidant that has been found to protect against cardiotoxicity after TAM-based chemotherapy (Yasueda et al., 2016). Several research studies have looked into the combined effectiveness of TAM and CoQ10 (Perumal et al., 2005; Saddar et al., 2019). According to a new study, CoQ10 may have a crucial role in reducing the negative effects of TAM, hence enhancing its overall safety and tolerability (Zahrooni et al., 2019).

2.6. A recent trial on CoQ10 metabolism of unresolved issues

The information given will demonstrate that there are still a significant number of issues with CoQ10 metabolism that require fixing. Gaining a deeper The first thing that has to be done is to understand the method by which CoQ10 molecules are carried from the intestinal environment into enterocytes (especially the identification of potential CoQ10 carriers) and then into the circulation via the lymphatic system. This might thus offer a foundation for enhancing the CoQ10 supplement's initial bioavailability and help to explain why certain persons have a lower natural capacity to absorb the supplement than the typical person. Second, it is necessary to determine the process by which excess CoQ10 is delivered to target cells from the circulation, i.e., whether this is a diffusion-controlled mechanism or a transporter-mediated one, the blood level of CoQ10 must be higher than that of the cell in order to allow for net access. It's crucial to find out whether exogenous The blood-brain barrier can be crossed by CoQ10 in humans in particular since doing so might assist in highlighting some of the underwhelming results of clinical trials using CoQ10 supplements for neurological conditions. Thirdly, additional studies should be conducted to develop alternative administration techniques that showed promise in preclinical animals for application in clinical settings. Among these are intravenous, intraperitoneal, and intramuscular techniques; in some neurological diseases, intrastriatal injection may also be necessary. Even though the assessment of plasma CoQ10 levels is routinely used to track CoQ10 levels or identify CoQ10 deficiencies after therapy, more study needs to be done to understand how indicative the levels of CoQ10 in plasma are similar to those in other tissues (Mantle et al., 2023).

This investigation looked at breast cancer using CoQ10. There is research on CoQ10's utility in treating breast cancer. The intention of a review of the available literature had to be conducted for this study to discover and analyze proof of the impact of CoQ10 as a supplement while breast cancer is being treated. This whole paper describes how to treat breast cancer with CoQ10. CoQ10 serves as an antioxidant and facilitates the cellular synthesis of energy. The immune system has been demonstrated to be stimulated by CoQ10, and it has also been found to protect the heart against the adverse effects of several chemotherapeutic drugs. Levels of CoQ10 in cancer patients have reportedly had low blood counts.

3. Conclusions

Coenzyme Q10 (CoQ10) research on breast cancer is a growing area with some fascinating findings. While there is evidence linking CoQ10 levels to the risk of breast cancer, further study is needed to completely understand this association. CoQ10 has the ability to lower the toxicity of some anti-cancer medicines such as Doxorubicin and Tamoxifen (TAM) as an adjuvant treatment. More thorough research is needed, however, to confirm its efficacy and safety in clinical settings. Breast cancer is a complicated illness impacted by several variables, and CoQ10 is just one avenue of investigation in the search for better preventative and treatment techniques. More research is needed, with bigger sample sizes and longer-term follow-ups, to determine the impact of CoQ10 on breast cancer.

Ethical consideration

Not applicable.

Conflict of Interest

The authors declare no conflicts of interest.

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