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# Ascorbic Acid (Vit. C) as a Positive Effective Factor to Treatment of Breast Cancer Patients

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***Abstract:*** Breast cancer is a prominent cause of mortality and the most prevalent malignancy in women. Numerous pharmacological treatments that have enabled the tumor to be cured and resolved are currently available. The use of complementary medicine is increasing due to the various side effects of cancer treatments, with studies exploring high-dose intravenous vitamin C injections to enhance anticancer effectiveness and reduce side effects in patients. This study delves at vitamin C's function in cancer therapy, proposing that large dosages could lessen the side effects of pharmaceutical therapies while increasing their efficacy for breast cancer patients.

***Key points:*** Breast cancer, ascorbic acid, anticancer mechanisms, alternative medicine.

## Introduction

Breast cancer remains the most prevalent disease affecting women globally, with over 2 million cases annually, according to the World Health Organisation. Despite a decline in mortality since the 1990s, it ranks second in the European Union for cancer-related deaths among women [1]. The multifactorial pathogenesis of breast cancer is influenced by a family history of breast and ovarian cancer, lifestyle choices, hormone imbalances, and genetic abnormalities [2]. If you have a first-degree family, such as a mother, sister, or daughter, with the illness, your chance of acquiring breast cancer is about quadrupled. The presence of two first-degree relatives increases your risk fivefold.

Additionally, women who have a male family member with a previous diagnosis of breast cancer are at an increased risk of developing the disease themselves [2]. A group of breast tumor subtypes with different cellular and molecular origins, characterized by unique pathophysiology, sensitivity to treatment, and molecular traits, are collectively referred to as breast cancer. The vast majority of these subtypes are ductal or lobular epithelial tumors. Receptor status divides breast tumours into four classes: HER2, ER, and progesterone. Luminal A has strong ER and/or PR receptors but negative HER2, luminal B is HER2-positive and has ER and/or PR receptors, and basal-type tumours have all receptors negative [3].

Heterogeneity in tumors has emerged as a crucial clinical characteristic for diagnosis and treatment selection. Breast cancer mortality has decreased in the EU as a result of effective systemic treatments and early detection. The number of treatments that can save the lives of people with breast cancer has increased recently. Indeed, the cancerous cells can be destroyed by a variety of treatments. Various early and late treatments can cause various side effects, influenced by the specific medication, dosage, and timing of the treatment, which can vary [4]. Using alternative medicine to improve one's quality of life might be seen as a significant treatment adjunct.

Women with cancer in its early stages who have a worse quality of life should use these alternative treatments [5]. In this regard, the outcomes of these supplementary treatments could enhance the quality of life for these individuals [6]. Therefore, the present work is to examine the usage of vitamin C as a complementing treatment for breast cancer.

**Metabolic Biochemistry of Ascorbic acid (Vit. C)**

A carbohydrate like glucose ascorbic acid is soluble in water. The very reactive "ene-diol" group is present, unlike glucose. Dehydroascorbic acid (DHA) and stable monodehydroascorbate (MDHA) radicals are produced when this group converts sugar into a powerful reducing agent, which may then donate electrons to oxidants and radicals. These radicals can be turned back into ascorbate reversibly [7,8].

DHA is transported throughout the body's cells via sodium vitamin C transporters 1 and 2 (SVCT1 and SVTC2, respectively) [9]. DHA can be broken down inside the cell to produce L-threonate, oxalate, and 2,3-diketogulonate, which the kidney can eliminate [10]. Reactive oxygen species (ROS) or free radicals can oxidize ascorbate inside and outside cells. As a result, ascorbate's antioxidant properties can lower ROS concentrations [11]. However, ascorbate can reach millimolar quantities when administered intravenously, which causes it to operate as a prooxidant [12]. The interaction with metal ions like Fe3+ and Cu2+, which ascorbate can chelate, causes the prooxidant activity [13]. Through the Fenton and Haber-Weiss chemical process, hydrogen peroxide and oxygen-reduced iron ions mix to form reactive hydroxyl radicals (HO) or peroxide ions (O2) [14,15].

Vitamin C, an essential cofactor for several iron- and copper-dependent enzymes, preserves the reduced state of transition metals. This state is essential for the optimal activity of these enzymes [16,17].

**Mechanism of Action to Vitamin C as Anticancer**

The research on vitamin C's anticancer properties has sparked various hypotheses due to a deeper understanding of ascorbate's role in cells and cancer development molecular mechanisms [18,19]. Vitamin C's role in preventing cancer metastases is attributed to its role in collagen formation, which is hindered by its absence [20].

The stroma around a tumor, similar to scurvy, can form a thick barrier that encloses neoplastic cells within dense fibrous tissue, thereby preventing their spread. Vitamin C can be administered in large amounts to improve the resistance of intercellular ground substance to local infiltration. Thus, using vitamin C helps control collagen production at suitable levels, thereby preventing the spread of metastases [21]. Ewan Cameron and Rotman's research supports the theory that vitamin C reduces hyaluronidase enzyme, reducing tissue disturbance and cancer cell spread [22].

Vitamin C has been suggested to inhibit the production of series 2 prostaglandins by cancer cells [23]. Angiogenesis, migration, and cell proliferation are well-recognized effects of these bioactive lipids. Numerous solid tumors strongly express prostaglandin E2 (PGE2) [24]. Furthermore, vitamin C stabilizes the transcription factor protein 53 (P53), which inhibits cell growth [25]. Kim et al. suggest that p53 may contribute to the variability in ascorbate cytotoxicity across cancer cell lines [26].

Glucose transporters 1 (GLUT), which are often elevated in cancer cells because of their higher glucose requirements, allow vitamin C to enter the body. This rise in GLUT1 transporters helps cancer cells absorb vitamin C, hence improving its selective, nontoxic potency as a treatment [12]. In the 2000s, cell culture experiments demonstrated that ascorbate's pro-oxidative activity, producing H2O2 and OH, can effectively destroy cancer cells at a millimolar vitamin C plasma concentration [27,28]. The pro-oxidative action of vitamin C depends on iron ions; tumour cells show larger levels of labile iron in their microenvironment than do control cells [29].

Moreover, extracellular H2O2 may help raise the extracellular DHA level, improving the intracellular oxidative milieu upon cell entrance. The conversion of DHA to ascorbate by tumor cells with high levels of GLUT1 leads to intracellular oxidative stress. This response causes oxidative cell damage by lowering the antioxidant content in the cells and raising the endogenous ROS levels [30].

**Ascorbic acid (Vit. C) Effects on Breast Cancer Cell Lines**

Vitamin C has been found to trigger cell death in human breast cancer cell lines, despite the lack of in vivo evidence on breast cancer [31]. More evidence suggests that vitamin C and chemotherapy medications work together synergistically. Kurbacher et al. investigated if several chemotherapeutics used to treat breast cancer would synergistically impact vitamin C. Furthermore, paclitaxel, doxorubicin, and cisplatin were administered to two human breast cancer cell lines, MCF-7 and MDA-MB-231.

Additionally, 1 Üm and 100 Ш m of ascorbate were also provided to these cell lines. Moreover, it was shown that the impact was synergistic with doxorubicin at concentrations of 1 Üm and 100 Ш m in MCF-7 and MDA-MB-231. This was the case regardless of whether the ascorbate concentrations were within the normal range on either of the two cells.

In addition, the effect was affected differently depending on the dose in MDA-MB-231 cells. One meter and one hundred meters of ascorbate were shown to be synergistic with cisplatin in MCF-7 cells; however, in MDA-MB-231 cells, only one hundred meters of ascorbate was found to be efficacious. The quantities evaluated in MCF-7 cells had no influence on the effectiveness of vitamin C; however, in MDA-MB-231 cells a lower concentration had a synergistic effect and a larger dose had an additive effect [32]. Zeng et al. found that the epithelial-mesenchymal transition is impeded by significant dosages of vitamin C infusions, thereby obstructing the metastasis of human breast cancer. xenografts in rodents with atherosclerosis [33].

In vivo, animal models suggest that vitamin C administration can potentially inhibit breast cancer metastasis despite limited human patient studies on this relationship. For example, vitamin C, which Gulo knockout mice and humans both cannot produce, may prevent the spread of breast cancer in mice [34].

**Ascorbic acid (Vit. C) Uses to Breast Cancer Therapy**

Studies indicate that Vitamin C therapy can improve hunger, reduce discomfort, and enhance the quality of life for cancer patients, particularly those battling breast cancer [35]. In addition, vitamin C was used as an additional therapeutic method for patients going through chemotherapy, and the life expectancy of certain patients was increased. Vitamin C appears to be effective in reducing oxidative stress, a significant negative impact of chemotherapy and radiation on the body. Indeed, oxidative stress is brought on by the metabolic processes of cancer cells and the effects of radiation, chemotherapy, and other therapies that increase reactive oxygen species (ROS) levels [36]. The level of vitamin C in patients is correlated with the stage of the illness, with those in a more advanced stage exhibiting a lower level and those in a less advanced stage exhibiting a higher level [37,38].

A study evaluating intravenous chemotherapy (IVC) treatment for primary, non-metastasized breast cancer patients found it to be equally effective as chemotherapy and radiation therapy, with no negative side effects [39]. As previously stated, the immune system could be enhanced by the improved quality of life that the patients experienced due to their IVC treatment. A meta-analysis suggests that post-diagnosis vitamin C therapy may reduce the mortality risk in breast cancer patients. The risk of mortality, particularly that induced by breast cancer, can be substantially reduced by the administration of vitamin C [40].

**Conclusions**

IVC is an optimal adjunctive therapy for patients with breast cancer due to its numerous benefits. IVC is an effective strategy for restoring the physiological concentrations of vitamin C, which is frequently deficient in cancer patients. Furthermore, it has been shown that IVC may improve the quality of life for cancer patients. There is evidence from both pre-clinical and clinical trials that suggest intravenous chemotherapy (IVC) has the potential to lessen the negative effects of chemotherapeutic medicines without reducing the effectiveness of these treatments in treating cancer. The possible explanation is that IVC has both antioxidant and anti-inflammatory effects.

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