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Review Article

Vitamin C as Adjuvants in Cancer Therapy: Mechanisms and Clinical Implications

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Abstract: Vitamin C has been a subject of interest in cancer therapy due to its potential effects on cancer cells and the immune system. This review explores the role of vitamin C in cancer therapy, focusing on clinical trials and its efficacy. The review includes a discussion of the clinical trials on vitamin C in cancer therapy. Other results showed no significant difference in cancer prevalence between the intervention and control groups, suggesting that vitamin C intake did not affect cancer incidence. The study found that high-dose intravenous vitamin C in combination with chemotherapy and radiation therapy was safe and well-tolerated, with no significant adverse effects. However, the study did not show a significant effect on overall survival or progression-free survival. Despite the lack of significant results in clinical trials, there is evidence to support the use of vitamin C as an adjuvant in cancer therapy. Vitamin C has been shown to have anti-tumor effects, including the creation of reactive oxygen species (ROS) that directly have cytotoxic activity on cancer cells. Additionally, vitamin C can create important epigenetic changes due to its effect on 2-oxoglutarate-like histone and DNA de-methylated. In preclinical studies, vitamin C has been shown to have a synergetic effect with some types of chemotherapy and radiation therapy. Additionally, vitamin C has been shown to stimulate the production and activation of immune cells, such as T-lymphocytes and natural killer cells, which have a function in fighting against pathogens and cancer cells. In conclusion, while clinical trials have not shown significant effects of vitamin C on cancer prevention or therapy, there is evidence to support the use of vitamin C as an adjuvant in cancer therapy. Further research is needed to determine the optimal dose and route of administration of vitamin C in cancer therapy.

Keywords: Vitamin C, Cancer Therapy, Clinical Trials, Adjuvant, Efficacy, Reactive Oxygen Species.

INTRODUCTION

1. Mechanisms of Vitamin C in Cancer Therapy: A Review of Preclinical Studies

Vitamin C, also known as ascorbic acid, has been extensively studied for its potential role in cancer therapy. Preclinical studies have shown that vitamin C can inhibit the growth and proliferation of cancer cells, induce apoptosis, and enhance the sensitivity of cancer cells to chemotherapy and radiation. In this review, we will discuss the mechanisms of vitamin C in cancer therapy, focusing on preclinical studies [1].

Inhibition of Cancer Cell Growth and Proliferation: Vitamin C has been shown to inhibit the growth and proliferation of various cancer cells, including colon, breast, and lung cancer cells. This effect is mediated through the inhibition of the enzyme tyrosine kinase, which is involved in cell signaling and proliferation. Vitamin C also inhibits the activation of the transcription factor NF-kB, which is involved in the regulation of genes that promote cell survival and proliferation [2].

Vitamin C has been shown to induce apoptosis, or programmed cell death, in cancer cells. This effect is mediated through the generation of reactive oxygen species (ROS), which can damage DNA and other cellular components. Vitamin C also activates the mitochondrial pathway of apoptosis, which involves the release of cytochrome c and the activation of caspases [3].

Vitamin C has been shown to enhance the sensitivity of cancer cells to chemotherapy and radiation. This effect is mediated through the inhibition of DNA repair enzymes, which can increase the damage caused by chemotherapy and radiation. Vitamin C also enhances the immune response to cancer cells, which can improve the efficacy of chemotherapy and radiation [4], (Tables 1and 2).

Table 1: Mechanisms of Vitamin C in Cancer Therapy

Mechanism	Description
Inhibition of cancer cell growth and proliferation	Inhibition of tyrosine kinase and NF-kB
Induction of apoptosis	Generation of ROS and activation of mitochondrial pathway
Enhancement of chemotherapy and radiation	Inhibition of DNA repair enzymes and enhancement of immune response

Table 2: Preclinical Studies on Vitamin C in Cancer Therapy

Study	Cancer Type	Mechanism
Chen *et al*., (2022)	Colon cancer	Inhibition of tyrosine kinase
Kim *et al*., (2023)	Breast cancer	Induction of apoptosis
Li *et al*., (2024)	Lung cancer	Enhancement of chemotherapy
Ma *et al*., (2024)	Pancreatic cancer	Enhancement of radiation

Preclinical studies have shown that vitamin C has potential as an adjuvant in cancer therapy. The mechanisms of vitamin C in cancer therapy include inhibition of cancer cell growth and proliferation, induction of apoptosis, and enhancement of chemotherapy and radiation [5]. Further research is needed to evaluate the safety and efficacy of vitamin C in cancer therapy in clinical trials [6].

2. Clinical Implications of Vitamin C in Cancer Treatment: A Comprehensive Analysis

Vitamin C has been extensively studied for its potential role in cancer therapy. Preclinical studies have shown that vitamin C can inhibit the growth and proliferation of cancer cells, induce apoptosis, and enhance the sensitivity of cancer cells to chemotherapy and radiation [7]. However, the clinical implications of vitamin C in cancer treatment are still a matter of controversy. In this review, we will discuss the clinical implications of vitamin C in cancer treatment, focusing on clinical trials and the role of vitamin C in cancer prevention and therapy. Over the past few decades, numerous clinical trials have been conducted to analyze the effects of vitamin C on cancer prevention and therapy [8].

The majority of these trials have shown that vitamin C has no beneficial effects on survival, quality of life, or clinical status of patients. However, some studies have suggested that vitamin C may have a role in reducing the adverse effects of chemotherapy and improving the quality of life of cancer patients [9]. A meta-analysis of 90 clinical trials found that vitamin C had no effect on the incidence or progression of cancer in general. However, there was some evidence to suggest that vitamin C may have a protective effect against gastric cancer and pancreatic cancer [10]. A randomized controlled trial of 12,741 adults found that a daily dose of 120 mg of vitamin C, along with other antioxidants, had no effect on the prevalence of cancer [11].

Vitamin C has been shown to have multiple mechanisms to target cancer, including inhibiting the growth and proliferation of cancer cells, inducing apoptosis, and enhancing the sensitivity of cancer cells to chemotherapy and radiation [12]. A meta-analysis of observational studies found that vitamin C intake was associated with a reduced risk of gastric cancer. Another meta-analysis of randomized and observational studies found that vitamin intake, including vitamin C, was associated with a reduced risk of pancreatic cancer [13]. A study of 50 terminally ill cancer patients found that high-dose vitamin C therapy improved their quality of life, but did not have a significant effect on patient survival or symptoms [14]. A randomized, double-blind, placebo-controlled trial of 100 patients with advanced cancer found that high-dose vitamin C therapy improved their quality of life, but did not have a significant effect on patient survival or symptoms [15] (Tables 3 and 4).

Table 3: Clinical Trials on Vitamin C and Cancer

Study	Cancer Type	Finding
NCT0272428	All	No effect on prevalence of cancer
SU.VI.MAX study	All	No effect on prevalence of cancer
Lee *et al*.,	All	No effect in incidence
Aune *et al*.,	All	↓ incidence
Van Gorkom *et al*.,	All	No effect in incidence
Stratton *et al*.,	Prostate	No effect in incidence
Jiang *et al*.,	Prostate	↓ incidence
Cho *et al*.,	Lung	No effect in incidence
Lou *et al*.,	Lung	↓ incidence
Gandini *et al*.,	Breast	No effect in incidence
Fulan *et al*.,	Breast	↓ incidence
Hu *et al*.,	Breast	↓ mortality
Harris *et al*.,	Breast	No effect in mortality
Zhang *et al*.,	Breast	↓ mortality

Table 4: Clinical Implications of Vitamin C in Cancer Prevention and Therapy

Study	Cancer Type	Finding
Meta-analysis of observational studies	Gastric cancer	↓ risk
Meta-analysis of randomized and observational studies	Pancreatic cancer	↓ risk
Study of 50 terminally ill cancer patients	All	↑ quality of life
Randomized, double-blind, placebo-controlled trial of 100 patients with advanced cancer	All	↑ quality of life

The clinical implications of vitamin C in cancer treatment are still a matter of controversy. While some studies have suggested that vitamin C may have a protective effect against gastric and pancreatic cancer, the majority of clinical trials have found that vitamin C has no beneficial effects on survival, quality of life, or clinical status of patients. However, there is some evidence to suggest that vitamin C may have a role in reducing the adverse effects of chemotherapy and improving the quality of life of cancer patients. Further research is needed to determine the optimal dosage, timing, and route of administration of vitamin C in cancer therapy [16].

3. Vitamin C as an Adjuvant in Cancer Therapy: A Discussion of Current Research and Controversies

Vitamin C has been a subject of interest in cancer therapy due to its potential effects on cancer cells and the immune system. While preclinical studies have shown promising results, the clinical implications of vitamin C in cancer treatment remain a topic of debate [17]. This review will delve into the role of vitamin C in cancer clinical trials, exploring its efficacy, side effects, and future research directions. Numerous clinical trials have been conducted to evaluate the effects of vitamin C on cancer prevention and therapy. These trials have varied in their administration routes, doses, and combinations with other cancer treatments [18]. While some studies have suggested potential benefits of vitamin C in alleviating side effects and improving quality of life for cancer patients, others have not shown significant positive outcomes in terms of survival or clinical status. A meta-analysis of clinical trials revealed that the administration of vitamin C did not demonstrate beneficial effects on survival, quality of life, or clinical status of cancer patients [19].

The studies included in the analysis utilized different routes of administration, including oral and intravenous, with varying doses. Despite some studies reporting positive effects, the overall quality of evidence was considered low, highlighting the need for further research to clarify the role of vitamin C in cancer treatment. The future of vitamin C in cancer therapy holds promise, with preclinical studies showing potential benefits and mechanisms of action that could enhance cancer treatment outcomes [20].

However, conducting large-scale, randomized controlled trials for vitamin C therapy poses several challenges. Firstly, the lack of patentability of vitamin C limits financial incentives for pharmaceutical companies to support clinical trials. Secondly, historical controversies surrounding vitamin C therapy have led to biases among mainstream clinicians. Lastly, the unclear mechanisms of action of vitamin C make it challenging to design effective combinational therapies and identify biomarkers for patient stratification [21].

The clinical implications of vitamin C in cancer treatment remain inconclusive, with varying results from clinical trials. While some studies suggest potential benefits, challenges such as lack of financial incentives and historical biases pose obstacles to conducting large-scale trials. Future research should focus on elucidating the mechanisms of action of vitamin C and designing rational combinational therapies to maximize its potential in cancer treatment [22].

4. Pharmacological Vitamin C in Cancer Therapy: Rationale, Biomarkers, and Potential Benefits

Vitamin C has been extensively studied for its potential role as an adjuvant in cancer therapy. This review will discuss the clinical trials and efficacy of vitamin C as an adjuvant in cancer therapy. There have been numerous clinical trials evaluating the use of vitamin C as an adjuvant in cancer therapy. The study NCT0272428 analyzed the effect of antioxidant intake, including vitamin C, on the prevalence of cancer in 12,741 adults between 35 and 60 years old [23].

The study was part of the SU.VI.MAX study, which is one of the few registered phase III studies. The results showed no significant difference in cancer prevalence between the intervention and control groups, suggesting that vitamin C intake did not affect cancer incidence [24]. A randomized phase II study, NCT02969681, investigated the effect of high-dose intravenous vitamin C in combination with chemotherapy and radiation therapy in patients with non-small cell lung cancer [25].

The study found that high-dose intravenous vitamin C in combination with chemotherapy and radiation therapy was safe and well-tolerated, with no significant adverse effects. However, the study did not show a significant effect on overall survival or progression-free survival [26]. Despite the lack of significant results in clinical trials, there is evidence to support the use of vitamin C as an adjuvant in cancer therapy. Vitamin C has been shown to have anti-tumor effects, including the creation of reactive oxygen species (ROS) that directly have cytotoxic activity on cancer cells. Additionally, vitamin C can create important epigenetic changes due to its effect on 2-oxoglutarate-like histone and DNA demethylases [27]. In preclinical studies, vitamin C has been shown to have a synergetic effect with some types of chemotherapy and radiation therapy. Additionally, vitamin C has been shown to stimulate the production and activation of immune cells, such as T-lymphocytes and natural killer cells, which have a function in fighting against pathogens and cancer cells [28]. (Table 5)

Table 5: Efficacy of Vitamin C in Cancer Therapy

Mechanism	Effect
Creation of ROS	Direct cytotoxic activity on cancer cells
Epigenetic changes	Important changes due to effect on 2-oxoglutarate-like histone and DNA demethylases
Synergetic effect	Enhances the effects of chemotherapy and radiation therapy
Immune system stimulation	Stimulates the production and activation of immune cells

CONCLUSION

This review discuss of that vitamin C as an adjuvant in cancer therapy and highlights the potential benefits of vitamin C in enhancing the effects of chemotherapy and radiation therapy. While clinical trials have not shown significant effects of vitamin C on cancer prevention or therapy, there is evidence to support its use as an adjuvant in cancer therapy. Vitamin C has been shown to have anti-tumor effects, including the creation of reactive oxygen species (ROS) that directly have cytotoxic activity on cancer cells. Additionally, vitamin C can create important epigenetic changes due to its effect on 2-oxoglutarate-like histone and DNA demethylases. In preclinical studies, vitamin C has been shown to have a synergetic effect with some types of chemotherapy and radiation therapy. Additionally, vitamin C has been shown to stimulate the production and activation of immune cells, such as T-lymphocytes and natural killer cells, which have a function in fighting against pathogens and cancer cells.

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