#### Check for updates

#### **OPEN ACCESS**

EDITED BY Dunja Miletić, University of Belgrade, Serbia

REVIEWED BY Ilinka Pećinar, University of Belgrade, Serbia Gabriele Carullo, University of Siena, Italy

\*CORRESPONDENCE Kalyani Gorrepati kalyanigorrepati@gmail.com P.S. Soumia soumiaps@gmail.com

RECEIVED 18 September 2024 ACCEPTED 31 October 2024 PUBLISHED 14 November 2024

#### CITATION

Gorrepati K, Krishna R, Singh S, Shirsat DV, Soumia PS and Mahajan V (2024) Harnessing the nutraceutical and therapeutic potential of *Allium* spp.: current insights and future directions. *Front. Nutr.* 11:1497953.

doi: 10.3389/fnut.2024.1497953

#### COPYRIGHT

© 2024 Gorrepati, Krishna, Singh, Shirsat, Soumia and Mahajan. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

# Harnessing the nutraceutical and therapeutic potential of *Allium* spp.: current insights and future directions

# Kalyani Gorrepati<sup>1</sup>\*, Ram Krishna<sup>2</sup>, Saurabh Singh<sup>3</sup>, Dhananjay V. Shirsat<sup>1</sup>, P.S. Soumia<sup>1</sup>\* and Vijay Mahajan<sup>1</sup>

<sup>1</sup>ICAR-Directorate of Onion and Garlic Research, Rajgurunagar, Pune, India, <sup>2</sup>ICAR-Indian Institute of Vegetable Research, Varanasi, India, <sup>3</sup>Institute of Environment and Sustainable Development, Banaras Hindu University, Varanasi, India

Apart from the culinary usage, Alliums are known for their therapeutic potential since antiguity. Alliums contain diverse bioactive compounds such as, sulfur-containing compounds (allicin, diallyl sulfides), flavonoids, and saponins. These compounds have demonstrated a wide range of pharmacological actions, including antioxidant, anticancer, anti-inflammatory, antimicrobial, neuroprotective, cardioprotective activities and treatment of metabolic disorders such as diabetes and hyperlipidemia. Despite encouraging preclinical results, translating these findings into clinical practice remains difficult, necessitating more rigorous human trials and molecular research. One of the major constrain in enhancing the therapeutic efficacy of these bioactive compound is to develop large-scale extraction techniques besides improving their stability, solubility, and bioavailability. The current scenario urges to focus research on optimizing the bioavailability of these compounds, evaluate their synergistic effects with existing therapies, as well as their long-term safety. This perspective article provides a comprehensive overview of the therapeutic potential of Allium spp. and suggests the key avenues for future research aiming at realising their full clinical potential.

#### KEYWORDS

Allium, bioactive compounds, health benefits, nutraceuticals, therapeutic properties

# Introduction

Alliums are well-known for their diverse medicinal and therapeutic properties and have been a part of various medicinal systems for centuries. The genus Allium belongs to the family Amaryllidaceae of the order Asparagales. More than 920 species have been reported in the Allium genus, of which garlic (*Allium sativum*), onion (*A. cepa and A. cepa var. aggregatum*), leek (*A. ampeloprasum*), chive (*A. schoenoprasum*), Welsh onion (*A. fistulosum*), and shallot (*A. ascalonicum*), being some well-known and widely cultivated species (1). Various parts of allium plant (i.e., leaves, flowers, pseudostem, bulb, and seeds) are consumed in different forms due to their versatility. The characteristic taste and smell of these species is attributed to certain bioactive compounds, including organosulfurs (allicin, diallyl disulfide), flavonoids (quercetin, kaempferol), saponins and other phytochemicals (2–5). Due to these versatile bioactive compounds, the consumption of Allium species has been associated to numerous health benefits, such as cardiovascular benefits, gastrointestinal health, antimicrobial and antiviral properties, anticancer potential, anti-inflammatory and antioxidant effect etc.

Globally, onion and garlic are the highly valued allium crops for the unique aroma and pungency. Beyond enhancing the flavour and taste, they act as functional foods with

significant health benefits. Nevertheless, the demand for these crops are often unmet due to several factors. This urges for the need of an alternative source that provide nutritional diversity without compromising the taste and flavour. In addition, leeks and Welsh onions are utilized extensively in some parts of western and Asian countries. Therefore, as an alternative to the onion and garlic, underutilized alliums such as Allium tuberosum, Allium fragrance, and Allium chinense can be incorporated into the daily diet. Furthermore, these plants are ideal for kitchen gardens or small pots due to the ease in cultivation, require minimal space and low maintenance, making them perfect for nuclear families. These crops can be regenerated from their stubbles, as they only need to be planted once for ongoing harvests. Furthermore, Alliums are low in calories and rich in essential nutrients such as vitamins (such as vitamin C and B vitamins), minerals (such as potassium and selenium), and dietary fibers which play a pivotal role in enhancing the nutritional quality of diets besides their therapeutic properties. Due to their importance as a staple in both diet and medicine, reinforcing the proverb, "Let food be thy medicine and medicine be thy food." With the advent of various technological advancements, the important bioactive compounds from these allium species have also been extracted, encapsulated and consumed as supplements for preventing and treating various lifestyle diseases. Despite the numerous health benefits of Allium species, there are some concerns regarding the stability, dosage, bioavailability and synergistic effect with other compounds. In this, we have tried to comprehend the information related to bioactive compounds and their diverse medicinal and therapeutic benefits.

# Bioactive compounds in Allium species

Allium spp. contain several bioactive compounds that exhibit a range of health-promoting properties, including antioxidant, antiinflammatory, antimicrobial, and anticancer activities (Table 1). Among the various Allium spp., garlic is rich in vitamins, enzymes, organosulfur compounds (OSCs), phenolic compounds etc. OSCs like allicin in garlic, and thiosulfinates (isoalliin) in onions, are associated with anticancer, cardiovascular, and antimicrobial effects (6, 7). Likewise, phenolic compounds such as flavonoids are abundant in Allium spp. Quercetin in onions is associated with antioxidant, antiobesity, anti-cancer, and cardiovascular benefits (8, 9). Alliums are also rich in non-structural carbohydrates like Fructans which acts as a prebiotics. For instance, onion contain 2.8% of fructooligosaccharides (FOS) whereas garlic contains 1.0% FOS (10). FOS aid in improving the gut health and enhancing mineral absorption, thereby supporting bone health and reducing atherosclerosis (11). Furthermore, garlic and onion are rich in minerals such as selenium (Se) that acts as a cofactor for various antioxidant enzymes (12). Although A. tuberosum has higher antioxidant activity in compared to A. sativum (13), it also protects against CCl4 induced liver injury (14). Meanwhile, consuming leek (A. ampeloprasum) can help reduce the risks of hypercholesterolemia, high blood pressure, arteriosclerosis, and platelet aggregation there by preventing cardiovascular diseases (15). Similarly, Alliums are rich in vitamins such as Vitamin C, K, B12 etc., which enhances the immune system (16).

# Health benefits of Allium species

Several health benefits of *Allium* spp., including cardiovascular health, enhance immune function, and reduce the risk of cancer has been well documented in various research. Besides, they also help decrease cholesterol, regulate blood pressure, and have antidiabetic qualities. All these are attributed to their antioxidant, antiinflammatory, and antimicrobial properties. The details of the bioactive and their mode of action is described below (Table 1 and Figure 1).

## Prevention of cardiovascular disease (CVD)

Cardiovascular disease (CVD) is the leading global cause of morbidity and mortality, responsible for 32% of global deaths (17). It is primarily caused by the atherosclerotic plaques or thrombi blocking coronary arteries, as a result of oxidative modification of low-density lipoprotein (LDL) by reactive oxygen species (ROS) contributing to the progression of atherosclerosis (18). Plaque formation constricts the blood vessels the deposition of cholesterol, lipids, and lipoproteins, which can either block arteries or break off and restrict blood flow elsewhere. Besides, increased plasma fibrinogen and platelet aggregation promote thrombus formation, consequently narrowing arteries and causing CVD (19).

Still, CVD can be effectively managed through addressing the major factors such as aberrant cholesterol levels, hypertension, platelet aggregation, and oxidative stress (18). Garlic and onion consumption has been linked to reduce lipid and cholesterol levels (20). Garlic is especially noted for its cardiovascular benefits, such as reducing blood pressure, preventing atherosclerosis, lowering cholesterol and triglycerides, inhibiting platelet aggregation, and increasing fibrinolytic activity (21). Key bioactive compounds in Allium spp. such as allicin, flavonoids, and polysulfides in garlic, and quercetin and thiosulfinates in onion contribute to these effects (22, 23). The bioactive compounds in garlic reduces platelet aggregation by inhibiting calcium mobilization (24, 25) and promote fibrinolysis, which aids in dissolution of clots (26). Moreover, these bioactive compounds also scavenges ROS, thereby preventing LDL oxidation (27, 28).

### Anticancerous properties

Globally millions of deaths are reported due to cancer, a complex disease characterized by uncontrolled cell division and the spread of abnormal cells to nearby tissues (29, 30). Asia houses 60% of the global population, and bears nearly half of the global cancer burden (30, 31). Cancer development involves several stages: initiation, promotion, progression, and metastasis (32). The anticancer activity involves multiple cellular mechanisms. Garlic contains allicin, S-allylmercaptocysteine, S-propargyl-L-cysteine, polysulfanes, and other sulfur-based compounds known for their anticancer activity (32–34). Organosulfur compounds, such as allicin, have ability to induce apoptosis (programmed cell death) in cancer cells and inhibit their proliferation. Additionally, the antioxidant properties of the flavonoids help to neutralize

TABLE 1 Medicinal properties of bioactive compounds in Allium spp. along with their mode of action.

Bioactive compound	Plant organ	Medicinal properties	Mode of action	Reference
Onion (Allium cepa)				
Quercetin	Bulb, bulb peel, foliage	Antioxidant, anti-inflammatory, anticancer	Inhibits free radical formation, reduces inflammation markers, induces apoptosis in cancer cells	(104–106)
Sulfur Compounds		Antimicrobial, cardiovascular health, anticancer	Inhibits microbial growth, reduces cholesterol, induces cancer cell death	(102, 107)
Saponins		Antimicrobial, cholesterol-lowering	Disrupts microbial cell membranes, inhibits cholesterol absorption in the intestines	(108, 109)
Flavonoids		Antioxidant, cardioprotective, anticancer	Scavenges free radicals, enhances nitric oxide production, inhibits cancer proliferation	(110–112)
Alk(en)yl Cysteine Sulfoxides		Antioxidant, antihypertensive, antiplatelet	Reduces oxidative stress, lowers blood pressure, inhibits platelet aggregation	(113, 114)
Garlic (Allium sativum)				
Allicin	Bulb, bulb peel, foliage	Antimicrobial, antioxidant, anti-inflammatory, antitumor	Inhibits bacterial enzyme activity, reduces oxidative stress, modulates inflammatory pathways	(115–118)
Ajoene		Antimicrobial, anticoagulant	Inhibits platelet aggregation, has antifungal properties	(116, 119, 120)
Sulfur Compounds (Diallyl Disulfide, Diallyl		Anti-cancer, Antioxidant, anti-inflammatory,	Lowers cholesterol and blood pressure level, has anti-	(121–123)
Sulfide, S-Allylcysteine)		cardioprotective, liver protective, neuroprotective	inflammatory and anticancer properties.	
			Induces apoptosis in cancer cells and inhibits tumor	
			growth; neutralizes free radicals.	
Chives (Allium schoenoprasum)				
Allicin	Pseudo stem, foliage	Antimicrobial, anti-inflammatory, antioxidant, cardiovascular benefits	Inhibits bacterial growth, reduces inflammation and oxidative stress.	(124–126)
Quercetin		Antioxidant, anti-inflammatory, antihistamine,	Scavenges free radicals, reduces inflammation, and	(14, 125)
		anticancer, anti-diabetic	inhibits histamine release. Inhibit cancer cell	
			proliferation.	
Leek (Allium ampeloprasum)				
Allicin	Pseudo stem, foliage	Antimicrobial, anti-inflammatory, antioxidant	Inhibits microbial growth by disrupting cellular	(15, 127)
			processes and has anti-inflammatory effects by	
			reducing cytokine production.	
Quercetin		Anti-inflammatory, antioxidant, antihypertensive	Scavenges free radicals and inhibits inflammatory	(128, 129)
			pathways, relaxes blood vessels, reduce blood pressure.	
Sulfides		Cardioprotective, anti-inflammatory	Enhance cardiovascular health by improving lipid	(129, 130)
			profiles and reduce inflammation.	
Flavonoids		Antioxidant, anti-inflammatory, anticancer	Modulate cell signaling pathways, reduce oxidative	(131–133)
			stress, and inhibit cancer cell proliferation.	

(Continued)

10.3389/fnut.2024.1497953

#### TABLE 1 (Continued)

Bioactive compound	Plant organ	Medicinal properties	Mode of action	Reference
Welsh onion (Allium fistulosum)				
Quercetin	Pseudo stem, foliage	Antioxidant, Anti-inflammatory, Anticancer	Scavenges free radicals, inhibits inflammatory	(39, 134–136)
			pathways, induces apoptosis in cancer cells	
Allicin		Antibacterial, Antifungal, Antioxidant	Inhibits microbial enzyme activities, reduces oxidative	(127, 137)
			stress	
Sulfur Compounds		Cardioprotective, Anticancer, Detoxifying	Modulates detoxification enzymes, inhibits tumor	(138, 139)
			growth, protects cardiovascular health	
Flavonoids		Anti-inflammatory, Antioxidant	Reduces inflammation, scavenges reactive oxygen species	(136)



Frontiers in Nutrition

10.3389/fnut.2024.1497953



harmful free radicals and reduce oxidative stress, a contributing factor in cancer development (35). Several in vitro and in vivo studies have been documented the anticancerous properties of garlic (29). At early stages of cancer initiation, the bioactive compounds of garlic act as potent antioxidants by scavenging the ROS, promoting detoxification, and aid in DNA repair. This will reduce oxidative stress and suppress the production of tumorpromoting agents like 12-O-tetradecanoylphorbol-13-acetate (TPA). Activating the p53 pathway, allicin could arrest the cell cycle and death in breast cancer cells (36). Furthermore, allicin suppresses the discomfort in oral cancer through inhibiting pain mediators such as endothelin, IL-8, and TNF- $\alpha$  (37). Additionally, it can also limit proliferation of cancer cells through suppression of telomerase activity in a dose-dependent manner (38). Likewise, bioactive compounds such as onionin A, fisetin, diosgenin, and quercetin in onion, whereas thiosulfinates and tuberoside M in Chinese chives possess anticancer properties (23). The in vitro study on the A. fistulosum and A. sativum extract, shows the inhibition of the human fibroblasts and keratinocyte growth. This suggests a potential role of these extracts in cancer treatment as they exhibit anti proliferative effects on cancer cells (39).

## Antidiabetic effect

Diabetes mellitus (DM) is a serious global health concern during this modern era, with a projected 325 million cases by 2025 (40). Diabetes is classified into two types: Type 1, an autoimmune disorder in which the pancreas produces little or no insulin, and Type 2, which is characterized by insulin resistance and/or impaired insulin secretion. Predominantly, Type 2 diabetes prevails in 90-95% of the cases reported whereas only 5-10% in Type 1 diabetes. In most cases, it is the children and young adults who are affected than old generation (41). This scenario is due to the sedentary lifestyle, calorie rich foods, obesity, and longer life spans. Hyperglycemia in diabetes is caused by abnormalities in insulin secretion (42), which could be managed effectively through proper diet and enzyme inhibition (43, 44). Alliums especially onion and garlic, have been reported to suppress Type 2 diabetes (45, 46). Functional compounds such as S-methyl L-cysteine, S-allyl cysteine, and diallyl disulphide of garlic while S-methylcysteine and flavonoids of onion possess antidiabetic activities (23). Moreover, polyphenols (allicin) in garlic exhibit both antioxidant and antidiabetic properties, and mimic insulin in glucose metabolism (47). Also, garlic extracts have shown effectiveness in reducing insulin resistance (48). Previous reports suggests that both onion and garlic can inhibit carbohydratemetabolizing enzymes which results in decreased hyperglycemia in diabetic model animals (49, 50). The butanol fraction of the A. tuberosum leaf extract demonstrated significant antidiabetic activity in the alloxan treated mice (14). However the bioactive compounds responsible for this activity remain unidentified, and further research is needed to isolate and characterize these compound. Nevertheless, Quercetin found in onion play a crucial role in inhibiting  $\alpha$ -glucosidase and enhancing insulin action, along with rutin (51, 52). Besides, sulfur compounds in Allium spp. act as free radical scavengers and stimulate insulin secretion (53).



## Osteoporosis (OP)

Osteoporosis (OP) is a hidden, dangerous disease induced by lifestyle choices, resulting in fatal or disabling fractures. One in three women, and one in every 12 males are affected by OP. Among women, 50% over the age of 45, and 90% over the age of 75 are vulnerable. The primary cause include low bone mineral density (BMD) (54), oxidative stress from an imbalance between reactive ROS and antioxidants (55), and an imbalance between osteoclasts osteoblasts due to estrogen deficiency and inflammation, marked by increased pro-inflammatory cytokines like  $TNF\alpha$  and T-cell expression of RANKL (56, 57). Flavonoids, particularly quercetin, and sulfur compounds found in Allium species, have been shown to help reduce osteoporosis. Matheson et al. (58) reported that women who frequently consume onion may lower their risk of hip fractures by over 20% compared to non-consumers. Several preclinical studies have suggested that consumption of onion prevents bone resorption and osteoclast differentiation, hence maintaining normal BMD (59, 60). Quercetin, a phytoestrogen is a potent natural osteogenic agent due to its anti-inflammatory, antioxidant and estrogen-like actions (61-63). It also promotes osteoclast apoptosis and has anti-cancer, anti-depression, and antiviral effects (64, 65). Studies also demonstrate quercetin and its derivatives.

### Antimicrobial, antiviral and anti-inflammatory properties

Antimicrobial and antiviral properties of various *Allium* spp., is attributed to their sulfur rich compounds such as allicin, ajoene, and thiosulfinates. These compounds have exhibited efficacy against a wide

range of bacteria, including Escherichia coli, Enterococcus faecalis, Staphylococcus aureus, Salmonella typhi, Pseudomonas, Proteus, and Helicobacter pylori, as well as viruses like Influenza (A and B viruses), Rhinovirus and Herpes simplex virus (HSV-1 and HSV-2) (66-71). Quercetin in onion is found to be effective against various bacterial and viral infections. Recent studies highlight that allicin disrupts microbial cell walls and inhibits viral replication by targeting essential enzymes. Since the COVID-19 pandemic, there has been interest in the antiviral effects of Allium spp. against SARS-CoV-2, the virus responsible for COVID-19 (72). Nevertheless, there is no conclusive evidence that bioactive compounds in garlic inhibit viral proliferation or boost immune response. Therefore, rigorous clinical trials are required to validate these results (73, 74). Similarly, ajoene found in Allium spp. possess antifungal properties against various fungi such as Candida albicans, Scopulariopsis spp., and Aspergillus spp. (75). The leaf extract of the A. tuberosum highest antimicrobial activity against Staphylococcus aureus and Bacillus subtilis, compared to A. sativum (13). Additionally, the green leaves of A. fistulosum contains fructans which possesses potent anti-influenza properties inhibiting the replication of the influenza virus (76). Compounds such as A, B and C isolated from A. fistulosum have been found effective against fungal pathogens (77). The A. schoenoprasum exhibited antimicrobial activity against strains of Staphylococcus aureus and Bacillus cereus (78). Moreover, the vitamin C and flavonoids in A. fistulosum play a vital role in mitigating inflammatory responses caused by oxidative stress there by reducing inflammation and enhancing body's defense mechanism (79). The in vivo evaluation using a turpentine oil-induced inflammation model in rats has shown that the Allium schoenoprasum leaf extract of has inhibitory activity on phagocytosis and oxidative stress (80). Furthermore, ongoing research emphasizes the potential of Allium-derived compounds in combating resistant pathogens (Methicillin-resistant *Staphylococcus aureus* [MRSA] and vancomycinresistant *Enterococcus* [VRE]) (81).

#### Neuroprotective effects

Neurological disorders (Alzheimer's, Parkinson's, and brain injuries) are associated with oxidative stress, misfolded proteins, and neuronal loss (82-84). Globally the cases of dementia are expected to hit more 150 million by 2050 (85). Allicin, S-allyl cysteine (SAC), and diallyl disulfide (DADS) in garlic, and quercetin in onion are potent neuroprotective agents. These compounds exhibit antioxidant activities thereby protecting the neurons from oxidative stress, inhibit apoptosis, and reduce inflammation thus preventing neurodegenerative diseases (86). Allicin has the property to enhance cognitive function through restoring neurotransmitter levels, regulating microglial activity and decreasing neuroinflammation (83). Furthermore, in vitro studies on mice with cognitive impairments, demonstrated the potential of quercetin in supporting cognitive health by improving behavior and brain redox activity (87).

## Anti-aging effects

Aging, an inevitable biological process often accompanied by reproductive and regenerative decline (88), with skin aging being particularly complex (89, 90). Bioactive compounds present in Allium species are reported to reduce oxidative stress, inflammation, and improve overall cellular health. Allicin in garlic neutralizes free radicals due to its antioxidant effect and protects skin from damaging thereby reduce premature aging (91, 92). Furthermore, it has the potential to inhibit leukocyte elastase thus act as anti-aging agent (93). Likewise, quercetin in onion scavenges free radicals, reduces UV damage, and promotes DNA repair which results in improved skin health (94). Anthocyanins protect the skin from harmful UV radiations while, FOS boost gut health due to their prebiotic activities that eventually leads to healthy aging (95).

# **Toxicological implications**

Several studies highlight the health benefits of allium and is considered safe for consumption in most individuals. Daily consumption of 1/2-1 onion and 1-2 garlic cloves (2-5g) per day is generally considered safe (96). In most individuals, consumption of alliums at large quantities may not affect their metabolism, however in sensitive individuals can exhibit toxic reactions at high doses. Gastrointestinal symptoms such as nausea, vomiting, and diarrhea is often associated with consumption of garlic at large quantities (97, 98). However, it may also cause allergic reactions and skin irritations rarely (99). Long-term consumption of large amounts of garlic may lead to hematologic effects, including bleeding, as garlic inhibits platelet aggregation due to its sulfur compounds. Though garlic is prescribed clinically in the treatment of some disorders, care should be taken regarding its usage with other medications due to possible drug interactions that might arise as a result. Similarly, onion when consumed at large quantities, result in gastrointestinal discomfort and allergic reactions (100). Like any product, consuming large quantities of Alliums can pose risks. It is imperative to consume fresh Alliums in moderation and adhere to recommended supplement dosages to avoid any unintended reactions.

# Challenges and future directions

Allium species highlights their potential therapeutic benefits, but several gaps remain that require further investigation. Out of approximately 700 Allium species, only about 30 have been extensively studied. Further research is required to fully explore their bioactive compounds, with particular emphasis on developing new drugs and therapies for carcinogenesis, immune-related, and cardiovascular diseases (101). Extensive work has been done on substantiating the health benefit of bioactive compounds such as allicin and quercetin, whereas several other phytochemicals remain underexplored. Most studies focused on their individual effects in preventing and alleviating these lifestyle diseases, however their synergistic action in complex mixtures are not fully understood. Furthermore, low stability and bioavailability of these compounds poses challenges for deciding the recommended dose. Similarly, the precise molecular mechanisms underlying their mode of action remain unclear. It is imperative to gain a deeper understanding of how these compounds are absorbed, metabolized, and excreted in the human body, as well as their precise effects on cellular pathways and gene expression.

Besides the uncertainty in dosage and physiological pathways, extraction of specific bioactive compound and its preservation using modern extraction methods such as steam distillation and solvent extraction poses significant challenge. Technologies like supercritical fluid extraction (SFE), ultrasound-assisted extraction (UAE), and microwave-assisted extraction (MAE), improved the yield and purity of extracted bioactive compound. With the advent of advanced chromatographic techniques like High-performance liquid chromatography (HPLC) and molecular imprinting, the selective isolation of bioactive compounds has become increasingly feasible. These techniques help to identifying and isolating the precise compound from the mixture, contributing to the development of effective drugs for therapeutic interventions. Most bioactive compounds are sensitive to heat, light, and oxygen, leading to degradation during extraction and storage. For instance, allicin is highly unstable and degrades rapidly upon oral consumption due to its interaction with stomach acids (102). Therefore, innovative stabilization methods such as encapsulation is required to safeguard these heat- and oxygen-sensitive bioactive compounds during extraction and storage. Currently, traditional polymers and lipids are used for encapsulation. However, future research should focus on developing novel materials that both are biocompatible and biodegradable, aligning with sustainability goals. Furthermore, enhancing the loading capacity of encapsulation systems and developing target specific controlled-release formulations could maximize therapeutic efficacy while improving bioavailability. Scaling up encapsulation techniques for industrial applications is crucial. Advanced methods such as nanocarriers, coacervation, and electrospinning hold significant promise for achieving large-scale production while preserving the stability and efficacy of bioactive compounds. These approaches offer enhanced efficiency and scalability, ensuring that the encapsulated materials retain their desired properties during processing and storage.

Robust human clinical trials to compare the bioavailability and efficacy of encapsulated versus non-encapsulated forms is crucial for validating their therapeutic potential. Furthermore, while research on *Allium* spp. has demonstrated their health benefits, particularly in cancer and chronic disease management, more studies are needed to investigate their long-term effects and safety, especially in relation to genetic variability and interactions with other medications. Genetic differences and dietary habits among individuals can influence the response to Allium-derived compounds, underscoring the need for personalized health strategies. To fully harness the therapeutic potential of *Allium* spp., it is essential to develop sustainable cultivation practices that ensure a consistent supply of high-quality products. Integrating *Allium* spp. into public health recommendations and dietary guidelines could also promote their use for disease prevention and health promotion.

The increasing interest in Allium supplementation to enhance health benefits requires several factors to be considered like supplementation dose, formulation and delivery, clinical trials, personalized approaches and dietary integration. For instance, in most clinical studies, the daily dose of dehydrated garlic powder has been approximately 900 mg. 1–7.2 g/d of Aged garlic extract (AGE) which contains allicin is often recommended for various health benefits including cardio vascular health. Studies also showing that 1.8–10 g/d of AGE have immune enhancement in humans (103). However, development of bioavailable formulation of Allium supplementation is crucial as Allicin is highly unstable and degrade quickly due to which garlic supplementation often undergoes like aging to preserve its active ingredients. Furthermore, clinical trials to evaluate the side effects of Allium supplements administered for various health conditions is important.

Harnessing the nutraceutical and therapeutic potential of *Allium* spp. also supports several Sustainable Development Goals (SDGs). By offering plant-based treatments for non-communicable diseases like cardiovascular conditions and cancer, they contribute to SDG 3: Good Health and Well-being. As nutrient-rich crops, Allium species can be integrated into food security programs, aligning with SDG 2: Zero Hunger. Their cultivation promotes eco-friendly practices, reducing reliance on synthetic drugs and pesticides, contributing to SDG 12: Responsible Consumption and Production. Additionally, Allium plants require low environmental input, supporting sustainable agriculture and resilience to climate change, which ties into SDG 13: Climate Action. In summary, advancing research on *Allium* spp. requires a multifaceted approach, combining novel extraction and

# References

1. Khandagale K, Krishna R, Roylawar P, Ade AB, Benke A, Shinde B, et al. Omics approaches in Allium research: progress and way ahead. *PeerJ*. (2020) 8:e9824. doi: 10.7717/peerj.9824

2. Diretto G, Rubio-Moraga A, Argandoña J, Castillo P, Gómez-Gómez L, Ahrazem O. Tissue-specific accumulation of sulfur compounds and saponins in different parts of garlic cloves from purple and white ecotypes. *Molecules*. (2017) 22:1359. doi: 10.3390/molecules22081359

3. Gorrepati K, Thangasamy A, Kumar A, Satpute P, Singh M. Biochemical differences between bolted and non-bolted onions. *J Exp Agric Int.* (2020) 30-35:30–5. doi: 10.9734/ JEAI/2020/v42i630534

4. Szychowski KA, Rybczyńska-Tkaczyk K, Gawel-Bęben K, Świeca M, Karaś M, Jakubczyk A, et al. Characterization of active compounds of different garlic (*Allium sativum* L.) cultivars. *Polish J Food Nutr Sci.* (2018) 68:73–81. doi: 10.1515/pjfns-2017-0005

encapsulation methods, detailed molecular studies, and large-scale clinical trials to fully understand and optimize their therapeutic potential.

# Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

# Author contributions

KG: Conceptualization, Writing – original draft, Writing – review & editing. RK: Conceptualization, Writing – original draft, Writing – review & editing. SS: Writing – original draft, Writing – review & editing. DS: Writing – original draft, Writing – review & editing. PS: Conceptualization, Writing – original draft, Writing – review & editing. VM: Writing – original draft, Writing – review & editing.

# Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

# **Conflict of interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

# Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

 Zamri N, Abd Hamid H. Comparative study of Onion (Allium cepa) and Leek (Allium ampeloprasum): identification of Organosulphur compounds by UPLC-QTOF/ MS and anticancer effect on MCF-7 cells. Plant Foods Hum Nutr. (2019) 74:525–30. doi: 10.1007/s11130-019-00770-6

6. Itakura Y, Ichikawa M, Mori Y, Okino R, Udayama M, Morita T. How to distinguish garlic from the other Allium vegetables. *J Nutr.* (2001) 131:9638–7S. doi: 10.1093/jn/131.3.9638

7. Tocmo R, Liang D, Lin Y, Huang D. Chemical and biochemical mechanisms underlying the cardioprotective roles of dietary organopolysulfides. *Front Nutr.* (2015) 2:1. doi: 10.3389/fnut.2015.00001

 Choi IS, Cho EJ, Moon JH, Bae HJ. Onion skin waste as a valorization resource for the by-products quercetin and biosugar. *Food Chem.* (2015) 188:537–42. doi: 10.1016/j. foodchem.2015.05.028 9. Moon J, Do HJ, Kim OY, Shin MJ. Antiobesity effects of quercetin-rich onion peel extract on the differentiation of 3T3-L1 preadipocytes and the adipogenesis in high fat-fed rats. *Food Chem Toxicol.* (2013) 58:347–54. doi: 10.1016/j.fct.2013.05.006

10. Gidado A, Daja A, Kasim Z, Audu MM, Idris A. Free glucose, fructose, sucrose and total fructan contents of some commonly consumed vegetables in Maiduguri Metropolis, North East Nigeria. *Food Sci Qual Manag.* (2018) 80:80–8.

11. Sabater-Molina M, Larqué E, Torrella F, Zamora S. Dietary fructooligosaccharides and potential benefits on health. *J Physiol Biochem*. (2009) 65:315–28. doi: 10.1007/BF03180584

12. Pappa EC, Pappas AC, Surai PF. Selenium content in selected foods from the Greek market and estimation of the daily intake. *Sci Total Environ*. (2006) 372:100–8. doi: 10.1016/j.scitotenv.2006.08.008

13. Khalid N, Ahmed I, Latif MSZ, Rafique T, Fawad SA. Comparison of antimicrobial activity, phytochemical profile and minerals composition of garlic *Allium sativum* and *Allium tuberosum*. *J Korean Soc Appl Biol Chem*. (2014) 57:311–7. doi: 10.1007/s13765-014-4021-4

14. Tang X, Olatunji OJ, Zhou Y, Hou X. Allium tuberosum: antidiabetic and hepatoprotective activities. *Food Res Int.* (2017) 102:681–9. doi: 10.1016/j. foodres.2017.08.034

15. Shelke PA, Rafiq SM, Bhavesh C, Rafiq SI, Swapnil P, Mushtaq R. Leek (*Allium ampeloprasum* L.) In: Eds. Nayik G.A., Gull A. Antioxidants in vegetables and nuts-properties and health benefits. (Singapore: Springer) (2020). 309–31.

16. Adeniyi TT, Ajayi GO, Sado MA, Olopade HJ. Vitamin C and garlic (*Allium sativum*) ameliorate nephrotoxicity and biochemical alterations induced in lead-exposed rats. *J Med Med Sci.* (2012) 3:273–80.

17. Schwingshackl L, Hoffmann G, Buijsse B, Mittag T, Stelmach-Mardas M, Boeing H, et al. Dietary supplements and risk of cause-specific death, cardiovascular disease, and cancer: a protocol for a systematic review and network meta-analysis of primary prevention trials. *Syst Rev.* (2015) 4:34–6. doi: 10.1186/s13643-015-0029-z

18. Santhosha SG, Jamuna P, Prabhavathi SN. Bioactive components of garlic and their physiological role in health maintenance: a review. *Food Biosci.* (2013) 3:59–74. doi: 10.1016/j.fbio.2013.07.001

19. Luc G, Fruchart JC. Oxidation of lipoproteins and atherosclerosis. *Am J Clin Nutr.* (1991) 53:206S–9S. doi: 10.1093/ajcn/53.1.206S

20. Harenberg J, Giese C, Zimmermann R. Effect of dried garlic on blood coagulation, fibrinolysis, platelet aggregation and serum cholesterol levels in patients with hyperlipoproteinemia. *Atherosclerosis.* (1988) 74:247–9. doi: 10.1016/0021-9150(88)90244-4

21. Chan JYY, Yuen ACY, Chan RYK, Chan SW. A review of the cardiovascular benefits and antioxidant properties of allicin. *Phytother Res.* (2013) 27:637–46. doi: 10.1002/ptr.4796

22. Qidwai W, Tabinda A. Role of garlic usage in cardiovascular disease prevention: an evidence-based approach. *Evid Based Complement Alternat Med.* (2013) 2013:1–9. doi: 10.1155/2013/125649

23. Zeng Y, Li Y, Yang J, Pu X, Du J, Yang X, et al. Therapeutic role of functional components in alliums for preventive chronic disease in human being. *Evid Based Complement Alternat Med.* (2017) 2017:9402849. doi: 10.1155/2017/9402849

24. Allison GL, Lowe GM, Rahman K. Aged garlic extract and its constituents inhibit platelet aggregation through multiple mechanisms. *J Nutr.* (2006) 136:782S–8S. doi: 10.1093/jn/136.3.782S

25. Qi R, Liao F, Inoue K, Yatomi Y, Sato K, Ozaki Y. Inhibition by diallyl trisulfide, a garlic component, of intracellular Ca2+ mobilization without affecting inositol-1, 4, 5-trisphosphate (IP3) formation in activated platelets. *Biochem Pharmacol.* (2000) 60:1475–83. doi: 10.1016/S0006-2952(00)00467-6

26. Moriguchi T, Takasugi N, Itakura Y. The effects of aged garlic extract on lipid peroxidation and the deformability of erythrocytes. *J Nutr.* (2001) 131:1016S–9S. doi: 10.1093/jn/131.3.1016S

27. Dillon SA. Aged garlic extract as an antioxidant in cardiovascular disease. (PhD Dissertation). United Kingdom: Liverpool John Moores University (2002).

28. Dillon SA, Burmi RS, Lowe GM, Billington D, Rahman K. Antioxidant properties of aged garlic extract: an in vitro study incorporating human low density lipoprotein. *Life Sci.* (2003) 72:1583–94. doi: 10.1016/S0024-3205(02)02475-X

29. De Greef D, Barton EM, Sandberg EN, Croley CR, Pumarol J, Wong TL, et al. Anticancer potential of garlic and its bioactive constituents: a systematic and comprehensive review In: Theresa Vincent T. (eds) Seminars in cancer biology, vol. 73: (New York, USA: Academic Press) (2021). 219–64.

30. Vafaee K, Dehghani S, Tahmasvand R, Saeed Abadi F, Irian S, Salimi M. Potent antitumor property of Allium bakhtiaricum extracts. *BMC Complement Altern Med.* (2019) 19:116–2. doi: 10.1186/s12906-019-2522-8

31. Sankaranarayanan R, Ramadas K, Qiao YL. Managing the changing burden of cancer in Asia. *BMC Med.* (2014) 12:1–17. doi: 10.1186/1741-7015-12-3

32. Raghu H, Nalla AK, Gondi CS, Gujrati M, Dinh DH, Rao JS. uPA and uPAR shRNA inhibit angiogenesis via enhanced secretion of SVEGFR1 independent of GM-CSF but dependent on TIMP-1 in endothelial and glioblastoma cells. *Mol Oncol.* (2012) 6:33–47. doi: 10.1016/j.molonc.2011.11.008

33. Antony ML, Singh SV. Molecular mechanisms and targets of cancer chemoprevention by garlic-derived bioactive compound diallyl trisulfide. *Indian J Exp Biol.* (2011) 49:805–16.

34. Herman-Antosiewicz A, Powolny AA, Singh SV. Molecular targets of cancer chemoprevention by garlic-derived organosulfides 1. *Acta Pharmacol Sin.* (2007) 28:1355–64. doi: 10.1111/j.1745-7254.2007.00682.x

35. Pan Y, Zheng YM, Ho WS. Effect of quercetin glucosides from Allium extracts on HepG2, PC-3 and HT-29 cancer cell lines. *Oncol Lett.* (2018) 15:4657–61. doi: 10.3892/ ol.2018.7893

36. Maitisha G, Aimaiti M, An Z, Li X. Allicin induces cell cycle arrest and apoptosis of breast cancer cells in vitro via modulating the p53 pathway. *Mol Biol Rep.* (2021) 48:7261–72. doi: 10.1007/s11033-021-06722-1

37. Alamir AH, Patil S. Allicin could potentially alleviate oral cancer pain by inhibiting "pain mediators" TNF-alpha, IL-8, and endothelin. *Curr Issues Mol Biol.* (2021) 43:187–96. doi: 10.3390/cimb43010016

38. Almatroodi SA, Almatroudi A, Alsahli MA, Khan AA, Rahmani AH. Thymoquinone, an active compound of *Nigella sativa*: role in prevention and treatment of cancer. *Curr Pharm Biotechnol.* (2020) 21:1028–41. doi: 10.217 4/1389201021666200416092743

39. Țigu AB, Moldovan CS, Toma VA, Farcaș AD, Moț AC, Jurj A, et al. Phytochemical analysis and in vitro effects of *Allium fistulosum* L. and *Allium sativum* L. extracts on human normal and tumor cell lines: A comparative study. *Molecules*. (2021) 26:574. doi: 10.3390/molecules26030574

40. Hou LQ, Liu YH, Zhang YY. Garlic intake lowers fasting blood glucose: metaanalysis of randomized controlled trials. *Asia Pac J Clin Nutr.* (2015) 24:575–82. doi: 10.6133/apjcn.2015.24.4.15

41. Eldin IMT, Ahmed EM, Abd EH. Preliminary study of the clinical hypoglycemic effects of *Allium cepa* (red onion) in type 1 and type 2 diabetic patients. *Environ Health Insights*. (2010) 4:71. doi: 10.4137/EHI.S5540

42. DeFronzo RA. Insulin resistance: a multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidaemia and atherosclerosis. *Neth J Med.* (1997) 50:191–7. doi: 10.1016/S0300-2977(97)00012-0

43. Deshpande MC, Venkateswarlu V, Babu RK, Trivedi RK. Design and evaluation of oral bioadhesive controlled release formulations of miglitol, intended for prolonged inhibition of intestinal  $\alpha$ -glucosidases and enhancement of plasma glucagon like peptide-1 levels. *Int J Pharm.* (2009) 380:16–24. doi: 10.1016/j. ijpharm.2009.06.024

44. Grea A, Formicki G, Kapusta E, Szaroma W, Muchacka R, KopaÅ M, et al. Effect of some foodstuffs on the development in diabetes. *J Microbiol Biotechnol Food Sci.* (2013) 2:1205–14.

45. Eidi A, Eidi M, Esmaeili E. Antidiabetic effect of garlic (*Allium sativum* L.) in normal and streptozotocin-induced diabetic rats. *Phytomedicine*. (2006) 13:624–9. doi: 10.1016/j.phymed.2005.09.010

46. Ohaeri OC. Effect of garlic oil on the levels of various enzymes in the serum and tissue of streptozotocin diabetic rats. *Biosci Rep.* (2001) 21:19–24. doi: 10.1023/A:1010425932561

47. Su CC, Chen GW, Tan TW, Lin JG, Chung JG. Crude extract of garlic induced caspase-3 gene expression leading to apoptosis in human colon cancer cells. *In Vivo*. (2006) 20:85–90.

48. Padiya R, Banerjee SK. Garlic as an anti-diabetic agent: recent progress and patent reviews. *Recent Pat Food Nutr Agric.* (2013) 5:105–27. doi: 10.2174/18761429113059990002

49. Cazzola R, Camerotto C, Cestaro B. Anti-oxidant, anti-glycant, and inhibitory activity against  $\alpha$ -amylase and  $\alpha$ -glucosidase of selected spices and culinary herbs. *Int J Food Sci Nutr.* (2011) 62:175–84. doi: 10.3109/09637486.2010.529068

50. Oboh G, Ademiluyi AO, Agunloye OM, Ademosun AO, Ogunsakin BG. Inhibitory effect of garlic, purple onion, and white onion on key enzymes linked with type 2 diabetes and hypertension. *J Diet Suppl.* (2019) 16:105–18. doi: 10.1080/19390211.2018.1438553

51. Gautam S, Pal S, Maurya R, Srivastava AK. Ethanolic extract of *Allium cepa* stimulates glucose transporter type 4-mediated glucose uptake by the activation of insulin signaling. *Planta Med.* (2015) 81:208–14. doi: 10.1055/s-0034-1396201

52. Kim OY, Lee SM, Do H, Moon J, Lee KH, Cha YJ, et al. Influence of quercetin-rich onion peel extracts on adipokine expression in the visceral adipose tissue of rats. *Phytother Res.* (2012) 26:432–7. doi: 10.1002/ptr.3570

53. Kumari N, Kumar M, Lorenzo JM, Sharma D, Puri S, Pundir A, et al. Onion and garlic polysaccharides: a review on extraction, characterization, bioactivity, and modifications. *Int J Biol Macromol.* (2022) 219:1047–61. doi: 10.1016/j. ibiomac.2022.07.163

54. Compston J. Practical guidance for the use of bisphosphonates in osteoporosis. *Bone.* (2020) 136:115330. doi: 10.1016/j.bone.2020.115330

55. Chen JR, Haley RL, Hidestrand M, Shankar K, Liu X, Lumpkin CK, et al. Estradiol protects against ethanol-induced bone loss by inhibiting up-regulation of receptor activator of nuclear factor-κB ligand in osteoblasts. *J Pharmacol Exp Ther.* (2006) 319:1182–90. doi: 10.1124/jpet.106.109454

56. Sylvester F. Skeletal health in pediatric inflammatory bowel disease In: Mamula, P., Markowitz, J. E., and Baldassano, R. N. (eds) Pediatric inflammatory bowel disease. (Boston, MA: Springer US) (2007). 119–32. doi: 10.1007/978-0-387-73481-1\_11

57. Turk N, Cukovic-Cavka S, Korsic M, Turk Z, Vucelic B. Proinflammatory cytokines and receptor activator of nuclear factor κB-ligand/osteoprotegerin associated with bone deterioration in patients with Crohn's disease. *Eur J Gastroenterol Hepatol.* (2009) 21:159–66. doi: 10.1097/MEG.0b013e3283200032

58. Matheson EM, Mainous AG III, Carnemolla MA. The association between onion consumption and bone density in perimenopausal and postmenopausal non-Hispanic white women 50 years and older. *Menopause*. (2009) 16:756–9. doi: 10.1097/ gme.0b013e31819581a5

59. Huang TH, Mühlbauer RC, Tang CH, Chen HI, Chang GL, Huang YW, et al. Onion decreases the ovariectomy-induced osteopenia in young adult rats. *Bone*. (2008) 42:1154–63. doi: 10.1016/j.bone.2008.01.032

60. Rassi CM, Lieberherr M, Chaumaz G, Pointillart A, Cournot G. Modulation of osteoclastogenesis in porcine bone marrow cultures by quercetin and rutin. *Cell Tissue Res.* (2005) 319:383–93. doi: 10.1007/s00441-004-1053-9

61. Huang Y, Yin Y, Gu Y, Gu Q, Yang H, Zhou Z, et al. Characterization and immunogenicity of bone marrow-derived mesenchymal stem cells under osteoporotic conditions. *Sci China Life Sci.* (2020) 63:429–42. doi: 10.1007/s11427-019-1555-9

62. Siddiqui JA, Swarnkar G, Sharan K, Chakravarti B, Gautam AK, Rawat P, et al. A naturally occurring rare analog of quercetin promotes peak bone mass achievement and exerts anabolic effect on osteoporotic bone. *Osteoporos Int.* (2011) 22:3013–27. doi: 10.1007/s00198-010-1519-4

63. Wong RWK, Rabie ABM. Effect of quercetin on preosteoblasts and bone defects. Open Orthop J. (2008) 2:27–32. doi: 10.2174/1874325000802010027

64. Veronesi F, Desando G, Fini M, Parrilli A, Lolli R, Maglio M, et al. Bone marrow concentrate and expanded mesenchymal stromal cell surnatants as cell-free approaches for the treatment of osteochondral defects in a preclinical animal model. *Int Orthop.* (2019) 43:25–34. doi: 10.1007/s00264-018-4202-6

65. Yang J, Dong D, Luo X, Zhou J, Shang P, Zhang H. Iron overload-induced osteocyte apoptosis stimulates osteoclast differentiation through increasing osteocytic RANKL production in vitro. *Calcif Tissue Int.* (2020) 107:499–509. doi: 10.1007/s00223-020-00735-x

66. Kyung KH. Antimicrobial activity of volatile sulfur compounds in foods In: Qian, M. C., Xuetong Fan, X, and Mahattanatawee, K. (eds). Volatile sulfur compounds in food: American Chemical Society (2011). 323–38. doi: 10.1021/bk-2011-1068.ch016

67. Mehrbod P, Amini E, Tavassoti-Kheiri M. Antiviral activity of garlic extract on influenza virus. *Iran J Virol.* (2009) 3:19–23. doi: 10.21859/isv.3.1.19

68. O'Gara EA, Hill DJ, Maslin DJ. Activities of garlic oil, garlic powder, and their diallyl constituents against *Helicobacter pylori*. *Appl Environ Microbiol*. (2000) 66:2269–73. doi: 10.1128/AEM.66.5.2269-2273.2000

69. Perry CC, Weatherly M, Beale T, Randriamahefa A. Atomic force microscopy study of the antimicrobial activity of aqueous garlic versus ampicillin against *Escherichia coli* and *Staphylococcus aureus*. J Sci Food Agric. (2009) 89:958–64. doi: 10.1002/jsfa.3538

70. Rawat S. Evaluation of synergistic effect of ginger, garlic, turmeric extracts on the antimicrobial activity of drugs against bacterial phatogens. Int J Biopharm. (2015) 6:60–5.

71. Yadav S, Trivedi NA, Bhatt JD. Antimicrobial activity of fresh garlic juice: an: in vitro: study. Int Quart J Res Ayurveda. (2015) 36:203–7. doi: 10.4103/0974-8520.175548

72. Ali SG, Ansari MA, Alzohairy MA, Almatroudi A, Alomary MN, Alghamdi S, et al. Natural products and nutrients against different viral diseases: prospects in prevention and treatment of SARS-CoV-2. *Medicina*. (2021) 57:169. doi: 10.3390/medicina57020169

73. Lengbiye EM, Mbadiko CM, Falanga CM, Matondo A, Inkoto CL, Ngoyi EM, et al. Antiviral activity, phytochemistry and toxicology of some medically interesting Allium species: a mini review. *Int J Pathogen Res.* (2020) 5:64–77. doi: 10.9734/ijpr/2020/v5i430145

74. Rouf R, Uddin SJ, Sarker DK, Islam MT, Ali ES, Shilpi JA, et al. Antiviral potential of garlic (*Allium sativum*) and its organosulfur compounds: a systematic update of preclinical and clinical data. *Trends Food Sci Technol.* (2020) 104:219–34. doi: 10.1016/j. tifs.2020.08.006

75. Davis SR. An overview of the antifungal properties of allicin and its breakdown products–the possibility of a safe and effective antifungal prophylactic. *Mycoses.* (2005) 48:95–100. doi: 10.1111/j.1439-0507.2004.01076.x

76. Lee JB, Miyake S, Umetsu R, Hayashi K, Chijimatsu T, Hayashi T. Anti-influenza A virus effects of fructan from welsh onion (*Allium fistulosum L.*). *Food Chem.* (2012) 134:2164–8. doi: 10.1016/j.foodchem.2012.04.016

77. Sohn HY, Ku EJ, Ryu HY, Jeon SJ, Kim NS, Son KH. Antifungal activity of fistulosides, steroidal saponins, from *Allium fistulosum L. J Life Sci.* (2006) 16:310–4. doi: 10.5352/JLS.2006.16.2.310

78. Ghasemian A, Mostafavi S, Kh S. Antimicrobial effects of aqueous and alcoholic extracts of *Allium schoenoprasum* on some bacterial pathogens. *Infect Epidemiol Microbiol.* (2018) 4:1–4.

79. Kim SH, Yoon JB, Han J, Seo YA, Kang BH, Lee J, et al. Green onion (*Allium fistulosum*): an aromatic vegetable crop esteemed for food, nutritional and therapeutic significance. *Food Secur.* (2023) 12:4503. doi: 10.3390/foods12244503

80. Parvu AE, Parvu M, Vlase L, Miclea P, Mot AC, Silaghi-Dumitrescu R. Antiinflammatory effects of *Allium schoenoprasum* L. leaves. *J Physiol Pharmacol.* (2014) 65:309–15.

81. Magryś A, Olender A, Tchórzewska D. Antibacterial properties of *Allium sativum* L. against the most emerging multidrug-resistant bacteria and its synergy with antibiotics. *Arch Microbiol.* (2021) 203:2257–68. doi: 10.1007/s00203-021-02248-z

82. Liu Y, Ding R, Xu Z, Xue Y, Zhang D, Zhang Y, et al. Roles and mechanisms of the protein quality control system in Alzheimer's disease. *Int J Mol Sci.* (2021) 23:345. doi: 10.3390/ijms23010345

83. Nadeem H, Zhou B, Goldman D, Romley J. Association between use of ß2adrenergic receptor agonists and incidence of Parkinson's disease: retrospective cohort analysis. *PLoS One*. (2022) 17:e0276368. doi: 10.1371/journal.pone.0276368

84. Shabab T, Khanabdali R, Moghadamtousi SZ, Kadir HA, Mohan G. Neuroinflammation pathways: a general review. *Int J Neurosci*. (2017) 127:624–33. doi: 10.1080/00207454.2016.1212854

85. Patterson KM, Clarke C, Wolverson EL, Moniz-Cook ED. Through the eyes of others-the social experiences of people with dementia: a systematic literature review and synthesis. *Int Psychogeriatr.* (2018) 30:791–805. doi: 10.1017/S1041610216002374

86. Lanzotti V. The analysis of onion and garlic. J Chromatogr A. (2006) 1112:3–22. doi: 10.1016/j.chroma.2005.12.016

87. Hayashi Y, Hyodo F, Nakagawa K, Ishihara T, Matsuo M, Shimohata T, et al. Continuous intake of quercetin-rich onion powder may improve emotion but not regional cerebral blood flow in subjects with cognitive impairment. *Heliyon.* (2023) 9:e18401. doi: 10.1016/j.heliyon.2023.e18401

88. Sadowska-Bartosz I, Bartosz G. Effect of antioxidants supplementation on aging and longevity. *Biomed Res Int.* (2014) 2014:404680. doi: 10.1155/2014/404680

89. Mukherjee PK, Maity N, Nema NK, Sarkar BK. Bioactive compounds from natural resources against skin aging. *Phytomedicine*. (2011) 19:64–73. doi: 10.1016/j. phymed.2011.10.003

90. Ndlovu G, Fouche G, Tselanyane M, Cordier W, Steenkamp V. In vitro determination of the anti-aging potential of four southern African medicinal plants. *BMC Complement Altern Med.* (2013) 13:1–7. doi: 10.1186/1472-6882-13-304

91. Capasso A. Antioxidant action and therapeutic efficacy of *Allium sativum* L. *Molecules*. (2013) 18:690–700. doi: 10.3390/molecules18010690

92. Majewski M. Allium sativum: facts and myths regarding human health. Rocz Panstw Zakl Hig. (2014) 65:1–8.

93. Pangastuti A, Indriwati SE, Amin M. Investigation of the anti-aging properties of allicin from *Allium sativum* L bulb extracts by a reverse docking approach. *Trop J Pharm Res.* (2018) 17:635–9. doi: 10.4314/tjpr.v17i4.10

94. Cui Z, Zhao X, Amevor FK, Du X, Wang Y, Li D, et al. Therapeutic application of quercetin in aging-related diseases: SIRT1 as a potential mechanism. *Front Immunol.* (2022) 13:943321. doi: 10.3389/fimmu.2022.943321

95. Kherade M, Solanke S, Tawar M, Wankhede S. Fructooligosaccharides: a comprehensive review. J Ayurvedic Herb Med. (2021) 7:193–200. doi: 10.31254/jahm.2021.7305

96. Kumar KS, Bhowmik D, Chiranjib B, Tiwari P. Allium cepa: a traditional medicinal herb and its health benefits. J Chem Pharm Res. (2010) 2:283–91.

97. Alam K, Hoq O, Uddin S. Medicinal plant *Allium sativum*. A review. *J Med Plant Stud.* (2016) 4:72–9.

98. Friedman T, Shalom A, Westreich M. Self-inflicted garlic burns: our experience and literature review. *Int J Dermatol.* (2006) 45:1161–3. doi: 10.1111/j.1365-4632.2006.02860.x

99. Yin J, Li H. Anaphylaxis caused by younger garlic. J Allergy Clin Immunol. (2007) 119:34.

100. Mikaili P, Maadirad S, Moloudizargari M, Aghajanshakeri S, Sarahroodi S. Therapeutic uses and pharmacological properties of garlic, shallot, and their biologically active compounds. *Iran J Basic Med Sci.* (2013) 16:1031–48.

101. Najeebullah S, Shinwari ZK, Jan SA, Khan I, Ali M. Ethno medicinal and phytochemical properties of genus Allium: a review of recent advances. *Pak J Bot.* (2021) 53:135–44. doi: 10.30848/PJB2021-1(34)

102. Bisen PS, Emerald M. Nutritional and therapeutic potential of garlic and onion (*Allium* sp.). *Curr Nutr Food Sci.* (2016) 12:190–9. doi: 10.217 4/1573401312666160608121954

103. Amagase H, Petesch BL, Matsuura H, Kasuga S, Itakura Y. Intake of garlic and its bioactive components. J Nutr. (2001) 131:955S–62S. doi: 10.1093/jn/131.3.955S

104. Rohman MM, Hossain MD, Suzuki T, Takada G, Fujita M. Quercetin-4'glucoside: a physiological inhibitor of the activities of dominant glutathione S-transferases in onion (*Allium cepa* L.) bulb. *Acta Physiol Plant.* (2009) 31:301–9. doi: 10.1007/s11738-008-0234-7

105. Olszowy-Tomczyk M, Garbaczewska S, Wianowska D. Correlation study of biological activity with quercetin and phenolics content in onion extracts. *Molecules*. (2022) 27:8164. doi: 10.3390/molecules27238164

106. Azeem M, Hanif M, Mahmood K, Ameer N, Chughtai FRS, Abid U. An insight into anticancer, antioxidant, antimicrobial, antidiabetic and anti-

inflammatory effects of quercetin: a review. Polym Bull. (2023) 80:241-62. doi: 10.1007/s00289-022-04091-8

107. Petropoulos S, Di Gioia F, Ntatsi G. Vegetable organosulfur compounds and their health promoting effects. *Curr Pharm Des.* (2017) 23:2850–75. doi: 10.217 4/1381612823666170111100531

108. Oleszek M, Oleszek W. Saponins in food In: Xiao, J., Sarker, S., and Asakawa, Y. (eds) Handbook of dietary phytochemicals, Singapore: Springer, (2020). 1–40. doi: 10.1007/978-981-13-1745-3\_34-1

109. Corzo-Martínez M, Villamiel M. An overview on bioactivity of onion In: Aguirre C. B (eds) Onion consumption and health. Nova Science Publishers, Inc., New York, United States (2012) 1–48.

110. Park S, Kim MY, Lee DH, Lee SH, Baik EJ, Moon CH, et al. Methanolic extract of onion (*Allium cepa*) attenuates ischemia/hypoxia-induced apoptosis in cardiomyocytes via antioxidant effect. *Eur J Nutr.* (2009) 48:235–42. doi: 10.1007/s00394-009-0007-0

111. Kothari D, Lee WD, Kim SK. Allium flavonols: health benefits, molecular targets, and bioavailability. *Antioxidants*. (2020) 9:888. doi: 10.3390/antiox9090888

112. Khan J, Deb PK, Priya S, Medina KD, Devi R, Walode SG, et al. Dietary flavonoids: Cardioprotective potential with antioxidant effects and their pharmacokinetic, toxicological and therapeutic concerns. *Molecules*. (2021) 26:4021. doi: 10.3390/molecules26134021

113. Pareek S, Sagar NA, Sharma S, Kumar V. Onion (*Allium cepa* L.) In: Yahia, E. M. (ed) Fruit and vegetable phytochemicals: chemistry and human health. Wiley Online Library, Hauppauge, New York, United State (2017). 1145–62. doi: 10.1002/9781119158042.ch58

114. Suleria HAR, Butt MS, Anjum FM, Saeed F, Khalid N. Onion: nature protection against physiological threats. *Crit Rev Food Sci Nutr.* (2015) 55:50–66. doi: 10.1080/10408398.2011.646364

115. Nouroz F, Mehboob M, Noreen S, Zaidi F, Mobin T. A review on anticancer activities of garlic (*Allium sativum* L.). *Middle East J Sci Res.* (2015) 23:1145–51. doi: 10.5829/idosi.mejsr.2015.23.06.9381

116. Hussein HJ, Hameed IH, Hadi MY. A review: anti-microbial, anti-inflammatory effect and cardiovascular effects of garlic: *Allium sativum. Res J Pharm Technol.* (2017) 10:4069–78. doi: 10.5958/0974-360X.2017.00738.7

117. el-Saber Batiha G, Magdy Beshbishy A, Wasef LG, Elewa YHA, al-Sagan AA, Abd el-Hack ME, et al. Chemical constituents and pharmacological activities of garlic (*Allium sativum L.*): A review. *Nutrients.* (2020) 12:872. doi: 10.3390/nu12030872

118. Stępień AE, Trojniak J, Tabarkiewicz J. Anti-cancer and anti-inflammatory properties of black garlic. Int J Mol Sci. (2024) 25:1801. doi: 10.3390/ijms25031801

119. Espinoza T, Valencia E, Albarrán M, Díaz D, Quevedo RA, Díaz O, et al. Garlic (*Allium sativum* L) and its beneficial properties for health: A review. *Agroind Sci.* (2020) 10:103–15. doi: 10.17268/agroind.sci.2020.01.14

120. Jikah AN, Edo GI. Mechanisms of action by Sulphur compounds in *Allium* sativum, a review. *Pharmacol Res Modern Chinese Med.* (2023) 9:100323. doi: 10.1016/j. prmcm.2023.100323

121. Yi L, Su Q. Molecular mechanisms for the anti-cancer effects of diallyl disulfide. *Food Chem Toxicol.* (2013) 57:362–70. doi: 10.1016/j.fct.2013.04.001

122. Mitra S, Das R, Emran TB, Labib RK, Islam F, Sharma R, et al. Diallyl disulfide: a bioactive garlic compound with anticancer potential. *Front Pharmacol.* (2022) 13:943967. doi: 10.3389/fphar.2022.943967

123. Farhat Z, Hershberger PA, Freudenheim JL, Mammen MJ, Hageman Blair R, Aga DS, et al. Types of garlic and their anticancer and antioxidant activity: a review of the

epidemiologic and experimental evidence. *Eur J Nutr.* (2021) 60:3585–609. doi: 10.1007/s00394-021-02482-7

124. Sutejo IR, Efendi E. Antioxidant and hepatoprotective activity of garlic chives (*Allium tuberosum*) ethanolic extract on doxorubicin-induced liver injured rats. *Int J Pharm Med Biol Sci.* (2017) 6:20–3. doi: 10.18178/ijpmbs.6.1.20-23

125. Lee JH, Yang HS, Park KW, Kim JY, Lee MK, Jeong IY, et al. Mechanisms of thiosulfinates from *Allium tuberosum* L.-induced apoptosis in HT-29 human colon cancer cells. *Toxicol Lett.* (2009) 188:142–7. doi: 10.1016/j.toxlet.2009.03.025

126. Lee KH, Yoon YT. Antioxidant activity of kimchi seasoning with black garlic. *Korean J Food Nutr.* (2017) 30:175–80. doi: 10.9799/ksfan.2017.30.1.175

127. Vuković S, Popović-Djordjević JB, Kostić AŽ, Pantelić ND, Srećković N, Akram M, et al. Allium species in the Balkan region—major metabolites, antioxidant and antimicrobial properties. *Horticulturae*. (2023) 9:408. doi: 10.3390/horticulturae9030408

128. Shahrajabian MH, Sun W, Cheng Q. A review of Leek (*A. ampeloprasum* L.), an important vegetable and food ingredient with remarkable pharmaceutical activities. *Pharmacogn Commun.* (2021) 11:9–12. doi: 10.5530/pc.2021.1.3

129. Xie T, Wu Q, Lu H, Hu Z, Luo Y, Chu Z, et al. Functional perspective of leeks: active components, health benefits and action mechanisms. *Food Secur*. (2023) 12:3225. doi: 10.3390/foods12173225

130. Alves-Silva JM, Zuzarte M, Girão H, Salgueiro L. Natural products in cardiovascular diseases: the potential of plants from the Allioideae subfamily (ex-Alliaceae Family) and their Sulphur-containing compounds. *Plan Theory.* (2022) 11:1920. doi: 10.3390/plants11151920

131. Ali MY, Hassan DR, Soltan SS, El Sharbiny M. The effect of Egyptian leek seeds and leaves on colon and breast cancer based on their antioxidant activity and DFT approach. *African J Biol Sci.* (2024) 20:45–66. doi: 10.21608/ajbs.2024.373509

132. Al-Khayri JM, Sahana GR, Nagella P, Joseph BV, Alessa FM, Al-Mssallem MQ. Flavonoids as potential anti-inflammatory molecules: a review. *Molecules*. (2022) 27:2901. doi: 10.3390/molecules27092901

133. Fattorusso E, Lanzotti V, Taglialatela-Scafati O, Cicala C. The flavonoids of leek, *Allium porrum. Phytochemistry.* (2001) 57:565–9. doi: 10.1016/S0031-9422(01)00039-5

134. Alam A, al Arif Jahan A, Bari MS, Khandokar L, Mahmud MH, Junaid M, et al. Allium vegetables: traditional uses, phytoconstituents, and beneficial effects in inflammation and cancer. *Crit Rev Food Sci Nutr.* (2023) 63:6580–614. doi: 10.1080/10408398.2022.2036094

135. Zhao C, Wang Z, Cui R, Su L, Sun X, Borras-Hidalgo O, et al. Effects of nitrogen application on phytochemical component levels and anticancer and antioxidant activities of *Allium fistulosum*. *PeerJ*. (2021) 9:e11706. doi: 10.7717/peerj.11706

136. Nazir S, Afroz S, Tauseef H, Afsheen H, Farooqui R, Rizvi A. Phytochemical analysis, safety profile, analgesic, and anti-inflammatory effect of ethanol extract of *Allium fistulosum L. Pak-Euro J Med Life Sci.* (2022) 5:135–46. doi: 10.31580/pjmls. v5i1.2511

137. Chang TC, Jang HD, Lin WD, Duan PF. Antifungal activities of commercial rice wine extracts of Taiwanese *Allium fistulosum*. *Adv Microbiol*. (2016) 6:471–8. doi: 10.4236/aim.2016.67046

138. Kurnia D, Ajiati D, Heliawati L, Sumiarsa D. Antioxidant properties and structure-antioxidant activity relationship of Allium species leaves. *Molecules*. (2021) 26:7175. doi: 10.3390/molecules26237175

139. Rais N, Ved A, Ahmad R, Kumar M, Barbhai MD, Chandran D, et al. S-allyl-L-cysteine—a garlic bioactive: physicochemical nature, mechanism, pharmacokinetics, and health promoting activities. *J Funct Foods*. (2023) 107:105657. doi: 10.1016/j. jff.2023.105657