

Review Article

Beetroot (*Beta vulgaris L.*): evidence-based review of phytochemistry, functional properties, anti-cancer mechanisms and clinical translation

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ABSTRACT

Due to its high nutritional composition and complex phytochemical profile, beetroot (*Beta vulgaris L.*) has been increasingly studied scientifically as a functional food. This comprehensive review summarises the existing knowledge about beetroot botanical traits, nutritional composition, phytochemical contents, biological activities, anti-cancer activity, molecular pathways, processing methods, and clinical uses. Beetroot is a rich source of carbohydrates, dietary fibre, important vitamins and minerals, dietary nitrates and bioactive compounds such as betalains, polyphenols, flavonoids and pectic chemicals. These ingredients combine to provide it with powerful antioxidant, anti-inflammatory and antibacterial capabilities. Beetroot has demonstrated significant anticancer activity in models of breast, prostate, colorectal and liver cancer, with considerable *in vitro* and *in vivo* evidence to support its activity via mechanisms involving reactive oxygen species modulation, apoptosis induction, cell cycle arrest, angiogenesis inhibition, autophagy regulation and immune modulation. Further improvements in the bioavailability, stability and therapeutic efficiency of beetroot bioactives have resulted from advances in fermentation, probiotic enhancement and nanoliposomal formulations. Clinically, beetroot has been used in functional foods, sports nutrition, cardiovascular health interventions and cancer supportive therapy and has a favourable safety profile. Results are promising, however there are still issues with standardising the dose and lack of confirmation in large-scale clinical trials. In conclusion, this review identifies beetroot as an evidence-based functional food with great nutraceutical and therapeutic potential, while outlining future research pathways required for its effective translation into clinical and personalised nutrition applications.

Keywords: Beetroot (*Beta vulgaris L.*), Functional food, Betalains, Anticancer activity, Antioxidant and anti-inflammatory properties, Bioavailability enhancement, Fermentation and nanotechnology, Nutraceutical applications

INTRODUCTION

Beetroot (*Beta vulgaris L.*) is a widely cultivated root vegetable that has been used for many centuries as a food ingredient, a natural colourant and as a traditional medicine throughout Europe, Asia, the Middle East and parts of Africa. Beetroot, long regarded for its nutritional richness and culinary diversity, has in more recent times attracted considerable scientific interest owing to its various bioactive ingredients and the health-promoting aspects linked with them.^{1,2} Beetroot is well accepted

globally and it is used in various forms such as raw roots, juices, fermented goods, powders, and functional food formulations in traditional and current dietary systems.³⁻⁵ Functional foods are foods that have health advantages beyond basic nutrition. Over the last several decades there has been a significant change to the idea of functional foods in the field of nutritional science. This change is driven by the global growth in non-communicable diseases such as cancer, cardiovascular diseases, diabetes and chronic inflammatory diseases.^{6,7} In this respect, beetroot has been identified as a potential functional food, owing to

its high presence of biologically active substances such as betalains (betanin and betaxanthins), polyphenols, flavonoids, dietary nitrates, pectins, and necessary micronutrients.⁸⁻¹¹ These compounds have been demonstrated to exhibit antioxidant, anti-inflammatory, anti-microbial and cytoprotective effects through several molecular pathways.¹²⁻¹⁵

Among these bioactive compounds, betalains have received considerable interest due to their strong antioxidant activity and their participation in the modulation of oxidative stress, which is involved in carcinogenesis and other chronic disorders.¹⁶⁻¹⁸ Experimental investigations have shown that beetroot extracts and purified betalains reduce lipid peroxidation, scavenge free radicals, protect DNA from oxidative damage and control redox sensitive signalling pathways.¹⁹⁻²¹ Beetroot also contains dietary nitrates which are precursors for the generation of nitric oxide that has positive effects on vascular health, metabolic control, and physiological performance.²²⁻²⁴ These multiple features have placed beetroot among the nutraceutical candidates that can be used in very different fields, such as sports nutrition, disease prevention and supportive therapy.²⁵⁻²⁷

In particular, the rising body of in vitro and in vivo evidence indicating the substantial anticancer potential of beetroot and its derivatives is noteworthy. Cytotoxic, antiproliferative, and pro-apoptotic actions of beetroot extracts on a range of cancer cell lines, including breast, prostate, colorectal, liver, esophageal and pancreatic malignancies.²⁸⁻³⁵ Mechanistic studies have shown that these effects are mediated by mechanisms that include activation of apoptosis, cell-cycle arrest, suppression of angiogenesis, control of reactive oxygen species, and regulation of autophagy and immunological responses.³⁶⁻⁴⁰ Furthermore, synergistic interactions between beetroot extracts and conventional chemotherapeutic drugs like doxorubicin have been reported, indicating a possible role for beetroot-based techniques as adjuvant or supportive tools in cancer care.⁴¹⁻⁴³ In addition to traditional extraction methods, recent studies have explored fermentation, delivery systems based on nanotechnology and food processing technologies to improve the bioavailability, stability and therapeutic efficacy of beetroot bioactives.⁴⁴⁻⁴⁸

Products based on fermented beetroot, formulations loaded with probiotics and nanoencapsulated betalains have been shown to have higher antioxidant activity and greater cytotoxic effects against cancer cells, underscoring the role of processing procedures in maximising functional advantages.⁴⁹⁻⁵² However, despite these developments, the literature has produced fragmented and often conflicting findings, due to diversity in extraction methods, dosage and experimental design. While numerous studies and narrative reviews have been conducted on specific aspects of beetroot, such as nutritional composition, antioxidant capacity, or isolated anticancer effects, there remains a lack of a comprehensive, integrative review that

systematically consolidates recent evidence on beetroot's phytochemistry, biological activities, mechanistic pathways, and therapeutic applications in a unified framework.⁵³⁻⁵⁷ Existing reviews generally address restricted time periods, specific disease models or only a single class of bioactive chemicals, and hence important knowledge gaps exist with respect to the broader translational potential of beetroot as a functional food and nutraceutical agent.⁵⁸⁻⁶⁰

However, the rapid growth of research from 2009 to 2025, especially in the fields of cancer biology, functional foods, fermentation technology, and nano-formulations, calls for a consolidated and up-to-date synthesis of current evidence. Such evaluation is needed to clarify the present knowledge, to identify the research gaps, issues in standardisation, safety concerns and future directions in clinical and industrial applications. Additionally, the integration of results from in vitro, in vivo and nascent clinical investigations can provide a more comprehensive knowledge of the therapeutic value and limitations of beetroot.⁵²⁻⁵⁶

Thus, the present review aims to systematically collect, critically analyse and synthesise the available scientific literature on *Beta vulgaris* with emphasis on its nutritional composition, phytochemical profile, biological activities, anticancer mechanisms, processing strategies, and functional food applications. The aim of this review is to synthesise the latest high-quality studies, and to give a strong scientific basis for future research, product development and evidence-based use of beetroot for health promotion and disease prevention.

DESCRIPTION OF THE PLANT AND NUTRITIONAL COMPOSITION OF BEETROOT

Classification of plants

Beetroot (*Beta vulgaris* L.) is a biennial herb belonging to the family Amaranthaceae, previously placed in the family Chenopodiaceae. The genus *Beta* includes a number of cultivated varieties, such as the table beetroot (beetroot), sugar beetroot, fodder beetroot and Swiss chard, all of which are derived from the wild parent *Beta vulgaris* subsp. *Maritima*.^{2,12,22} Among them, table beetroot (*Beta vulgaris* L. subsp. *vulgaris*) is mainly cultivated for its edible taproot and widely used for nutrition and medicinal purposes.^{9,21} Morphologically, beetroot has a large, fleshy taproot that functions as a storage organ for carbohydrates and medicinal substances. The root is normally deep red to purple because of the presence of water-soluble nitrogenous pigments called betalains, including betacyanins and betaxanthins.^{18,24} The above-ground part of the plant is a rosette of broad and ovate to heart-shaped leaves with long petioles, which are also edible and nutritionally beneficial.^{2,16} In the second year of growth, if the plant is allowed to finish its life cycle, it develops an erect flowering stalk with little greenish flowers arranged in dense inflorescences.²¹ Beetroot is highly adapted to

temperate regions and is farmed around the world in Europe, Asia, the Americas and portions of Africa. In addition, its agronomic resilience, relatively short growth cycle and high yield contribute to its wide availability and economic relevance.^{15,53} The morphological buildup of colours, nitrates and phenolic compounds in the taproot, besides its culinary value, is the biological basis for the known functional and medicinal benefits of the taproot.^{10,17}

Nutritional value

Beetroot is a major dietary component of traditional and current nutrition systems, rich in nutrients and fat free. It has a nutritional profile characterised by a balanced combination of macronutrients, micronutrients and bioactive substances, which together justify its definition as a functional food.^{1,9,10}

Carbohydrates

Beetroot's main macronutrient is carbohydrate, which accounts for its mild sweetness and energy delivering ability. The main carbohydrates are sucrose, glucose and fructose, sucrose being the main sugar accumulated in the taproot.^{22,55} These carbohydrates are a significant energy source and are especially interesting in sports nutrition and recovery formulations.^{26,60} The carbohydrate portion also promotes fermentation processes, allowing the production of probiotic and functional beetroot-based products.^{44,49}

Fibre

Beetroot is a good source of dietary fibre which consists of soluble and insoluble portions. The presence of fibre improves the gastrointestinal function, regulates the microbiota in the gut, and controls the glucose and lipid metabolism.^{21,55} Prebiotic effects have been observed for pectins and hemicelluloses contained in beetroot cell walls, and in modified form they may possess antiproliferative effects on colorectal cancer cells.^{45,67} Fibre also increases feelings of fullness and plays a role in cardiovascular health by helping regulate cholesterol.^{24,60}

Vitamins

Beetroot includes a number of vital vitamins, especially vitamin C, folate (vitamin B9) and other B-complex vitamins, including B1, B2 and B6.^{9,55} Folate is important for DNA synthesis, methylation and cell division making beetroot nutritionally important during periods of fast growth and when cellular metabolism is compromised.²² Vitamin C improves antioxidant defence and immunological function, which complements the antioxidant actions of betalains and polyphenols.^{16,19}

Mineral

Beetroot contains a high mineral content with high quantities of potassium, magnesium, iron, calcium,

phosphorus, manganese and copper.^{9,21,55} Potassium is the most prevalent mineral, and it plays an essential role in electrolyte balance, blood pressure regulation and neuromuscular function.^{24,26} The iron concentration is non-heme but adds to the traditional usage of beetroot as a dietary supplement in anaemia, especially when ingested with vitamin C rich foods that promote iron absorption.^{17,54} Magnesium and manganese are also involved in the support of enzymatic processes and antioxidant defence systems.^{12,60}

Nitrate

Beetroot has a very unique nutritional property, which is its high nitrate level, making it different from many plants. Dietary nitrates are transformed endogenously to nitric oxide by the nitrate–nitrite–nitric oxide pathway resulting to vasodilation, better endothelial function and increased oxygen utilization.^{22,24} These qualities explain the well-documented effects of beetroot on cardiovascular health, metabolic control and physical performance.^{26,51,60} In addition to cardiovascular effects, increasing evidence indicates the role of nitric oxide signalling in immunological modulation and regulation of tumour microenvironment, indirectly contributing to anticancer effects.³⁶ The botanical properties and high nutritional value of beetroot provide a good biological foundation for functional and therapeutic uses. The combination of carbohydrates, dietary fibre, vitamins, minerals and nitrates, as well as, its particular phytochemical profile makes *Beta vulgaris* a crop of nutritional value with important implications in health promotion and illness prevention.^{1,10,21,55}

BEETROOT PHYTOCHEMICALS

Beetroot (*Beta vulgaris* L.) offers a unique and diversified phytochemical composition which accounts for its functional, nutraceutical and medicinal qualities. The biological activity of beetroot is due to the synergistic combination of pigments, phenolic chemicals, nitrogenous elements and structural polysaccharides. Among these, betalains, polyphenols, flavonoids, nitrates and pectic compounds have been most intensively explored for their functions in antioxidant defence, metabolic control and disease prevention including cancer.^{1,10,18}

Betalains (Betalain and Betaxanthins)

Betalains are water soluble nitrogen pigments that provide beets with their characteristic red-violet and yellow colour. Unlike anthocyanins, betalains are found only in the order Caryophyllales and are divided into two primary classes: betacyanins (red-violet pigments) and betaxanthins (yellow-orange pigments).^{18,24,55} The major betacyanin in beetroot is betanin, which is regarded as the main bioactive pigment in beetroot, contributing to most of the antioxidant capacity.^{16,19} Betalains are structural derivatives of betalamic acid, with a high redox potential and an efficient scavenging of reactive oxygen and

nitrogen species. Many studies have shown that betanin and other betalains protect biomolecules from oxidative damage, prevent lipid peroxidation and stabilise cellular membranes.^{16,19,24}

In addition to antioxidant action, betalains have been reported to alter inflammatory signalling pathways, induce apoptosis and decrease proliferation in several cancer cell lines including colorectal, breast, prostate and liver malignancies.²⁸⁻³⁵ Due to their ability to modulate redox-sensitive transcription factors and mitochondrial pathways, they are relevant for cancer chemoprevention and supportive therapy.³⁶⁻⁴⁰

Phenolic

Another key class of bioactive chemicals in beetroot that are responsible for its antioxidant and cytoprotective effects are polyphenols. Polyphenols dispersed in free and bound forms in the root matrix have been identified as phenolic acids including ferulic acid, caffeic acid, p-coumaric acid, and syringic acid.^{10,21,55} Besides betalains, polyphenols are present in lower amounts but act synergistically with pigments and vitamins to increase the total antioxidant efficiency.^{12,19}

The polyphenolic chemicals from beetroot have demonstrated to reduce DNA damage generated by oxidative stress, to modulate phase I and phase II detoxification enzymes, and to interfere with signalling pathways implicated in inflammation and carcinogenesis.^{16,37} Moreover, processing techniques like as fermentation and thermal treatment might impact the bioavailability of polyphenols, sometimes boosting their biological activity by structural modification or microbial metabolism.^{44,49,52}

Flavonoids

Flavonoids are a subset of polyphenols and comprise vitexin, isovitexin, rutin and quercetin derivatives which have been discovered in beetroot roots and leaves.^{21,55} These chemicals are notably plentiful in beetroot leaves but also present in the edible taproot, and they have systemic antioxidant and anti-inflammatory properties.^{22,60} Flavonoids has many biological effects, such as scavenging free radicals, inhibiting pro-inflammatory mediators, and regulating cell signalling cascades related to proliferation and apoptosis.³⁶

Vitexin in particular has drawn attention because of its reported anticancer mechanisms including cell-cycle arrest, mitochondrial malfunction, and regulation of MAPK and PI3K/Akt pathways. Beetroot contains betalains and flavonoids, which co-exist in beetroot,

increasing functional complexity and allowing for complimentary and overlapping modes of action.^{18,36}

Nitrates and nitric oxide precursors

Beetroot is one of the greatest dietary sources of inorganic nitrates, which are transformed in vivo to nitrites and then to nitric oxide through the nitrate–nitrite–nitric oxide pathway.^{22,24} Nitric oxide is an important signalling molecule for vasodilation, mitochondrial efficiency, glucose metabolism, and immunological modulation.^{26,60}

The nitrate concentration of beetroot underpins its well-established effects on cardiovascular health and exercise performance, but there is accumulating evidence that nitric oxide signalling also modulates tumour biology and immune surveillance.³⁶ Nitric oxide can affect angiogenesis, apoptosis, and dynamics of the tumour microenvironment, suggesting that nitrates can indirectly contribute to the anticancer effects of beetroot within a complex phytochemical matrix.⁴⁰

Importantly, it is believed that nitrates of beetroot are safer and more physiologically regulated than synthetic nitrate sources because of their interaction with antioxidants, which prevent the development of nitrosamines.^{22,24}

Pectins and dietary fibers

Beetroot is rich in dietary fibre like cellulose, hemicellulose and pectic polysaccharides, which are important for gastrointestinal health and metabolic regulation.^{21,55} Especially, pectins have been studied for their capacity to bind bile acids, alter the gut microbiota and modulate immunological responses.⁴⁵

Modified pectins from beetroot have shown antiproliferative and pro-apoptotic effects in colorectal cancer models, probably due to binding with galectin-3 and other cell surface receptors implicated in tumour growth.⁴³ Furthermore, fermentation and enzyme modification may improve the bioactivity of fiber-associated compounds, paving the way to the development of functional foods and therapeutic adjuncts.^{44,49}

The phytochemical richness of beetroot is due to the integrated presence of betalains, polyphenols, flavonoids, nitrates, and structural polysaccharides. These compounds have antioxidant, anti-inflammatory, metabolic and anticancer effects through complementing biochemical and molecular processes.

The interactions between these chemicals are critical for the development of beetroot-based functional foods, nutraceutical formulations, and medicinal techniques.^{1,10,18,36,55}

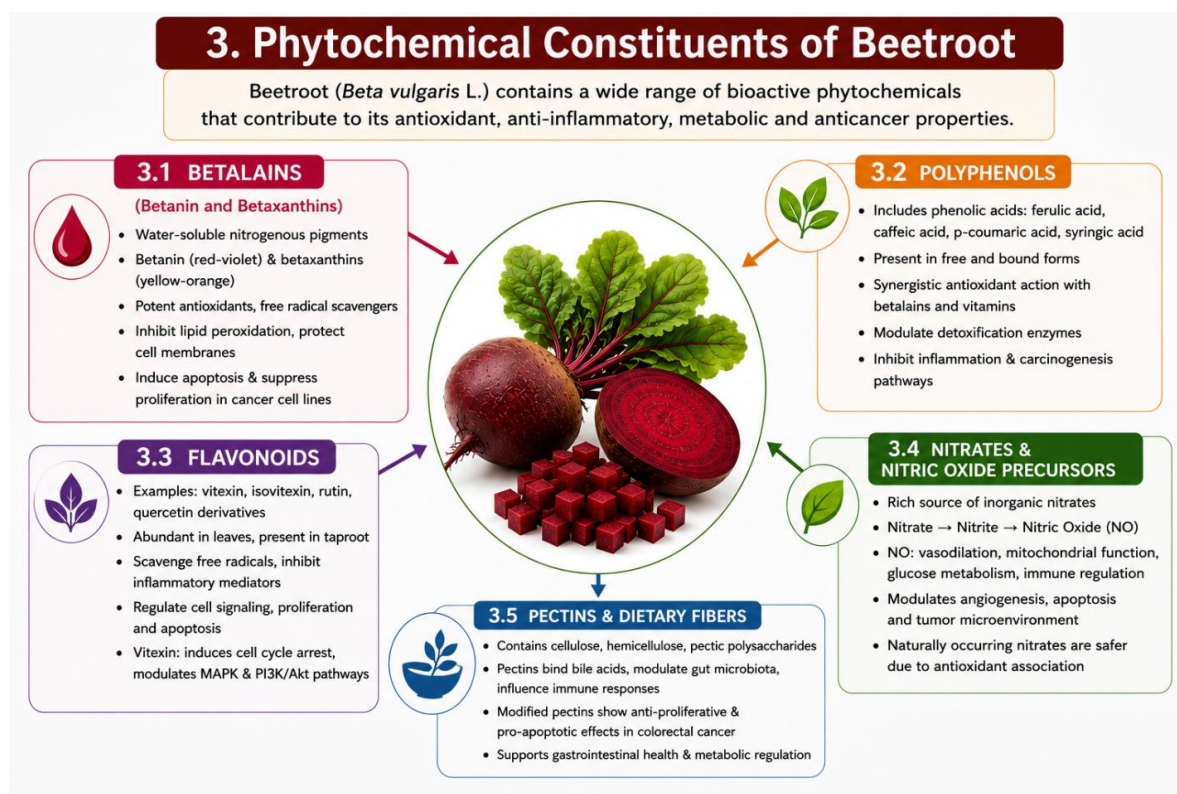


Figure 1: Beetroot phytochemicals.

BIOLOGICAL ACTIVITIES OF BEETROOT

The biological actions of beetroot (*Beta vulgaris* L.) are mainly due to its rich phytochemical makeup, including betalains, polyphenols, flavonoids, nitrates and related antioxidants. These chemicals operate individually and synergistically to give antioxidant, anti-inflammatory and antibacterial activities, which collectively contribute to beetroot's protective role against oxidative stress related illnesses and chronic diseases.^{1,10,18}

Antioxidant activity

Oxidative stress, an imbalance between production of reactive oxygen species (ROS) and antioxidant defence systems, is a key factor in ageing, inflammation, carcinogenesis and metabolic diseases. Beetroot has proven a high antioxidant activity in several experimental scenarios, being a powerful source of dietary antioxidants.^{16,19,55}

Scavenging of free radicals

Beetroot demonstrates potent free radical scavenging ability against a wide array of ROS including superoxide anions, hydroxyl radicals and peroxyl radicals. This activity is mainly due to the betalains, particularly betanin, which has strong electron-donating capacity and redox stability.^{16,18,24} In vitro tests, such as DPPH, ABTS and FRAP, have shown consistently the considerable radical scavenging capacity of beetroot extracts and juices.^{12,19,55}

Polyphenols and flavonoids also contribute to this activity by neutralising free radicals and rebuilding oxidised antioxidant molecules, therefore prolonging antioxidant defence.^{21,36}

The synergistic effect of betalains, vitamin C and phenolic compounds leads to a higher antioxidant efficiency than that seen for isolated substances alone.^{19,60} Fermentation and processing procedures are also shown to enhance the antioxidant activity by enhancing the bioavailability of the compounds and the formation of bioactive metabolites.^{44,49,52}

Inhibition of lipid peroxidation

Lipid peroxidation is an important event leading to membrane damage, dysregulated cell signalling and development of chronic illnesses. Lipid peroxidation in biological membranes and lipid rich systems has been shown to be potently inhibited by beetroot bioactives.^{16,24} Betalains stabilise membrane lipids by scavenging lipid peroxyl radicals and chelating pro-oxidant metal ions to inhibit chain reactions of lipid oxidation.^{18,55}

In experimental research, it has been shown that beetroot extracts dramatically decrease levels of malondialdehyde (MDA), a major marker of lipid peroxidation, in both in vitro and in vivo models.^{19,60} This protective effect is particularly relevant in cancer prevention, as oxidative degradation of lipids contributes to genomic instability and tumour growth.³⁶

Anti-inflammatory activity

Oxidative stress is intimately associated with chronic inflammation and is a key factor in the development of cancer, cardiovascular disease, and metabolic disorders. Beetroot shows significant anti-inflammatory effect through the regulation of inflammatory mediators and signalling pathways.^{36,55} Beetroot contains betalains and flavonoids that have been proven to decrease pro-inflammatory cytokines such as tumour necrosis factor- α (TNF- α), interleukin-6 (IL-6), and interleukin-1 β (IL-1 β) and promote anti-inflammatory mediators.³⁶

In addition, beetroot chemicals inhibit the cyclooxygenase (COX) and lipoxygenase (LOX) pathways, decreasing the synthesis of pro-inflammatory prostaglandins and leukotrienes.^{18,55} Dietary nitrates-derived nitric oxide also helps to the management of inflammation through the improvement of endothelial function and modulation of immune cell activity.^{22,24} The synergistic antioxidant and anti-inflammatory properties of beetroot serve to reduce oxidative-inflammatory feedback loops that are crucial to the evolution of chronic disease and maintenance of the tumour microenvironment.⁴⁰

Antimicrobial activity

Beetroot has shown modest but strong antibacterial activity against many pathogenic microorganisms including Gram-positive and Gram-negative bacteria and some fungi.^{21,55} This is due to phenolic acids, flavonoids and betalains, which damage microbial cell membranes, block enzyme systems and interfere with nucleic acid production.^{12,21} Beetroot extracts have been demonstrated to suppress the development of *Escherichia coli*, *Staphylococcus aureus*, *Salmonella* spp. and *Candida* spp., supporting its traditional usage as a medicinal food ingredient and preservative.^{55,60} Fermented beetroot products generally show an increased antibacterial potency due to the synergistic effect of organic acids, bioactive metabolites and probiotic microbes.^{44,49} These qualities suggest a potential application of beetroot in functional meals, food preservation and complementing antibacterial methods.

The antioxidant, anti-inflammatory and antibacterial effects of beetroot are attributed to the synergistic action of its phytochemical ingredients. These biological features provide the mechanistic explanation for the reported protective effects of beetroot in chronic disease prevention and support its classification as a functional food with therapeutic value.^{1,10,18,36,55}

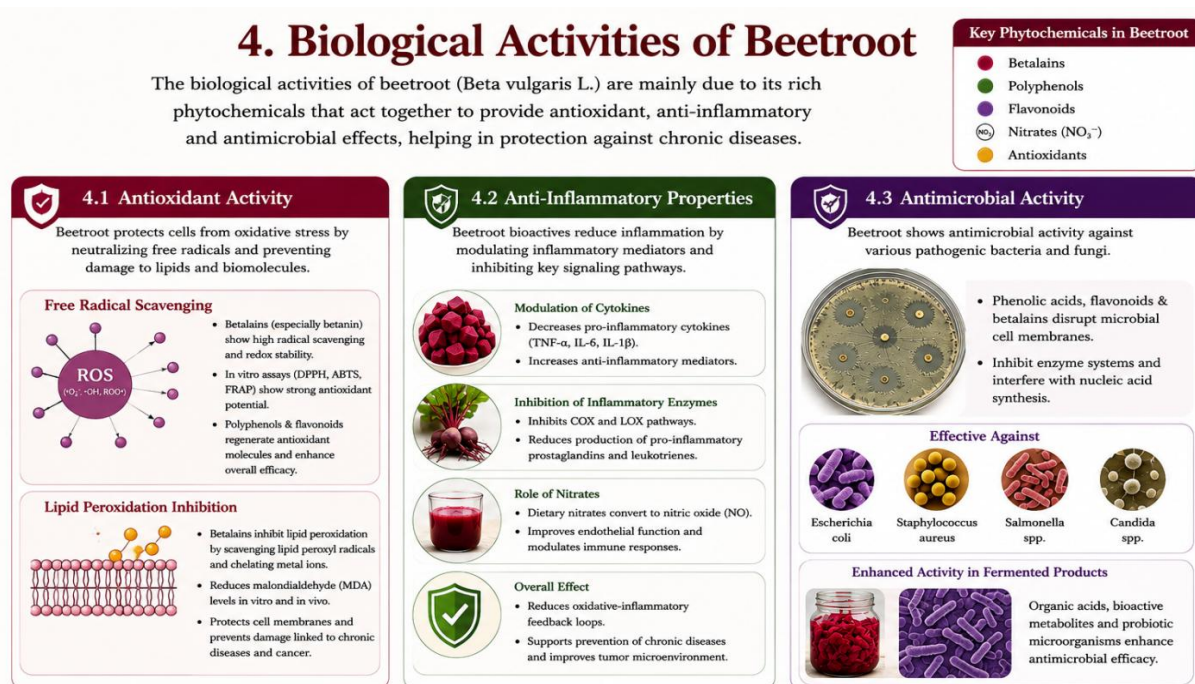


Figure 2: Biological activities of beetroot.

ANTICANCER POTENTIAL OF BEETROOT

Cancer is still one of the leading causes of morbidity and mortality worldwide, which has led to the significant exploration of plant-derived bioactive chemicals as supplemental or supporting treatment agents. Beetroot

(*Beta vulgaris* L.) has been gaining momentum as a prospective anticancer functional food due to its rich phytochemical content including betalains, polyphenols, flavonoids, nitrates and dietary fibres. Accumulating evidence from in vitro, in vivo and synergistic investigations supports its potential significance in cancer prevention and adjuvant therapy.^{1,10,18}

In Vitro data

Current information of the anticancer effect of beetroot is based on in vitro investigations. We have tested extracts, juices, separated pigments and processed formulations in a wide range of human cancer cell lines and they show cytotoxic, antiproliferative and pro-apoptotic effects.

Breast cancer (MCF-7 cells)

Beetroot extracts and purified betalains displayed substantial cytotoxic effect against estrogen-receptor-positive breast cancer cell line MCF-7. Studies have demonstrated a dose-dependent reduction of cell proliferation with associated morphological alterations indicative of apoptosis including chromatin condensation and membrane blebbing.^{28,41} Mechanistically, these effects have been associated with mitochondrial dysfunction, increased production of reactive oxygen species (ROS) in cancer cells and stimulation of intrinsic apoptotic pathways.^{36,40} Importantly, beetroot extracts presented decreased cytotoxicity in normal cells, suggesting selective anticancer action.^{28,35}

Prostate cancer (PC-3)

Beetroot has been utilised extensively to assess its anticancer efficacy on prostate cancer cell lines, especially androgen-independent PC-3 cells. In vitro, beetroot and leaf extracts dramatically reduced proliferation, migration and invasion of PC-3 cells.^{41,56} These effects were linked to regulation of growth-signaling pathways, inhibition of matrix metalloproteinases, and induction of cell-cycle arrest.^{36,56} The antiproliferative effects were associated with the presence of betalains and polyphenols.^{18,55}

Colorectal cancer (HT-29 and HCT-116)

The evidence for anticancer activity of beetroot in colorectal cancer models is robust. Beetroot hydro-alcoholic extracts, betanin and modified beetroot pectins have been reported to exhibit substantial cytotoxicity against HT-29 and HCT-116 cell lines.^{35,45} The effects observed include induction of apoptosis, inhibition of DNA synthesis and suppression of inflammatory mediators involved in colorectal carcinogenesis.^{36,45} Pectic polysaccharides from beetroot were demonstrated to interact with galectin-3, a major regulator of tumour growth, limiting the proliferation of cancer cells.⁴⁵

Liver cancer (HepG2)

Hepatocellular carcinoma cell line HepG2 has been widely utilised to assess anticancer properties of beetroot. The viability of HepG2 cells was strongly inhibited with fermented beetroot juice, betalain-rich extracts and polyphenol fractions in a concentration dependent manner.^{52,60} These effects were connected with an oxidative stress imbalance inside the cancer cells, mitochondrial membrane depolarisation, and activation of

caspase-mediated death.^{36,52} It has been established that fermentation can improve cytotoxic efficacy, likely due to enhanced bioavailability of active metabolites.^{49,52}

In-Vivo studies

Further evidence for the anticancer potential of beetroot is provided by in vivo studies, which have demonstrated tumour inhibition and systemic protective benefits in animal models. Experimental investigations employing chemically produced and transplanted tumour models have shown a reduction of tumour incidence, slowed tumour progression and better antioxidant status due to beetroot or betalain supplementation.³⁶ There was also a decrease in lipid peroxidation, improved activity of endogenous antioxidant enzymes and modification of inflammatory markers with beetroot supplementation showing direct and indirect anticancer benefits.^{16,19,60} Importantly, beetroot-based therapies have shown the favourable safety profiles in animal investigations with no substantial toxicity detected at physiologically relevant doses. These findings increase the translational value of beetroot as a dietary supplement in cancer prevention and supportive therapy.

Synergistic effects with chemotherapy

Beetroot with doxorubicin

One of the most interesting research areas on beetroot is its synergistic interaction with conventional chemotherapy drugs.⁴¹ showed that beetroot extracts increase the cytotoxic effect of doxorubicin on breast, prostate and pancreatic cancer cell lines. Such a synergy enables the possible dose reduction of chemotherapeutic medicines, thus reducing systemic toxicity and retaining anticancer activity.⁴¹ The combined treatment was found to be more effective in enhancing apoptosis and disrupting redox equilibrium in cancer cells than either drug alone.

Formulations based on nanoparticles

Recent advances in nanotechnology have resulted in the production of beetroot mediated metallic nanoparticles such as silver, zinc oxide and copper oxide nanoparticles with increased anticancer action.^{59,60} These nano-formulations enhance cellular absorption, target specificity and sustained release of bioactive substances. In vitro studies have reported higher cytotoxicity against breast, liver, and colorectal cancer cells due to increased ROS production and mitochondrial damage.⁵⁹

Fermented beetroot juice

Fermentation is a viable approach to boost the anti-cancer efficacy of beetroot. Lactic acid bacteria fermented beetroot juice showed better cytotoxic action against liver and colorectal cancer cell lines compared to unfermented juice.^{49,52} Fermentation causes the rise in the content and bioavailability of phenolics, organic acids and betalain derivatives, as well as probiotic-mediated

immunomodulatory effects.^{44,49} The results of this study suggest that fermented beetroot products may be regarded as new functional foods with potential for use in cancer supportive therapy. There is a lot of in vitro and in vivo research showing that beetroot has a great anticancer

potential against many types of cancer. Its capacity to synergise with chemotherapeutic drugs and sophisticated delivery technologies makes beetroot a scientifically supported functional food and a prospective adjuvant in integrative cancer management.^{1,18,36,41,49,55}

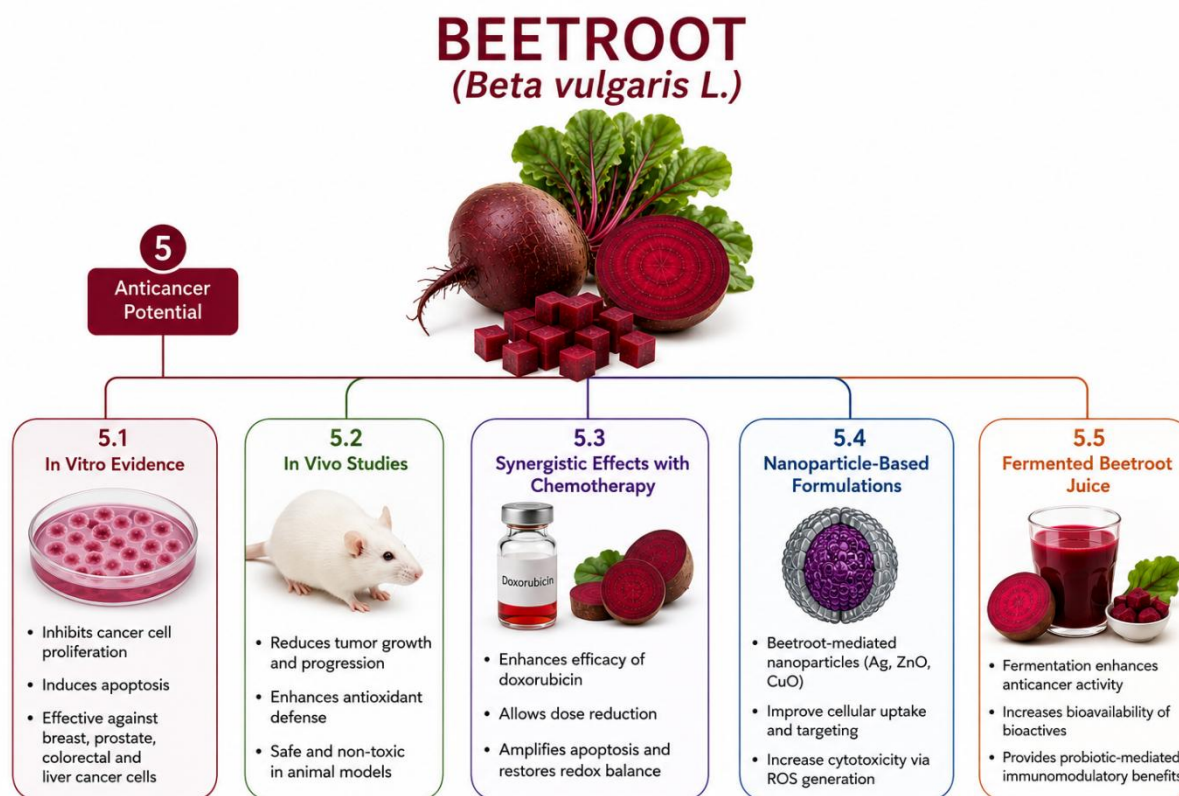


Figure 3: Anticancer potential of beetroot.

MECHANISMS OF ACTION

The anticancer and chemopreventive properties of beetroot (*Beta vulgaris* L.) is mediated by numerous interrelated molecular processes. Beetroot bioactive chemicals (betalains, polyphenols, flavonoids, nitrates and dietary fibres) influence the main cellular processes involved in the start, progression and metastasis of cancer, and not through a single pathway. The mechanisms involved are oxidative stress regulation, activation of programmed cell death, inhibition of uncontrolled proliferation, angiogenesis suppression, autophagy modulation and regulation of immune system.^{18,36,40}

Modulation of reactive oxygen species (ROS)

Oxidative stress is a double-edged sword in cancer biology; low levels of ROS encourage tumour proliferation, yet high ROS levels may induce cancer cell death. The redox-modulating characteristics of beetroot chemicals allow for selective targeting of cancer cells.^{16,19}

Furthermore, betalains, especially betanin, are highly effective antioxidants, eliminating reactive oxygen and

nitrogen species, chelating pro-oxidant metal ions, and stabilising cellular membranes.^{18,24} Beetroot extracts can paradoxically raise intracellular ROS beyond tolerable limits in cancer cells, resulting in mitochondrial malfunction and apoptosis, while shielding normal cells from oxidative damage.^{36,52} This selective regulation of ROS is a crucial mechanism for the specificity of beetroot towards cancer.⁴⁰

Induction of apoptosis

Induction of apoptosis is one of the most commonly documented mechanisms of beetroot mediated anticancer action. In vitro investigations have shown that beetroot extracts and purified betalains induce the intrinsic (mitochondrial) mechanism of apoptosis in cancer cells.^{28,35}

This process includes reduction of mitochondrial membrane potential, cytochrome c release, caspase-9 and caspase-3 activation, increase of pro-apoptotic proteins (Bax) and decrease of anti-apoptotic proteins (Bcl-2).

These processes lead to DNA fragmentation and programmed cell death in breast, prostate, colorectal and liver cancer cell lines.^{36,40,52} The capacity of beetroot chemicals to recover the apoptosis, which is frequently dysregulated in cancer, increases their chemopreventive pertinence.⁴¹

Cell cycle inhibition

Cancer is the result of cells dividing without control. Bioactives included in beetroot have been demonstrated to interfere with the advancement of cell cycle by inducing arrest at various checkpoints, notably during G0/G1 and G2/M phases.^{36,56} Mechanistically, beetroot chemicals downregulate cyclins (cyclin D1, cyclin B1) and cyclin-dependent kinases (CDKs), but upregulate CDK inhibitors such as p21 and p27.³⁶ This cell cycle arrest restricts DNA replication and mitosis and so inhibits the development of tumour cells.^{28,56} Cell cycle arrest has been reported in colon, prostate and breast cancer models treated with beetroot extracts and derivatives.^{35,45}

Inhibition of angiogenesis

Angiogenesis, the development of new blood vessels, is critical for tumour growth and metastasis. Angiogenic signalling has been shown to be inhibited by beetroot chemicals, which block the expression of vascular endothelial growth factor (VEGF) and downstream pathways.³⁶ Betalains and polyphenols disrupt the hypoxia inducible factor-1 α signalling (HIF-1 α), hence decreasing endothelial cell proliferation and migration.⁴⁰ Furthermore, nitric oxide modulation by beetroot nitrates may normalise tumour vasculature, therefore restricting aberrant angiogenesis and enhancing tissue oxygenation.^{22,24} This anti-angiogenic activity contributes to in vivo inhibition of tumour growth.

Autophagy regulation

Autophagy is a complex cellular process that can either enhance cancer cell survival or induce cell death depending on the circumstances. Recent evidence suggests that beetroot bioactives could influence autophagic pathways, tilting the balance towards autophagy-mediated cancer cell death.^{36,54} Studies show that treatment with beetroot results in altered expression of autophagy-related proteins, including LC3, Beclin-1 and p62, indicative of the initiation of autophagic flux in cancer cells.⁴⁰ This process generally functions in tandem with apoptosis, enhancing cytotoxic consequences and overcoming resistance pathways.

Immune system modulation

Immune dysregulation is involved in every step of cancer progression. Beetroot helps to immunological regulation through boosting antioxidant defence, lowering chronic inflammation, and modulating immune cell function.^{36,55} Dietary nitrates and polyphenols from beets have been

demonstrated to enhance the function of endothelium and immunological cells while betalains decrease pro-inflammatory cytokines such as TNF- α , IL-6 and IL-1 β .³⁶ Such effects may improve antitumor immune surveillance and decrease immunosuppressive tumour microenvironment. Probiotic mediated actions of fermented beetroot products enhance immunological regulation.^{44,49}

Beetroot executes anticancer effects through a multitargeted mechanistic framework including redox regulation, programmed cell death, proliferation control, angiogenesis suppression, autophagy modulation and immune regulation. This molecular variety increases its translational significance and puts beetroot as a scientifically validated functional food with a high potential to be used in cancer prevention and adjuvant therapy strategies.^{18,36,40}

FERMENTATION, PROCESSING AND BIOAVAILABILITY

Processing methods affect stability, bioaccessibility and intestinal absorption, which largely influence the therapeutic efficacy of beetroot (*Beta vulgaris* L.) bioactives. Fermentation, probiotic enrichment and advanced delivery systems such as nanoliposomal encapsulation have appeared as efficient strategies to increase bioavailability and functional performance of compounds derived from beetroot, especially betalains and phenolics.^{44,49,52}

Fermented beetroot Juice

Fermentation is a traditional bioprocess that enhances the nutritional content and biological activity of plant-based foods by microbial metabolism. Fermented beetroot juice, generally produced by lactic acid bacteria (LAB), has been found to possess more antioxidant and anticancer activity compared to unfermented juice.^{49,52} The bioaccessibility of active ingredients is enhanced by the fermentation mediated by LAB, which enhances the release of bound phenolic compounds, organic acids, and the partial degradation of complex carbohydrates.^{44,49} In vitro studies reveal that fermented beetroot juice exhibits more potent cytotoxic effects on liver (HepG2) and colorectal cancer cell lines, along with increased intracellular oxidative stress and greater activation of apoptosis in cancer cells.⁵² Moreover, fermentation enhances sensory properties and shelf-life, therefore allowing its use in functional beverages and nutraceutical compositions.^{5,26,42,44,60}

Probiotic fortification

Probiotic augmentation is a synergistic strategy in which beetroot is used as a substrate and carrier for helpful microbes. Probiotics can be stimulated by the natural carbohydrate content of beets and the fermentation-derived metabolites may contribute to modulate the gut

microbiota.^{44,49} Probiotic supplemented beetroot products have been reported to promote the intestinal barrier function, reduce inflammation and boost immunological responses all of which indirectly influence the cancer prevention and metabolic health.⁴⁹

Moreover, probiotics can also assist in the biotransformation of polyphenols and betalains into smaller, more bioavailable metabolites, thus enhancing their systemic bioavailability and biological activity.^{44,52} This dual effect, i.e. nutrient delivery and microbiota modification, makes probiotic beetroot compositions intriguing candidates for integrative health applications.

Nanoliposomal formulations

Betalains and polyphenols are known to have high bioactivity, but their stability and bioavailability are limited due to breakdown during digestion and fast metabolism. Nanoliposomal encapsulation has evolved as an improved delivery technique to circumvent these constraints.⁵⁹ Nanoliposomal beetroot compositions encapsulate hydrophilic and lipophilic chemicals in phospholipid bilayers, thus preserving them from stomach degradation and allowing controlled release at target areas.

In cancer cell models, studies demonstrate improved cellular absorption, extended circulation time and higher anticancer activity of nanoliposomal beetroot pigments.⁵⁹ Moreover, nanocarriers facilitate targeted delivery and minimise off-target toxicity, lending support to their potential application in adjunct cancer therapy and functional food innovation.

Stability of the betalains

Betalains are very sensitive to environmental conditions, such as pH, temperature, light and oxygen exposure. Pigment degradation and loss of bioactivity can occur due to thermal processing, long-term storage and unfavourable pH conditions.^{18,24,55} Processing techniques, such as low-temperature treatment, fermentation, encapsulation and the application of antioxidant co-factors, have been demonstrated to greatly improve betalain stability.^{44,49,59} Fermentation reduces pH and oxidative conditions, which helps to preserve the structure of betalains. The use of nanoliposomal encapsulation provides a physical barrier to degradation.^{18,59} Stability of betalains is important to maintain consistent functional performance and therapeutic efficacy of beetroot-based products.⁵⁵ fermentation, microbial incorporation and nanotechnology-based delivery technologies improve bioavailability, stability and therapeutic potential of beetroot bioactives substantially. These processing solutions overcome key constraints associated with ordinary beetroot intake and facilitate the creation of next-generation functional foods and nutraceuticals with enhanced health outcomes.^{44,49,52,59}

CLINICAL AND NUTRACEUTICAL USES

There is increasing experimental and translational evidence that beetroot (*Beta vulgaris L.*) is a flexible ingredient in clinical nutrition and nutraceutical development. The rich composition of betalains, nitrates, polyphenols, flavonoids, and dietary fibres in beetroot has led to its inclusion in functional foods, sports nutrition products, interventions for cardiovascular health, and supportive strategies in oncology.^{1,10,18}

Functional food

Beetroot has been extensively used in the development of functional meals with the purpose of providing health advantages beyond basic nutrition. The antioxidant content and the nutritional profile of products including beetroot juice, fermented drinks, powders, fortified snacks, yoghurts and bread goods have been improved.^{44,49,55} Beetroot is also a clean label food colouring as the natural pigmentation produced by betalains can replace synthetic additives and provide biological activity.^{5,18,26,55} Beetroot-based functional foods have been found to improve oxidative status and to reduce inflammatory markers and to support gastrointestinal health via dietary fibre and prebiotic actions.^{21,60} Fermented and probiotic-enriched beetroot products further increase the functional value by modifying gut microbiota and increasing the absorption of phenolic chemicals.^{44,49} These features encourage beetroot's incorporation into everyday meals as a preventive nutritional strategy against chronic illnesses.

Sports dietetics

One of the more documented clinical applications of beetroot is in sports nutrition and exercise physiology. Nitrate-rich beetroot improves endogenous synthesis of nitric oxide, providing better vasodilation, oxygen delivery and mitochondrial efficiency.^{22,24} Clinical and performance-based studies showed that beetroot supplementation improves endurance, decreases oxygen expenditure during exercise and promotes overall athletic performance.^{26,60} Beetroot juice and concentrates are commonly promoted to athletes and physically active individuals as ergogenic aids. Besides performance enhancement, beetroot antioxidant and anti-inflammatory qualities can aid to reduce exercise-induced oxidative stress and muscle damage, facilitating recovery and long-term training adaption.^{19,60} These benefits make beetroot a scientifically supported nutraceutical for elite sports and overall fitness.²⁶

Cardiac health

Cardiovascular disease continues to be a major health problem worldwide and beetroot is shown to possess great promise in cardiovascular health management. It has been shown in clinical trials that regular intake of beetroot juice or products rich in nitrate reduces systolic and diastolic

blood pressure, improves endothelial function and increases arterial compliance.^{22,24,60}

Nitric oxide-mediated vasodilation is crucial to these benefits while concomitant antioxidant activity protects vascular tissues from oxidative damage and inflammation.^{16,19} Moreover, the dietary fibre and polyphenols of beetroot are involved in the control of the lipid profile and metabolic balance.^{21,55} These combined results justify the use of beetroot-based nutraceuticals as supplemental dietary therapies in hypertension and cardiovascular risk reduction.²⁴

Cancer supportive treatment

Beetroot has also acquired popularity as a helpful dietary supplement in cancer treatment besides prevention. Preclinical evidence suggests that beetroot bioactives may improve tolerance to chemotherapy, decrease oxidative stress, and modify inflammatory responses associated with cancer progression and treatment-related toxicity.^{36,41} Beetroot extracts in combination with chemotherapeutic drugs, such as doxorubicin, have shown synergistic effects with increased cytotoxic activity against cancer cells and this may allow for reduced doses and side effects.⁴¹ Fermented beetroot products and nanoliposomal formulations further improve absorption and therapeutic targeting and reinforce their significance as adjuncts in integrative oncology.^{42,52,49} Despite few data from large-scale clinical studies, the growing body of mechanistic and translational evidence make a compelling case for the inclusion of beetroot in dietary approaches to improve quality of life, immunological function and metabolic resilience in cancer patients.³⁶ Beetroot-based therapies are well tolerated which is important for long-term supportive use. Beetroot is a multifunctional nutraceutical with recognised applications in functional meals, sports nutrition, cardiovascular health and cancer supportive therapy. This, together with mechanistic and translational findings, encourages wider clinical use and further exploration in human intervention trials.^{1,5,18,24,26,36,60}

SAFETY, TOXICITY AND LIMITATIONS

The evidence of the functional and therapeutic potential of beetroot (*Beta vulgaris L.*) is increasing, but its application in clinical and nutraceutical practice should be treated with caution due to safety issues, uncertainty about the dosage, and the limitations of the current research.

Concerns about nitrate

Beetroot is among the richest dietary sources of inorganic nitrates, which are of importance for its cardiovascular and performance-enhancing effects through nitric oxide generation.^{22,24} The consumption of nitrates from vegetables in the diet is generally considered safe, although there are some concerns regarding high intake and the development of N-nitroso compounds that have been related with carcinogenicity in the past.²²

Importantly, the nitrates from beetroot are eaten in a complex matrix of antioxidants rich in vitamin C, polyphenols and betalains that limit the development of nitrosamines and attenuate the related dangers.^{16,24}

Current research suggests that dietary and supplementary nitrate consumption from beetroot in healthy populations do not offer major health hazards.^{22,24,60} But other populations, such as those with poor kidney function, babies, or those taking several nitrate supplements at the same time, may require a bit of caution. Standardised intake guidelines are still needed as long as the long-term safety evidence for high-dose beetroot supplements are lacking.⁵⁹

Gaps in dosage and problems of standardisation

One of the important constraints in beetroot research is the absence of standardised dosing procedures. The great variability in forms (fresh root, juice, extracts, fermented products, isolated betalains, nano-formulations), concentrations and length of treatments in existing research make it difficult to compare them directly and to extrapolate them clinically.^{36,49,52} In anticancer trials, the effective doses in vitro are generally greater than the physiologically attainable values via dietary consumption alone.^{28,35,45} Also, whilst tumour suppressive effects are observed in animal research, there is no sufficient dose equivalency for human application. The reproducibility and translational relevance of present findings are constrained by the absence of consensus on appropriate dosage, frequency and formulation.

Absence of large-scale clinical trials

There is a lot of pre-clinical data supports beetroot's biological and anti-cancer effects, however there are very few large scale, randomised controlled clinical trials. Most human investigations to date have been concerned with cardiovascular performance, blood pressure regulation and exercise physiology with insufficient exploration of cancer associated outcomes.^{22,24,60}

In oncology, evidence is mostly built on in vitro and in vivo models, mechanistic and supportive studies of possible benefit in oxidative stress reduction and treatment tolerance.^{36,41} However, robust clinical trials examining efficacy, safety, pharmacokinetics and long-term outcomes are urgently needed before beetroot-based therapies may be suggested as evidence-based therapeutic adjuncts in cancer patients,

General limitations and research gaps

Additional constraints are the differences in beetroot cultivar, growing circumstances, processing methods, and storage, which all have a substantial impact on the phytochemical content and biological activity.^{10,55} Furthermore, the interaction of beetroot bioactives with pharmaceuticals has been little investigated, particularly in

the context of polypharmacy such as in oncology. Future study should focus on standardised extract characterisation, dose–response assessment, long-term toxicity and well-designed clinical studies. Addressing these gaps will be important to position beetroot as a safe, effective, and evidence-based component of functional nutrition and integrative health initiatives.^{56,57} While beetroot is largely accepted as a safe dietary component or functional food, its clinical translation is currently hindered by concerns around nitrate consumption, dose standardisation, and the lack of large-scale clinical validation. With thorough human trials and standardised formulations, these issues will be key to responsible development of beetroot-based nutraceuticals and supportive therapies.^{22,36,60}

FUTURE PERSPECTIVES AND RESEARCH GAPS

Although there has been progress in understanding the functional and anticancer characteristics of beetroot (*Beta vulgaris* L.), important knowledge gaps still need to be addressed for successful clinical translation and wider nutraceutical use.

Necessity of clinical validation

A key future priority is the creation of good quality clinical evidence. While preclinical research consistently show antioxidant, anti-inflammatory and anticancer benefits of beetroot bioactives, human data, especially in oncology, are scarce and varied.^{36,41} So far, most clinical trials have focused on cardiovascular and exercise outcomes rather than disease-modifying endpoints.^{22,24,60} Well-designed, randomised, placebo-controlled trials are needed to examine efficacy, safety, dose–response relationships and long-term effects of beetroot-based therapies in varied groups including patients undergoing cancer therapy. Such studies should contain validated indicators (oxidative stress, inflammation, angiogenesis) to enhance causal inference and translational relevance.

Standardization of extracts and formulations

Another major difficulty is the lack of standardisation of beetroot preparations. The phytochemical profiles and biological activity are highly variable and greatly influenced by cultivar, agronomic circumstances, maturity of harvest, processing (juicing, fermentation, drying) and storage.^{10,55} Future study should prioritise standardised extraction techniques, chemical fingerprinting (e.g., measurement of betalains and polyphenols) and stability testing to ensure repeatability across studies.^{18,55} Reference materials and reporting requirements will be important to enable comparisons of outcomes and to facilitate regulatory acceptance of beetroot-based nutraceuticals.

Molecular mechanistic studies

Several modes of action have been hypothesised but need to be further validated at the molecular level. Several

studies utilise phenotypic endpoints (cell viability, apoptotic markers) without full pathway-level confirmation.^{36,40} Future studies should utilise omics approaches (transcriptomics, proteomics, metabolomics) and advanced imaging to identify specific targets of beetroot bioactives, their interactions with signalling networks (e.g., PI3K/Akt, MAPK, NF-κB, HIF-1α), and their effects on the tumour microenvironment.³⁶ Such mechanistic clarity will boost credibility, promote sensible combination methods and encourage IP creation.

Precision medicine and personalised nutrition

Emerging approaches in personalised nutrition are promising for beetroot study.⁴⁹ Inter-individual variability in nitrate metabolism, gut microbiota composition, genetic polymorphisms and illness status can dramatically alter the response to beetroot supplementation. Future research should include monitoring of the microbiome, nutrigenomics, and metabolite tracking to identify responder characteristics and personalise beetroot-derived therapies.^{44,49} Personalised techniques may be especially significant in supportive care in cancer because the tolerance to treatment and metabolic resilience differ greatly between patients. Translating beetroot research from bench to bedside will require concerted efforts focused on rigorous clinical validation, standardised formulations, mechanistic depth and personalised dietary frameworks. Addressing these research gaps will contribute to both increase the evidence foundation and to unlock the full translational potential of beetroot as a scientifically based functional food and nutraceutical agent.^{36,55}

CONCLUSION

This review provides a holistic and detailed synthesis of the existing scientific evidence on beetroot (*Beta vulgaris* L.) with respect to its botanical background, nutritional composition, phytochemical diversity, biological activities, anticancer potential, mechanistic pathways, processing technologies, and clinical and nutraceutical applications. The overall results clearly indicate that beetroot is not only a traditional dietary vegetable but also a complex functional matrix that contains biologically active constituents like betalains, polyphenols, flavonoids, nitrates, and dietary fibres acting in a coordinated and synergistic manner. The amount of experimental and translational research summarised above confirms the therapeutic value of beetroot throughout different physiological systems. Its antioxidant and anti-inflammatory qualities are the basis of protective benefits against illnesses connected to oxidative stress. Its nitrate-mediated nitric oxide pathway is the basis of cardiovascular function and metabolic efficiency.

Importantly, a large body of preclinical research suggests the anticancer potential of beetroot through pathways including oxidative stress modulation, apoptosis induction, proliferation of unregulated cell proliferation,

angiogenesis inhibition, autophagy regulation and immunological modulation. These multifarious actions, in combination with the established synergistic benefits with conventional medicines and innovative delivery modalities, underline the relevance of beetroot as a supportive agent in integrative health and disease management.

Overall, the present evidence positions beetroot as a scientifically validated, evidence-based functional food with substantial promise in preventive nutrition, therapeutic support and nutraceutical research. Despite the need for more clinical validation and standardisation, the current knowledge base strongly supports the responsible inclusion of beetroot in modern dietary strategies to promote health, improve physiological resilience and complement conventional therapeutic approaches.

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