Vitamin C and Cancer: Is There A Use For Oral Vitamin C?

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Abstract *For several decades, the role of vitamin C in the treatment of cancer has been a subject of clinical research and controversy. It has been established that ascorbate is potentially a safe and effective anti-cancer agent, able to kill cancer cells while leaving healthy cells unharmed. However, its role has been viewed in the context of existing cytotoxic chemotherapy models of medicine. Consequently, many doctors and patients have come to believe that only intravenous vitamin C administration is an effective treatment for cancer. We suggest that this view is misguided and oral intakes are preferable.*

Introduction

Methods and technologies designed for drug therapies do not always apply to orthomolecular medicine. One current debate is the use of cytotoxic chemotherapy as a model for the use of vitamin C in cancer. Some claim that intravenous (IV) ascorbate is required to produce cytotoxic levels in the body. Here we show that restricting delivery to the IV route is inconsistent with available clinical,[1] animal,[2] and experimental data.[3] Furthermore, there are strong indications that, as a treatment for cancer, oral vitamin C is potentially more effective than IV administration.

The use of intravenous vitamin C in clinical trials has not delivered the promising results of early studies.[4] Recent studies have assumed that, in the early clinical trials, IV administration resulted in successful life extension. By contrast, Hickey and others have suggested that the use of IV ascorbate may generate resistance to treatment, rather than the expected benefits.[5,6] This contrasting idea has also been challenged.[7,8] We point out the main differences between oral and IV administration of ascorbate, and explain why oral intakes are likely to be more effective for the treatment of cancer.

Cancer Biology

Cancer is often misunderstood as a disease based on genetic mutation. Thus, modern cancer research often attempts to find the gene, or genes, that lead to the illness. In some cases, there are correlations between cancer and either oncogenes (which are activated or increased) or tumour suppressor genes (which are deactivated or lowered). However, the genetic differences between healthy cells—or, indeed, benign cancer cells—and malignant cells are enormous. Malignant cells are aneuploid[9,10] and, even in a single tumour, they can have vastly different numbers of chromosomes from the standard 23 matched pairs of healthy cells (ranging, say, from only 10 chromosomes to 100+). This change can be explained parsimoniously as a failure of the cancer cells' mechanisms for control of chromosome copying and cell division.

Biology is normally considered within the framework of evolution. Similarly, cancer can be viewed in terms of cellular microevolution, towards what we might refer to as "selfish cells."[11] The implication for carcinogenesis is that anything that causes error-prone cell proliferation will, in the long-term, result in cancer. For example, local oxidation drives cell proliferation via redox signalling and free radical damage. When this happens, a lack of antioxidants—whether through dietary deficiency or because cells lack the energy to produce them—will drive carcinogenesis and increase the risk of cancer. This explains the widespread finding that dietary antioxidants prevent cancer.

The changes that occur during a cell's transition from healthy to malignant include varying responses to antioxidants and oxidants. Typically, malignant cells rely on oxidation to drive growth; however, they must strike a balance, as too much oxidation can kill the cells.[12] To a first approximation, both chemotherapy and radiotherapy work by increasing local oxidation and causing free radical damage, with the aim of either killing cancer cells directly, or stimulating apoptosis (cell suicide).

Antioxidants function in the opposite way: they decrease oxidation and may thus protect malignant cells from the oxidative effects of conventional treatments. For this reason, the use of standard dose antioxidant supplements in treating cancer is highly suspect, despite them being one of the main ways a person can avoid getting the disease in the first place.

Fortunately, within tumours, vitamin C and certain other dietary "antioxidants" act as oxidants, rather than antioxidants. Moreover, the same substances act as antioxidants within healthy cells. This means they can destroy cancer cells, while simultaneously improving the health of the rest of the body. This consequence of the redox chemistry of vitamin C and related substances is crucial to how they should be used for the prevention and treatment of cancer.

Microevolution provides a parsimonious explanation for the development of cancer.[11] One common consequence of carcinogenic microevolution is that tumours have a different metabolism than healthy cells. According to the microevolutionary model, the development of anaerobic metabolism is not surprising because, in its early stages, a tumour's growth is restricted by its lack of blood vessels.[13] Cells that are relatively far from blood vessels become short of oxygen and other metabolites. Thus, selection pressure favours anaerobic cells, which use glycolysis for energy, avoiding the need for oxygen. Until the tumour learns (i.e., evolves) to stimulate local blood vessel growth, it remains small and its growth is limited. However, given time and a diversity of cell types, cancer cells that can stimulate the growth of local blood vessels will probably occur and will have a selective advantage over those that cannot.

Cells that divide with errors are likely to diverge from the normal, healthy form.[11] Slightly abnormal cells become subject to selection pressures, as the body responds with immune and other mechanisms to help prevent cancer. In abnormal and varying cells, such pressure favours those cells that have increased fitness. In this context, "increased fitness" means they behave like malignant cells, reproducing, spreading into their local environment, and setting up distant colonies (metastases).

The biochemistry of human cells includes essential core mechanisms that we share with microorganisms; over an evolutionary timescale, these have become stable. By contrast, the signalling and other cooperative mechanisms, needed in the tissues of multicellular organisms, are more recent and less robust. Damaged human cells thus have a tendency to revert to the precursor forms that helped microorganisms to become so successful. When cells from a multicellular animal, such as a human, regress to such single-celled behaviour, we call the cells cancerous.

Adaptation

The large variation in chromosome numbers found in some tumours is an indication of biological diversity. A malignant tumour is not a clonal multiplication of a single cell

type, but a diverse ecosystem. Malignant cells compete, cooperate, and communicate between themselves and with nearby healthy cells. Even among inanimate agents, populations with these characteristics often display an emergent property, sometimes called swarm intelligence.[14] Classic examples of flocking behaviour include the behaviour of flocks of birds or shoals of fish. Such populations often exhibit adaptation to threats, and this is also apparent in the way cancer cells develop resistance to treatment.

Resistance is perhaps the single most important issue in the treatment of cancer. Its eradication would be less demanding without its rapid development of tolerance to treatment. By definition, an anticancer drug is toxic to the population of cancer cells. However, some cells may get a lower than average dose: perhaps they have a relatively poor blood supply or are otherwise shielded from the drug. Alternatively, the duration of treatment may be insufficient for the drug to penetrate the whole tumour, allowing certain cells to survive the treatment. Furthermore, because of biological variation, some cancer cells are naturally more resistant to toxicity. Chemotherapy and radiotherapy kill the most susceptible cancer cells, while sparing the resistant cells. These resistant cells are now free from competition from cells that were easy to kill or damage and can thus grow more rapidly. In such cases, a tumour may be seen to shrink temporarily but then to grow back, as the aggressive cancer cells assert their dominance. Such adaptation is usually described as resistance to treatment, but it is an example of natural selection, occurring in a population of cells. Since the days of Wallace and Darwin, this selective process has been one of the well-studied phenomena in biology.

The primary problem in treating cancer is to deal with the cancer's natural variability and its resultant capacity to adapt to toxicity. It is well known that a cancer may respond to any single drug or other treatment, by avoiding its mechanisms of action. If the drug blocks an oncogene, for example, a cell using a different oncogene may proliferate. Alternatively, a cell with a disabled tumour suppressor gene may thrive, as competition is reduced. Generally, toxicity is not absolute and resistance can evolve rapidly.

Once again, nutrients need particular consideration. By definition, a nutrient is used for cellular health and growth. Providing nutrients to strengthen patients, or their immune systems, can equally deliver growth promoters, e.g., folic acid or iron, to a tumour. However, the cancer needs nutrients to grow and may be sensitive to the depletion of specific molecules. Relative deprivation of required nutrients will slow or reverse cancer growth, but the specific nutrients need to be identified and may vary with the individual and condition. One nutritional approach that a cancer cannot avoid is if it is starved of usable energy. Physically, the cancer needs energy to grow or even to continue to survive. "Starving" the cancer is a potential treatment,[2] and is part of the reason patients should avoid carbohydrates and sugars.

A standard way of dealing with the issue of adaptation was developed as a result of experience with antibiotics. Bacteria have been found to adapt to antibiotic drugs, which are therefore given continuously, in order to apply a constant selection pressure on the infectious microorganism. In tuberculosis and some other chronic infections, multiple antibiotics may be given together. Bacterial adaptation to the treatment would then require a response that simultaneously overcomes multiple antibiotic mechanisms of action; this is far less likely to occur.

A critical point in preventing antibiotic resistance is to avoid starting and stopping the treatment, thus patients are warned to complete the whole course. This is because each break in treatment provides respite to the microorganisms and makes it more likely that they will develop an adaptive response. In principle, the mechanisms of resistance of bacteria to antibiotics are similar to those of cancer cells to chemotoxic therapies. By analogy, therefore, cancer treatment should be given continuously. Unfortunately, most conventional therapies are too toxic to be given long-term.

The Chemotherapy Model

Conventional chemotherapy exploits a difference in the susceptibility of cancer cells and healthy cells to toxic treatments. Cancer cells are slightly more susceptible to ionizing radiation and to some poisons, particularly those that involve free radical damage. However, the difference in response is small: a dose of a drug that is high enough to kill cancer cells will typically be toxic to the host's other cells as well. The side-effects of radiation and chemotherapy are well known and form part of the media image of a cancer patient. In giving such treatment, oncologists aim to give the maximum effective dose, while minimizing harm to the patient.

For some rare cancers, such as childhood leukaemia and testicular cancer, conventional chemotherapy is beneficial. However, chemotherapy is a hotly debated topic.[15] For the vast majority of adult solid tumours, it offers little, if any, life extension and the side effects may dominate any potential benefit. Importantly, the more precisely targeted the therapy, the greater is the chance that diverse cancer cells can adapt. Chemotherapy generally cannot be given in high enough doses to kill the tumour outright, without also killing the patient. Moreover, it cannot be continued at a lower level for a prolonged period, since a heuristic in pharmacology is that the toxicity is proportional to the total dose.

Natural Redox Agents

The development of cancer cells is a consequence of microevolutionary processes. Another consequence of evolution is that some natural substances have powerful anticancer properties. Cells in multicellular organisms, including plants, have evolved the ability to cooperate and to suppress the development of cancer. The list of natural anticancer substances is long and includes curcumin (turmeric), green tea extract, selenium, alpha-lipoic acid, and many other supplements. Every so often, a research group claims a breakthrough in finding a safe anticancer molecule,[16,17] without realizing that such substances are ubiquitous. We are particularly interested in vitamin C, which acts safely as an antioxidant in healthy tissues and an oxidant in tumours. In other words, it is the archetype for anti-cancer treatments.[3]

A range of redox active molecules have the property of killing cancer cells, while helping healthy cells. Vitamin C may be considered unique in the respect it can be given in massive doses, with a high degree of safety. Although it is theoretically possible to give a toxic dose of vitamin C, it is less likely than an overdose of water, which occasionally results in death. Oral doses of vitamin C have a single established but minor side effect: loose stools (diarrhoea). Obviously, clinicians giving large intravenous doses need to realize the potential for toxic reactions, particularly with cancer patients, as tumour necrosis can occur.

Bowel Tolerance and Dynamic Flow

The late Dr. Robert Cathcart described how tolerance to oral doses varies with the individual's state of health.[18] In healthy people, as the dose of vitamin C is increased, progressively less is absorbed. The concentration of vitamin C builds up in the intestines, attracting water. At some point, usually after consuming several grams in a single dose, the unabsorbed vitamin C causes diarrhoea. Cathcart noticed, however, that sick or stressed individuals could take exceptionally large doses, without reaching their bowel tolerance level. This bowel tolerance effect is large and obvious. So, for example, a person might tolerate well over 100 grams per day when acutely ill but have a bowel tolerance of 3 grams per day when healthy. The magnitude and easy reproducibility of this effect suggests that it is important to the mechanism of action with oral intakes.

Cathcart's bowel tolerance observations imply that, during illness, the body responds by absorbing as much vitamin C as possible from the gut. A healthy person will absorb only a fraction of a single gram dose, whereas a sick person seemingly absorbs almost all of a 10 gram dose. This increased absorption does not necessarily produce an abundance of vitamin C in the blood. During illness, the use of vitamin C by the tissues appears

to increase dramatically, producing a relative deficit in the blood plasma. Together with Cathcart, we explained these findings in relation to high oral doses of vitamin C, in terms of a dynamic flow through the body.[19]

Dynamic flow occurs when "excess" vitamin C is available in the diet and gut. In good health, a proportion is absorbed and the rest is excreted. During illness, the body absorbs more from the gut, in an attempt to match the increased tissue requirements for antioxidants (or, to be more precise, for redox reactions). The result is a flow of vitamin C through the body; absorbed into the blood, it acts as an antioxidant (or oxidant) in the tissues, following which spent ascorbate is excreted in the urine. According to this model, the oft-cited "expensive urine" argument[20] against high doses of vitamin C is reinterpreted, as an essential and beneficial aspect of its biological function.

Blood Plasma Levels

When given by injection, the initial ascorbate level is determined by the mass of the vitamin dose and the volume of plasma. Even a small, gram level dose can produce immediate plasma levels in the millimole range.[21] However, the plasma level drops rapidly, with a half-life of 0.5 hours.[19] The baseline for this rapid excretion is a plasma level of about 60-70 μM/L. Below this level, the vitamin is conserved and excretion is slow, with a half-life measured in days to weeks, in healthy individuals. This conservation of ascorbate protects against acute scurvy and, thus, the baseline maintenance level may be taken as the minimum level for short-term health. In a healthy adult, 200 mg/day can preserve this baseline. However, such an intake assumes an unrealistic absence of illness or stress, which can rapidly deplete plasma levels.

When healthy people take high doses of vitamin C orally, absorption is incomplete and gradual, reflecting a balance between excretion and absorption. The plasma levels increase over an hour or two, to a level of about 250 μM/L, then gradually decay, returning to baseline after, perhaps, six hours. It is sometimes claimed that the plasma levels are saturated, or tightly controlled, at <100 μM/L, with a 200 mg/day oral intake,[21] but this is a misunderstanding. Firstly, the data for dynamic flow using repeated oral doses indicates that an intake of 20 g/day (20,000 mg/day in divided doses) can maintain plasma levels at approximately 250 μM/L.[22] Moreover, the massively increased Cathcart bowel tolerance in sick people, who can sometimes consume up to 200-300 g/day, reflects a greater absorptive capacity.

The availability of liposomal vitamin C has increased the plasma levels attainable with oral doses. These formulations greatly increase absorption in healthy individuals, to perhaps 90% of an oral dose. Our preliminary results indicated that a large single oral dose of liposomes could increase plasma levels of free ascorbate to a maximum of at least 400 μM/L.[22] We point out that this is free ascorbate, so does not include the amount that remains in intact liposomes, or that might be expected to have been absorbed into the tissues, given the form of administration.[23] Initial measurements suggest that liposomes and standard oral ascorbic acid are absorbed by independent mechanisms and that a combination of both can yield free molecule plasma levels at >800 μM/L. Importantly, such plasma levels can be sustained indefinitely using oral doses.

Clinical Trials

Cameron and Pauling performed a preliminary clinical trial, on the use of vitamin C in 100 terminal cancer patients.[24] Their results were remarkable, with vitamin C increasing the mean survival time more than 4.2 times, from 50 days (controls) to more than 200 days (treated). They reported that most treated patients had a lower risk of death and improved quality of life, while about 10% (13 patients) had survival times around 20 times longer than those of the control patients.

Cameron treated 100 patients, who he compared with 1,000 matched controls. The lack of randomization of the groups was later criticized as a limitation of the study.[25]

However, this objection does not explain the observed difference in survival rates, as any selection bias would have needed to be unusually large to produce such results, and is inconsistent with the experiment as described. We have estimated that in order to select 100 patients with the observed characteristics, the experimenters would have needed about 7,000 patient records and the process would have taken nearly four person-years, assuming one hour per patient. Given the selection described for the study, it is implausible that patients were selected in this way. The survival curves for Cameron's experiment are shown in **Figure 1** (p.39).

The protocol included an initial 10 day course of IV ascorbate, at a relatively low daily dose of 10 g/day, followed by continuous oral intakes of 10-30 g/day, in divided doses. Notably, Cameron emphasized multiple oral dosing, to maintain plasma levels.[26] He warned against intermittent injections, which would give saw-tooth plasma levels and might produce a rebound effect.

In 1982, Murata and Morishige also reported extended survival times from the use of vitamin C in cancer.[27] These Japanese researchers used oral doses of up to 30 g/day, supplemented with relatively low-dose 10-20 g IV infusions. Their reported survival times were 43 days for 44 low-ascorbate patients, compared to 246 days for 55 high-ascorbate patients (5.7 times longer). In another Japanese hospital, the researchers reported survival times of 48 days for 19 control patients, compared to 115 days for six treated patients. Furthermore, at the time of publication, some treated patients were still alive. In 1982 Murata and Morishige had replicated the Cameron and Pauling trial with similar encouraging results, as shown in their survival chart, reproduced in **Figure 2** (p.39).

Results have not all been so positive. In 1985, Creagan and Moertel of the Mayo Clinic published the results of clinical trials, claiming to replicate Cameron and Pauling's study. They compared 60 patients, who received 10 g/day vitamin C orally, to 63 controls.[28] In a further study, they randomized one hundred patients with colorectal cancer into two groups: the treatment group received 10 g of vitamin C per day and control patients were given a placebo.[29] Creagan and Moertel failed to demonstrate a benefit. We would be keen to take a closer look at their findings, as was the late Linus Pauling, but these researchers have declined to release their raw data for independent analysis.

Since the Mayo Clinic studies, some researchers have attempted to explain away the negative findings by suggesting that the positive studies used IV ascorbate, whereas the negative studies used oral intakes.[30,31] The implication of this is that oral intakes cannot reach the levels needed to kill cancer cells, whereas injected ascorbate can reach the necessary cytotoxic levels. This interpretation is an error, which seems to have arisen through analogy with chemotherapy.

Although there were technical problems with the control selection in the Cameron and Pauling study, these were not sufficient to invalidate the results. By contrast, the Creagan and Moertel trials demonstrate a lack of understanding of the basic science, particularly the pharmacokinetics and short half-life of vitamin C. Perhaps Mayo Clinic researchers have begun to appreciate the difficulties with these negative studies, since the Mayo Clinic website currently states "more well-designed studies [on vitamin C and cancer] are needed before a firm recommendation can be made."[32] We agree, and would place the emphasis on "well-designed."

Unfortunately, the Mayo Clinic studies did not take into account the short half-life of high-dose vitamin C, so their studies were flawed in terms of the basic science.[19] Ironically, proponents of vitamin C as chemotherapy suggest that the early positive trial results were just serendipity.[30,31] They claim that Pauling, arguably one of the greatest scientists in history, "may not have fully appreciated the critical difference between intravenous and oral administration."[31] This odd suggestion is easily refuted from Pauling's writings and those of his colleague Cameron.[1]

With some irony, we must point out that the suggestion that oral doses are ineffective is a fallacy. Firstly, however, we restate

Figure 1. Cameron and Pauling's results indicate that (mostly oral) high-dose vitamin C can produce a large increase in survival time for a range of tumours.

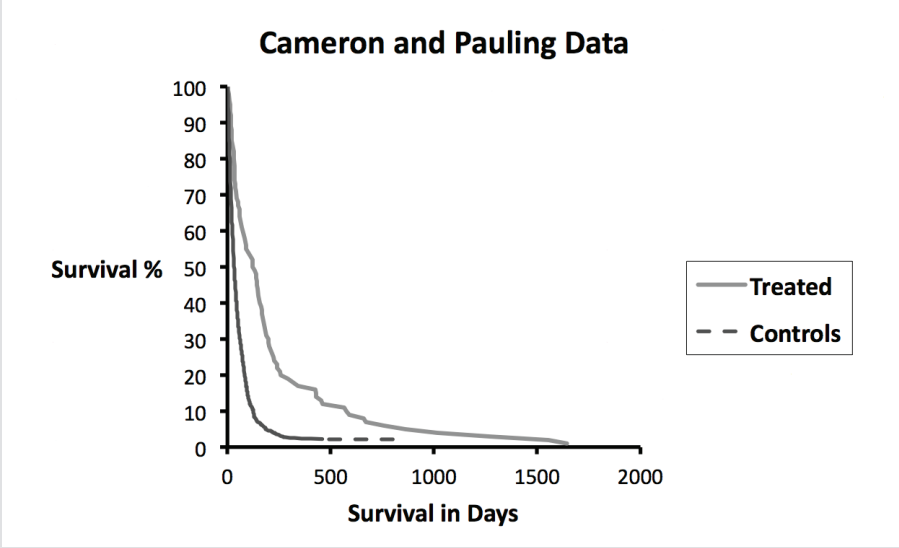
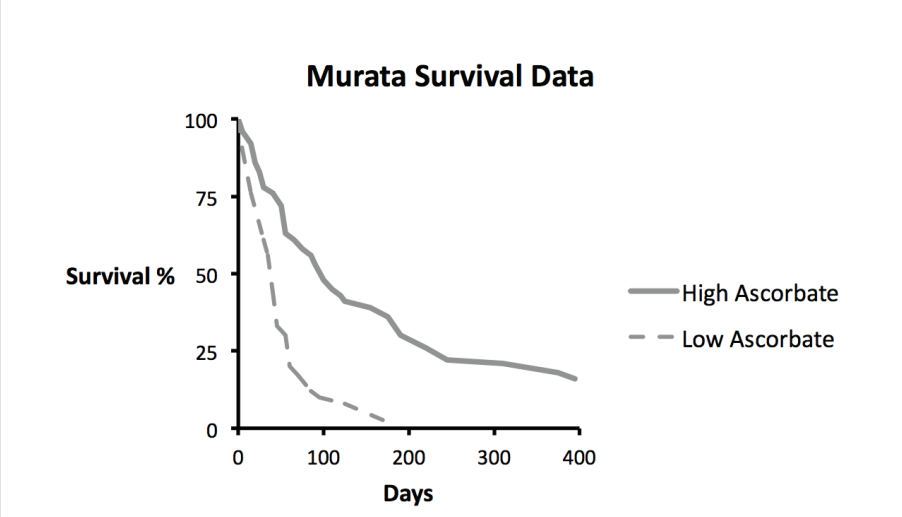


Figure 2. Representation of the Murata and Morishiga survival data, extracted from their figure. Low ascorbate (≤4g a day) and high ascorbate (≥5g a day) groups are shown (dashed and solid lines respectively). The increase in survival with dose is clear.



that Cameron and Pauling, and Murata and Morishige, used predominantly oral doses, with the stated aim of maintaining plasma levels. Furthermore, Hoffer also replicated the early trials, using oral vitamin C in cancer patients, and obtained similar positive results,[33] as shown in **Figure 3**, (p.41).

The mean survival time for his 31 controls was 5.7 months. He treated approximately one hundred patients, of whom he classified 20% as "poor responders," even though they lived for approximately twice as long as controls (10 months). The remaining 80% of patients he classed as "good responders." Of these, 32 patients, with cancers of the breast, ovary, cervix, or uterus, had a mean survival time of 122 months, and 47 patients, with other cancers, had a mean survival time of 72 months. The assertion that oral doses of vitamin C are ineffective is not consistent with the data from these trials.

Selective Cytotoxicity

An understanding of the short-term toxicity of ascorbate to cancer cells is relevant to the chemotherapy model of vitamin C treatment. In such experiments, either a cancer cell line or healthy cells are treated with vitamin C for about an hour, and its toxicity is estimated. As an example, **Figure 4** (p.41) shows results from Chen et al,[34] showing the selective toxicity of vitamin C to tumour cells and healthy white blood cells (monocytes). The results show that Burkitt's lymphoma tumour cells start to die at relatively low levels of ascorbate, and with an hour's exposure at a concentration of 1,000 μM/L, cell death is approximately complete. Similar results have been demonstrated with other cancer cell lines, although experimental cell lines differ in their sensitivity.[35,36]

The "vitamin C as chemotherapy" model assumes delivery of a relatively short, high burst of ascorbate. However, this does not apply to oral doses, which can be used to produce long term, sustained plasma levels. The question arises, what happens when the treatment with ascorbate is maintained over a prolonged time period? **Figure 5** (p.42) illustrates data calculated from Takemura et al, using mesothelioma cell lines.[37] These data show a large increase in cancer toxicity when the experimental exposure time was increased from 1 hour to 24 hours. In some cases, a prolonged exposure to vitamin C at a concentration of 100 μM/L, a level easily sustained with oral supplementation, was found to be more effective than a short exposure at the much higher level of 1,000 μM/L.

Despite this, it is important to remember that vitamin C on its own is a relatively weak anticancer agent. Crucially, however, it can be used as a driver, to supply electrons to synergistic redox agents. Often, such substances combine in a Fenton style reaction, generating hydrogen peroxide which kills cancer cells. Numerous other mechanisms may also be involved, such as inhibition by the combination of vitamin C and alpha-lipoic acid of NF-kappaB, which is involved in the control of DNA copying during cell replication.[38] When combined with vitamin K3, the concentration of vitamin C needed to kill cells is massively reduced (by a factor of 10-50).[39] Similarly, alpha-lipoic acid,[40] copper,[41] selenium, and other redox active supplements greatly increase the selective cytotoxicity of ascorbate.[12]

Conclusions

Establishing the role of vitamin C in cancer is a challenging research endeavour. The pharmacokinetics of vitamin C is more complicated than that of a typical drug. It has dual phase pharmacokinetics, with a short half-life for high doses and a long half-life for lower intakes. Importantly, the mechanisms underlying Cathcart's bowel tolerance effect during illness and stress do not yet have a scientific explanation. Although the effect is easily reproduced, it has been ignored by medical and nutritional research. With hindsight, it is clear that the simplistic "vitamin C as chemotherapy" research paradigm was likely to be misleading. We need to reconsider the available data, using orthomolecular concepts.

The rather startling clinical results of Cameron, Pauling, Murata, and Hoffer were not a result of the use of intravenous admin-

Figure 3. Representation of Hoffer's results on vitamin C treated patients and controls. These results with oral doses support those obtained by Cameron and Pauling, and Murata and Morishiga.

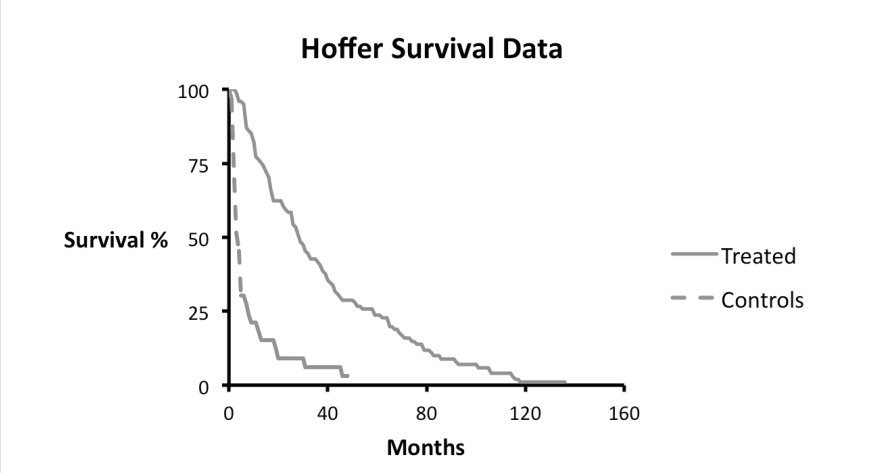


Figure 4. Experimental cell death following a one hour exposure to ascorbate in Burkitt's lymphoma cells (solid line) and healthy monocyte white blood cells (dotted line). The response of the tumour cells is approximately sigmoid. The majority of cell death occurs in the range of blood plasma values achievable using oral ascorbic acid and liposomal vitamin C (250-800 μM/L).

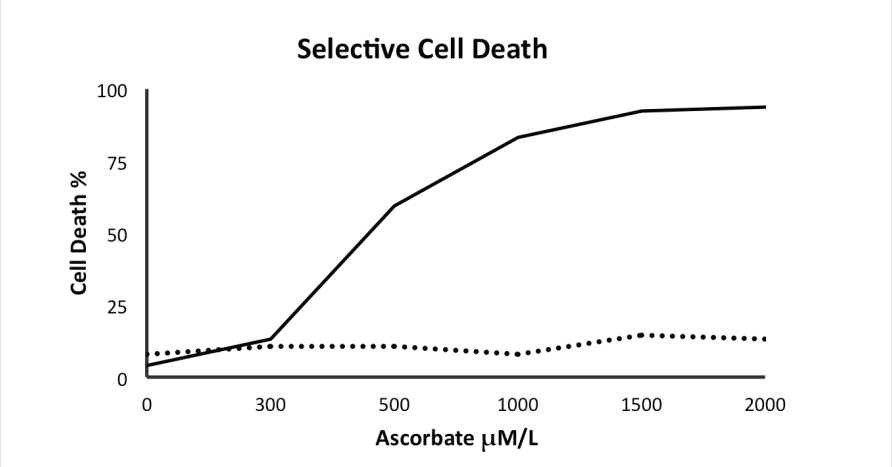
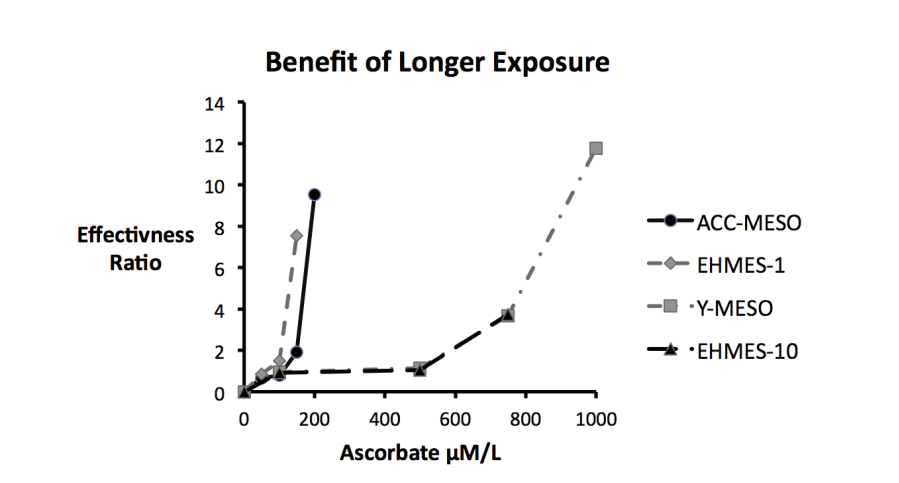


Figure 5. Increasing the experimental exposure of cancer cells from 1 to 24 hours greatly increases the anticancer activity. The ratio is relative to the effectiveness of 1,000 µM/L for one hour for mesothelioma cell lines.



istration. Hoffer used oral doses exclusively, yet obtained results consistent with those of Cameron and Pauling. Cameron used some intravenous administration, but the majority of vitamin C in his studies was given orally. Indeed, he urged that levels should be sustained and warned against fluctuations, which are inevitable with intermittent intravenous infusions. Some have assumed that Murata and Morishiga's study used intravenous administration of ascorbate,[42] but the paper states that supplemental (0.5 g-1 g), oral (6 g to 30 g), and intravenous routes (10-20 g) were employed.[27]

Clinical results using intravenous ascorbate as chemotherapy have not lived up to the promise of the early trials.[4] One reason for this is that IV administration produces high but short-lived blood plasma levels. The assumption that a short sharp pulse of vitamin C will be more effective than a lower level prolonged exposure is not supported by the experimental data. As we have described, extending the exposure time more than compensates for a reduction in concentration. Indeed, longer exposures can be orders of magnitude more effective than short ones. The concentrations required to be cytotoxic over longer periods are much lower. Oral intakes, particularly with combined use of ascorbic acid and liposomal vitamin C, can easily achieve and maintain adequate levels for selective cytotoxicity.

Finally, the use of vitamin C as a sole anticancer agent is not recommended, as its anticancer actions are known to be greatly enhanced through use of synergistic supplements, such as alpha-lipoic acid. In clinical trials, it might be appropriate to study vitamin C in isolation, if the medical problem were to determine the details of its mechanism of action. However, such mechanisms can be determined using animal and experimental studies. We therefore see little reason to deprive patients of a more optimal therapy, purely in an attempt to determine the action of vitamin C in isolation. There is a more pressing and practical issue: the real

medical problem is to keep cancer patients alive and healthy, for as long as possible.

Competing Interests

The authors declare that they have no competing interests.

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