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## Nanotechnology as a tool to enhance the pharmacological potential of phytochemicals derived from horticultural crops

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### Abstract

Horticultural crops, encompassing fruits, vegetables, spices, plantation and ornamental plants, are abundant sources of bioactive phytochemicals such as phenolics, flavonoids, alkaloids, terpenoids, carotenoids, saponins, glycosides and sulfur-containing compounds. These phytochemicals exhibit diverse pharmacological properties, including antioxidant, anti-inflammatory, antimicrobial, antiviral, anticancer, antidiabetic, cardioprotective and neuroprotective activities and are strongly associated with reduced risk of chronic and lifestyle-related diseases. Despite their promising therapeutic potential, the practical application of horticultural crop phytochemicals is limited by several challenges, including poor aqueous solubility, low gastrointestinal absorption, rapid metabolism and clearance, chemical instability, dose-related toxicity and limited target specificity. Nanotechnology has emerged as an effective strategy to overcome these limitations and enhance phytochemical pharmacology. Nanoencapsulation and nano-delivery systems improve solubility, stability, bioavailability and pharmacokinetic behavior of phytochemicals, while enabling controlled, sustained and targeted delivery. A wide range of nanocarriers, including lipid-based and polymeric nanoparticles, metallic and metal oxide nanoparticles, nanoemulsions, nanogels, solid lipid nanoparticles and nanostructured lipid carriers, have demonstrated improved therapeutic efficacy and safety profiles for phytochemical-based formulations. The development of green and phytoengineered nanotechnology further strengthens this approach by utilizing horticultural crop extracts for eco-friendly nanoparticle synthesis. Plant-mediated fabrication reduces the use of toxic chemicals and energy-intensive processes while enhancing biocompatibility and therapeutic synergy through phytochemical-mediated reduction and stabilization. At the cellular and molecular levels, nano-phytochemical systems exhibit enhanced cellular uptake, efficient intracellular trafficking, improved interaction with biomolecules and receptors and modulation of key signaling pathways and gene expression, leading to superior pharmacological outcomes at lower doses. Overall, the integration of nanotechnology with horticultural crop phytochemicals offers a transformative pathway for developing sustainable, effective and evidence-based plant-derived therapeutics, with expanding applications in pharmaceutical, nutraceutical, functional food and cosmeceutical industries.

### 1. Introduction

Horticultural crops, encompassing fruits, vegetables, spices, plantation crops and ornamental plants, represent one of the most valuable biological resources for human nutrition, health promotion and disease prevention. Beyond their traditional role as sources of vitamins, minerals, dietary fiber and essential nutrients, horticultural crops are increasingly recognized for their richness in diverse phytochemicals that exert significant biological and pharmacological activities. These phytochemicals, which include phenolic acids, flavonoids, carotenoids, alkaloids, terpenoids, glucosinolates, saponins and sulfur-containing compounds, are secondary metabolites

synthesized by plants as part of their defense mechanisms and adaptive strategies. Over the past few decades, extensive scientific evidence has demonstrated that such bioactive compounds contribute substantially to antioxidant, anti-inflammatory, antimicrobial, anticancer, antidiabetic, cardioprotective, neuroprotective and immunomodulatory effects, thereby playing a crucial role in reducing the risk of chronic and lifestyle-related diseases. The increasing global interest in plant-derived therapeutics, functional foods and nutraceuticals has further intensified research on horticultural crop phytochemicals as safer and more sustainable alternatives to synthetic drugs.

Despite the immense pharmacological promise of phytochemicals derived from horticultural crops, their practical application in therapeutic systems remains limited by several inherent physicochemical and biological constraints. Many phytochemicals exhibit poor aqueous solubility, low stability under physiological and processing conditions, limited permeability across biological membranes, rapid metabolism and low oral bioavailability. These

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limitations significantly reduce their therapeutic efficacy and hinder their translation from laboratory research to clinical and commercial applications. For instance, phenolic compounds and flavonoids, though potent antioxidants and anti-inflammatory agents, often undergo rapid degradation in the gastrointestinal tract or first-pass metabolism in the liver, resulting in minimal systemic availability. Similarly, carotenoids and other lipophilic compounds show poor absorption due to their hydrophobic nature. Such challenges necessitate higher dosages to achieve desired pharmacological effects, which may increase the risk of toxicity or adverse interactions. Consequently, overcoming these delivery and bioavailability barriers has emerged as a critical research priority in phytochemical-based pharmacology (Khan *et al.*, 2022). In this context, nanotechnology has emerged as a transformative and enabling platform capable of addressing many of the limitations associated with conventional phytochemical utilization. Nanotechnology involves the design, characterization, production and application of materials at the nanoscale, typically ranging from 1 to 100 nanometers, where unique physicochemical properties such as increased surface area, enhanced reactivity, tunable surface chemistry and improved biological interactions become evident. When applied to phytochemicals, nanotechnology offers innovative strategies for nanoencapsulation, targeted delivery, controlled release and protection of bioactive compounds from degradation. Nanoformulation of phytochemicals can significantly enhance their solubility, stability, absorption and pharmacokinetic behavior, thereby improve their therapeutic potential while reduce required dosages and side effects. The convergence of nanotechnology with plant-based bioactives has thus given rise to the rapidly expanding field of nano-phytopharmacology.

Horticultural crops occupy a unique and strategic position in this nano-enabled paradigm due to their abundant and diverse phytochemical profiles. Fruits such as berries, citrus, grapes and apples; vegetables including tomato, onion, garlic, crucifers and leafy greens; spices like turmeric, ginger, pepper and cinnamon; and plantation crops such as tea, coffee and cocoa are rich sources of bioactive molecules with proven pharmacological relevance. Integrating nanotechnology with these phytochemicals not only enhances their medicinal value but also adds economic and functional value to horticultural produce. Moreover, the use of edible plant-derived compounds in nanoformulations aligns well with the growing consumer preference for natural, plant-based and minimally processed health products. This synergy supports the development of next-generation nutraceuticals, functional foods and plant-based therapeutic systems that are both effective and sustainable. Nanotechnology-based delivery systems employed for phytochemicals derived from horticultural crops include polymeric nanoparticles, lipid-based nanoparticles, nanoemulsions, nanogels, solid lipid nanoparticles, nanostructured lipid carriers and metallic or metal oxide nanoparticles. These nanocarriers can be engineered to encapsulate single or multiple phytochemicals, protect them from environmental and enzymatic degradation and facilitate their targeted delivery to specific tissues or cells. Controlled and sustained release mechanisms further enhance therapeutic efficacy by maintaining optimal bioactive concentrations over extended periods. Importantly, nanocarriers can be functionalized with ligands or surface modifiers to improve cellular uptake and site-specific action, which is particularly relevant in the treatment of cancer, inflammatory disorders and metabolic diseases. Such advancements mark a significant departure from conventional phytochemical administration

methods and open new avenues for precision phytotherapy (Rani *et al.*, 2023). An additional and increasingly important dimension of this field is the integration of green and phytoengineered nanotechnology approaches. In contrast to conventional chemical and physical nanoparticle synthesis methods, green nanotechnology employs plant extracts, including those from horticultural crops, as reducing, stabilizing and capping agents for nanoparticle synthesis. This approach not only reduces environmental toxicity and energy consumption but also enhances biocompatibility and therapeutic synergy. Phytochemicals present in horticultural crop extracts play a dual role by participating in nanoparticle formation while simultaneously contributing to biological activity. Such phytoengineered nanoparticles exhibit improved pharmacological performance due to the combined effects of nanostructures and plant-derived bioactives. This eco-friendly strategy aligns with global sustainability goals and supports the development of safer nanomedicine platforms.

While the potential benefits of nano-enabled phytochemicals are substantial, their application also raises important concerns related to biosafety, toxicity and regulatory compliance. Nanoparticles possess unique biological interactions that differ from their bulk counterparts and their long-term effects on human health and the environment remain incompletely understood. Issues such as nanoparticle accumulation, oxidative stress induction, immune responses and unintended ecological impacts require careful evaluation. For phytochemical-based nanoformulations, additional challenges include standardization of plant extracts, reproducibility of nanoformulation processes and variability in phytochemical composition due to genetic, environmental and agronomic factors. Addressing these concerns through rigorous toxicological assessment, standardized protocols and robust regulatory frameworks is essential for the responsible advancement of nanotechnology in phytochemical pharmacology.

From a translational perspective, nanotechnology-enhanced phytochemicals derived from horticultural crops hold immense promise for pharmaceutical, nutraceutical and cosmeceutical industries. Nanoformulated plant bioactive can be incorporated into oral, topical, transdermal and injectable formulations with improved efficacy and consumer acceptability. In the nutraceutical and functional food sectors, nanoencapsulation can protect sensitive phytochemicals during processing and storage, thereby extending shelf life and maintaining bioactivity. Furthermore, the integration of nanotechnology with traditional knowledge systems and modern pharmacology provides a powerful framework for evidence-based validation of plant-derived therapeutics. This convergence is particularly relevant in regions where horticultural crops and herbal medicines form the backbone of primary healthcare systems. In recent years, advances in molecular biology, omics technologies and computational modeling have further strengthened the scientific foundation of nano-phytochemical research. Studies investigating cellular uptake mechanisms, intracellular trafficking, signaling pathway modulation and gene expression changes induced by nanoformulated phytochemicals are providing deeper insights into their modes of action. Such mechanistic understanding is critical for optimizing nanoformulation design and ensuring targeted therapeutic outcomes. Additionally, the integration of artificial intelligence and machine learning in nanotechnology research is expected to accelerate the identification of optimal nanocarrier systems and predict

biological responses, thereby reducing trial-and-error approaches. Given the rapid expansion of research in this interdisciplinary domain, there is a pressing need for comprehensive and critical reviews that synthesize current knowledge, identify key challenges and highlight future research directions. While numerous studies have independently explored phytochemicals, pharmacology and nanotechnology, integrated analyses focusing specifically on horticultural crop-derived phytochemicals remain limited (Talebi *et al.*, 2025). A holistic evaluation of how nanotechnology can enhance the pharmacological potential of these bioactive is essential for bridging existing knowledge gaps and guiding future innovation. Such reviews are particularly valuable for researchers, clinicians, industry stakeholders and policymakers seeking to harness the full potential of horticultural crops for health and therapeutic applications.

In this context, the present review aims to critically examine the role of nanotechnology as a tool to enhance the pharmacological potential of phytochemicals derived from horticultural crops. It focuses on the diversity of horticultural phytochemicals, their established pharmacological activities, the limitations associated with their conventional use and the innovative nanotechnological strategies employed to overcome these challenges. Emphasis is placed on nanoformulation approaches, green nanotechnology, mechanistic insights, biosafety considerations and translational prospects. By providing an integrated and up-to-date synthesis of current research, this review seeks to contribute to the rational development of nano-enabled phytochemical therapeutics and support the advancement of sustainable, plant-based healthcare solutions.

## 2. Phytochemicals in horticultural crops

Horticultural crops are among the richest natural reservoirs of phytochemicals, a diverse group of plant-derived secondary metabolites that play crucial roles in plant growth, defense, adaptation and interaction with the environment. Unlike primary metabolites, which are directly involved in growth and development, phytochemicals are synthesized primarily for protective and regulatory functions, enabling plants to withstand biotic and abiotic stresses. From a human health perspective, these compounds have attracted considerable scientific interest due to their wide-ranging pharmacological activities. Fruits, vegetables, spices, plantation crops and ornamental plants collectively contribute an enormous diversity of phytochemicals, many of which have been linked to disease prevention and therapeutic effects. The concentration, composition and bioactivity of phytochemicals in horticultural crops vary significantly depending on genetic makeup, plant part, maturity stage, cultivation practices, environmental conditions and postharvest handling. Understanding the major classes of phytochemicals and their distribution across horticultural crop groups is fundamental to exploiting their pharmacological potential and developing nano-enabled delivery strategies.

### 2.1 Major classes of phytochemicals

Among the various classes of phytochemicals present in horticultural crops, phenolics and polyphenols constitute one of the most abundant and extensively studied groups. These compounds are characterized by one or more hydroxyl groups attached to aromatic rings and are synthesized primarily through the shikimate and phenylpropanoid pathways. Phenolics play a vital role in plant defense against pathogens, ultraviolet radiation and oxidative stress,

while also contributing to color, flavor and astringency. Simple phenolic acids such as gallic acid, caffeic acid, ferulic acid and chlorogenic acid are widely distributed in fruits and vegetables, whereas complex polyphenols, including tannins and lignans, are abundant in berries, grapes, apples, pomegranates and plantation crops such as tea and coffee. From a pharmacological standpoint, phenolics and polyphenols exhibit strong antioxidant activity due to their ability to donate hydrogen atoms or electrons, neutralize free radicals and chelate metal ions. These properties underpin their reported anti-inflammatory, cardioprotective, anticancer, neuroprotective and antimicrobial effects. Despite their potent bioactivity, many phenolic compounds suffer from limited stability and bioavailability, which restricts their therapeutic application and underscores the need for advanced delivery systems. Flavonoids represent a major subclass of polyphenols and are ubiquitously present in horticultural crops. Structurally, flavonoids are characterized by a common C6-C3-C6 skeleton and are further categorized into flavonols, flavones, flavanones, flavanols, anthocyanins and isoflavones. These compounds are responsible for the vivid pigmentation of many fruits and vegetables, contributing to red, blue, purple and yellow hues. Anthocyanins are particularly abundant in berries, grapes, cherries, plums and purple vegetables, whereas flavonols such as quercetin and kaempferol are commonly found in onions, apples, leafy vegetables and cruciferous crops (Parvin *et al.*, 2025). Citrus fruits are rich sources of flavanones, including hesperidin and naringenin. Flavonoids play multifunctional roles in plants, including UV protection, pollinator attraction and defense against herbivores and pathogens. Pharmacologically, flavonoids are associated with antioxidant, anti-inflammatory, antidiabetic, antihypertensive, anticancer and neuroprotective activities. They modulate key cellular signaling pathways, inhibit pro-inflammatory enzymes, regulate gene expression and influence cell cycle progression. However, their poor water solubility, susceptibility to degradation and rapid metabolism pose significant challenges for effective therapeutic use, making them prime candidates for nanoformulation strategies.

Alkaloids constitute another important class of phytochemicals found in several horticultural crops, particularly in vegetables, spices and certain ornamental plants. Alkaloids are nitrogen-containing compounds with diverse chemical structures and pronounced physiological effects. In plants, they function primarily as defense molecules against herbivores and pathogens due to their bitter taste and potential toxicity. Common alkaloids found in horticultural crops include solanine and chaconine in potatoes, capsaicin in chili peppers, caffeine in coffee and tea and piperine in black pepper. Although, alkaloids are often associated with toxicity, many exhibit significant pharmacological activities at controlled doses. These include analgesic, stimulant, antimicrobial, anticancer and neuroactive effects. Capsaicin, for instance, is widely studied for its analgesic, anti-inflammatory and metabolic regulatory properties, while caffeine exhibits central nervous system stimulation and antioxidant effects. The potent biological activity of alkaloids necessitates precise dose control and targeted delivery, highlighting the relevance of nanotechnology in improving their safety and therapeutic efficacy. Terpenoids form the largest and most structurally diverse group of phytochemicals in horticultural crops. Derived from isoprene units, terpenoids include monoterpenes, sesquiterpenes, diterpenes, triterpenes and tetraterpenes. Carotenoids, a subclass of terpenoids, are pigmented compounds responsible for yellow, orange and red colors in many

fruits and vegetables (Siafaka *et al.*, 2025). Lycopene in tomatoes,  $\beta$ -carotene in carrots, lutein in leafy greens and zeaxanthin in maize are well-known examples. Terpenoids are widely distributed in fruits, vegetables, spices and aromatic plants, contributing to aroma, flavor and plant defense. Pharmacologically, terpenoids and carotenoids exhibit antioxidant, anti-inflammatory, anticancer, cardioprotective and immunomodulatory properties. Carotenoids, in particular, play a crucial role in eye health, oxidative stress reduction and modulation of immune responses. However, their lipophilic nature limits their bioavailability, as they require dietary fats for absorption and are prone to oxidative degradation. Nanoencapsulation offers a promising approach to enhance the solubility, stability and targeted delivery of terpenoids and carotenoids.

Saponins, glycosides and sulfur-containing compounds constitute additional classes of phytochemicals with significant pharmacological relevance. Saponins are glycosylated triterpenes or steroidal compounds known for their surface-active properties, which enable them to form stable foams. They are widely distributed in legumes, certain vegetables and medicinal horticultural crops. Saponins exhibit a broad range of biological activities, including cholesterol-lowering, immunomodulatory, antimicrobial and anticancer effects. Glycosides, which consist of a sugar moiety linked to a non-sugar aglycone, encompass a diverse group of compounds with varied pharmacological activities depending on their aglycone structure. Sulfur-containing compounds, particularly glucosinolates and organosulfur compounds, are characteristic of cruciferous vegetables such as cabbage, broccoli, cauliflower and radish, as well as allium crops like garlic and onion. These compounds are responsible for the pungent aroma and taste of these vegetables and are known for their strong chemopreventive, antimicrobial and anti-inflammatory properties. Upon enzymatic hydrolysis, glucosinolates yield biologically active products such as isothiocyanates, which have been extensively studied for their anticancer potential. Despite their efficacy, sulfur-containing compounds are often unstable and susceptible to degradation, necessitating protective delivery systems to preserve their bioactivity.

## 2.2 Sources and distribution

Fruits represent one of the most important sources of phytochemicals in the human diet and contribute significantly to daily antioxidant intake. The phytochemical profile of fruits is highly diverse and includes phenolics, flavonoids, carotenoids and organic acids. Berries such as blueberries, strawberries, raspberries and blackberries are particularly rich in anthocyanins, flavonols and phenolic acids, making them among the most potent antioxidant-rich foods. Citrus fruits are abundant in flavanones, vitamin C and phenolic acids, while grapes contain resveratrol, flavanols and tannins. Tropical fruits such as mango, papaya, pineapple and guava are notable sources of carotenoids, polyphenols and bioactive enzymes. The distribution of phytochemicals within fruits varies across peel, pulp and seeds, with peels and seeds often containing higher concentrations of bioactive compounds than the edible pulp. This uneven distribution highlights the potential of fruit by-products as valuable sources of phytochemicals for pharmacological applications. Vegetables constitute another major group of horticultural crops with substantial phytochemical diversity. Leafy vegetables such as spinach, kale and lettuce are rich in flavonoids, carotenoids and phenolic acids, while cruciferous vegetables are distinguished by their high glucosinolate

content. Root and tuber vegetables, including carrots, beetroot and potatoes, contain carotenoids, betalains, phenolics and alkaloids. Allium vegetables such as garlic, onion and leek are particularly rich in organosulfur compounds with well-documented antimicrobial and cardioprotective properties. Leguminous vegetables contribute saponins, flavonoids and phenolic acids, while solanaceous vegetables like tomato and eggplant are important sources of carotenoids, phenolics and glycoalkaloids. The phytochemical composition of vegetables is strongly influenced by cultivation practices, environmental stress, maturity stage and cooking methods, which can either enhance or reduce bioactive content.

Spices and condiments, although, consumed in relatively small quantities, are among the most concentrated sources of phytochemicals in the human diet. These crops are rich in essential oils, phenolics, flavonoids, alkaloids and terpenoids that contribute to their characteristic aroma, flavor and medicinal properties. Turmeric contains curcuminoids with potent anti-inflammatory and anticancer activities, ginger is rich in gingerols and shogaols with antioxidant and digestive benefits and black pepper contains piperine, which enhances bioavailability of other phytochemicals. Cinnamon, clove, cardamom and coriander are also rich sources of bioactive compounds with antimicrobial and metabolic regulatory properties. Due to their strong biological activity and poor solubility, phytochemicals from spices and condiments are particularly suitable for nano-enabled delivery systems aimed at enhancing their pharmacological efficacy (Ulas *et al.*, 2025). Plantation crops such as tea, coffee, cocoa and coconut contribute significantly to global phytochemical intake and possess immense economic and medicinal importance. Tea is rich in catechins, theaflavins and flavonoids, coffee contains chlorogenic acids and caffeine and cocoa is abundant in flavanols with cardioprotective effects. These crops are often consumed as beverages, providing a continuous dietary source of bioactive compounds. Ornamental horticultural crops, although, primarily cultivated for aesthetic purposes, are increasingly recognized as valuable sources of unique phytochemicals. Many ornamental plants synthesize alkaloids, flavonoids, terpenoids and glycosides with potent pharmacological activities. Extracts from ornamental flowers and leaves are being explored for antioxidant, antimicrobial and anticancer properties, expanding the scope of horticultural phytochemical research beyond edible crops.

## 3. Pharmacological potential of horticultural crop phytochemicals

Phytochemicals derived from horticultural crops exert a wide spectrum of pharmacological effects that collectively contribute to disease prevention, health promotion and therapeutic intervention. These bioactive compounds act through multiple molecular and cellular mechanisms, including modulation of oxidative stress, regulation of inflammatory signaling pathways, inhibition of pathogenic microorganisms, interference with cancer cell proliferation and improvement of metabolic and cardiovascular functions. The pharmacological relevance of horticultural crop phytochemicals is strongly supported by *in vitro*, *in vivo* and epidemiological studies, which consistently associate high consumption of fruits, vegetables, spices and plantation crops with reduced incidence of chronic and degenerative diseases. However, the biological efficacy of these compounds is influenced by factors such as bioavailability, metabolism, target specificity and synergistic interactions, underscoring the importance of advanced delivery strategies to maximize their therapeutic potential.

### 3.1 Antioxidant and anti-inflammatory activities

Oxidative stress and chronic inflammation are central contributors to the pathogenesis of numerous diseases, including cancer, diabetes, cardiovascular disorders, neurodegenerative diseases and aging-related conditions. Horticultural crop phytochemicals play a pivotal role in counteracting these processes through their potent antioxidant and anti-inflammatory activities. Antioxidant phytochemicals, particularly phenolics, flavonoids, carotenoids and certain alkaloids, neutralize reactive oxygen species (ROS) and reactive nitrogen species (RNS) by donating electrons or hydrogen atoms, chelating transition metal ions and enhancing endogenous antioxidant defense systems. Fruits such as berries, grapes, citrus and pomegranates, as well as vegetables like tomatoes, spinach and crucifers, are especially rich in antioxidant phytochemicals that contribute to cellular redox homeostasis. Beyond direct free radical scavenging, phytochemicals modulate the activity of key antioxidant enzymes, including superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase (Osman *et al.*, 2024). Polyphenols and flavonoids activate transcription factors involved in antioxidant defense, thereby upregulating the expression of cytoprotective genes. This indirect antioxidant mechanism is particularly significant, as it provides sustained protection against oxidative damage. Carotenoids such as lycopene,  $\beta$ -carotene, lutein and zeaxanthin are highly effective in quenching singlet oxygen and protecting lipid membranes from peroxidation, which is crucial for maintaining cellular integrity.

Anti-inflammatory activity is another hallmark of horticultural crop phytochemicals. Chronic inflammation is mediated by the overproduction of pro-inflammatory cytokines, chemokines and enzymes such as cyclooxygenase, lipoxygenase and inducible nitric oxide synthase. Phytochemicals inhibit these mediators by suppressing inflammatory signaling pathways and reducing the expression of inflammatory genes. Flavonoids and phenolic acids interfere with nuclear transcription factors that regulate inflammation, while terpenoids and organosulfur compounds modulate immune cell activation and cytokine release. Spices and condiments such as turmeric, ginger, garlic and chili peppers are particularly notable for their strong anti-inflammatory properties. Despite their efficacy, many antioxidant and anti-inflammatory phytochemicals exhibit low stability and rapid metabolism, which limits their *in vivo* effectiveness and highlights the importance of formulation-based enhancement strategies.

### 3.2 Antimicrobial and antiviral properties

The emergence of antimicrobial resistance and viral pandemics has intensified the search for alternative and complementary therapeutic agents derived from natural sources. Phytochemicals from horticultural crops exhibit broad-spectrum antimicrobial and antiviral activities, making them promising candidates for combating infectious diseases. These compounds act through diverse mechanisms, including disruption of microbial cell membranes, inhibition of enzyme activity, interference with nucleic acid synthesis and modulation of host immune responses. Phenolics, flavonoids, alkaloids, terpenoids and sulfur-containing compounds contribute significantly to the antimicrobial defense of plants and retain this activity when consumed or applied therapeutically. Vegetables such as garlic, onion and crucifers are rich in organosulfur compounds and glucosinolate-derived metabolites that exhibit strong antibacterial and antifungal effects (Godase *et al.*, 2023). These compounds disrupt

microbial membranes and inhibit key metabolic enzymes, leading to growth suppression or cell death. Fruits such as citrus, berries and grapes contain phenolics and flavonoids that inhibit the adhesion and colonization of pathogenic bacteria. Spices and condiments are particularly potent antimicrobial agents due to their high concentration of bioactive compounds. Essential oils and alkaloids from spices interfere with microbial cell integrity and metabolic pathways, contributing to their traditional use as preservatives and medicinal agents.

Antiviral activity of horticultural crop phytochemicals has gained increasing attention, particularly in the context of respiratory and gastrointestinal viral infections. Polyphenols and flavonoids inhibit viral entry, replication and assembly by interacting with viral proteins or host cell receptors. Certain phytochemicals modulate host immune responses, enhancing antiviral defense mechanisms. Additionally, plantation crops such as tea and coffee contain bioactive compounds that exhibit antiviral properties through multiple modes of action. However, the clinical application of phytochemical-based antimicrobials is often constrained by poor solubility, limited bioavailability and variability in activity, necessitating innovative approaches to improve their pharmacological performance.

### 3.3 Anticancer and chemopreventive effects

Cancer remains one of the leading causes of mortality worldwide and horticultural crop phytochemicals have emerged as key agents in cancer prevention and therapy. Epidemiological studies consistently demonstrate an inverse relationship between fruit and vegetable consumption and cancer risk, underscoring the chemopreventive potential of plant-derived bioactives. Phytochemicals exert anticancer effects by modulating multiple stages of carcinogenesis, including initiation, promotion, progression and metastasis. Their multi-targeted nature distinguishes them from conventional chemotherapeutic agents and reduces the likelihood of resistance development. Phenolics and flavonoids inhibit oxidative DNA damage, thereby preventing mutation and tumor initiation. They also regulate cell cycle progression, induce apoptosis in cancer cells and inhibit angiogenesis and metastasis. Carotenoids play a crucial role in protecting cellular membranes and regulating gene expression involved in cell growth and differentiation. Alkaloids and terpenoids interfere with microtubule dynamics, signal transduction pathways and hormone metabolism, contributing to their anticancer activity (Arabestani *et al.*, 2024). Sulfur-containing compounds from cruciferous and allium vegetables enhance detoxification enzymes and promote the elimination of carcinogens. Chemopreventive effects of horticultural crop phytochemicals are particularly significant in hormone-related and gastrointestinal cancers. These compounds modulate estrogen metabolism, inhibit inflammatory mediators and suppress tumor-promoting signaling pathways. Despite promising preclinical evidence, the translation of phytochemicals into effective anticancer therapies is limited by challenges related to bioavailability, pharmacokinetics and target specificity. High doses required to achieve therapeutic concentrations may result in adverse effects, highlighting the need for delivery systems that enhance efficacy while minimizing toxicity.

### 3.4 Antidiabetic and metabolic regulatory effects

Metabolic disorders such as diabetes mellitus, obesity and metabolic syndrome represent major global health challenges. Horticultural crop phytochemicals exhibit significant antidiabetic and metabolic

regulatory effects by influencing glucose metabolism, insulin sensitivity, lipid homeostasis and energy balance. Fruits, vegetables and spices contribute bioactive compounds that modulate key enzymes and signaling pathways involved in carbohydrate and lipid metabolism. Polyphenols and flavonoids inhibit carbohydrate-digesting enzymes, reduce glucose absorption and improve insulin signaling, thereby contributing to glycemic control. Certain phytochemicals enhance pancreatic  $\beta$ -cell function and protect against oxidative stress-induced damage, supporting insulin secretion and glucose homeostasis. Terpenoids and saponins influence lipid metabolism by reducing cholesterol absorption, enhancing bile acid excretion and regulating adipogenesis. Spices such as cinnamon, turmeric and ginger have been traditionally used for metabolic regulation and are now supported by scientific evidence demonstrating their role in improving insulin sensitivity and reducing inflammation associated with metabolic disorders (Adhikari *et al.*, 2025). Plantation crops and fruits rich in phenolic acids and flavonoids contribute to improved lipid profiles and reduced oxidative stress, which are critical factors in preventing diabetes-related complications. However, the effectiveness of phytochemicals in metabolic regulation is often compromised by low oral bioavailability and rapid clearance. Interindividual variability in metabolism further complicates their therapeutic application, emphasizing the importance of formulation strategies that ensure consistent and sustained bioactivity.

### 3.5 Cardioprotective and neuroprotective activities

Cardiovascular and neurodegenerative diseases are among the leading causes of morbidity and mortality worldwide and oxidative stress, inflammation and metabolic dysfunction play central roles in their pathogenesis. Phytochemicals from horticultural crops exert cardioprotective and neuroprotective effects by modulating these underlying mechanisms. Fruits and vegetables rich in polyphenols and flavonoids improve endothelial function, reduce oxidative damage to blood vessels and inhibit platelet aggregation, thereby lowering the risk of atherosclerosis and hypertension. Carotenoids and phenolic compounds contribute to lipid regulation and protect low-density lipoproteins from oxidation, a key step in the development of cardiovascular disease. Organosulfur compounds from allium vegetables enhance nitric oxide bioavailability, improve vascular tone and reduce blood pressure. Regular consumption of phytochemical-rich horticultural crops is consistently associated with reduced incidence of coronary heart disease and stroke. Neuroprotective effects of horticultural crop phytochemicals are attributed to their ability to cross the blood-brain barrier, modulate neurotransmitter systems and protect neuronal cells from oxidative and inflammatory damage. Flavonoids and phenolic acids enhance cognitive function, improve cerebral blood flow and inhibit neuroinflammatory mediators. These compounds also interfere with protein aggregation and neuronal apoptosis, which are characteristic features of neurodegenerative disorders (Solanki *et al.*, 2022). Plantation crops such as tea and coffee contain neuroactive phytochemicals that improve alertness, cognitive performance and neuroprotection. Despite their potential, the delivery of cardioprotective and neuroprotective phytochemicals to target tissues remains challenging due to metabolic barriers and limited tissue penetration. Achieving therapeutic concentrations in cardiovascular and neural tissues often requires innovative strategies to enhance stability, bioavailability and targeted delivery.

## 4. Role of nanotechnology in enhancing phytochemical pharmacology

The integration of nanotechnology into phytochemical-based pharmacology represents a paradigm shift in the utilization of bioactive compounds derived from horticultural crops. While phytochemicals possess immense therapeutic potential, their practical application has long been constrained by poor solubility, instability, low bioavailability, rapid metabolism and limited target specificity. Nanotechnology offers innovative solutions to these challenges by enabling precise manipulation of materials at the nanoscale, where unique physicochemical and biological properties emerge. Through nanoscale engineering, phytochemicals can be protected, stabilized and delivered more efficiently to target tissues, thereby significantly enhancing their pharmacological performance. The role of nanotechnology in phytochemical pharmacology extends beyond simple delivery enhancement and includes controlled release, targeted action, synergistic bioactivity and improved safety profiles. Nanotechnology-based approaches are particularly well suited for horticultural crop phytochemicals due to their structural diversity and varying physicochemical characteristics. Phenolics, flavonoids, alkaloids, terpenoids, carotenoids and sulfur-containing compounds differ widely in polarity, molecular size and stability, necessitating adaptable and versatile delivery platforms. Nanotechnology provides a toolbox of nanocarriers that can be tailored to encapsulate both hydrophilic and hydrophobic compounds, protect them from environmental and biological degradation and modulate their interaction with biological systems. As a result, nano-enabled phytochemicals demonstrate improved pharmacokinetics, enhanced cellular uptake, prolonged circulation time and superior therapeutic efficacy compared to their conventional counterparts.

### 4.1 Nanotechnology concepts relevant to phytochemicals

Nanoencapsulation is one of the most fundamental and widely employed nanotechnology concepts in phytochemical pharmacology. It involves the incorporation of bioactive phytochemicals within nanoscale matrices or shells that physically isolate the compound from the external environment. This protective encapsulation shields phytochemicals from chemical degradation, enzymatic breakdown and unfavorable pH conditions encountered during processing, storage and digestion. Nanoencapsulation also improves solubility by dispersing poorly water-soluble phytochemicals in nanoscale carriers with enhanced surface area and wettability. For lipophilic compounds such as curcumin, lycopene, resveratrol and quercetin, nanoencapsulation dramatically increases dissolution rates and bioaccessibility, thereby improving absorption and systemic availability. Beyond protection and solubility enhancement, nanoencapsulation enables controlled modulation of phytochemical release profiles. Encapsulated phytochemicals can be released gradually over time rather than rapidly dissipating following administration. This sustained release ensures prolonged therapeutic action, reduces dosing frequency and minimizes fluctuations in plasma concentration. Nanoencapsulation also allows the co-delivery of multiple phytochemicals or the combination of phytochemicals with conventional drugs, facilitating synergistic interactions and multi-targeted therapeutic strategies. Such approaches are particularly valuable in managing complex diseases that involve multiple pathological pathways (Sharma *et al.*, 2025).

Nanocarriers and nanodelivery systems form the structural backbone of nano-enabled phytochemical pharmacology. These systems are designed to transport phytochemicals across biological barriers and deliver them to specific tissues, cells, or intracellular compartments. Nanocarriers possess dimensions that allow them to interact efficiently with biological membranes, enter cells through endocytosis and evade premature clearance by the immune system. Surface modification of nanocarriers with polymers, ligands, or targeting moieties further enhances their biological performance by improving stability, circulation time and target specificity. For phytochemicals with limited permeability or rapid clearance, nanocarriers act as vehicles that optimize pharmacokinetic behavior and maximize therapeutic impact. Controlled and targeted release mechanisms represent another critical nanotechnology concept relevant to phytochemical pharmacology. Controlled release systems regulate the rate and duration of phytochemical release, ensuring that bioactive compounds are delivered at therapeutically optimal concentrations. Targeted release systems, on the other hand, are designed to deliver phytochemicals preferentially to diseased tissues while minimizing exposure to healthy cells. Targeting can be achieved through passive mechanisms, such as enhanced permeability and retention effects, or active mechanisms involving ligand-receptor interactions. By concentrating phytochemicals at specific sites of action, targeted nanodelivery enhances efficacy, reduces systemic toxicity and improves safety profiles. These mechanisms are particularly relevant for anticancer, anti-inflammatory and neuroprotective applications, where localized delivery is crucial for therapeutic success.

#### 4.2 Types of nanocarriers used

Lipid-based nanoparticles are among the most extensively studied nanocarriers for phytochemical delivery due to their biocompatibility, biodegradability and ability to encapsulate lipophilic compounds. These nanoparticles are composed of natural or synthetic lipids that form stable nanostructures capable of solubilizing hydrophobic phytochemicals. Lipid-based systems mimic biological membranes, facilitating efficient interaction with cells and enhancing absorption across gastrointestinal and cellular barriers. Phytochemicals such as carotenoids, terpenoids and polyphenols exhibit significantly improved bioavailability when delivered through lipid-based nanoparticles. Additionally, these systems protect sensitive compounds from oxidative degradation and enzymatic breakdown, extending shelf-life and therapeutic activity. Polymeric nanoparticles represent another versatile class of nanocarriers widely used in phytochemical pharmacology. These nanoparticles are constructed from natural or synthetic polymers and offer precise control over particle size, surface characteristics and release kinetics. Polymeric nanocarriers are particularly effective for sustained and controlled release applications, as their degradation rates can be tailored to match desired therapeutic profiles. They are capable of encapsulating a wide range of phytochemicals, including both hydrophilic and hydrophobic compounds. The structural flexibility of polymeric nanoparticles allows for surface functionalization with targeting ligands, enhancing site-specific delivery and cellular uptake. As a result, polymeric nanocarriers have demonstrated improved efficacy and reduced toxicity in phytochemical-based therapeutic systems.

Metallic and metal oxide nanoparticles have gained attention for their unique physicochemical properties and potential synergistic interactions with phytochemicals. These nanoparticles exhibit high surface area, tunable surface chemistry and intrinsic biological activity.

When combined with phytochemicals, metallic nanoparticles can enhance antimicrobial, anticancer and antioxidant effects through additive or synergistic mechanisms. Phytochemical-mediated synthesis of metallic nanoparticles, often referred to as green or phytoengineered nanotechnology, further enhances biocompatibility and sustainability. In such systems, phytochemicals serve dual roles as reducing agents and therapeutic molecules, resulting in nanoparticles with enhanced pharmacological functionality. However, careful evaluation of toxicity and long-term safety is essential for the responsible use of metallic nanocarriers. Nanoemulsions and nanogels represent soft nanocarrier systems that are particularly suitable for delivering phytochemicals with poor solubility and stability. Nanoemulsions consist of nanoscale droplets dispersed in a continuous phase, providing a high surface area for improved solubilization and absorption of lipophilic phytochemicals (Ghosh *et al.*, 2025). These systems are kinetically stable and can be administered through oral, topical, or parenteral routes. Nanogels, on the other hand, are three-dimensional polymeric networks capable of holding large amounts of water while maintaining structural integrity. They offer excellent loading capacity, responsiveness to environmental stimuli and controlled release properties. Nanoemulsions and nanogels are especially valuable in nutraceutical, cosmeceutical and topical therapeutic applications involving horticultural crop phytochemicals.

Solid lipid nanoparticles and nanostructured lipid carriers represent advanced lipid-based nanocarrier systems designed to overcome limitations associated with earlier lipid formulations. Solid lipid nanoparticles are composed of solid lipids that provide a rigid matrix for encapsulating phytochemicals, offering improved stability and controlled release. Nanostructured lipid carriers incorporate both solid and liquid lipids, creating a less ordered internal structure that enhances drug loading capacity and reduces expulsion during storage. These systems combine the advantages of lipid-based delivery with improved stability and scalability, making them attractive for industrial applications. Phytochemicals delivered through solid lipid nanoparticles and nanostructured lipid carriers exhibit enhanced bioavailability, prolonged circulation time and improved therapeutic outcomes. Collectively, these nanocarrier systems demonstrate the transformative role of nanotechnology in enhancing phytochemical pharmacology (Singh *et al.*, 2023). By addressing solubility, stability, bioavailability and targeting challenges, nanotechnology enables the effective translation of horticultural crop phytochemicals into clinically and commercially viable therapeutic agents. The continued refinement of nanocarrier design, coupled with advances in green synthesis and regulatory frameworks, is expected to further expand the application of nanotechnology in phytochemical-based pharmacology. This convergence of horticulture, pharmacology and nanoscience holds significant promise for the development of sustainable, effective and safe plant-based therapeutics.

#### 5. Nanoformulation of horticultural crop phytochemicals

Nanoformulation represents a critical translational step in converting horticultural crop phytochemicals from promising bioactive molecules into effective pharmacological agents. While nanotechnology provides the conceptual and structural framework for enhanced delivery, nanoformulation focuses on the practical design, optimization and functional performance of phytochemical-loaded nanosystems. Through nanoformulation, phytochemicals are encapsulated, stabilized and engineered to overcome physicochemical

and biological barriers that limit their therapeutic efficacy. This approach not only improves solubility and bioavailability but also enables controlled, targeted and synergistic delivery, thereby maximizing pharmacological outcomes. Nanoformulation strategies are particularly relevant for horticultural crop phytochemicals due to their structural diversity, sensitivity to degradation and complex interactions with biological systems.

### 5.1 Encapsulation and stabilization strategies

Encapsulation is the cornerstone of nanoformulation and plays a vital role in stabilizing phytochemicals derived from horticultural crops. Many phytochemicals are highly sensitive to environmental conditions such as light, heat, oxygen, pH fluctuations and enzymatic activity. Nanoencapsulation physically isolates these bioactive compounds within protective matrices, thereby preserving their chemical integrity during processing, storage and physiological transit. This protective effect is especially important for polyphenols, carotenoids and sulfur-containing compounds, which are prone to oxidative and hydrolytic degradation. Encapsulation strategies are tailored based on the physicochemical nature of the phytochemical and the intended route of administration. Hydrophobic phytochemicals are typically encapsulated within lipid or polymeric cores, whereas hydrophilic compounds may be incorporated into aqueous compartments or surface-bound systems. The nanoscale size of encapsulated systems provides a high surface-to-volume ratio, improving dispersion and stability in biological fluids. Additionally, encapsulation reduces direct exposure of phytochemicals to harsh gastrointestinal conditions, minimizing premature degradation and loss of bioactivity (Jadoun *et al.*, 2021).

Stabilization through nanoformulation also involves the use of surface modifiers and protective coatings that prevent aggregation, oxidation and chemical transformation. Polymers, surfactants and biopolymers are often employed to enhance colloidal stability and prolong shelf life. In the context of horticultural phytochemicals, stabilization is particularly important for nutraceutical and functional food applications, where long-term storage and processing stability are essential. By maintaining phytochemical integrity, nanoformulation ensures consistent dosing and reproducible pharmacological effects.

### 5.2 Enhancement of bioavailability and pharmacokinetics

One of the most significant advantages of nanoformulation is its ability to dramatically enhance the bioavailability and pharmacokinetic profile of phytochemicals. Bioavailability is influenced by solubility, dissolution rate, permeability, metabolism and systemic clearance, all of which can be favorably modulated through nanoscale delivery systems. Nanoformulated phytochemicals exhibit improved dissolution rates due to reduced particle size and increased surface area, enabling faster and more efficient absorption across biological membranes. Nanoformulation also enhances intestinal permeability by facilitating transcellular and paracellular transport mechanisms. Nanoparticles can interact with epithelial cells and be internalized through endocytic pathways, bypassing traditional absorption barriers. This is particularly advantageous for phytochemicals that exhibit poor membrane permeability in their free form. Furthermore, nanoformulated systems can protect phytochemicals from enzymatic degradation and first-pass metabolism, thereby increasing systemic exposure and prolonging circulation time.

Pharmacokinetic parameters such as absorption rate, peak plasma concentration, half-life and area under the curve are significantly improved through nanoformulation. Sustained release properties of nanocarriers ensure prolonged therapeutic levels, reducing the need for frequent dosing. Improved pharmacokinetics not only enhance therapeutic efficacy but also reduce interindividual variability in response, which is a common challenge in phytochemical-based therapies (Kumar *et al.*, 2023). These improvements are particularly relevant for chronic disease management, where consistent and long-term exposure to bioactive compounds is required.

### 5.3 Targeted and sustained drug delivery

Targeted and sustained delivery is a defining feature of nanoformulated phytochemicals and represents a major advancement over conventional delivery approaches. Sustained delivery systems are designed to release phytochemicals gradually over extended periods, maintaining therapeutic concentrations while minimizing peak-related toxicity. This controlled release is achieved through matrix degradation, diffusion-controlled mechanisms, or stimulus-responsive release triggered by pH, enzymes, or redox conditions. Targeted delivery further enhances pharmacological efficacy by directing phytochemicals to specific tissues, cells, or intracellular compartments. Passive targeting exploits physiological differences between healthy and diseased tissues, such as enhanced vascular permeability in inflamed or tumor tissues. Active targeting involves surface modification of nanocarriers with ligands that recognize specific receptors or biomarkers, enabling selective uptake by target cells. For horticultural crop phytochemicals with broad biological activity, targeted delivery reduces off-target effects and improves therapeutic precision (Xu *et al.*, 2024).

Targeted and sustained nanoformulations are particularly valuable in anticancer, anti-inflammatory and neuroprotective applications, where localized and prolonged action is essential. By concentrating phytochemicals at the site of action, nanoformulation enhances efficacy while reducing systemic exposure and toxicity. This targeted approach aligns with modern precision medicine paradigms and expands the clinical relevance of plant-derived therapeutics.

### 5.4 Synergistic effects of phytochemicals and nanomaterials

An emerging and highly promising aspect of nanoformulation is the synergistic interaction between phytochemicals and nanomaterials. In many nanoformulated systems, nanocarriers are not merely passive delivery vehicles but actively contribute to biological activity. Certain nanomaterials possess intrinsic antimicrobial, antioxidant, or anticancer properties that complement the pharmacological effects of encapsulated phytochemicals. When combined, these components produce additive or synergistic effects that enhance overall therapeutic performance. Synergy also arises from the co-delivery of multiple phytochemicals within a single nanocarrier. Horticultural crops naturally contain complex mixtures of bioactive compounds that act through multiple pathways. Nanoformulation enables the preservation and controlled delivery of these phytochemical combinations, maintaining their natural synergistic interactions. This multi-component delivery strategy is particularly effective in managing complex diseases that involve oxidative stress, inflammation, metabolic dysregulation and cellular signaling abnormalities. Green and phytoengineered nanoformulations further enhance synergy by integrating phytochemicals into nanoparticle synthesis itself. In such systems, phytochemicals function as both reducing agents and

therapeutic agents, resulting in nanoparticles with enhanced bioactivity and biocompatibility (Ashfaq *et al.*, 2023). These synergistic nano-phytochemical systems exhibit improved pharmacological efficacy compared to isolated phytochemicals or nanomaterials alone. Importantly, synergy allows for dose reduction, minimizing toxicity while maintaining or enhancing therapeutic outcomes.

## 6. Green and phytoengineered nanotechnology approaches

Green and phytoengineered nanotechnology has emerged as a sustainable and biologically compatible alternative to conventional nanoparticle synthesis methods. Traditional chemical and physical synthesis techniques often involve high energy inputs, toxic solvents, hazardous reducing agents and complex processing steps, raising concerns regarding environmental safety, cost and biomedical applicability. In contrast, green nanotechnology exploits biological systems-particularly plants and plant-derived biomolecules-to synthesize nanoparticles in an eco-friendly manner. Horticultural crops, owing to their rich phytochemical composition, play a pivotal role in this paradigm by serving as natural factories for nanoparticle fabrication.

### 6.1 Plant-mediated synthesis of nanoparticles

Plant-mediated synthesis of nanoparticles relies on the intrinsic reducing, stabilizing and capping properties of phytochemicals present in plant tissues. Extracts obtained from leaves, fruits, peels, seeds, flowers, or roots contain a diverse array of bioactive compounds such as phenolics, flavonoids, terpenoids, alkaloids, sugars, proteins and organic acids. These compounds facilitate the reduction of metal ions into nanoscale particles while simultaneously stabilizing the formed nanoparticles. The process is typically conducted under mild conditions, such as ambient temperature and pressure, eliminating the need for harsh chemicals or extreme physical conditions (Tenchov *et al.*, 2025). The use of horticultural crops for nanoparticle synthesis is particularly advantageous due to their accessibility, renewability and chemical diversity. Phytochemicals act synergistically during nanoparticle formation, influencing particle size, morphology, surface charge and stability. This biological control over nanoparticle characteristics enhances reproducibility and biocompatibility, which are critical for pharmacological applications. Moreover, plant-mediated synthesis aligns with traditional medicinal practices, creating a seamless bridge between ethnobotany and modern nanotechnology.

### 6.2 Use of Horticultural crop extracts in nanoparticle fabrication

Horticultural crop extracts are increasingly employed as multifunctional agents in nanoparticle fabrication. These extracts not only reduce metal ions but also impart therapeutic functionality to the resulting nanoparticles. Fruits, vegetables, spices and plantation crops rich in polyphenols and antioxidants are particularly effective in producing stable and bioactive nanoparticles. The phytochemical profile of the extract determines the physicochemical properties and biological behavior of the nanoparticles, enabling tailored synthesis for specific pharmacological applications. Extract-based synthesis offers flexibility in nanoparticle design by allowing modulation of synthesis parameters such as extract concentration, pH, temperature and reaction time (Aker *et al.*, 2022). This tunability facilitates the production of nanoparticles optimized for drug delivery, antimicrobial activity, or anticancer applications. Importantly, phytochemical-coated nanoparticles often exhibit enhanced biological activity compared to chemically synthesized counterparts, owing to the synergistic action of surface-bound phytochemicals.

### 6.3 Advantages over chemical and physical synthesis methods

Green and phytoengineered nanotechnology offers several advantages over conventional chemical and physical synthesis methods. First, it eliminates or significantly reduces the use of toxic reagents and solvents, minimizing environmental contamination and health risks. Second, the process is energy-efficient and cost-effective, as it operates under mild conditions without the need for sophisticated equipment. Third, biologically synthesized nanoparticles exhibit superior biocompatibility, making them more suitable for biomedical and nutraceutical applications. Another critical advantage is the inherent functionalization provided by plant-derived biomolecules. In chemical synthesis, additional steps are often required to functionalize nanoparticle surfaces for stability or targeting (Yousaf *et al.*, 2025). In contrast, phytochemicals naturally cap and functionalize nanoparticles during synthesis, simplifying processing and enhancing biological performance. This intrinsic functionalization improves dispersion, reduces aggregation and enhances interaction with biological systems.

### 6.4 Sustainability and eco-friendly aspects

Sustainability is a defining feature of green nanotechnology. The use of renewable plant resources, biodegradable biomolecules and environmentally benign processes aligns with global sustainability goals and circular bioeconomy principles. Utilizing agricultural by-products such as fruit peels, seeds and processing waste further enhances sustainability by converting waste into high-value nanomaterials. This approach not only reduces environmental burden but also adds economic value to horticultural production systems (Hsu *et al.*, 2023). From a regulatory and societal perspective, eco-friendly nanoparticle synthesis enhances public acceptance of nanotechnology-based products, particularly in food, nutraceutical and herbal medicine sectors. The integration of green nanotechnology with horticultural sciences thus represents a holistic and sustainable strategy for advancing phytochemical pharmacology.

## 7. Mechanisms of nanophytochemical interaction

Understanding the mechanisms underlying nano-phytochemical interactions is essential for optimizing therapeutic efficacy and ensuring safety. At the nanoscale, phytochemicals exhibit altered biological behavior due to enhanced cellular uptake, modified pharmacokinetics and improved molecular interactions. Nanoformulation fundamentally changes how phytochemicals interact with cells, tissues and molecular targets (Fahim *et al.*, 2024).

### 7.1 Cellular uptake and intracellular trafficking

Nanoformulated phytochemicals are internalized by cells primarily through endocytic pathways, including clathrin-mediated endocytosis, caveolae-mediated uptake and macropinocytosis. The small size and surface properties of nanoparticles enable them to cross cellular membranes more efficiently than free phytochemicals. Once internalized, nanoparticles are trafficked to intracellular compartments such as endosomes and lysosomes, where controlled release of phytochemicals occurs. Intracellular trafficking pathways influence the fate and activity of delivered phytochemicals. Properly engineered nanoparticles can escape endosomal entrapment, allowing phytochemicals to reach cytoplasmic or nuclear targets. This enhanced intracellular delivery is particularly relevant for anticancer and neuroprotective applications, where intracellular signaling modulation is critical (Liu *et al.*, 2024).

## 7.2 Interaction with biomolecules and receptors

Nanoformulated phytochemicals exhibit enhanced interaction with biomolecules such as proteins, enzymes, nucleic acids and membrane receptors. Nanoparticles increase the local concentration of phytochemicals at target sites, improving binding efficiency and biological response. Surface-functionalized nanoparticles can interact selectively with specific receptors, facilitating targeted delivery and receptor-mediated signaling modulation. At the molecular level, phytochemical-nanoparticle conjugates influence enzyme activity, inhibit pathogenic proteins and modulate receptor-mediated pathways more effectively than free phytochemicals. These interactions enhance specificity and reduce off-target effects, contributing to improved therapeutic outcomes (Raj *et al.*, 2025).

## 7.3 Modulation of signaling pathways and gene expression

Nano-phytochemical systems exert profound effects on cellular signaling pathways and gene expression profiles. By enhancing intracellular availability, nanoformulated phytochemicals more effectively regulate oxidative stress responses, inflammatory cascades, apoptotic pathways and metabolic signaling networks. They influence transcription factors, kinases and regulatory proteins involved in disease progression. At the genomic level, nanoformulated phytochemicals modulate gene expression patterns associated with cell survival, inflammation, metabolism and differentiation (Muzammil *et al.*, 2023). This molecular reprogramming underpins their enhanced pharmacological efficacy and supports their use in chronic and complex diseases.

## 7.4 Enhanced therapeutic efficacy at molecular levels

The convergence of improved delivery, targeted interaction and molecular modulation results in significantly enhanced therapeutic efficacy. Nano-phytochemical systems achieve higher potency at lower doses, reducing toxicity while maintaining or enhancing biological activity. The ability to act on multiple molecular targets simultaneously makes these systems particularly effective in multifactorial diseases such as cancer, metabolic disorders and neurodegeneration (Khan *et al.*, 2024).

## 8. Applications and translational prospects

The integration of nanotechnology with horticultural crop phytochemicals has opened new avenues for translational applications across multiple industries. The versatility of nanoformulated phytochemicals enables their deployment in pharmaceutical, nutraceutical, food and cosmetic sectors. In the pharmaceutical industry, nanoformulated phytochemicals are being explored as therapeutic agents, adjuvants and drug delivery enhancers. Improved bioavailability, targeted delivery and reduced toxicity make them attractive alternatives or complements to synthetic drugs. In the nutraceutical sector, nanoencapsulation enhances stability, absorption and efficacy of dietary bioactives, supporting the development of evidence-based supplements. Nano-enabled phytochemicals are increasingly incorporated into functional foods and beverages to enhance health benefits without compromising sensory attributes. Nanoencapsulation protects phytochemicals during processing and storage, ensuring consistent bioactivity. This approach supports the development of next-generation functional foods aimed at disease prevention and health promotion.

In cosmeceuticals, nanoformulated phytochemicals improve skin penetration, stability and efficacy of active ingredients. Anti-aging, antioxidant and anti-inflammatory formulations benefit significantly from nano-delivery systems. Herbal formulations also gain improved standardization, efficacy and shelf-life through nanoformulation, bridging traditional medicine with modern technology (Eker *et al.*, 2025). The clinical translation of nano-phytochemical systems is progressing steadily, supported by advances in formulation science and safety evaluation. Commercial prospects are strong, particularly in markets favoring natural, plant-based and sustainable products. Strategic collaboration between academia, industry and regulatory bodies will be essential for successful commercialization.

## 9. Future perspectives

The future of nano-phytochemical pharmacology lies in interdisciplinary integration, technological innovation and regulatory harmonization. The integration of nanotechnology with genomics, proteomics, metabolomics and artificial intelligence will enable rational design and optimization of nanoformulations. AI-driven modeling can predict biological responses, optimize carrier design and accelerate discovery pipelines. Personalized medicine approaches will tailor nano-phytochemical therapies based on individual genetic, metabolic and lifestyle factors. This precision strategy promises improved efficacy and reduced adverse effects. Smart nanoformulations responsive to pH, enzymes, redox state, or temperature will enable on-demand and site-specific phytochemical release. These systems represent a major advancement in controlled and precision therapeutics. Robust regulatory frameworks are essential to ensure safety, quality and efficacy of nano-phytochemical products. Harmonization of guidelines and long-term safety studies will facilitate clinical translation and public acceptance.

## 10. Conclusion

This review highlights the transformative potential of nanotechnology in enhancing the pharmacological efficacy of phytochemicals derived from horticultural crops. By addressing fundamental limitations such as poor solubility, instability, low bioavailability and lack of target specificity, nano-enabled strategies unlock new therapeutic possibilities for plant-derived bioactives. Green and phytoengineered nanotechnology further strengthens this paradigm by offering sustainable, eco-friendly and biologically compatible solutions. The convergence of horticulture, phytochemistry, pharmacology and nanotechnology pave the way for innovative, sustainable and evidence-based therapeutic systems. With continued interdisciplinary research, technological refinement and regulatory support, nanoformulated horticultural phytochemicals are poised to play a significant role in next-generation healthcare, functional nutrition and plant-based therapeutics.

### Availability of data and material

All data are provided within the manuscript.

### Authorship contribution statement

**M. Kabilan:** Contributed to conceptualization, supervision, critical review, and overall guidance of the manuscript; **M. Jayakumar:** Contributed to literature survey, data curation, and critical analysis of published studies; **K. Sundharaiya:** Contributed to software handling, reference management, and visualization of review content;

**G. Sathish:** Contributed to writing the original draft, reviewing, and editing of the manuscript; **Adnan A. Khan:** Contributed to critical review, validation of scientific content, and final approval of the manuscript.

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