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Bioactive compounds of *Allium cepa* L. and their pharmaceutical prospects

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Abstract

Rich in a variety of bioactive components with substantial pharmacological potential, onion (*Allium cepa* L.) is a key medicinal and food plant. The main phytochemical families found in onion such as flavonoids, anthocyanins, organosulfur compounds, phenolic acids, fructo-oligosaccharides and saponins are critically summarized in this study along with their molecular mechanisms and potential medical applications. Targets including different pathways and mitochondrial signalling cascades are used to modulate oxidative stress, inflammatory signalling, apoptosis, metabolic control and neuroprotective pathways. The anticancer potential of onion phytochemicals through mechanisms including cell cycle arrest, apoptosis induction, antiangiogenic action and metastasis suppression is further covered. Onion-derived compounds have appealing biological properties, but their practical translation is still restricted due to their poor solubility, instability, accelerated metabolism, low bioavailability and inadequate tissue selectivity. Current developments in nanoformulation techniques such as liposomes, phytosomes, polymeric nanoparticles, nanoemulsions, solid lipid nanoparticles, nanostructured lipid carriers and plant-derived extracellular vesicles are thoroughly assessed in order to get around these restrictions. Recent investigation indicates that delivery methods based on nanotechnology significantly enhance the stability, pharmacokinetics, therapeutic effectiveness and targeted distribution of onion phytochemicals. The paper also discusses future directions for precision phytomedicine, safety concerns, regulatory obstacles and clinical prospects. All bioactive substances produced from onion are potential prospects for the creation of pharmacological and nutraceutical treatments of the future.

1. Introduction

Due to their varied pharmacological characteristics and very low toxicity profiles, medicinal plants continue to be essential sources of bioactive chemicals for contemporary therapies and the creation of functional foods (Teshika *et al.*, 2019; Zhao *et al.*, 2021). One of the earliest vegetable crops to be cultivated, onion (*A. cepa*) has been widely used in many cultures, including Ayurvedic medical systems as well as a traditional medicinal plant (Griffiths *et al.*, 2002). The onion is a member of the genus *Allium*, which has over 900 species found all over the world and the family is Amaryllidaceae (Lanzotti, 2006; Zhao *et al.*, 2021). Onion are the most consuming vegetables worldwide due to its culinary appeal, nutritional worth and potential for medicinal application (Pareek *et al.*, 2017). The vast number of physiologically active phytochemicals found in onion such as organosulfur compounds, anthocyanins, flavonoids, phenolic acids and steroidal saponins are primarily responsible for their therapeutic value (Marrelli *et al.*, 2019). Numerous pharmacological properties including antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, anticancer, antidiabetic, cardioprotective,

neuroprotective and immunomodulatory effects can be observed by these substances (Teshika *et al.*, 2019; Fredotovic *et al.*, 2020). According to recent research, onion phytochemicals control molecular pathways linked to metabolic diseases, oxidative damage, inflammatory processes, cell death and angiogenesis (Iwar *et al.*, 2024). While sulfur-containing substances like thiosulfonates, cepaenes and onionin A contribute to anti-inflammatory and immunomodulatory activities, flavonoids like quercetin have potent antioxidant and chemo preventive qualities (Slimestad *et al.*, 2007; Fredotovic *et al.*, 2020). Onion cultivars, environmental factors, processing techniques and storage methods all affect the phytochemical makeup of onion (Nile and Park, 2013; Zhao *et al.*, 2021). Onion peels are especially rich in phenolic compounds and flavonoids whereas red onion often have higher amounts of anthocyanins and flavanols than white onion, leading to enhanced antioxidant activity (Benítez *et al.*, 2011). Advances in molecular pharmacology and nutraceutical research are contributing to the growing interest in onion phytomedicine (Gorrepati *et al.*, 2024). Regular onion consumption may lower the risk of cancer, cardiovascular disease, diabetes, obesity and neurodegenerative disorders through synergistic interactions among several phytochemicals, as demonstrated by experimental and epidemiological studies (Griffiths *et al.*, 2002; Zhao *et al.*, 2021). However, low absorption, volatility and fast metabolism restrict the medicinal use of onion phytochemicals (Fredotovic *et al.*, 2020). In order to enhance the pharmacokinetic and therapeutic qualities of chemicals obtained from onion, contemporary research increasingly focuses on nanoformu-

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lation and advanced delivery methods (Bozzuto *et al.*, 2024). This review paper emphasizes onion phytochemical diversity, the molecular processes behind its therapeutic actions, current developments in nanoformulation techniques and potential future uses for integrative phytochemistry.

2. Phytochemical diversity of onion

The colour, flavour, scent, defensive mechanisms and therapeutic potential of *A. cepa* (onion) are all influenced by a variety of naturally occurring bioactive compounds known as phytochemicals (Table 1).

Table 1: Major phytochemical groups identified in *A. cepa* and their biological activities

Phytochemical group	Compounds	Biological activities	Functional significance	References
Organosulfur compounds	Isoalliin, methiin, propiin, thiosulfates and cepaenes	Antimicrobial, antioxidant, anti-inflammatory and cardioprotective	Responsible for onion pungency, generated through alliinase mediated hydrolysis of ACSOs	Lanzotti, 2006
Flavonoids	Quercetin, quercetin-3-glucoside, kaempferol and rutin	Antioxidant, antihypertensive, anti-inflammatory and anticancer	Quercetin derivatives are the predominant flavonoids in onion	Slimestad <i>et al.</i> , 2007
Anthocyanins	Cyanidin and delphinidin derivatives	Antioxidant, vasoprotective and anti-inflammatory	Responsible for red and purple pigmentation in onion cultivars	Teshika <i>et al.</i> , 2019
Phenolic acids	Gallic acid, caffeic acid, ferulic acid and p-coumaric acid	Antioxidant, antimicrobial and anti-inflammatory	Onion peels contain high concentrations of phenolic acids	Benítez <i>et al.</i> , 2011
Fructooligosaccharides	Inulin and fructans	Prebiotic, immunomodulatory and gut protective	Promote growth of beneficial intestinal microbiota	Pareek <i>et al.</i> , 2017
Saponins	Steroidal saponins	Antifungal, cholesterol-lowering and anticancer	Contribute to membrane disruption and apoptosis induction	Marrelli <i>et al.</i> , 2019

2.1 Sulfur containing compounds

Among the most distinctive phytochemicals found in onion are sulfur-containing compounds, which are mostly responsible of the onion's strong flavour, scent and possible medicinal uses. Thio sulfinates, cysteine sulfoxides, allyl propyl disulfides, S-allyl cysteine derivatives and newly identified thiolane compounds are some of these substances. When onion tissues are damaged, sulfur metabolites are created enzymatically, which releases volatile chemicals with antibacterial, antioxidant, anti-inflammatory and anticancer properties (Iwar *et al.*, 2024). According to recent study, Tropea red onion have higher sulphate contents, which are associated with improved antioxidant activity and production of sulfur-rich bioactive metabolites. Onion sulfur compounds have biological characteristics that are multifunctional and have potential uses in medicine (Hosek *et al.*, 2025; Muscolo *et al.*, 2025).

2.2 Quercetin derivatives and flavonoids

Quercetin and its glycoside derivatives are the main antioxidant phytochemicals found in *A. cepa*. Onion is one of the best dietary sources of quercetin, especially in the dry outer layers and peel tissues, according to Kothari *et al.* (2020). Quercetin, spiraeoside, catechin, kaempferol, rutin, vicenin-2 and isorhamnetin-3-glucoside are the main flavonoids found in onion. Due to the presence of extra anthocyanin pigments and quercetin derivatives, red onion has much greater flavonoid concentrations than yellow onion (Samota *et al.*, 2022). Numerous biological actions such as antioxidant, anti-inflammatory, cardioprotective, neuroprotective and antiproliferative

One of the most abundant dietary sources of sulfur-containing compounds, flavonoids, phenolic acids, vitamins and antioxidant metabolites is found in onion. The cultivar, bulb colour, environmental factors, growing approaches, storage conditions and characterization techniques all have a substantial impact on the concentration and distribution of these chemicals. According to recent research, onion peels have significantly higher levels of flavonoids and phenolics than the edible pulp, emphasising the significance of onion by-products as important sources of nutraceutical chemicals (Muscolo *et al.*, 2025; Ren and Zhou, 2021).

properties are displayed by these flavonoids (Panche *et al.*, 2016). Peel of onion regularly exhibits the largest concentration of flavonoids, highlighting its potential utility in nutraceutical applications.

2.3 Pigmented onion varieties and anthocyanins

The water-soluble pigments called anthocyanins give certain onion varieties their red and purple hues. The main anthocyanins in red onion are cyanidin derivatives, a variety of delphinidin substances and cyanidin-3-glucoside. According to Samota *et al.* (2022), anthocyanins have anti-inflammatory, cardioprotective and regulating the metabolic actions in addition to greatly increasing antioxidant capacity. Tropea red onion have higher antioxidant activity than yellow onion types because they are particularly high in anthocyanins and flavonoids (Russo *et al.*, 2012). Red onion has improved functional and medicinal qualities due to the combination of anthocyanins and quercetin derivatives.

2.4 Antioxidant components and vitamins

Additionally, a number of antioxidant vitamins including C, A and E are found in onion. The most prevalent of these is vitamin C, which is mostly found in the peel tissues. Red onion has the greatest vitamin C content of any evaluated cultivar, as stated by Muscolo *et al.* (2025). Collagen formation, oxidative stress reduction and immunological protection all depend on vitamin C (Carr and Maggini, 2017). Despite being present in very small amounts, vitamin E can be utilized in combination with flavonoids and phenolic substances to enhance cellular defence and oxidative stability (Krinsky and

Johnson, 2005). Onion, due to their greater accumulation of flavonoids, phenol compounds and vitamins are regularly show better radical-scavenging activity in antioxidant tests (Cheng *et al.*, 2013; Muscolo *et al.*, 2025). Total biological activity of onion is increased by these vitamins and other compounds.

2.5 Phenolic compounds and acids

Another notable class of phytochemicals found in onion are phenolic acids, which have a major impact on antioxidant activity. Ferulic acid, chlorogenic acid, caffeic acid, gallic acid, syringic acid, protocatechuic acid and coumaric acid derivatives are the main phenolic acids found in onion (Muscolo *et al.*, 2025). These substances serve as organic antioxidants that can scavenge free radicals and lessen cellular damage brought on by oxidative stress. Furthermore, several phenolic acids such as ellagic acid and syringic acid have been proven possessing anticancer, neuroprotective, antidiabetic and anticonvulsant properties (Daglia *et al.*, 2014; Chen, 2015).

2.6 Fructooligosaccharides and saponins

Onion bulbs naturally contain fructooligosaccharides (FOS), which are significant non-digestible prebiotic carbohydrates that support the growth of beneficial gut microorganisms like *Bifidobacterium* and *Lactobacillus* species. This improves gut health, immune system function, absorption of minerals and regulation of metabolism (Zhao *et al.*, 2021). Short-chain fatty acids that support intestinal integrity and have anti-inflammatory properties are produced when FOS

ferments in the colon (Teshika *et al.*, 2019). Steroidal saponins, bioactive substances with antibacterial, antifungal, anti-inflammatory, cholesterol-lowering and perhaps anticancer activities through membrane contact and apoptosis induction pathways, are also found in onion (Iwar *et al.*, 2024). Furthermore, through antioxidant and anti-inflammatory processes, flavonoid-rich onion phytochemicals work in concert to improve this compound therapeutic potential (Kothari *et al.*, 2020). *A. cepa*, nutraceutical and therapeutic potential as a functional medicinal food is greatly raised when FOS and saponins are combined (Gorrepati *et al.*, 2024).

3. Molecular targets and mechanistic pharmacology

3.1 Oxidative stress signalling

Bioactive components of onion including as quercetin, fisetin, cepaenes and sulfur-containing compounds, modulate oxidative stress signalling pathways to provide potent antioxidant effects. These phytochemicals improve endogenous antioxidant enzymes including superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase while neutralizing reactive oxygen species (ROS) and lowering lipid peroxidation (Marefati *et al.*, 2021). Additionally, onion-derived chemicals protect cells from oxidative damage and mitochondrial dysfunction linked to chronic illnesses by regulating redox-sensitive signalling pathways such as Nrf2 (Nuclear factor erythroid 2-related factor 2), ERK (extracellular signal-regulated kinase) and MAPK (mitogen-activated protein kinase) (Dorrigiv *et al.*, 2021).

Table 2: Therapeutic applications of *A. cepa* phytochemicals and their molecular mechanisms

Therapeutic application	Major onion phytochemicals	Mechanism of action	Reported biological effects	References
Antioxidant activity	Quercetin, anthocyanins, phenolic acids and sulfur compounds	Scavenging ROS, enhancing antioxidant enzymes (SOD, CAT, GPx)	Reduction of oxidative stress and cellular damage	Marefati <i>et al.</i> , 2021; Dorrigiv <i>et al.</i> , 2021
Anti-inflammatory activity	Quercetin, organosulfur compounds and flavonoids	Suppression of inflammatory mediators and cytokines	Reduced inflammation and immune modulation	Boskabady <i>et al.</i> , 2021; Marefati <i>et al.</i> , 2021
Anticancer activity	Quercetin, diallyl disulfide, anthocyanins and phenolic acids	Inhibition of tumour growth and signalling	Antiproliferative and chemo preventive effects	Zhao <i>et al.</i> , 2021; Gupta <i>et al.</i> , 2025
Cell cycle arrest	Quercetin and sulfur compounds	Arrest at G1/S and G2/M phases	Suppression of uncontrolled cancer cell proliferation	Gupta <i>et al.</i> , 2025
Apoptosis induction	Quercetin and organosulfur compounds	Activation of intrinsic apoptotic pathways	Programmed cancer cell death	Dorrigiv <i>et al.</i> , 2021
Antiangiogenic activity	Flavonoids and sulfur compounds	Inhibition of neovascularization	Reduced tumour blood supply and growth	Zhao <i>et al.</i> , 2021
Antimetastatic activity	Quercetin and flavonoids	Inhibition of migration and invasion	Suppression of metastasis	Zhao <i>et al.</i> , 2021
Metabolic regulation	Quercetin, fructooligosaccharides and sulfur compounds	Improvement of glucose and lipid metabolism	Antidiabetic and anti-obesity effects	Gupta <i>et al.</i> , 2025; Zhao <i>et al.</i> , 2021
Neuroprotective activity	Quercetin, phenolic acids and anthocyanins	Reduction of neuroinflammation and oxidative injury	Protection against neuro-degeneration	Dorrigiv <i>et al.</i> , 2021
Gut health and prebiotic effects	Fructooligosaccharides (FOS)	Promotion of beneficial bacteria and SCFA production	Improved gut health and immunity	Zhao <i>et al.</i> , 2021
Synergistic chemotherapeutic effects	Quercetin and sulfur compounds	Sensitization of tumor cells to chemotherapy	Enhanced efficacy and reduced toxicity	Gupta <i>et al.</i> , 2025; Dorrigiv <i>et al.</i> , 2021

3.2 Pathways of inflammatory signalling

By inhibiting important inflammatory mediators and signalling pathways, onion phytochemicals have significant anti-inflammatory effect (Table 2). Inflammatory cytokines including TNF- α , IL-1 β , IL-6 and prostaglandin E2 are produced less often when quercetin and organosulfur compounds block NF- κ B activation, cyclooxygenase (COX), lipoxygenase (LOX), STAT-1, JNK and p38 MAPK pathways (Marefati *et al.*, 2021). Onion bioactives also lessen oxidative inflammatory responses and leukocyte chemotaxis which helps prevent immunological dysregulation and chronic inflammatory diseases (Boskabady *et al.*, 2022).

3.3 Cancer signalling and apoptosis

Onion contains bioactive chemicals that control a number of biological processes related to cancer proliferation, survival and death. Diallyl disulfide, quercetin and similar sulfur compounds decrease proliferative pathways including Wnt/ β -catenin, PI3K/Akt and MAPK signalling while modulating apoptotic proteins like Bax, Bcl-2, caspases and p53 (Dorrigiv *et al.*, 2021). In several cancer cell types, these pathways suppress tumour development and encourage programmed cell death. The chemo preventive potential of onion phytochemicals is highlighted by their interference with oxidative and inflammatory pathways linked to carcinogenesis (Zhao *et al.*, 2021).

3.4 Regulation of metabolism

Phytochemicals of onion influence insulin sensitivity, lipid homeostasis and glucose metabolism, all of which contribute to metabolic control. By controlling AMP-activated protein kinase (AMPK), lowering oxidative stress and inhibiting inflammatory mediators linked to obesity and metabolic syndrome, onion flavonoids and sulfur-containing substances enhance metabolic balance (Gupta *et al.*, 2025). Additionally, onion polysaccharides and fructooligosaccharides promote the formation of short-chain fatty acids and the makeup of the gut microbiota, which improves immunological control and metabolic health (Zhao *et al.*, 2021).

3.5 Mechanisms of neuroprotection

The neuroprotective properties of onion phytochemicals are mainly due to their anti-inflammatory and antioxidant properties. By lowering ROS production, maintaining mitochondrial function and inhibiting neuroinflammatory mediators such NF- κ B and pro-inflammatory cytokines, quercetin and other flavonoids shield neuronal cells from oxidative injury (Dorrigiv *et al.*, 2021). Furthermore, these substances may alter signalling pathways related to cognitive function and neuronal survival, lowering the risk of neurodegenerative illnesses including Parkinson's and Alzheimer's (Gupta *et al.*, 2025).

4. Nanoformulations of onion phytochemicals

Since several beneficial components, like quercetin and organosulfur compounds, show poor solubility, instability and limited bioavailability under physiological settings, nanoformulations of onion phytochemicals are chosen over traditional formulations. In addition to lowering degradation and enhancing pharmacological performance, nanoencapsulation improves their stability, controlled release, cellular absorption and targeted therapeutic efficacy.

4.1 Liposomes

Liposomes are phospholipid-based vesicular nanocarriers that have been extensively studied to enhance the transport of phytochemicals produced from onion, including quercetin, anthocyanins and compounds containing sulfur. Liposomal encapsulation increases the stability of onion bioactive, shields them from oxidation and enzymatic destruction and improves gastrointestinal absorption because many of them have weak water solubility and restricted membrane permeability. Liposomes can improve pharmacokinetic behaviour and controlled release by encasing hydrophilic and lipophilic substances in lipid bilayers with aqueous cores. According to previous studies (Akbarzadeh *et al.*, 2013; Mozafari *et al.*, 2008), liposomal administration dramatically boosts cellular absorption and therapeutic efficiency of flavonoids while lowering systemic toxicity and degradation throughout circulation.

4.2 Phytosomes

Phytochemicals create molecular complexes with phospholipids in phytosomes, which are advanced phospholipid-complex delivery systems that enhance membrane transport and lipid solubility. When added to phytosomal preparations, onion flavonoids like quercetin show improved oral bioavailability and extended systemic circulation. Better gastrointestinal absorption is made possible by the phospholipid association, which also shields phytochemicals from metabolic and enzymatic breakdown. Therefore, phytosomes have garnered a lot of interest for enhancing the therapeutic efficacy of plant-derived anti-inflammatory and antioxidant chemicals with otherwise inadequate pharmacokinetic characteristics (Semalty *et al.*, 2010; Rasaie *et al.*, 2014).

4.3 Nanoparticles made of polymers

Onion phytochemicals are delivered in a sustained and targeted approach via polymeric nanoparticles made of biodegradable polymers as PLGA, chitosan and alginate. These nanoparticles permit regulated release of encapsulated chemicals, increase medication stability and extend circulation time. Through the increased permeability and retention (EPR) effect, polymeric nanoparticles promote tumour accumulation in cancer treatment, raising therapeutic concentrations at pathological locations while reducing systemic toxicity. Due to increased cellular absorption and prolonged intracellular release, quercetin-loaded polymeric nanoparticles have shown better antioxidant, anticancer and anti-inflammatory properties than free quercetin (Kumari *et al.*, 2010; Pool *et al.*, 2012).

4.4 Nanoemulsions

The purpose of nanoemulsions is to improve the solubility and absorption of hydrophobic phytochemicals by creating nanosized oil-in-water or water-in-oil dispersions. Because of their incredibly small droplet size and huge surface area, onion-derived flavonoids and sulfur compounds produced as nanoemulsions show better dispersion, greater intestinal permeability and enhanced bioavailability. Furthermore, nanoemulsion technologies promote quick cellular uptake and increase formulation stability. For nutraceutical and pharmaceutical applications requiring poorly soluble plant-derived bioactive chemicals, these formulations are being investigated in as many ways (Gupta *et al.*, 2016; McClements, 2012).

4.5 Nanoparticles of solid lipids

Physiologically compatible solid lipids are used to create solid lipid nanoparticles (SLNs), which are lipid-based nanocarriers that stay solid at body temperature and room temperature. SLNs allow for continuous and regulated medication release while successfully shielding onion phytochemicals from oxidation, hydrolysis and chemical degradation. These nanocarriers are appropriate for medicinal delivery systems because of their great physical stability, superior biocompatibility and minimal toxicity. Flavonoid encapsulation in SLNs greatly extends the shelf-life, bioavailability and therapeutic stability of phytochemicals that are vulnerable to environmental deterioration (Muller *et al.*, 2000; Mehnert and Mader, 2001).

4.6 Lipid carriers using nanostructures

Second-generation lipid nanocarriers made of a combination of liquid and solid lipids are called nanostructured lipid carriers (NLCs). Because to their flawed lipid matrix structure, NLCs have better drug-loading capacity and less drug leakage than SLNs. NLCs can effectively encapsulate onion phytochemicals such as anthocyanins and sulfur-containing compounds, enhancing stability, controlled release and systemic bioavailability. Because they reduce drug ejection caused by crystallization and improve long-term formulation stability, NLCs are especially beneficial for unstable phytochemicals (Pardeike *et al.*, 2009; Naseri *et al.*, 2015).

4.7 Extracellular vesicles derived from plants

Extracellular vesicles formed from plants are naturally occurring nanoscale vesicles that may transfer proteins, lipids, RNAs and phytochemicals throughout biological systems. Extracellular vesicles generated from onion are a viable option for precision phytomedicine because of their inherent biocompatibility, minimal immunogenicity and natural medicinal payload. These vesicles shield their contents from enzymatic destruction while delivering therapeutic compounds straight into inflammatory tissues and tumour microenvironments by overcoming biological barriers. According to recent research, plant-derived vesicles might serve as effective and safe natural nanocarriers for applications in regenerative medicine and targeted drug delivery (Mu *et al.*, 2014; Zhuang *et al.*, 2015).

5. Precision phytomedicine with onion-derived nanovesicles

5.1 Cellular uptake mechanisms

Numerous internalization routes, including as endocytosis, membrane fusion, micropinocytosis and receptor-mediated uptake, enabling onion-derived nanovesicles to enter target cells. Their nanoscale size improves intracellular transport efficiency and makes it easier to pass through biological membranes. These vesicles improve therapeutic concentrations at diseased locations by releasing encapsulated phytochemicals into the cytoplasm after internalization. Additionally, sensitive bioactive chemicals are shielded from premature degradation in extracellular environments and digestive systems *via* nanovesicle-mediated transport. According to new research, plant-derived vesicles can assist targeted therapeutic applications by interacting selectively with immune cells, inflammatory tissues and tumour microenvironments (Woith *et al.*, 2019; Teng *et al.*, 2018).

5.2 Precise therapeutics

To increase the specificity and effectiveness of onion phytochemicals, precision phytomedicine combines nanotechnology with customized delivery methods. While reducing systemic exposure and toxicity, functionalized nanoparticles and extracellular vesicles can collect specifically in fatigued tissues such as tumours inflammatory organs and neurodegenerative diseases. Additionally, prolonged therapeutic administration and customized treatment plans based on disease-specific molecular targets are made possible by controlled release systems. According to Patra *et al.* (2018) and Mitchell *et al.* (2021), precision techniques have the potential to greatly enhance treatment results in cancer, inflammatory illnesses, metabolic disorders and neurological problems while minimizing side effects that are frequently linked to traditional medications.

6. Translational prospects and clinical evidence

6.1 Toxicity and safety

When compared to many manufactured pharmacological drugs, phytochemicals produced from onion often have better safety profiles and are less toxic. By improving targeted distribution and lowering necessary treatment doses, nanoencapsulation techniques might further lessen systemic side effects. However, because nanoparticle composition, size, surface charge and long-term deposition may affect biological interactions and toxicity, thorough toxicological assessments are still necessary. Although, more research on chronic exposure, biodistribution, immunogenicity and nanoparticle clearance is required before widespread clinical application, current evidence suggests that biodegradable lipid and polymeric nanocarriers exhibit comparatively good biocompatibility (Fadeel and Garcia-Bennett, 2010; Ventola, 2017).

6.2 Regulatory issues

The clinical translation of onion-derived nanoformulations confronts significant production and regulatory obstacles despite their great medicinal promise. Before granting permission for medical applications, regulatory bodies need stringent evaluation of nanoparticle size, shape, drug-loading efficiency, stability, repeatability and safety. Inadequate standardization, inconsistent phytochemical composition and a lack of coordinated international regulatory frameworks are other problems for herbal nanomedicines. To enable the commercialization and therapeutic application of onion-based nanophytomedicines, there are still many obstacles that need to be overcome, including large-scale manufacturing, quality control, long-term safety evaluation and clinical validation (Ehmann *et al.*, 2013; Halamoda-Kenzaoui *et al.*, 2019).

7. Pharmacological uses of onion

7.1 Antioxidant activity

Bioactive substances with potent antioxidant qualities including quercetin, anthocyanins, phenolic acids and organosulfur compounds are abundant in onion. The activity of endogenous antioxidant enzymes such as glutathione peroxidase (GPx), catalase (CAT) and superoxide dismutase (SOD) is increased by these phytochemicals. They prevent oxidative damage to cellular proteins, lipids and DNA by scavenging reactive oxygen species (ROS) and lowering lipid peroxidation. Red onion often has stronger antioxidant activity due to their high anthocyanin and flavonoid content. The

nuclear factor erythroid 2-related factor 2 (Nrf2) signalling pathway, which controls the production of genes dependent on the antioxidant response element (ARE), may be triggered by onion phytochemicals. By increasing the production of phase II detoxifying enzymes including glutathione S-transferase (GST) and hemeoxygenase-1 (HO-1), activation of this pathway strengthens the cellular defence system. Onion phenolic compounds have the ability to chelate transition metal ions like copper and iron that lowers the production of very reactive hydroxyl radicals through Fenton reactions. The antioxidant defence capability of onion is further strengthened by these coupled methods (Marefati *et al.*, 2021; Dorigiv *et al.*, 2021).

7.2 Anti-inflammatory activity

Quercetin, flavonoids and sulfur containing compounds found in onion all have significant anti-inflammatory effects. These compounds decrease pro-inflammatory cytokines such as interleukin-6 (IL-6), interleukin-1 β (IL-1 β) and tumour necrosis factor- α (TNF- α). onion phytochemicals lower chronic inflammation and modify immune responses by blocking inflammatory pathways including nuclear factor-kappa B (NF- κ B) and cyclooxygenase (COX). Flavonoids produced by onion may decrease excessive nitric oxide (NO) generation during inflammatory reactions and inhibit the activity of inducible nitric oxide synthase (iNOS). It has also been shown that organosulfur compounds prevent the formation of inflammatory leukotrienes *via* lipoxygenase (LOX). Onion phytochemicals could decrease tissue damage linked to chronic inflammatory conditions including arthritis, asthma and cardiovascular illnesses by reducing oxidative stress-induced inflammation and modulating macrophage activation (Boskabady *et al.*, 2021; Marefati *et al.*, 2021).

7.3 Anticancer activity

Onion phytochemicals accompanied by powerful anticancer potential include quercetin, anthocyanins, phenolic acids and diallyl disulfide. These compounds stop tumours from initiation, developing and spreading by changing signalling pathways linked to the development of cancer. Quercetin has been demonstrated to avoid oxidative stress induced DNA damage and limit the growth of a number of cancer cell lines that including cancer cells from the breast, colon and prostate. In addition, organosulfur compounds may decrease the activation of carcinogens and increase the activity of detoxifying enzymes. Onion phytochemicals may disrupt signalling pathways linked to cancer particularly Wnt/ β -catenin, mitogen activated protein kinase (MAPK) and phosphatidylinositol 3-kinase/protein kinase B (PI3K/Akt). These actions lead to an increase in apoptosis and a decrease in the growth of cancer cells. In addition, certain sulfur compounds may cause epigenetic alterations especially DNA methylation and histone acetylation can control the expression of tumour suppressor genes. Thus, eating onion has been linked to a lower risk of certain gastrointestinal and hormone-related malignancies (Zhao *et al.*, 2021; Gupta *et al.*, 2025).

7.4 Antiangiogenic and antimetastatic activity

Onion includes sulfur compounds and flavonoids that prevent angiogenesis, tumour cell invasion and migration. Quercetin inhibits the production of vascular endothelial growth factor (VEGF) which restricts the development of new blood vessels necessary for the growth of tumours. Additionally, matrix metalloproteinases (MMPs) which are specialized enzymes implicated in cancer cell invasion and metastasis are interfered with the onion phytochemicals.

These steps contribute to preventing tumours from spreading to other tissues. Onion phytochemicals may prevent the epithelial-mesenchymal transition (EMT), a critical stage in tumour metastasis. Quercetin has been found to regulate adhesion molecules such as E-cadherin and N-cadherin, which reduces the invasiveness of cancer cells. Certain sulfur compounds may also suppress hypoxia inducible factor-1 alpha (HIF-1 α) noted as crucial for angiogenic signalling and tumour adaptation to hypoxic environments. These techniques significantly increase the antimetastatic potential of onion (Zhao *et al.*, 2021).

7.5 Antidiabetic and anti-obesity effects

Quercetin, fructooligosaccharides (FOS) and sulfur compounds found in onion can promote improved metabolic health. These compounds enhance insulin sensitivity, regulate carbohydrate metabolism and reduce postprandial blood glucose levels. Onion phytochemicals may also inhibit fat accumulation, reduce blood triglyceride and cholesterol levels and stimulate adipocyte metabolism. Prebiotics and dietary fibre from onion additionally assist in making regulate weight and metabolism. Onion extracts may decrease the intestinal absorption of glucose and the digestion of carbohydrates by inhibiting digestive enzymes including α -amylase and α -glucosidase. Adenosine monophosphate activated protein kinase (AMPK), which is essential for the absorption of glucose and the oxidation of fatty acids, may be triggered by quercetin. Prebiotic components of onion also help to alter the composition of the gut microbiota, which has been connected to improved energy balance, decreased systemic inflammation and improved insulin signalling (Gupta *et al.*, 2025; Zhao *et al.*, 2021).

7.6 Antimicrobial activity

Sulfur-containing chemicals and onion extracts have antibacterial properties against a variety of bacteria, fungi and viruses. *Escherichia coli*, *Staphylococcus aureus* and *Candida* species are among the harmful bacteria whose growth can be inhibited by substances like thiosulfates. Antibacterial properties have been associated with microbial cell membrane rupture and microbial enzyme system suppression in onion. Onion phytochemicals may interfere with the formation of microbial biofilms, a critical pathogenicity mechanism in many pathogenic bacteria. Organosulfur chemicals change membrane permeability and disturb microbial energy metabolism results in impede microbial growth and cause internal components to filter out. Also, certain onion flavonoids can enhance the therapeutic efficacy of conventional antibacterial medications against resistant microbial strains (Zhao *et al.*, 2021).

7.7 Prebiotic, gut health benefits and chemosensitization

Onion contain fructooligosaccharides (FOS), which work as prebiotics by promoting the growth of good gut bacteria like *Lactobacillus* and *Bifidobacterium*. Short-chain fatty acids (SCFAs), which enhance intestinal integrity, nutritional absorption and immunological function, are produced when the gut microbiota ferments FOS. Improved host immunity and gastrointestinal health are two benefits of these actions (Zhao *et al.*, 2021). Some phytochemicals found in onion, especially sulfur compounds and quercetin, may make tumour cells more susceptible to chemotherapy drugs. When used with chemotherapy, these substances can increase apoptosis, decrease multidrug resistance and improve drug absorption. In addition to possibly lowering the dose and toxicity of anticancer medications, these chemosensitizing effects may improve treatment

effectiveness. The SCF like butyrate that is produced during the fermentation of onion FOS, provides colonocytes with energy and supports intestinal barrier function. Prebiotics from onion may also improve mucosal immunity and control gut-associated lymphoid tissue (GALT). In terms of chemosensitization, quercetin has been shown to increase intracellular accumulation of chemotherapeutic medicines in resistant cancer cells by inhibiting efflux transporters like P-glycoprotein. Improved response to anticancer treatments may be a result of these effects (Gupta *et al.*, 2025; Dorriv *et al.*, 2021).

7.8 Neuroprotective and cardioprotective activity

Onion phytochemicals improve cardiovascular health through lipid-lowering, anti-inflammatory and antioxidant qualities. It has been demonstrated that quercetin improves endothelial function, lowers blood pressure and stops platelet aggregation. Sulfur-containing compounds may reduce the risk of atherosclerosis by reducing the oxidation of low-density lipoprotein (LDL). Thus, frequent consumption of onion has been associated with improved cardiovascular protection (Marefati *et al.*, 2021). Quercetin, anthocyanins and phenolic acids have neuroprotective properties because they reduce oxidative stress and neuroinflammation in brain tissues. These compounds may protect neurons from damage caused by reactive oxygen species and inflammatory mediators. Onion phytochemicals have been shown to decrease the progression of neurodegenerative illnesses such as Parkinson's and Alzheimer's by improving neuronal survival and cognitive function (Dorriv *et al.*, 2021).

7.9 Regulation of apoptosis and the cell cycle

Quercetin and organosulfur compounds regulate the cancer cell cycle and prevent unregulated cell growth by halting cells at the G1/S and G2/M stages. Furthermore, these compounds initiate intrinsic apoptotic pathways that cause cytochrome-c release, caspase activation and mitochondrial dysfunction, all of which lead to programmed cancer cell death. Furthermore, onion phytochemicals may downregulate anti-apoptotic proteins like Bcl-2 while promoting pro-apoptotic proteins like Bax. The expression of cyclins and cyclin dependent kinases (CDKs) are essential regulators of cell cycle progression may be influenced by onion phytochemicals. Quercetin has been linked to the activation of tumour suppressor proteins including p53, which enhances apoptosis and the DNA damage response. Apoptotic signalling pathways may be further strengthened by reactive oxygen species-mediated mitochondrial depolarization carried on by sulfur compounds. The control of abnormal cell proliferation and tumour growth is facilitated by these interrelated processes (Dorriv *et al.*, 2021; Gupta *et al.*, 2025).

8. Prospects for the future

Designing highly targeted onion phytochemical nanoformulations with improved stability, bioavailability, tissue specificity and therapeutic accuracy should be the main goal of future research. Precision phytomedicine employing bioactive chemicals produced from onion might be revolutionized by integrating nanotechnology with omics technologies, artificial intelligence, molecular diagnostics and customized therapy. While reducing systemic toxicity, advanced extracellular vesicles, multifunctional nanoparticles and stimuli-responsive delivery methods may allow for the specific targeting of cancer cells, inflammatory tissues and neurodegenerative diseases.

To enable the clinical translation and commercialization of onion-based therapeutic nanoplatforms, more research on pharmacokinetics, biodistribution, toxicity and large-scale production is necessary.

9. Conclusion

Bioactive phytochemicals with antioxidant, anti-inflammatory, anticancer, antibacterial, cardioprotective and neuroprotective properties are abundant in *A. cepa*. However, poor water solubility, chemical instability, fast metabolism, low bioavailability and insufficient tissue targeting restrict the traditional medicinal use of onion phytochemicals. Promising ways to get beyond these pharmacokinetic and therapeutic restrictions include liposomes, phytosomes, polymeric nanoparticles, nanoemulsions and plant-derived extracellular vesicles. These advanced nanoformulations allow for the precise delivery of onion bioactive chemicals to sick tissues while also increasing stability, bioavailability and circulation time. It is anticipated that further developments in nanotechnology, precision medicine and phytopharmaceutical research would expedite the clinical translation of treatments derived from onion and position onion phytochemicals as significant competitors for next pharmaceutical and nutraceutical uses.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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