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Review Article

Pharmacology of Vitamin C in the Treatment of Cancer: A Comprehensive Review

Kartik Jamwal [1], Komal *[2], Kapil Kumar Verma [2]

[1] Department of Pharmacy, Minerva College of Pharmacy, Indora (H.P)
[2] Department of Pharmacology, Minerva College of Pharmacy, Indora (H.P)

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For Correspondence:

Ms. Komal, Department of Pharmacology, Minerva College of Pharmacy, Indora (H.P)

Abstract

Vitamin C (ascorbate) has re-emerged as a promising adjunct in oncology due to a clearer understanding of its distinct pharmacology when administered intravenously versus orally. Oral dosing is constrained by saturable intestinal absorption and tight renal regulation, limiting plasma concentrations to low micromolar levels. In contrast, intravenous (IV) administration achieves pharmacologic millimolar plasma concentrations, enabling mechanisms not accessible through dietary or supplemental intake. At these higher levels, ascorbate functions as a pro-drug to generate hydrogen peroxide (H_2O_2) in the extracellular space, selectively inducing oxidative stress and cytotoxicity in cancer cells, which often possess impaired antioxidant defences. Additional proposed mechanisms include modulation of redox signalling, enhancement of sensitivity to chemotherapy and radiotherapy, and regulation of epigenetic enzymes such as TET and HIF hydroxylases. Preclinical studies consistently demonstrate dose-dependent tumour cell killing and synergy with conventional therapies, while early-phase clinical trials report good tolerability, improved quality of life, and signals of therapeutic benefit in malignancies such as pancreatic, ovarian, and glioblastoma. However, definitive efficacy data remain limited due to small sample sizes and heterogeneous protocols. Safety concerns include haemolytic risk in G6PD deficiency and oxalate nephropathy in predisposed patients, underscoring the need for appropriate screening. Overall, current evidence supports the biological plausibility and safety of pharmacologic ascorbate as an adjunct to standard cancer therapy, but well-powered randomized trials and validated biomarkers are required before widespread clinical implementation.

Keywords: Vitamin C, Ascorbate, Intravenous Vitamin C, Cancer Therapy, Oxidative stress, Hydrogen Peroxide, Pharmacokinetics, Chemo-radiation Sensitization, Adjunctive oncology

1. INTRODUCTION:

Vitamin C (ascorbic acid) is an essential water-soluble micronutrient, fundamental to human health due to its critical role as a cofactor in numerous enzymatic processes, including collagen biosynthesis, catecholamine production, and peptide. Unlike most mammals, humans are incapable of synthesizing vitamin C endogenously due to a mutation in the L-gluconolactone oxidase (GULO) gene, making us entirely dependent on dietary intake to prevent deficiency syndromes like scurvy.[1] Beyond its classical nutritional role, vitamin C is a potent antioxidant, protecting cellular integrity from reactive oxygen species (ROS), and a key immunomodulator, with high concentrations accumulated in neutrophils and lymphocytes to bolster host defense.[2] The therapeutic potential of vitamin C, particularly in oncology, represents a paradigm shift from its essential nutritive function to a pharmacologic agent. The foundational hypothesis for its use in cancer was pioneered by Linus Pauling and Ewan Cameron in the 1970s, who reported that high-dose intravenous vitamin C improved survival and quality of life in terminal cancer patients.[3] This discrepancy was later explained by pharmacokinetics: oral administration is limited by saturable intestinal absorption, achieving peak plasma concentrations of only ~200 µM, while intravenous (IV) infusion bypasses this barrier, attaining plasma levels in the millimolar range (≥ 20,000 µM) necessary for anti-tumour activity. [4]

The anti-cancer mechanisms of pharmacological vitamin C are multifaceted and distinct from its physiological antioxidant role. At high plasma concentrations, it exhibits a pro-oxidant effect, selectively generating cytotoxic hydrogen peroxide (H_2O_2) in the extracellular tumour microenvironment, which induces oxidative stress and cell death in malignant cells with compromised antioxidant defences.[5] Furthermore, vitamin C functions as a cofactor for Fe^{2+}/α-ketoglutarate-dependent dioxygenases, including Ten-Eleven Translocation (TET) enzymes responsible for DNA demethylation. By promoting an epigenetic reprogramming that reactivates silenced tumour suppressor genes, vitamin C can potentially suppress tumour growth and differentiation.[6] Emerging evidence also points to its role in modulating the tumour immune microenvironment, enhancing the cytotoxicity of T-cells and natural killer (NK) cells, and even inducing novel cell death pathways like ferroptosis.[7]

1.1 Historical Context: From Scurvy to Pharmacological Agent

The therapeutic journey of vitamin C began long before its isolation, rooted in the fight against scurvy. Descriptions of this debilitating deficiency disease appear in ancient medical texts from Egypt and Greece, with Hippocrates documenting its symptoms. Its most devastating impact was felt during the naval explorations of the 15th to 18th centuries, where prolonged voyages without fresh provisions led to catastrophic mortality rates; for example, nearly two-thirds of Vasco da Gama's crew perished from scurvy in 1499.[8]

A pivotal turning point occurred in 1747, when British naval surgeon James Lind conducted one of the first controlled clinical experiments in history. Aboard the HMS Salisbury, he demonstrated that citrus fruits provided a rapid and effective cure for scurvy. Despite this compelling evidence, the British Admiralty did not officially mandate the provision of lemon juice to sailors until 1795, a policy that ultimately eradicated scurvy from the Royal Navy and altered the course of maritime history.[9]

The scientific basis for this cure remained unknown for another century. The key breakthrough came in 1932, when Albert Szent-Györgyi isolated a compound from adrenal glands and citrus fruits, which he named "hexuronic acid." Shortly thereafter, Charles Glen King independently identified the same compound as the antiscorbutic (anti-scurvy) factor. Szent-Györgyi's work was awarded the Nobel Prize in Physiology or Medicine in 1937, and the compound was renamed ascorbic acid.[10]

The modern therapeutic narrative of vitamin C, particularly in oncology, was catalyzed by double Nobel laureate Linus Pauling. In the 1970s, together with surgeon Ewan Cameron, Pauling proposed that high-dose vitamin C could significantly improve outcomes for terminal cancer patients.[11] From an evolutionary perspective, the human requirement for dietary vitamin C is a relatively recent development. A mutation in the L-gulonolactone oxidase (GULO) gene, which occurred approximately 60 million years ago in primate ancestors, rendered humans unable to synthesize ascorbic acid endogenously. This loss was likely non-deleterious due to a fruit-rich diet, making endogenous synthesis unnecessary.[12]

2. PHYSIOLOGICAL ROLES AND PHARMACOKINETICS: A FOUNDATION FOR THERAPY

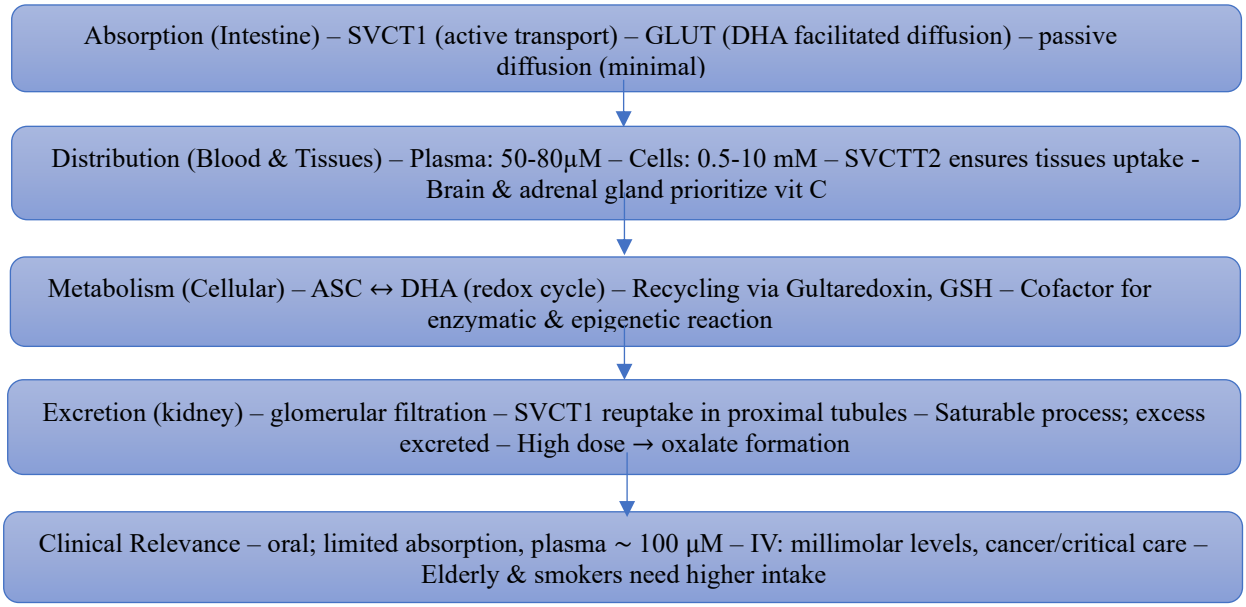
2.1 Essential Physiological Function

Vitamin C functions as a potent antioxidant, neutralizing reactive oxygen species (ROS) that otherwise cause oxidative damage to lipids, proteins, and DNA. Such oxidative stress contributes to the development of aging, cardiovascular disease, and cancer. In addition to its antioxidant role, vitamin C is a critical cofactor in the hydroxylation reactions required for collagen biosynthesis, thereby maintaining the structural integrity of skin, connective tissues, and blood vessels. Another important physiological role is its contribution to iron absorption from plant-based sources, which helps prevent iron-deficiency anaemia.[13]

2.2 The Critical Pharmacokinetic Divide: Oral vs. Intravenous Administration

The bioavailability and therapeutic efficacy of vitamin C are profoundly influenced by its route of administration. Oral absorption is limited by saturable intestinal transporters (SVCT1), achieving a maximum plasma concentration of approximately 200 µM, even with gram-sized doses. This ceiling effect prevents oral supplementation from reaching the millimolar plasma levels required for many therapeutic effects, particularly in oncology.[14]

In contrast, intravenous (IV) administration bypasses gastrointestinal absorption limitations. IV infusion results in plasma concentrations that can exceed 20,000 µM (20 mM), a level that is 100-1000 times higher than achievable orally. This pharmacokinetic advantage is the fundamental reason why early oral trials failed while modern IV trials show promise, especially for anti-cancer applications.[15]



Flow Chart 1: Pharmacokinetic and Clinical Relevance of Vitamin C.[16]

2.3 Factors Affecting Bioavailability:

Several factors modulate the bioavailability of orally administered vitamin C:

Formulation: Liposomal encapsulation protects vitamin C from degradation and enhances its absorption, achieving 1.5–2 times higher bioavailability than conventional oral supplements.

Dietary Source: Vitamin C from whole fruits often exhibits higher bioavailability than synthetic ascorbic acid due to the presence of co-factors like flavonoids and organic acids that enhance uptake and stability.

Gut Microbiota: A healthy gut microbiome supports vitamin C absorption, while dysbiosis can impair it. Probiotic supplementation has been shown to improve bioavailability.[17]

3. MECHANISM OF ACTION OF THERAPEUTICS

The therapeutic applications of vitamin C are underpinned by a diverse set of biochemical mechanisms.

At physiological concentrations, vitamin C is a primary antioxidant, scavenging free radicals, reducing oxidative stress, and regenerating other antioxidants like vitamin E. This activity is foundational to its role in protecting against chronic inflammatory diseases, supporting cardiovascular health, and preventing photodamage in the skin.[18]

3.1 Pro-Oxidant Cytotoxic

A unique and therapeutically relevant feature is its dual role. At high plasma concentrations achieved via IV infusion, vitamin C acts as a pro-oxidant in the extracellular environment, particularly in tumorous tissue. It generates hydrogen peroxide (H_2O_2), which induces selective oxidative stress and cytotoxicity in cancer cells that often have impaired antioxidant defences, while sparing normal cells.[19]

3.2 Epigenetic Regulation

Vitamin C serves as a cofactor for Fe^{2+}/α-ketoglutarate-dependent dioxygenases, including TET enzymes, which are crucial for DNA demethylation. By enhancing TET activity, vitamin C promotes an epigenetic landscape that can reactivate silenced tumour suppressor genes, potentially slowing tumour growth and inducing differentiation.[20]

3.3 Immunomodulatory

Vitamin C accumulates in immune cells and supports numerous functions: enhancing neutrophil migration and phagocytosis, supporting lymphocyte proliferation, and modulating cytokine production. It may also reduce immunosuppressive factors in the tumour microenvironment, thereby improving anti-tumour immunity.[21]

3.2 Introduction of Ferroptosis

Emerging evidence indicates that vitamin C can trigger ferroptosis, an iron-dependent form of regulated cell death characterized by lipid peroxide accumulation. This mechanism may contribute to its selective anti-cancer toxicity.[22]

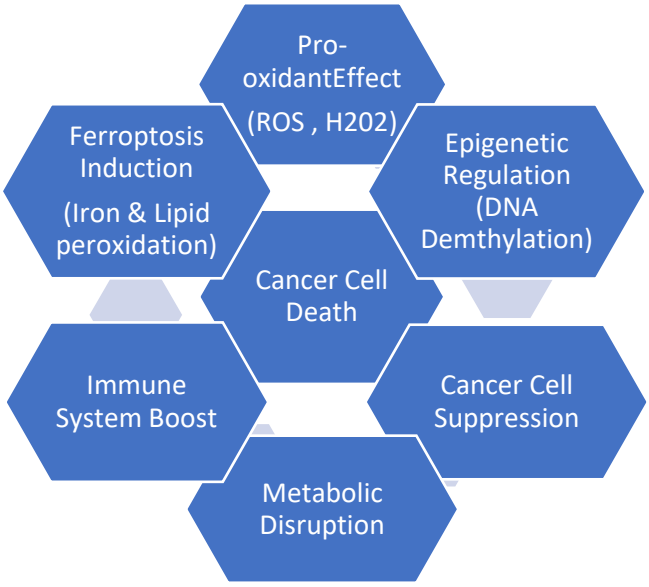


Figure 1: Mediated Cancer Cell Death.

4. THERAPEUTIC APPLICATIONS: EVIDENCE AND CONTEXT

4.1 Cancer Therapy:

The most investigated therapeutic application of high-dose IV vitamin C is in oncology, not as a cure but as an adjunct.

4.2.1 Clinical Evidence:

Studies in pancreatic, ovarian, and colorectal cancers have primarily reported benefits in improving quality of

life, reducing chemotherapy-induced toxicity (e.g., fatigue, nausea, neuropathy), and potentially enhancing overall survival in some patient cohorts. For instance, a combination of IV vitamin C with gemcitabine has shown prolonged progression-free survival in studies of pancreatic cancer.[23]

4.2.2 Supportive Care:

Its role in managing side effects and improving patient tolerance to conventional treatment is a significant area of promise. The evidence remains preliminary due to small sample sizes, lack of large-scale RCTs, and heterogeneity in dosing protocols. Its use is contraindicated in patients with G6PD deficiency (risk of haemolysis) and those with renal impairment or a history of kidney stones (risk of oxalate nephropathy).[24]

4.3 Vitamin C is a cornerstone of immune support:

Oral supplementation (1,000–2,000 mg/day) has been shown to reduce the duration and severity of the common cold, especially in individuals under physical stress. In critical care, high-dose IV vitamin C has been investigated for severe infections like sepsis and COVID-19 for its potential to modulate excessive inflammation (e.g., cytokine storm) and improve oxygenation. However, results from RCTs for sepsis and COVID-19 have been inconsistent, and its use in these settings remains experimental and not standard of care.[25]

4.4 Cardiovascular and Metabolic Health:

Vitamin C contributes to cardiovascular health through its antioxidant and cofactor activities. It improves endothelial function, aids in vasodilation, and reduces systolic blood pressure in hypertensive individuals. By preventing the oxidation of LDL cholesterol, it may slow the progression of atherosclerosis. Deficiency is a risk factor for cardiovascular disease.[26]

4.5 Dermatological Health and Wound Healing:

In dermatology, vitamin C is renowned for its anti-ageing and photoprotective effects. Topically, it reduces wrinkles, lightens hyperpigmentation, and improves skin elasticity by collagen synthesis and neutralizing UV-induced free radicals. Systemically, it is essential to all wound-healing processes, aiding recovery from surgical wounds, burns, and pressure ulcers.[27]

4.6 Neuroprotection and Cognitive Health:

The brain maintains high levels of vitamin C, where it acts as a key antioxidant and cofactor for neurotransmitter synthesis (e.g., catecholamines, serotonin). Higher plasma vitamin C levels are associated with a reduced risk of cognitive decline, Alzheimer's disease, and Parkinson's disease. Its neuroprotective effects are attributed to its ability to mitigate oxidative stress and support neuronal function.[28]

4.7 Other Applications:

Iron Absorption: Vitamin C significantly enhances the absorption of non-heme iron from plant-based foods, making it crucial for individuals with anaemia or those on vegetarian diets.

Detoxification: It has chelating properties that can aid in the excretion of heavy metals like lead and cadmium.[29]

Eye Health: Adequate intake may lower the risk of cataracts and age-related macular degeneration.

Common Side Effects: High oral doses (>2-3 g/day) can cause gastrointestinal disturbances, including diarrhoea, nausea, and abdominal cramps.

Serious Risks: Excessive intake can increase urinary oxalate excretion, raising the risk of kidney stones in predisposed individuals. In patients with hemochromatosis, it can promote iron overload. High-dose IV administration requires monitoring for these risks.

5. FUTURE DIRECTIONS AND CONCLUSION:

Future research on vitamin C should prioritize:

Large-Scale RCTs: Conducting definitive clinical trials to validate efficacy in cancer (as an adjunct), sepsis, and other critical illnesses.[30]

Precision Medicine: Identifying genetic and metabolic biomarkers to predict which patients are most likely to benefit from therapy.

Combination Therapies: Exploring synergies with existing treatments, particularly immunotherapy (e.g., checkpoint inhibitors) in oncology.

Delivery Systems: Advancing novel

In conclusion, vitamin C has evolved from a simple preventive nutrient against scurvy to a molecule of significant therapeutic interest. Its mechanism of action is complex and dose-dependent, featuring a fascinating dual role as an antioxidant and a pro-oxidant. While particularly promising in oncology as an adjunctive therapy, evidence also supports its benefits for immune function, skin health, and cardiovascular protection. However, translating this potential into mainstream medicine is contingent upon overcoming significant research hurdles, primarily by conducting large-scale clinical trials. Vitamin C remains a compelling example of how a common micronutrient, when understood in depth, can reveal novel and sophisticated therapeutic pathways.[31]

6. ADVANTAGES AND DISADVANTAGES OF VITAMIN C

6.1 Advantages:

6.1.1 Strengthens the Immune System

Helps stimulate the production and function of white blood cells, your body's front-line defenders against infections. May shorten the duration and reduce the severity of colds and respiratory infections—especially in those under physical stress (like athletes or soldiers). Supports immune defence by enhancing skin barriers and promoting antioxidant activity in immune cells.

6.1.2 Acts as a Powerful Antioxidant

Neutralises free radicals, which are unstable molecules that can damage cells and accelerate ageing. Reduces oxidative stress, a key driver of chronic diseases like heart disease, cancer, and type 2 diabetes. Protects vital

organs—including the lungs, brain, and blood vessels—from damage caused by pollution, stress, and poor diet.

6.1.3 Essential for Collagen Production

Plays a crucial role in the synthesis of collagen, the protein that maintains the strength and elasticity of skin, joints, tendons, and blood vessels. Aids in wound healing and recovery from surgical injuries. Promotes healthier, youthful-looking skin, helping reduce fine lines and wrinkles.[32]

6.1.4 Boosts Iron Absorption

Enhances the absorption of non-iron, the form of iron found in plant-based foods like spinach, lentils, and beans. This is especially beneficial for vegetarians, vegans, and those with anaemia, as it helps prevent or correct iron deficiency.

6.1.5 Supports Brain and Mental Health

Helps protect brain cells from oxidative damage, supporting long-term brain health. May slow down age-related cognitive decline and support memory and focus. Low vitamin C levels are linked to fatigue, poor mood, and even depression.

6.1.6 May Support Cancer Treatment (Adjunct Therapy)

High-dose intravenous (IV) vitamin C is being studied as a complementary therapy in cancer care. Some research suggests it may improve quality of life, reduce chemotherapy side effects, and in certain cases, help target cancer cells without harming healthy tissue.

6.1.7 Promotes Heart and Vascular Health

Helps lower blood pressure by improving blood vessel function and reducing arterial stiffness. May prevent the oxidation of LDL (bad cholesterol), a key factor in atherosclerosis (plaque buildup in arteries). Supports healthy circulation and reduces inflammation linked to heart disease.

6.1.8 May Aid in Detoxification

Vitamin C can bind to certain heavy metals, such as lead, mercury, and cadmium, helping the body eliminate them—particularly useful in polluted environments or for individuals exposed to industrial toxins.[33]

6.2 Disadvantages:

6.2.1 Digestive Upset

Taking high oral doses (usually over 2,000 mg per day) may lead to:

- Nausea
- Diarrhoea
- Stomach cramps

This is especially common when taken on an empty stomach.[34]

6.2.2 Kidney Stone Risk

Excess vitamin C is broken down into oxalate, which can form calcium oxalate stones—the most common type of kidney stone. People with a history of kidney stones or poor kidney function should avoid high-dose vitamin C supplements.

6.2.4 Iron Overload in Susceptible Individuals

In conditions like hemochromatosis (where the body stores too much iron), vitamin C can increase iron absorption, potentially leading to organ damage over time.

6.2.5 Can Interfere with Lab Tests

High levels of vitamin C may cause false readings in certain medical tests, including:

- Blood glucose tests (especially finger-prick monitors)
- Faecal occult blood tests (used for colon cancer screening)

It's important to inform your doctor if you're taking high-dose vitamin C before lab work.[35]

6.2.6 Limited Absorption and Wasted Excess

Your body can only absorb so much at a time—usually 200 to 400 mg per dose. Taking more than the body can use simply results in excretion through urine, which may waste supplements and money.

7. THERAPEUTIC APPROACHES OF VITAMIN C IN TREATMENT OF CANCER:

Cancer remains one of the biggest challenges in global health. At its core, it's a disease where abnormal cells grow and spread without control. The core concepts—first laid out by researchers Hanahan and Weinberg—still form the foundation of our understanding of cancer. But since 2020, there's been major progress. We've seen rapid developments in immunotherapy, cutting-edge technologies, rising attention to health disparities, and the ongoing effects of the COVID-19 pandemic.

7.1 The Shifting Global Burden.

Cancer cases are rising worldwide. The reasons? People are living longer, global populations are growing, and unhealthy lifestyle habits like poor diets, less physical activity, and increasing obesity are becoming more common, especially in developing countries.

The most commonly diagnosed cancers today are lung, breast, colorectal, prostate, and stomach. But some good news: in many high-income countries, cancer deaths are going down. This is thanks to better prevention, earlier detection, and improved treatment options.[36]

7.1.1 Immunotherapy 2.0: Going Beyond the First Generation.

The first major success with immune checkpoint inhibitors such as PD-1/PD-L1 and CTLA-4 was a game-changer. But now researchers are pushing the boundaries even further. New Immune Targets Scientists are exploring new checkpoint proteins like LAG-3, TIGIT, and TIM-3 to fight resistance. In 2022, the FDA approved a LAG-3 inhibitor (relatlimab) in combination with nivolumab for treating melanoma—an important milestone. Cell-Based Therapies CAR T-cell therapy has been a breakthrough for blood cancers like leukemia and lymphoma. Now researchers are trying to apply it to solid

tumours, which are harder to treat due to their complex microenvironments. Cancer Vaccines: mRNA technology, like what was used for COVID-19 vaccines, is now being tested for cancer. Early research into both general and personalized (neoantigen-based) vaccines is showing promise.

7.1.2 Precision Oncology and Multi-Omics Integration.

Cancer treatment is getting more personalized. Instead of just looking at where a tumour starts, doctors are now focusing on the tumours unique genetic blueprint. We've moved from analysing one gene at a time to studying the whole genome, plus other layers of biological data—a method called "multi-omics. This includes:

Transcriptomics – which genes are actively being expressed (RNA)

Proteomics – what proteins the tumour is producing

Metabolomics – the chemical activity inside the cells

By combining all this data, researchers can better understand how cancer behaves and identify smarter treatment strategies.

7.1.3 Liquid Biopsies: New Tools for Detection and Monitoring.

A simple blood test can now reveal traces of cancer DNA, known as **circulating tumor DNA (ctDNA)**. These tests have moved from research labs into real-world use. They're doing more than just identifying mutations[37]

Minimal Residual Disease (MRD): These tests can detect tiny amounts of cancer left behind after surgery, helping doctors decide if more treatment is needed, especially in colorectal cancer.

Early Detection: Multi-cancer early detection (MCED) tests are being developed to detect various types of cancer with a single blood draw. While promising, they're still being studied for routine.

7.1.4 Artificial Intelligence (AI) and Digital Pathology: Changing the Game.

AI and machine learning are transforming cancer care:

AI can interpret medical images (like X-rays and pathology slides) faster and often more accurately than humans, helping detect cancer earlier. (40)S

It can integrate huge datasets—from genomics, pathology, and patient history—to predict outcomes and guide treatment.[38]

AI is also speeding up drug development by identifying new drug targets and biomarkers.

7.1.5 Addressing Disparities and the Socioeconomic Divide.

The COVID-19 pandemic (2020–2022) highlighted just how unequal access to cancer care can be. Many patients experienced delays in diagnosis, treatment interruptions, or couldn't get the latest therapies. These problems hit hardest in lower-income and underserved communities.

7.1.6 A Call for Equity in Cancer Care.

With all the progress in cancer treatment, it's become increasingly clear: **everyone** should benefit, no matter their income, race, or location. Equal access is no longer just a noble goal—it's a public health and ethical priority. Mental Health and Survivorship as more people survive cancer, there's a growing need to support their emotional, physical, and social well-being.

7.2 History of Cancer:

Cancer isn't a new enemy—it's been around for thousands of years. Our understanding has grown from mystical ideas to cutting-edge science.[39] Here's how we got here

7.2.1 The Ancient Mystery (Prehistory – 1800s)

The First Recorded Case: An Egyptian scroll from around 3000 BC describes breast tumors and, sadly, says: "There is no treatment."

The "Crab" Theory: Greek doctor Hippocrates named the disease karkinos (crab) because tumors with swollen veins looked like crabs. He thought cancer was caused by too much "black bile.[40]

The First Big Clue: In the 1700s, doctors began doing autopsies and finally connected symptoms to physical changes inside the body.

The Microscope Era: In the 1800s, Rudolf Virchow used a microscope to show that cancer is made of abnormal cells—and these cells come from other diseased cells. This was the birth of modern cancer biology.

7.2.2 The First Big Weapons (Late 1800s – 1900s)

Surgery: Early treatment meant cutting out the tumour—and lots of surrounding tissue. It was aggressive, but sometimes effective.

Chemotherapy's Origin: Chemotherapy came from a tragic wartime discovery. Soldiers exposed to mustard gas had damaged immune cells. Scientists wondered: Could this be used to kill fast-growing cancer cells? It worked.

"War on Cancer": In 1971, the U.S. launched a national effort to fight cancer, leading to major discoveries—like the link between smoking and cancer.

7.2.3 The Genetic Revolution (1970s – 2010s)

DNA Discoveries: Scientists discovered that cancer is caused by mutations in our own genes—either genes that drive growth (oncogenes) or ones that fail to stop it (tumor suppressor genes).

Hallmarks of Cancer: Hanahan and Weinberg mapped out the key behaviors that make a cell cancerous—like avoiding death signals, spreading to other areas, and growing their own blood supply.

Targeted Therapy: Gleevec was the first drug designed to target a single cancer-causing protein, proving that precision medicine could work.

Immunotherapy Breakthroughs: Drugs that block immune "checkpoints" (like Keytruda) help the body

recognize and attack cancer. This discovery won the Nobel Prize in 2018.

7.2.4 Today's Cutting Edge (2020 – Now)

CAR-T Therapy: Doctors can now engineer a patient's immune cells to become cancer-fighting assassins. This therapy is already saving lives and is being improved to make it cheaper and more widely available.

Liquid Biopsies: A simple blood test can now detect fragments of cancer DNA. This allows earlier detection, better monitoring, and even screening for cancer before symptoms appear.

The Gut Connection: The bacteria in your gut can influence how well immunotherapy works. Researchers are even exploring faecal transplants to boost treatment response.

AI in Action: Artificial intelligence is now helping doctors find tumors earlier, read scans more accurately, and analyze complex medical data in ways humans can't.

7.3 Types of Cancer

Cancer is a group of diseases, and each type starts in different cells. Here's how they're classified:

7.3.1 Carcinomas

These are the most common and begin in epithelial cells—the ones that cover body surfaces.

Adenocarcinoma: Starts in glands that produce fluids.[41]

Common Sites: Lung, breast, prostate, pancreas, colon, oesophagus.

Squamous Cell Carcinoma: Grows in flat cells lining organs and skin.

Common Sites: Skin, lung, oesophagus, oral cavity, cervix, bladder.

Basal Cell Carcinoma: Begins in the skin's deepest layer. It rarely spreads but is very common.

Transitional Cell Carcinoma: Develops in the stretchy tissue lining the urinary tract.

Common Sites: Bladder, ureters, renal pelvis.

7.3.2 Sarcomas

These are rare and grow in connective tissue, such as bone, muscle, and fat. Soft Tissue Sarcomas include tumour cell in fat, blood vessels, and muscles. Examples: Liposarcoma, Leiomyosarcoma, Angiosarcoma. Bone Sarcomas originate in bone or cartilage. Examples: Osteosarcoma, Chondrosarcoma, Ewing sarcoma.

7.3.3 Leukaemia

These are blood cancers that begin in the bone marrow and result in an excess of abnormal white blood cells. Major Types: Acute Lymphoblastic Leukaemia (ALL), Chronic Lymphocytic Leukaemia (CLL), Acute Myeloid Leukaemia (ML), Chronic Myeloid Leukaemia (CML).

7.3.4 Lymphomas

Cancers of the lymphatic system, which is part of the immune system.

Hodgkin Lymphoma: Identified by the presence of Reed-Sternberg cells.

Non-Hodgkin Lymphoma (NHL): A diverse group of lymphoid cancers.

8. MECHNANISM ACTION OF VITAMIN C IN THE TREATMENT OF CANCER:

High-dose vitamin C (ascorbate) exerts anti-cancer effects through multiple, well-defined biochemical and molecular mechanisms that become active only when plasma concentrations reach pharmacologic levels achievable through intravenous infusion. At these high doses, vitamin C acts not as an antioxidant but as a pro-oxidant, undergoing rapid oxidation in the tumour microenvironment to generate large amounts of hydrogen peroxide (H_2O_2).[42]

Cancer cells, which typically possess weaker antioxidant systems, low catalase activity, and high iron availability, accumulate toxic levels of H_2O_2, leading to oxidative damage of DNA, lipids, and proteins, activation of caspase-mediated apoptosis, and metabolic collapse due to NAD^+ and ATP depletion.[43]

Vitamin C also enhances Fenton chemistry by reducing Fe^{3+} to Fe^{2+}, promoting hydroxyl radical formation and intensifying oxidative injury specifically in tumour cells. Beyond redox damage, high-dose ascorbate modulates cellular metabolism by inhibiting glycolytic enzymes such as GAPDH, thereby disrupting energy production in highly glycolytic cancer cells (Warburg phenotype).[44] Another major mechanism recently emphasized in 2024–2025 research is vitamin C's role as an essential cofactor for Fe^{2+}/2-oxoglutarate-dependent dioxygenases, especially TET enzymes, which promote DNA demethylation; by restoring TET activity that is often suppressed in cancer, vitamin C can reactivate silenced tumour-suppressor genes, enhance immune recognition, and drive differentiation in hematologic and some solid malignancies.[45] Vitamin C also influences the tumour immune microenvironment by improving T-cell activation, modulating macrophage phenotype, and supporting collagen synthesis that stabilizes tissue architecture and limits invasion.[46]

Furthermore, vitamin C can act as a radiosensitizer and chemosensitizer, increasing tumour susceptibility to radiation and certain cytotoxic drugs by heightening oxidative stress while potentially reducing treatment-related toxicity in normal tissues. Emerging studies even suggest roles in regulating ferroptosis, inhibiting hypoxia-inducible pathways, and targeting cancer stem-like cells, although these remain under investigation.[47] Overall, recent evidence supports vitamin C as a multifaceted anti-cancer agent whose selective cytotoxicity, epigenetic regulation, metabolic disruption, and immune-modulating properties make it a promising adjunctive therapy; however, clinical outcomes remain mixed, and high-dose IV vitamin C remains investigational pending larger, well-controlled trials.[48]

9. PATHOPHYSIOLOGY OF VITAMIN C IN CANCER TREATMENT:

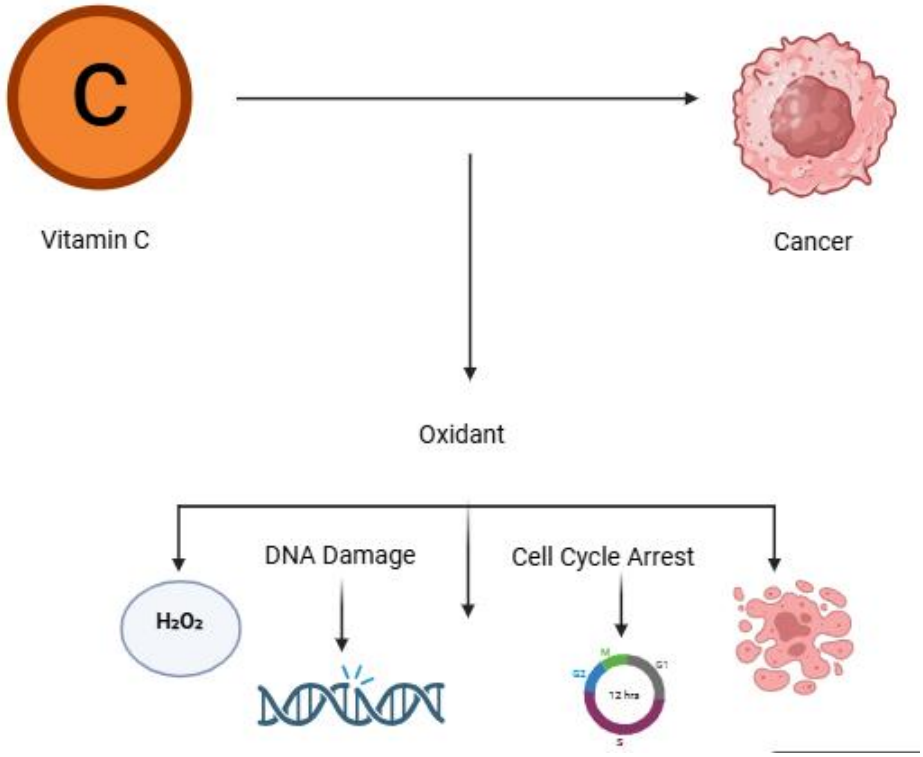


Figure 2: Pathophysiology Of Vitamin C.[49]

Vitamin C has long been recognized as an essential nutrient required for immune defence, collagen synthesis, antioxidant protection, and tissue repair, but growing scientific evidence suggests it may also play an important role in cancer management when administered at high pharmacologic doses. Early interest in vitamin C as a cancer therapy began with Linus Pauling in the 1970s, whose observations—although limited by methodological flaws—stimulated decades of further investigation.[50]

Modern research using advanced experimental models and clinical trials has renewed attention to its therapeutic potential, particularly when delivered intravenously, a route that can achieve plasma concentrations far higher than those achievable through diet or oral supplements.[51] At these elevated levels, vitamin C exhibits a distinct pro-oxidant effect by generating hydrogen peroxide (H_2O_2) within the tumour microenvironment; because many cancer cells have weakened antioxidant systems and reduced catalase activity, they are unable to detoxify H_2O_2 effectively,[52] leading to oxidative damage, DNA breakage, mitochondrial dysfunction, and ultimately selective cancer cell death. Vitamin C also exerts significant epigenetic effects, functioning as a cofactor for TET enzymes that regulate DNA demethylation; this process can reactivate silenced tumour-suppressor genes,[53] promote cellular differentiation, and inhibit malignant progression. In addition, high-dose vitamin C has been shown to enhance the efficacy of chemotherapy, radiotherapy, and even emerging immunotherapies, largely by increasing oxidative stress within tumour cells while simultaneously protecting normal tissues from treatment-related toxicity.[54]

Beyond these direct anti-tumour mechanisms, vitamin C strengthens the immune response by supporting the activity of T-lymphocytes, natural killer (NK) cells, and other components of the body's defence system, [55] thereby improving tumour surveillance and overall immune competence in cancer patients. Taken together, these mechanisms highlight how vitamin C—an old nutrient with well-established biological functions—may serve as a promising adjunct in modern cancer therapy, particularly when used in combination with standard treatments to enhance their effectiveness while limiting systemic harm.[56]

10. CONCLUSION:

Vitamin C has come a long way from its humble beginnings as the cure for scurvy. Today, we're seeing it in a new light: not just as a vital nutrient, but as a complex and promising player in the fight against cancer, especially when delivered in high doses directly into the bloodstream. This shift happened when scientists cracked a key puzzle: our guts can only absorb so much vitamin C from pills, but IV infusions can deliver amounts high enough to trigger powerful, targeted effects on cancer cells. So, how does it work? At these extreme levels, vitamin C actually flips the script. Instead of just protecting cells, it creates a mild hydrogen peroxide bath that selectively stresses and kills cancer cells, which are notoriously bad at cleaning up this kind of damage. But its strategy doesn't stop there. It also seems to help "reset" the genetic switches that cancer turns off, reviving our body's natural defenses against tumors. Perhaps

most excitingly, it gives our immune system a serious boost, helping our own T-cells recognize and attack cancer more effectively. For patients, this could mean a double win: making their standard therapies more effective while potentially reducing the brutal side effects like crushing fatigue and nerve pain, offering a much-needed improvement in quality of life. In the end, vitamin C's story is a fascinating one of scientific rediscovery. It shows us how a simple, everyday molecule can reveal hidden layers of complexity and hope. While it's not a magic bullet, it represents a compelling and versatile approach to cancer care—one that works with our body's own systems. The path forward now lies in rigorous science: running those critical trials, developing better delivery methods, and finally turning this decades-old promise into a tangible reality for patients.

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