Nutritional and Therapeutic Potential of Garlic and Onion (Allium sp.)

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REVIEW ARTICLE

Nutritional and Therapeutic Potential of Garlic and Onion (*Allium* sp.)

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Abstract: Genus *Allium* belongs to the family Liliaceae, which contains more than 600 species. Garlic (*Allium sativum*) and onion (*Allium cepa*) are two the most popular food ingredients widely used all over the world. During the last few decades, garlic and onion have received tremendous attention for their wide range of therapeutic properties and great health benefits. The variety of garlic and onion species' considerable differences in manufacturing process cause discrepancies in a spectrum of the ingredients derived. Current garlic preparations available on the market, including garlic powder, garlic oil, raw or cooked garlic and aged garlic extract. Garlic and onion extracts posses many therapeutic properties including antimicrobial, antiviral, antifungal, anti-protozoal, hepatoprotective, cardioprotective, anti-inflammatory, neuroprotective, anti-amnesic, anticarcinogenic, antimutagenic, antiasthmatic, immunomodulatory, hypolipidemic, anti-hypertensive, anti-diabetic and antioxidant. These therapeutic properties are caused by the combination and biological activity of organo-sulphur compounds such as S-allyl-l-cysteine, diallyl disulfide, diallyl trisulfide, ajoene, and allicin. Allicin, which is one of the most researched therapeutic compounds of garlic and onion, is extremely unstable and rapidly degrades with time, even at low temperatures, which causes its prompt degradation during contact with stomach acid during oral consumption. Present review discusses biochemical, pharmacological, therapeutic properties and nutritional value of garlic and onion, their use for prevention disease and maintenance of good health, as well as novel potential nanoparticles drug delivery systems for more effective oral and topical administration of natural organo-sulphur compounds.

Keywords: *Allium cepa*, *Allium sativum*, garlic, onion, allicin, organosulfur, flavonoids, sterols.

INTRODUCTION

Genus Allium belongs to the family Liliaceae having more than 700 species, differing in taste, form and colour, but have quite similar neutraceutical, phytochemical and biochemical properties [1, 2]. Garlic (*Allium sativum*) and onion (*Allium cepa*) are the two most popular food ingredients used widely all over the world. Crops are usually used fresh after harvest and/or dried and are ready for storage. During the last few decades, garlic and onion have received tremendous attention to their wide range of therapeutic properties and great health benefits as functional food [3-11]. The variety of garlic and onion species' considerable differences in manufacturing process cause discrepancies in a spectrum of the ingredients derived. Numerous meta studies have shown a protective relationship between high consumption of Allium sp. vegetable and the relative risk of both prevention of cancer and cardiovascular disorders [12-16]. Onion with estimated annual production over 47 million tons a year is usually consumed as fresh, and its commercial products are less abundant than those of garlic. Current garlic preparations available on the market include garlic powder, garlic oil, raw or cooked garlic and aged garlic extract. Garlic and onion extracts demonstrate strong antioxidant, hypocholesterolemic, hypolipidemic, anti-hypertensive, anti-diabetic, antithrombotic, anti-inflammatory, anti-spasmotic, anti-allergic, anti-viral, anti-protozoa, anti-hyperhomocysteinemic, anti-parasitic and neuroprotective properties [1, 15, 17]. Both plants are used in the prevention of vascular disease, and cancer of the bladder, brain, breast, colon, lungs, ovaries, and stomach [18-22]. Other potential benefits include, but are not limited to, kidney function [23], atherosclerosis [24] anti-bacterial/fungal activity [25-28], cataractogenesis [29], immune function [30, 31] and prebiotic effect [32, 33]. The therapeutic properties of onion and garlic are caused by the combination and biological activity of organo-sulfur compounds such as S-allyl-l-cysteine, diallyl disulfide, diallyl trisulfide, ajoene, and allicin. Studies suggest that the biological and therapeutic properties of garlic and onions are mainly due to their high organo-sulfur compounds [1].

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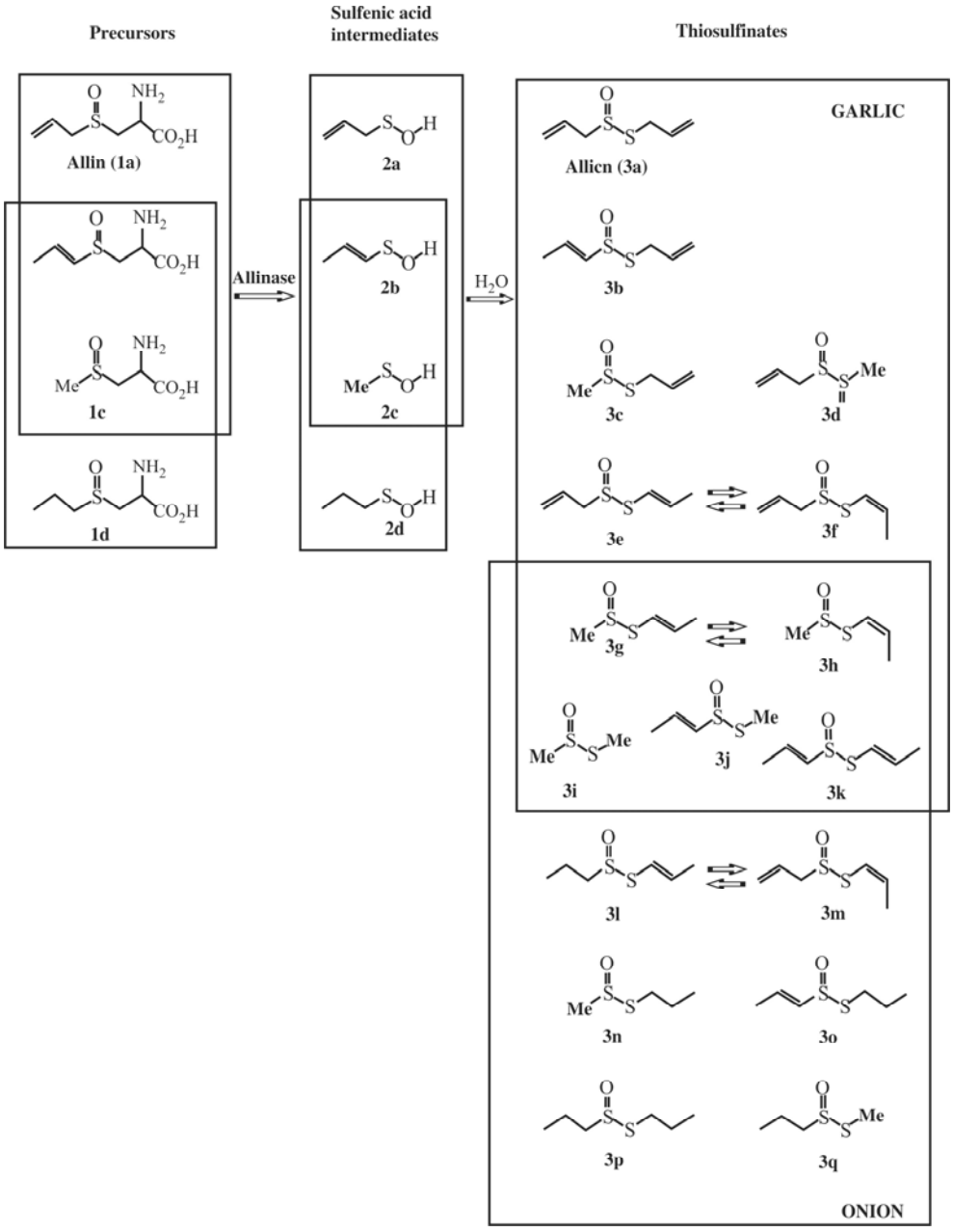

Fig. (1). Sulphur-containing constituents of onion and garlic.

Phytochemicals in *Allium* Genera

The primary sulphur containing constituents in both plants are the S-alkyl-L-cysteine sulphoxides (ACSOs), such as (a) Methiin and alliin (b) allicin (c) diallyl sulphide (DAS), and (d) diallyl disulphide (DADS) (Fig. **1**). These compounds provide to garlic and onion their characteristic odor and flavor, as well as most of their biological properties.

Of the countless phenolic compounds found in the onion, flavonoid formed by oxidation of C3 units, have persistently been assigned an important nutritional and therapeutic role [34]. The degree of oxidation identifies them in different subgroups like flavonols, flavanones, steroidal saponins, and anthocyanins (Fig. **2** and **3**). One of the major sources of two forms of dietary flavonoids found in onions are (a) anthocyanins in red and purple skinned bulbs and (b) quercetin and its derivatives in yellow skinned onion bulbes. Flavonoids are abundant in onion (Fig. **2** and **3**) while is completely lacking in garlic. Garlic contains a small amount of sallyl cysteine (SAC), non- volatile water-soluble sulphur compound (Fig. **1**). Fruto-kestose (GF2), nystose (GF3) fructofuranosylnystose (GF4), thiosulfinates are other sulphur containing bioactive compounds (Fig. **3**). Glycerophospholipids lectins, saponins (β-sitosterol, gitogenin, oleanolic acid, amyrin, diosgenin, cepagenin), glucosides, fructan, pectin, vitamins A, B1, B2, B3, B6, C, E, allixin and organoselenium compounds such as γ-glutamyl-Se-methylselenocysteine, Se-methylselenocysteine, "Se-alliins", Se-methionine, Se-cystine/Se-cysteine are the additional most abundant functional constituents in garlic and onion. Sulphur compounds do not exist as such in the intact cells. They are

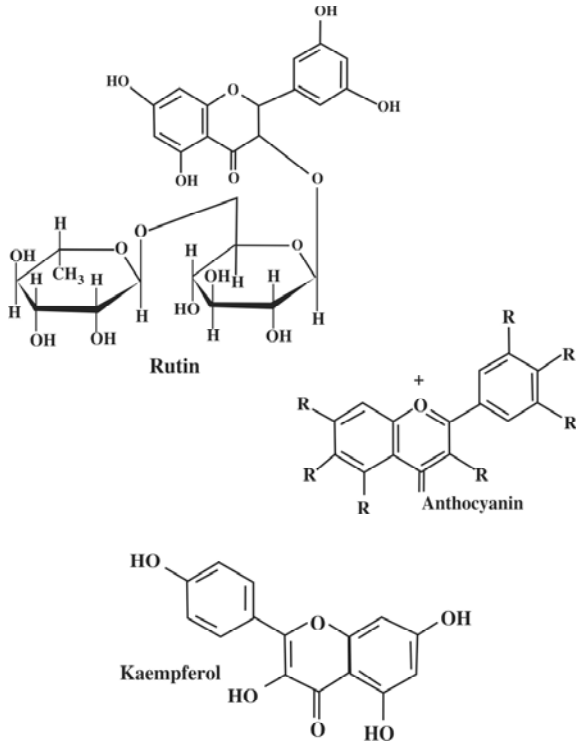

Fig. (2). Some common flavonoids of onion.

formed as a result of enzymic reaction between allinase and volatile precursors substrate S -alk(en)yl cysteine sulphoxide and sulphonic acid. Thiosulphinates and sulphonic acid compounds are derived when the cells are ruptured [35, 36]. Sulfur compounds are found in onion bulbs alongside with seleno derivatives thiosulfinates, thiosulfonates cepaenes, S-oxides, S,S'-dioxides, monosulfides, disulfides, trisulfides, zwiebelanes, and soluble sulphur (γ-glutamylcysteine peptides) (Fig. **1** and **4**).

A wide range of different flavonols, differentiated on the basis of degree of hydroxylation, are found in onions consisting of the aglycones and glycosylated derivatives. They are quercetin glucosides viz. the 4'-glucoside, the 7,4' -diglucoside, the 3,4'-diglucoside, the 3-glucoside, the 7-glucoside, the 3,7-diglucoside, the 3-rutinoside (rutin), the 3-rhanmoside (quercetrin), the 7,4'-, and 3-glucosides of kaempferol, isorhamnetin 4'-glucoside and rest are anthocyanins (Fig. **2** and **3**).

An abundance of flavonols is typical for flesh scale tissue compared to fresh white skinned onions, garlic and leek containing only trace amounts of flavonols. Onion is also a potential source of prostaglandins [37]. Bulbs and leaves of alliums possess flavonoids, sterols and steroidal glycosides. In garlic, 0.021% and in onion, 0.095%, saponin level has been reported [38, 39]. Fructans and fructosyl are the great source of soluble dietary fiber and the main stored carbohydrates in onion plant. The accumulation of fructans is associated with high concentration of thiosulfinate, soluble carbohydrates and pungency according to onion phenotype. Fructans, with maximum degree of polymerisation are typical for high dry matter onion bulbs. They are found in high concentration in onions bulbs (35-40% dry weight) constituting a major portion of the water-soluble carbohydrates. The chain

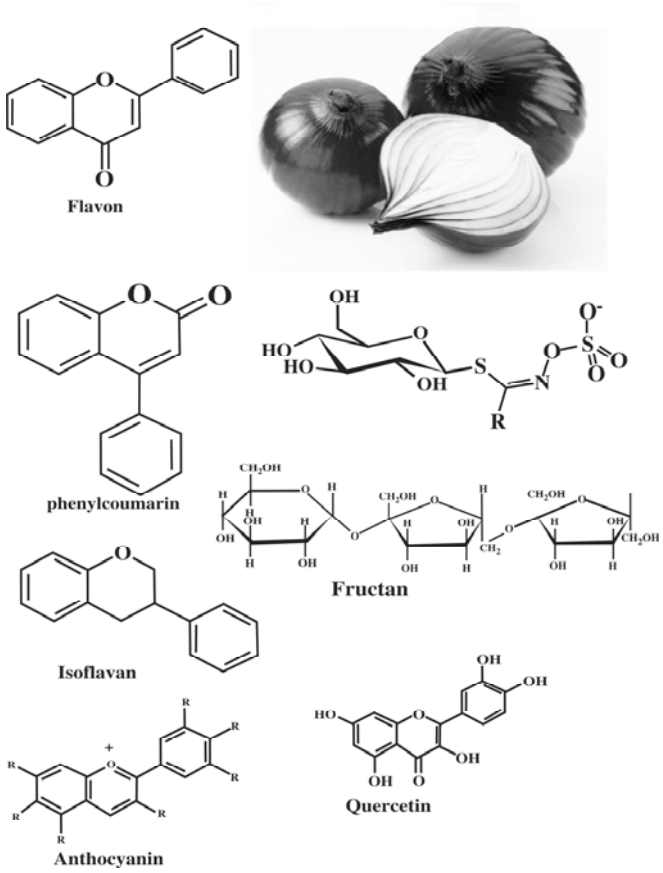

Fig. (3). Some common phytochemicals of onion (*Allium cepa*).

of fructans / fructosyl polymers of D-fructose molecules bonded by β (2→1) linkages is terminated by a D-glucose molecule linked to fructose by an α (1→2) bond during polymerisation [1, 39, 40]. Maximum concentration of lower molecular weight fructans with degree of polymerization 5 are found in the onion inner, younger leaf bases. Flavonols, anthocyanins and dihydroflavonols are found to occur in onion bulbs [1, 40]. Flavonols are the predominant pigments with 270-1187 mg per kilogram (FW) in yellow onions and 415-1917 mg of flavonols per kilogram in red onions (FW). Twenty five different flavonols are characterized with quercetin derivatives (Quercetin 4'-glucoside and quercetin 3,4'-diglucoside) as the most abundant dietary flavonoids with glycosyl moieties having glucose as exclusive moiety in all onion cultivars (Fig. **3**). Glycosyl moieties are mainly attached to the 4', 3, and/or 7- positions of the aglycones. Analogous derivatives of kaempferol (Fig. **2**) and isorhamnetin are minor pigments. Oligomeric structures of quercetin and the condensation products of quercetin and protocatechuic acid are found in the outer dry layers of onion bulbs. The anthocyanins and cyanidin glucosides acylated with malonic acid or nonacylated are found in red onions [40-42]. Essential and vegetable oils derived from the onion and garlic seeds have potential therapeutic value. The cold pressed onion seed oil contains fatty acids; palmitic acid (C16:0, 6.4-7.1%), oleic acid (C18:1, 24.8-26 %) and linoleic acid (C18:2, 65.2-64 %) [1, 43]. Oleic and linoleic acids are recognized for their anti-inflammatory, wound healing, procoagulant, cardioprotective, antiarrhythmic, hypotensive,

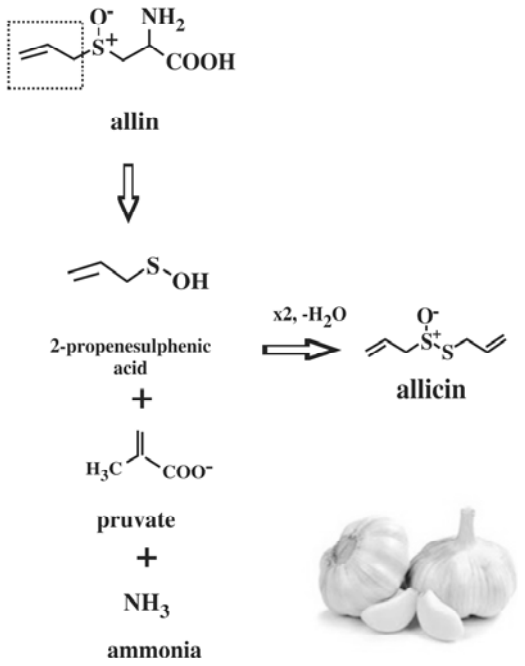

Fig. (4). Enzymic reaction of allinase.

neuroprotective properties and reduce the severity of both acute and the relapsing phases of chronic multiple sclerosis [1, 44]. Essential oil from different species of *Allium* viz. *Allium cepa*, *Allium sativum* L., *Allium jesdianum* Boiss, *Allium roseum* L., *Allium. sphaerocephalon* L., *Allium nigrum*, *Allium rotundum* and others demonstrate strong antibacterial activity [45-49]. The essential oil distilled from onion seeds contains about 48 active compounds, including 2-phenylethanol (0.42 % to 41.17 %), 1-pentanol, 2-heptanol, 2-octanol, 1-octen-3-ol, 1-heptanol, phenylmethanol, 1- dodecanol.1- pentanol, 2-heptanol, 1-octen-3-ol and phenylmethanol (up to 0.66 %), aromatic hydrocarbons (p-xylene and mesitylene), cyclic monoterpene α-phellandrene, bicyclic monoterpene, pcymene, esters (hexylacetate, nonylacetate, ethyloctanoate, methylhexanoate and nonylacetate) [49].

Garlic (*Allium sativum*)

Garlic (*Allium sativum*) is the herb known for its flavour and pungency and most widely quoted for medicinal properties [1, 9, 35, 36, 50]. Garlic ranks second best selling vegetable in the United States and used extensively as medicinal plant all over the world for over 5000 years for different ailments [51, 52]. Therapeutic potential of alliums was first recorded in collection of Zoroastrian holy writings followed by Sumerian and the ancient Egyptians. The Olympics in Greece used raw garlic to feed the athletes and increasing stamina [51]. In ancient medicine alliums and especially garlic was used to aid digestion, respiration and to treat leprosy [53]. Garlic gain especial attention as a plant with exceptional disease preventative and therapeutic properties used by Avicenna in treatment of variety of disease such as toothache, constipation, parasitic infestation, arthritis, insect bites, and infectious diseases as natural antibiotic [53]. Garlic demonstrates a number of pharmacological effects *viz.* cancer chemoprevention, antibiotic, antihypertensive, antidiabetic, antithrombotic and cholesterol- lowering properties [5]. The thiosulfinate extracts from garlic inhibit the tumor cells growth [20-22]. Abundance of natural oil and water-soluble sulfur-containing organosulfur compounds are responsible for the characteristic flavor and pungency of garlic having several pharmacological significance whereas intact, undisturbed bulbs of garlic contain only a few bioactive components. An odorless amino acid, alliin (Fig. **4**) is found in intact garlic which gets converted by an enzyme allinase into allicin responsible for the characteristic odor when cloves are crushed [37]. The spontaneous decomposition results to form numerous sulfur -containing compounds, some of which are having chemopreventive activity (Fig. **4**).

Onion (*Allium cepa*)

The onion (*Allium cepa*) (Latin 'cepa' = onion), most widely cultivated species of the genus *Allium*, commonly known as bulb onion, is used as a vegetable for its nutritive value (Table **1**). They are cultivated by many cultures and used globally for their medicinal qualities. The top global producers of onion during last 5 years are China and India with higher yields followed by Uzbegistan, Egypt, China, Korea and USA. They are usually eaten raw or used to make pickles or chutneys, served cooked as food stuff, as a vegetable or part of a prepared savoury dish.

Table 1. Nutritional value of raw onion in each 100 g.
(Source USDA www.onions-usa.org)

Energy	**166kJ (40 kcal)**
Carbohydrate	9.34 g
Sugars	4.24 g
Dietary fiber	1.7 g
Fat	0.1 g
Protein	1.1 g
Vitamins	
Thiamine (B_1)	(4%) 0.046 mg
Riboflavin (B_2)	(2%) 0.027 mg
Niacin (B_3)	(1%) 0.116 mg
Pantothenic acid (B_5)	(2%) 0.123 mg
Vitamin B_6	(9%) 0.12 mg
Folate (B_9)	(5%) 19 µg
Vitamin C	(9%) 7.4 mg
Trace Metals	
Calcium	(2%) 23 mg
Iron	(2%) 21 mg
Magnesium	(3%) 10 mg
Manganese	(6%) 0.129 mg
Phorphorus	(4%) 29 mg
Potassium	(3%) 146 mg
Zinc	(2%) 0.17 mg
Other constituents	
Water	89.11 g
Fluoride	1.1 µg

The plant has a fan like hollow bluish-green leaves with the bulb at the base. On maturation, bulb swells, the foliage dies down in the autumn and the outer layers of the bulb become dry and brittle. The crop is harvested, dried and are ready for use or storage. There are several other species; in this genera cultivated for food, such as shallots and potato onions with multiple bulbs, variously referred to as onions having a unique rich combination of fructans, dietary flavonoids and organosulfur compounds (Fig. **3**). These three families of compounds express salutary effects on human health with functional benefits against life style diseases including reduced risk of coronary heart disease, different types of cancer, anti-oxidative activity, metal ion chelation, lipid peroxidation inhibition, asthma, allergies, arthritis, diabetes, neurodegenerative disorders, osteoporosis and others. [54]. Onion pigments like 4'-glycosylation promote unique and unusual substitution patterns of sugar moieties. There are variation in structural identification of dihydroflavonols from onions compared to flavonols and anthocyanins and may be at high concentrations in some cultivars.

Shallot (*Allium ascalonicum*)

Shallot is used traditionally from the ancient times demonstrating a variety of health benefits including antioxidant, hypocholesterolemic, hepatoprotective, antidermatophytic, anti- angiogenic, anti-inflammatory, antibacterial (potential inhibitory activity against *Helicobacter pylori*), anti-fungal and peroxynitrite-scavenging properties [55]. The most effective pharmacological compounds of *Allium ascalonicum* are mannose-specific lectin, furostanol saponins, selenium, sulfur, antifungal peptide and flavonol glucosides [55]. The shallot extract inhibits proliferation and growth of tumor cell lines as HeLa and MCF-7 cells *in vivo* and *in vitro*, in combination with garlic is effective against human leukemia cells (HL-60) and human cervical carcinoma HeLa cells [56]. *A. ascalonicum* significantly decreases the inflammation *in vivo* via reduction of the vascular permeability or through inhibition of inflammatory mediators [55, 56].

Therapeutic Potential of Allium

Alliums are used as medicine for many major and minor disorders. Variety of data presently confirms the therapeutic properties and low toxicity of active ingredients in different cultivars of Allium by enhancing the blood's fibrinolytic activity and suppressing blood fibrinogen concentration, and increase the blood coagulation time [57, 58]. Garlic and onion also play a role in lowering serum cholesterol levels both in animals and humans [59]. Garlic and onion bulbs can also reduce the level of blood sugar [60, 61], thus they are beneficial to diabetes, obesity, respiratory and skin infections, insect bites, memory impairment, demonstrate strong anthelmintic properties [62] reduction of hypertension [63] and stimulation of the body's immune system [64]. Flavonoids present in the bulbs and leaves of alliums are very effective antioxidants with variable biochemical functions [35, 65, 66] like immune functionality, gene expression, liver function, enzyme activity, platelet aggregation, histamine metabolism, *etc* [34, 65]. Oligofructans are helpful in propogation of bifidobacteria and in reduction of deleterious bacteria in the colon, prevent wound infection and food spoilage, protection of liver function and detoxification, constipation prevention, reduction of serum cholesterol and blood pressure with various anticancer effects [67].

Anticarcinogenic Activity

Alliums have anticarcinogenic activity, but garlic is known to be more effective due to the interaction of the sulphur components of garlic with the tumour cell metabolism [68-70]. DNA adduct formation, mutagenesis, free radicals scavenging, cell proliferation, differentiation and angiogenesis can be modulated by different garlic derivatives and onion suppress/inhibit the platelet aggregation *i.e.*, induced by collagen, arachidonic acid, ADP, adrenaline and the thrombin and the effect is dose dependent. Studies have demonstrated that organosulfur compounds such as diallyl disulfide (DDS), S-allylcysteine (SAC), and S-methylcysteine (SMC) inhibit colon and renal carcinogenesis *in vitro* and *in vivo* [7, 71]. The steroidal saponins isolated from a variety of different species of onions demonstrate significant cytotoxic activity against murine fibrosarcoma, lung carcinoma, human melanoma and leukemia [72, 73]. The risk of *Helicobacter pylori* infection linked to stomach cancer through ulcer formation is reported to be decreased by providing protection from colon cancer by inhibiting both initiation and proliferation through the effect of both organosulfur and flavonoids compounds [74, 75] with high consumption of allium vegetables [74]. Organosulfur compounds modulate the cytokine pattern to inhibit NFB, the central regulator of pro- inflammatory gene expression and link between inflammation and tumor progression. They exert immunomodulatory effects through alterations in the production of cytokines and immune modulators. Diallyl trisulfide (DATS) has been shown to reduce tumor mitosis, decrease histone deacetylase activity, increase acetylation of H3 and H4, inhibited cell cycle progression, and decrease pro-tumor markers [76]. DATS inhibited cell growth of human melanoma and ajoene has been shown to induce apoptosis in leukemic cells via stimulation of peroxide production, through activation of caspase-3-like and caspase-8 activity [77].

Quercetin is known to heal the gastric ulcers and colonocytes through free radical scavenging by preventing the induction of gastric mucosal injury and relieves muscular spasm due to calcium-antagonistic properties [53, 64-66], highly effective in inducing apoptotic cell death in colorectal tumour cells while sparing normal cells [41, 80], gene transcription inhibition to protection against UV-induced immune-suppression [81,82] and inhibition of kinase activity in the signal transduction pathway as a mode of protective action [83, 84]. Antioxidant property of quercetin is reported to be inversely associated with cancer formation [78, 79]. Quercetin functions in multiple ways *viz*. (a) decrease cancer tumour initiation; (b) promote healing of stomach ulcers (c) inhibit the proliferation of cultured ovarian, breast, and colon cancer cells. There is a significant anti-proliferative effect of quercetin on ovarian carcinoma, breast cancer cells by increasing the activity of reductase enzymes known to inactivate cytotoxic carcinogenic compounds and synergistically increase the activation of quinoid anticancer drugs [41, 52]. The organosulfur compounds are largely responsible for the taste and smell of onion and also (a) reduce symptoms asso-

ciated with diabetes mellitus (b) inhibit platelet aggregation (involved in thrombosis) (c) prevent inflammatory processes associated with asthma. Many of these studies used non-human subjects. Some of the most common organosulfur compounds dipropyl sulfide (DPS) and dipropyl disulfide (DPDS) in onions protect SPF Wistar male rats against cancer at early and late stages of carcinogenesis in by triggering microsomal epoxide hydrolase, glutathione S-transferase, and UDP-glucuronosyltransferase activities in the liver [71]. Other two common organosulfur compounds cysteine and S-methylcysteine of onion showed chemopreventive activity against hepatocarcinogenesis and colon carcinogenesis in a rat model [7, 85]. Both organosulfur compounds and flavonoids found in onions have a protective effect against N- nitroso compounds (NOCs) known for increased risk of brain cancer in China [86]. Dietary intake of Allium vegetables intake diminishes the risk of sarcoma and carcinoma in various tissues and organs such as oral, skin, brain, pharyngeal, esophageal, stomach, colorectal, laryngeal, breast, ovarian, prostate, and renal cell cancers [77, 86-90]. Eruboside-B, a steroid saponin, kaempferol, and organo Se compounds [91] are largely responsible for the anticarcinogenic activity [92]. These effects appear to be mediated by various mechanisms such as (a) increasing the detoxification enzymatic systems activity (b) facilitating its excretion from the body (c) inhibiting the procarcinogens activation and (d) inhibition of oxidative damage due to their antioxidant action. The apoptotic effect of water soluble garlic extract on the human metastatic MDA-MB-435 cancer cells in mitosis is due to the modifications of the proapoptotic protein BimEL to mitochondria leading to execution of its proapoptotic function. Several epidemiologic studies show that garlic components may be effective to inhibit tumorigenesis in several experimental models [12] and in human cancer risks [4, 8]. There is a strong inverse relationship between stomach and colon cancer risk and increasing garlic intake [93, 94]. However, not all epidemiological studies have shown garlic to be protective against carcinogenesis. Additional reports have shown garlic to be ineffective [94]. The Inconclusive results are likely due to differences in the type of garlic compounds, quantity of organosulfur compounds available in fresh and/or commercially available preparations used by various investigators [95].

Cardiovascular Diseases (CVD)

CVD is affecting 1 billion people and expected to affect over 1.6 billion people by 2025. Garlic has been advocated for the prevention of antihypertensive properties responsible for CVD. However, due to insufficient available evidences, it has not been recommended as a routine clinical therapy for the treatment of hypertensive subjects [96]. The antihypertensive effect of garlic is shown to be related with the hydrogen sulphide production, allicin content, and alliinase, the enzyme which possesses angiotensin II inhibiting and vasodilating properties. Basically, one of the mechanisms of antihypertensive activity of garlic was suggested to be explained through its prostaglandin-like effects leading to eventual decrease of peripheral vascular resistance. Majority of studies suggest that the cardioprotective properties are more likely due to lowering of low- density lipoproteins (LDL) and blood pressure. The metaanalysis results showed that an average of 800-900 mg garlic/day could decrease total serum cholesterol levels by approximately 9-12% [96, 97]. Long term application of garlic was effective to reduce almost 50% cholesterol and triglycerides in serum and atheromatous lesions in the aorta [98]. Garlic significantly inhibited intracellular Ca2+ mobilization, thromboxane-A2 synthesis and protected against thrombosis. The aged garlic extract can inhibit blood platelet aggregation through suppression of the GPIIb/IIIa receptor and an increase in cAMP [99], can cause decrease of plasma viscosity, and increase the elastic property of blood vessels in mice [100]. A dietary intake of Allium is beneficial for normalizing platelet hyperactivation and prevention of cardiovascular diseases. The validity of these reports, however, is reduced by methodological shortcomings, including the fact that dietary intake, weight, and/or exogenous garlic ingestion was not always well-controlled. In a multicenter, randomized, placebo-controlled trial in which dietary assessment and supervision were strictly controlled, 12 weeks of garlic treatment was ineffective in lowering cholesterol levels in subjects with hypercholesterolemia [101]. However, it is yet not clear the specific component of garlic responsible for cholesterol lowering.

Immunomodulatory Properties

Allium sativum and its compounds significantly reduce the leukocyte- cytokine production in inflammatory conditions (IBS) [102]. Some garlic proteins modulate NK cell line activity in the mesenteric lymph node of mouse, and aged garlic extract increases NK activities against different cancerous cell lines [103].

Lipid Metabolism

Total serum cholesterol, LDL and very low density lipoproteins (VLDL) are drastically decreased in rats and rabbits after raw garlic consumption with significant increase in the level of high density lipoproteins (HDL). Allicin and its derivative compounds are the main active substances responsible for the hypolipidemic and hypocholesterolemic effects of onion and garlic [1]. Studies have shown that saponins and flavonoid quercetin are able to reduce level of serum cholesterol and arteriosclerosis severity, diabetes [39], and HIV suppression/AIDS blocking [104]. Most likely, the organosulfur compounds [7, 105], working through sulfur-sulfur or sulfur-oxygen linkages [6], are believed to possess anti-inflammatory, anti-allergic, anti-microbial, and anti-thrombotic activity through inhibition of cyclooxygenase and lipoxygenase [37].

Antimicrobial and Antifungal

Garlic and onion have been used for centuries in folk medicine in several societies against microbial infections. Sulphur compounds characterised from onion and garlic are considered as the main active antimicrobial agents [106-109]. Garlic and onion extracts are known to inhibit the growth of Gram-positive, Gram-negative and acid-fast bacteria [110] including *E. coli*, Shigella, Salmonella, Proteus, Klebsiella, Enterobacter, *Vibrio cholera, V. parahaemolyticus, Staphylococcus aureus* [106], *S. typhi, Pseudomonas. pyocaneus, P. vulgaris, Bacillus subtilis, Cryptococcal meningitis, Shigella dysenterae* and Aspergillus [111]. Garlic

suppresses beneficial intestinal microflora as well. However, probably due to a greater sensitivity of enterobacteria to allicin, it is more effective against potentially harmful enterobacteria [106-115].

Garlic extract with high content of ajoene is significantly effective against *Candida albicans*, *Paracoccidiodes*, *Aspergillus* sp., *Botrytis cinerea* and *Trichoderma harzianum*, *Scedosporium prolificans*, *Tinea pedis*, *Opalina ranarum*, *Entamoeba histolytica*, *Leishmania*, *Trypanosomes*, *Leptomonas*, *Crithidia*, etc. [38, 116, 117]. The identified main active antifungal agents from onion and garlic extracts are the breakdown products of allicin which is able of inhibit sulfhydryl enzymes, DAS, DADs, diallyl trisulphide (DATS) and ajoene having greater antifungal effect than allicin [38, 115]. The active antifungal compound of garlic and onion destroy fungal cells by (a) reducing the oxygen uptake potentiality (b) reduce cellular multiplication and (c) by inhibiting synthesis of lipids, proteins and nucleic acids [38]. In addition to effectiveness against variety of pathogens, allicin stimulates the endogenous immune system *via* immune-correlated signalling pathways in cells. Allicin is an electrophile molecule with positive charge attract towards cysteine, activate channel protein via modification of cysteine residues and activation of TRPA1 leading to cause alteration in the conductance of the ion channels in the cell membranes.

Antiparasitic and Antiprotozoal

About 1.5 million people, especially children die of the malaria initiated by *Plasmodium* sporozoites every year [http://www.who.int/malaria/media/world_malaria_report_2014/en/]. Cysteine protease and ajoene present in freshly crushed garlic cloves inhibits target preerythrocytic and erythrocytic stages of the Plasmodium development. Pure allicin inhibits cytopathological effects and the growth of the intestinal parasites *Entamoeba histolytica* and *Plasmodium berghei*. Garlic extract is effective against Leishmania protozoan which infects nearly 12 million people globally and have no effective vaccine yet. Aged garlic extract modulates cytokine patterns towards a Th1-type response, increasing nitric oxide production and macrophage activation, which are important for eradication of parasite [118].

Antiviral Activity

The antiviral activities of various commercial garlic products have been developed against influenza A and B viruses [119] human cytomegalovirus [120, 121], human immunodeficiency virus (HIV), viral pneumonia and rotavirus [122, 123]. Quercetin, lectins and sulphur compounds are reported to possess antiviral activity and enhance the bioavailability of some anti-viral drugs with pronounced anti-HIV activity [120, 123].

Antioxidant Activity

Quercetin, which is the major dietary flavonoid, found in onion, show the highest antioxidative activity comparable to α-tocopherol [124-126]. The dry outer layers of onion contains large amount of quercetin. S-allyl cysteine (SAC) and S allylmercaptocysteine (SAMC), bioavailable water-soluble organo-sulphur compounds of garlic, along with stable lipid-soluble allyl sulphides, as DAS, DATS, DADS and diallyl polisulphides, flavonoids (as allixin); saponins, essential micronutrients (selenium) and macronutrients, as lectins, are known to express potent antioxidant activity [125, 126].

Antihyperglycemic Activity

Diabetes mellitus (NIDDM, type 2 diabetes) is characterized by hyperglycemia, which is expressed with a rapid rise in blood glucose level due to hydrolysis of starch by pancreatic α-amylase and absorption of glucose in the small intestine by α-glucosidases [127]. The aqueous juice of various forms of raw onions and garlic and isolated compounds possess significant antihyperglycemic effect in laboratory settings. The root of the Welsh onion (*Allium fistulosum* L.) alleviates hyperglycemia via inhibiting α-glucosidase *in vitro*, as well as in animal model *in vivo* [127]. Quercetin, isoquercitrin and rutin demonstrate significant inhibitory activity on α-glucosidase from the rat intestine [127]. The Korean onions (*Allium cepa* L.) have strong inhibitory potential against rat α-glucosidases (sucrase, maltase, porcine pancreatic α-amylase) *in vitro* and *in vivo*. The consistent dietary intake of the onion (*Allium cepa* L.) extract in rat improves diabetes by decreasing triglyceride and free fatty acid levels. Aged garlic extract increase insulin secretion and sensitivity, increase nitric oxide production and significantly decrease inflammatory cytokines, glycosylated hemoglobin (HbA1c), postprandial blood glucose (PPBG) and fasting blood glucose (FBG) level in human studies [128]. Garlic oil demonstrates antioxidant activity in diabetic skeletal muscle via reversing insulin resistance, lowering the nitric oxide production and improving GLUT4 expression.

Effect on Respiratory System

A wide range of different flavonols, differentiated on the basis of degree of hydroxylation, are found in onions consisting of the aglycones and certain onion-derived compounds (not garlic), particularly thiosulfinates and cepaenes, show an anti-inflammatory and antiasthmatic properties *in vivo*. The main compounds found in *Allium cepa* L. extract (AcE) are the natural phenolics, flavonoids such as quercetin, exhibiting anti-inflammatory and antioxidant effects. There is a reduction in the production of inflammatory cytokines, a relaxation of tracheal rings, and a reduction in the total number of cells in BAL and EPO in the lungs by treatment with onion extract or quercetin [129]. Along with flavanols, the major bioactive constituents in *Allium cepa* L. are sulfurous compounds [130-133].

Effect on Skin

The nuclear transcription factor kappaB which is known to be linked to psoriasis can be interrupted by garlic compounds, such as diallyl sulfide, sallylmercaptocysteine and ajoene. These compounds play important role in development and progression of alopecia areata, wound healing, keloid scars, leishmaniasis. Garlic stimulates the proliferation of macrophages and lymphocytes, protecting against the suppression of immunity by ultraviolet radiation. *Allium cepa* improves the appearance of scars, their softness, diminish redness and improve the skin texture. Ingested fresh

Allium sativum delays formation of skin papillomas and protect against skin cancer [134].

Allium Products

Due to therapeutic properties of alliums, onion and garlic, diet supplements with capsules, tablets and lozenges are widely available on local and international markets. Onion products include dehydrated onion pieces, onion powder, oleoresins, onion salts, pickled onions, canned, frozen and packaged onions, *etc*. Dehydrated garlic powder, garlic juice, garlic salt, garlic flavouring are some of the advantageous garlic products being marketed [134]. Essential oil of garlic is extracted by distillation in boiling water in a still or by introducing live steam generated in a separate steam boiler [134, 135].

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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