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Phytoconstituents and Therapeutic Potential of *Allium cepa* Linn.– A Review

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ABSTRACT
In the present scenario, herbal medicines have gained global importance with both medicinal and economic implications. Widespread use of herbs throughout the world has raised serious concerns over their quality, safety and efficacy. Thus, accurate scientific assessment has become a prerequisite for acceptance of health claims. Onion (*Allium cepa* Linn.), a member of the genus *Allium*, is the second most important horticulture crop all over the world. It is used as an important source of phytoconstituents and food flavour. Onions are one of the richest sources of flavonoids and organosulphur compounds. They possess a high level of antioxidant activity attributable to flavonoids quercetin, kaempferol, myricetin; pigments such as anthocyanins, and organonosulphur compounds. The most important among the sulphur compounds are the cysteine derivatives non-volatile S-amino acids, S-alk(en)yl-substituted cysteine sulphoxides and their decomposition products such as thiosulfinates and polysulfides. These sulphure compounds and flavonoids possess antioxidant, antidiabetic, anti-inflammatory, anticancer, antimicrobial, antihyperlipidaemic, anticholesterolaemic, fibrinolytic, antiatherosclerotic, anticataractogenetic, antiplatelet aggregation, immunomodulatory, neuroprotective in ischemia and reperfusion-induced cerebral injury, and various other biological activities. Wide spectrum of biological activities makes *A. cepa* as potential therapeutic agent.
KEY WORDS: *Allium cepa,* Anticancer, Antioxidant, Flavonoids, S-cysteine sulphoxides

INTRODUCTION

Allium, a large genus containing about 4000 species is distributed throughout temperate regions of the world including Europe, Asia, North America and Africa (1). *Allium* species have a long history of folklore use and are potential sources of therapeutic principles. Of approximately 700 edible members, including economically important vegetables, flowering ornamentals and wild species, plants such as onion (*A. cepa* Linn.), garlic (*A. sativum* Linn.), chives (*A. schoenoprasum* Linn.), leek (*A. porrum* Linn.) and welsh onion (*A. stulosum* Linn.) are highly prized (2).

Onion, the underground bulb of *A. cepa* is a member of the family Liliaceae (3-5). Members of Liliaceae show a variety of different habits, and have varied classes of phytoconstituents. Therefore, the classification of the Liliaceae has been discussed for a long time. Hutchinson in 1959 assigned *A. cepa* to the subfamily Allioideae of the family Amaryllidaceae. But, because of the lack of alkaloids which are normally present in the family Amaryllidaceae, Allioideae was later classified as a subfamily of the Liliaceae (6). Recent taxonomic revisions assigned the plants of the genus *Allium* to an independent family Alliaceae (1, 7).

A. cepa is of great economic importance. It is widely cultivated all over the world, and was possibly one of the first domesticated vegetables by man (8). World onion production has increased by at least 25% over the past ten years with current production being around 44 million tones per year making it the second most important horticulture crop after tomatoes. Onion is famous for its use as food flavour, and as an important source of phytoconstituents. The average annual per capita intake of onion in the world is estimated to be 7 kg (9).

CHEMICAL CONSTITUENTS

A. cepa is a rich source of a variety of compounds and has been thoroughly investigated by phytochemists over the last 100 years. Various phytoconstituents of *A. cepa* have been reviewed under the following groups of constituents.

Alliinase

It is a 50 kDa glycoprotein, common to all *Allium* species isolated and characterized from several *Allium* species including *A. cepa*, *A. sativum*, *A. tuberosum*, *A. ursinum* and *A. porrum* (10-14). Purified onion alliinase shows optimum activity at 7.4 pH. In intact tissues, alliinase is compartmentalized within plant vacuoles and the non-volatile sulphur compounds located in the cytoplasm**.** Upon tissue disruption the vacuole and cytoplasmic contents mix, promoting the enzymatic hydrolysis of the respective sulphur compounds (15, 16).

Sulphur compounds

Like other species of the genus *Allium,* e.g. *A. sativum* or *A. ursinum*, *A. cepa* is especially characterized by a high content of both non-volatile and volatile organosulphur compounds. The most predominant of these sulphur containing compounds are the amino acids cysteine and methionine, the S-alk(en)yl-substituted cysteine sulphoxides and the γ-glutamyl peptides (17). The contents of these secondary sulfur compounds are strongly dependent on stage of development of the plant, temperature, water availability and the level of nitrogen and sulfur nutrition (18-21).

Non-volatile sulphur compounds of the unsubstituted S-containing amino acids L-cysteine, L-cystine and L-methionine are

relatively low in onions because of their rapid metabolism. A rapid oxidation of S-alk(en)ylated L-cysteine to related cysteine sulphoxides have been observed *in vivo*. Until now, four S-alk(en)yl-cysteine sulphoxides viz. (+)-S-methyl-, (+)-S-propyl-, trans-(+)-S-(1-propenyl)-L-cysteine sulphoxide and cycloalliin have been detected in *A. cepa*. When the tissues are disintegrated by chopping or squeezing, S-alk(en)yl-L-cysteine sulphoxides are metabolized to sulphenic acids by the action of alliinase. Sulphur compounds generated from the highly reactive sulphenic acids are responsible for the lachrymation, pungency, and for the typical smell, taste and pharmacological actions of onion extracts (17, 22). It is assumed that S-alk(en)yl-cysteine sulphoxides are predominantly synthesized in leaves, from where they are subsequently transferred to the attached bulb scale (23).

Volatile sulphur compounds in onion extracts are enzymatically generated upon chopping or squeezing of onion tissues (Fig. 1).

Among the volatile sulphur-containing compounds, probably the most famous is (Z)-propanthial-S-oxide. Its lachrymatory properties cause irritation to the eyes, and it is claimed that this constituent dimerizes to a further lachrymatory factor, i.e. (Z,Z)-d,l-2,3-dimethyl-1,4-butanthiol-S,S'-dioxide. Other volatile sulphur-containing compounds are zwiebelanes, the cepaenes and the mono-, di- and trisulphides originating from spontaneously formed thiosulfinates, which on the other hand are responsible for the characteristic onion flavour (17, 24). Interestingly, recent investigations hypothesize a specific enzymatic conversion of 1-propensulphenic acid to the lachrymatory factor, thus possibly enabling the production of non-lachrymatory onions by knocking-out the gene encoding for this enzyme without influencing the flavour and nutritional value of onions (25).

Volatile oil

Steam distillation of onion bulbs yields volatile oil known as onion oil. It has acid taste and unpleasant odour. Gas chromatography of the oil revealed the presence of monosulfides (R1-S-R2), disulfides (R1-S-S-R2), trisulfides (R1-S-S-S-R2), tetrasulfides (R1-S-S-S-S-R2) and thiols (RSH). Alkyl or alkenyl disulfides and trisulfides are primarily responsible for cooked onion flavour, which is characteristic of steam distilled onion oil (22).

Flavonoids

These are the major class of phytoconstituents that provide colour, texture and taste to the onion. They tend to accumulate in the outer cell layers (26, 27). The onions are known to contain anthocyanins and flavonoids quercetin and kaempferol (28, 29). However, anthocyanin pigments, concentrated in the outer scales of red onions, are only minor constituents of the edible portion (29). Kaempferol, while detectable in certain onion varieties, is present in much smaller quantities than quercetin (28, 30). Therefore, quercetin is the major flavonoid of interest in onions.

Amount of quercetin in onion varies with bulb colour, type, variety and growing location (31-34). Although the red onions are generally higher in total flavonoids than the white or sweet yellow onions due to the presence of anthocyanins (29). Red onions generally contain lower level of quercetin. Yellow onions have been found to contain maximum level of quercetin which tends to concentrate in outer ring (33, 35). In the underlying scales, quercetin is found as glucosides (28, 36). Predominant among the glucosides are quercetin 4'-glucoside (Q4'G) and quercetin 3,4'-diglucoside (Q3,4'G). These glucosides are mainly present in the abaxial epidermis of the scales. Concentrations of the two glucosides and ratios of Q4'G to Q3,4'G increase from the interior to the exterior scales (35, 36). Takahama and Hirota (2000) have suggested that quercetin is formed by the deglucosidation of its glucosides, followed by autoxidation to produce protocatechuic acid (37).

Saponins

A phytochemical investigation of the methanolic extract of the red bulbs of *A. cepa* var. *tropea*, typical of Calabria, a southern region of Italy, led to the isolation of four new furostanol saponins, named tropeoside A1/A2 (1a/1b) and tropeoside B1/B2 (3a/3b), along with the respective 22-O-methyl derivatives (2a/2b and 4a/4b), almost certainly extraction artifacts (38). High concentrations of ascalonicoside A1/A2 (5a/5b) and ascalonicoside B, previously isolated from *A. ascalonicum* Hort, were also found. This is the first report of furostanol saponins present in *A. cepa*.

γ-Glutamyl peptides

Until now, a total of 14 types of γ-glutamyl peptides have been identified in onions (39) and 9 of them contain sulphur atoms (Table 1).

Table 1: γ-Glutamyl peptides in A. cepa

γ-Glutamyl peptides	Sulphur-containing γ-Glutamyl peptides
γ-Glutamyl-isoleucine	γ-Glutamyl-methionine
γ-Glutamyl-valine	γ-Glutamyl-S-methyl-L-cysteine
γ-Glutamyl-leucine	γ-Glutamyl-S-methyl-L-cysteine sulphoxide
γ-Glutamyl-thyrosine	γ-Glutamyl-S-trans-(1-propenyl)-L-cysteine- sulphoxide
γ-Glutamyl-phenylalanine	γ-Glutamyl-S-(2-carboxypropyl)-cysteinylglycine
	Glutathione-γ-glutamyl-cysteine-disulphide
	Glutathione-cysteine-disulphide
	S-Sulphoglutathione
	Glutathione

γ-Glutamyl peptides which occur mainly in dormant seeds and resting bulbs, contribute to the germination of seeds, and act as a storage reserve. (+)-S-alk(en)yl-L-cysteine sulphoxides linked to γ-glutamyl peptides are not metabolized by alliinase. After cleavage by peptidases and transpeptidases, free alk(en)yl-L-cysteine sulphoxides are available to form volatile S-constituents in onion extracts. Because about 90% of soluble organically bound sulphur is present in the form of γ-glutamyl peptides, this class of compounds plays an important

Table 2: Composition of onion

Parameter	Value
Moisture	87-93%
	g /100 g wet wt.
Proteins	0.9-1.5
Fat	0.2-0.4
Carbohydrate	5.2-10.5
Ash	0.7
Energy	23-38 **calories**
Elements	**mg /100 g wet wt.**
Ca	190-540
P	200-430
K	80-110
Na	31-50
Mg	81-150
Al	0.5-1
Ba	0.1-1
Fe	1.8-2.6
Vitamins	**mg /100 g wet wt.**
Thiamin	0.3
Riboflavin	0.05
Nicotinic acid	0.2
Vitamin C	10
Vitamin B6	0.1
Pentothenic acid	0.14
	µg /100g wet wt.
Folic acid	16
Biotin	0.9
Retinol	25

role in the taste-quality of onions and for the formation of potentially pharmacologically active ingredients in onion extracts (17, 19).

Composition of fresh onion from nutritional point of view has been reported (Table 2) by Augusti (22). However, the particular composition depends on a large number of factors, such as growing conditions, time of harvest and length and conditions of storage (40).

ETHNOPHARMACOLOGY

A. cepa has been cultivated and used as a nutrient for more than 6000 years. People detected therapeutic properties of the plant and used it in traditional and folk medicine for many different major and minor disorders. Convincing scientific data to support most of these claims are, however, lacking (41).

Onion has been used as anthelmintic, aphrodisiac, carminative, emmenagogue, for vertigo, for migraine, expectorant, tonic and for the treatment of bruises, bronchitis, cholera, colic, earache, fever, high blood pressure, jaundice, pimples, dropsy and sores (5, 42). Fresh Onion juice is often recommended in folk medicine of various countries for pain and swelling after bee or wasp stings, which are followed by an allergy-induced reaction of the skin. The observed inhibitory effects of onion extracts on this kind of cutaneous reactions led to the discovery of anti-inflammatory and antiasthmatic, thiosulfinates and cepaenes (43, 44). Onions have also been used as adjuvant therapy for diabetes (42, 45).

PHARMACOLOGICAL REPORTS

A variety of traditional uses of onion have prompted the researchers world over to investigate pharmacological properties of onion.

Anticancer activity

Ethanol (95%) extract of onion, administered i.v. to cats and rats at dose of 50 mg/kg, produced weak activity on Sarcoma III (MKT) (46). Essential oil, applied externally on female mice at a dose of 1 mg/animal has been reported to be effective against carcinoma induced by twice weekly 12-o-tetradecanoyl-phorbol-13-acetate promotion for two week, followed by mezerein promotion for 18 week (47). The dose, when given with a second promoter, produced a 32% decrease in incidence of papilloma in DMBA-induced carcinogenesis. Hot water extract of the fresh bulb applied externally on mice (1 mg/animal) was active against DMBA-induced carcinogenesis (48).

The inhibitory effects of onion consumption on human carcinomas have been widely researched. Epidemiological data both support (49, 50) and refute (51), the concept that higher intake of onions is positively related to lower risk for carcinoma. It has been noted that persons in the highest consumption category versus the lowest had a 50% reduced risk of cancers of the stomach, alimentary and respiratory tracts (52). Organosulphur compounds such as diallyl disulfide (DDS), S-allylcysteine (SAC) and S-methylcysteine (SMC) have been shown to inhibit colon and renal carcinogenesis (53, 54).

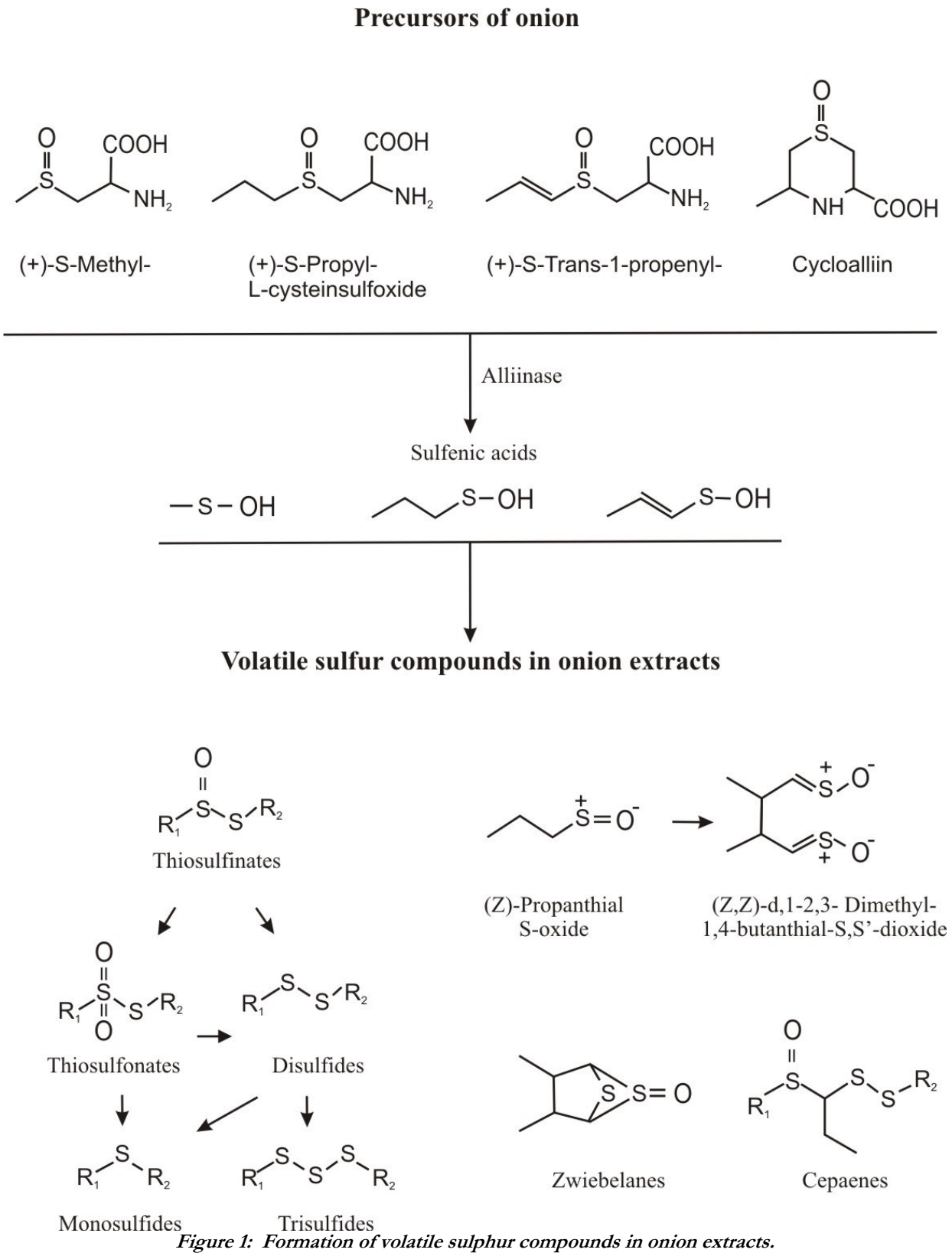

Figure 1: Formation of volatile sulphur compounds in onion extracts.

Mechanisms of protection ranged from induced cancer cell apoptosis (55) and gene transcription inhibition (56) to protection against UV-induced immunosuppression (57).

New evidence suggests that some of the most common organosulphur compounds in onions may protect against cancer in rats. Fukushima et al. (58) found that both cysteine and S-methyl cysteine, two common organosulphur compounds found in onions, have chemopreventive activity for hepatocarcinogenesis and colon carcinogenesis in rats. Various researchers have suggested that high onion consumption may have a strong impact on stomach cancer prevention (51), lung cancer (51), bladder cancer (59), breast cancer (60, 61) and ovarian cancer (62).

It has been have suggested that consumption of onion may be inversely linked while that of salt preserved foods positively related to risk of brain cancer (63). A case control of 129 subjects in north-east China paralleled these findings (50). In particular, a strong inverse relationship to cancer risk was found with high consumption of onions. It is well postulated that N-nitroso compounds (NOCs) from salted foods may be the reason for increased risk of brain cancer (63, 50). It has been shown that both organosulphur compounds (64) and flavonoids (65, 66) found in onions have a protective effect against NOCs.

Antihyperglycemic activity

The light petroleum extract of dried powder of onion (0.25 g/kg, p.o.) showed hypoglycemic activity comparable to tolbutamide in alloxan-induced diabetic rabbits (67). The ethyl ether extract (0.25 g/kg p.o.) of the juice expressed from onion revealed higher hypoglycemic activity both in the normal and alloxan-induced diabetic rabbits as compared to other extracts, and it was also observed that hypoglycemic effect was equivalent to that of tolbutamide and phenformin (42, 68-70).

Ether and ethanol (90%) extract of dried onion administered by gastric intubation to rats at dose of 50 g/kg (expressed as dry weight of the bulb) were active against alloxan- and adrenalin-induced hyperglycemia (71). Aqueous extract of fresh bulb taken orally by human adult at a dose of 100 g per person was active against glucose and adrenalin-induced hyperglycemia (42). Decoction of onion (4 ml/kg) showed hypoglycemic activity (72).

The organosulphur compounds S-methylcysteine sulphoxide (SMCS) and S-allylcysteine sulphoxide (SACS) were linked to significant amelioration of weight loss, hyperglycemia, low liver protein and glycogen, and other characteristics of diabetes mellitus in rats (73). The use of SMCS and SACS (200 mg/kg/day) gave results comparable to treatment with insulin or glibenclamide but without the negative side effect of cholesterol synthesis stimulation. *In vivo* analysis of the effects of quercetin on human diabetic lymphocytes showed a significant increase in the protection against DNA damage from hydrogen peroxide at the tissue level (74). Kumari et al. (75) also reported antidiabetic and hypolipidemic effect of S-methylcysteine sulphoxide isolated from onion. Diphenylamine isolated from onion has also been reported to exhibit antihyperglycemic activity (5, 76).

Antimicrobial activity

Onions have been shown to possess antibacterial and antifungal properties (10, 77). Volatile oil of onion has been shown to be highly effective against gram positive bacteria, dermatophytic fungi, growth and aflatoxin production of Aspergillus fungi genera including *Aspergillus niger, Brettanomyces anomalus, Candida albicans, C. lipolytica, Cladosporium werneckii, Fusarium oxysporium, Geotrichum candidum and Saccharomyces cerevisiae* (78, 79). Aqueous extract or the juice of onion has been reported to inhibit *in vitro* growth of *Escherichia coli, Serratia marcescens*, *Streptococcus* species, *Acetobacillus odontolyticus, Pseudomonas aeruginosa* and *Salmonella typhosa* (80, 81). A petroleum ether extract of onion inhibited the *in vitro* growth of *Clostridium paraputrificum* and *Staphylococcus aureus* (80). Welsh onion extracts have been reported to exert more inhibitory activity towards aflatoxin production than the preservatives sorbate and propionate at pH values near 6.5, even at concentrations 3-10 folds higher than maximum level used in foods (82). Organosulphur compounds have been reported to be responsible for antibacterial effects of onion extract against oral pathogenic bacteria causing dental caries (83).

In addition to inhibitory effects against pathogenic bacteria, onions have been found to promote beneficial micro-organisms. Onions contain fructo-oligosaccharides (FOS), probiotics which are non-digestible ingredients fermented by bifido bacteria in the body that help maintain the health of the gut and colon (84). Onions contain 2.8% FOS (wet wt.) as compared to 1.0% FOS in garlic, 0.7% in rye, and 0.3% in bananas.

Antioxidant activity

High intake of fruits and vegetables has been reported to prevent alteration of DNA by reactive oxygen species and subsequent cancer development (85). Flavonoids, ubiquitous in the plant kingdom, have been widely studied for their antioxidative effects (30, 52). Onions are known to contain anthocyanins and the flavonoids quercetin and kaempferol (28, 29). However, anthocyanin pigments, concentrated in the outer shell of red onions, are only minor constituents of the edible portion (29). Kaempferol, while detectable in certain onion varieties, is present in much smaller quantities than quercetin (28, 30). Therefore, quercetin is the major flavonoid of interest in onions. Mechanisms of action include free radical scavenging, chelation of transition metal ions, and inhibition of oxidases such as lipoxygenase (86, 87). Extracts from the outer scales of onion have exhibited potent free radical scavenging activities (88, 89).

The homogenate fresh onion and hot water extract of fresh aerial parts of *A. cepa* exhibit significant inhibition of lipid peroxidation (77). The antioxidative effects of consumption of onions have been associated with a reduced risk of neurodegenerative disorders (66), many forms of cancer (52, 90), cataract formation (91), ulcer development (87) and prevention of cardiovascular diseases by inhibition of lipid peroxidation and lowering of low density lipoprotein (LDL) cholesterol levels (92-94). Another antioxidant effect of onions and their extracts includes the reduction of rancidity in cooked meat (95). Protection from arachidonic acid

metabolites and lipoxygenase activity is important in prevention of vascular diseases (96). Quercetin has been shown to not only directly inhibit the lipoxygenase enzyme, but to also suppress consumption of α-tocopherol and to preserve human serum paraoxonase both are potent antioxidants against lipid peroxidation (93, 97).

Metal chelation involves formation of a complex with the flavonoid and prevention of catalytic radical production, whereas free radical scavenging activities relate to the flavonoid donating a hydrogen atom and creating a more stable radical (86). Direct scavenging of super oxide and hydroxyl anions has been reported (87, 98). However, Sestili et al. (99) in an experiment designed to distinguish the mechanism of action, found that quercetin effectively protected DNA strand scission from tetra-butylhydroperoxide, which can only be explained by iron chelation. Copper chelation has also been exhibited to have anti-peroxidative effects (92). Negre and Salvaryre (100), and Mc Anlis et al. (101) reported that although direct protection by quercetin against oxidative LDL modification had been found *in vitro*, the flavonoid exerted its protective effect *in vivo* at the cellular level by preventing cell damage from already oxidized LDL. Therefore, depending on the location of protective action (cellular, nuclear, or plasma) a different antioxidative mechanism may be at work.

Comparative studies of the antioxidative activities of different vegetables have been examined (102-106). It has been found that most vegetables contain antioxidant activity, which is associated with epidemiological hypothesis relating high vegetable intake with lower risk of diseases (105, 106). Absorption and bioavailability of flavonoids in onions have been shown to be more effective than from other sources (e.g. tea and apples) (107).

It has been demonstrated that the novel 3-mercapto-2-methylpantan-1-ol (3-MP), of which four possible diastereoisomers can occur in varying amounts in *A. cepa*, significantly inhibited peroxynitrite-mediated tyrosine nitration and inactivation of α-1-antiproteinase. Moreover, 3-MP also inhibited peroxynitrite-induced cytotoxicity, intracellular tyrosine nitration and intracellular reactive oxygen species (108, 109).

Cardiovascular protective effects

Experimental animals were studied for cardiovascular protective effects of onion. Rats fed 2 g/kg dry onion for six days while feeding on an atherogenic diet showed significant reductions in both serum cholesterol and triglyceride levels as compared to those only fed with atherogenic diet (110). Likewise, a group of volunteers fed a high fat diet plus 100 g onion once a day and those fed fat diet only showed a significant decrease in serum triglycerides, but not cholesterol (111). Investigators from both studies showed a possible inhibitory benefit of onion consumption on atherosclerotic formation.

Antihyperlipidimic and anticholesterolemic activities were observed after oral administration of minced bulbs, a water extract thereof, and essential oil (100 mg/kg) to rabbits and rats (112-116). However, one study reported no significant changes in cholesterol or lipid levels of the eye in rabbits, after treatment of the animals for six months with an aqueous extract (20% of diet) (5). Oral administration of butanol extract to patients with elementary lipaemia prevented an increase in total serum cholesterol, β-lipoprotein cholesterol, and β-lipoprotein and serum triglycerides (117). A saponin fraction (50 mg) or the bulb (100 mg) also decreased serum cholesterol and plasma fibrinogen levels (44). However, fresh onion extract (50 g) did not produce any significant effects on serum cholesterol, fibrinogen or fibrinolytic activity in normal subjects (118, 119).

It is reported that S-methylcysteine sulphoxide (SMCS) present in onion is active hypocholesteremic agent (120, 121). Volatile oil of onion and their precursor allins (SMCS) counteracted the lipogenic effect of sucrose, alcohol and cholesterol diets (122, 123).

Mechanism of action for anticholesterolaemic activity of onion includes inactivation of thiol enzymes (eg. HMG-CoA), which promote lipid/cholesterol synthesis by organosulphur compounds of *Allium*. Secondly, these compounds can reduce the level of NADPH in tissue so that they may not be available for cholesterol synthesis (124).

Reduction of heart diseases via dietary intake of phytochemicals has been examined (10, 52). Researchers who have studied 12,763 men from seven countries found an inverse relationship between flavonoid intake and coronary heart diseases (52). Inhibition of LDL oxidation and platelet aggregation was proposed as mechanisms of benefit against cardiovascular disease (125). Inhibition of platelet aggregation by onion has been demonstrated both *in vitro* and *in vivo*. Aqueous extract of onion has been reported to inhibit adenosine diphosphate, collagen, epinephrine and arachidonic acid-induced platelet aggregation *in vitro* (126). Platelet aggregation was inhibited in rabbits after administration of the essential oil, or a butanol or chloroform extract of the onion (127, 128). An ethanol, butanol or chloroform extract or the essential oil (10-60 μg/ml) of the onion inhibited aggregation of human platelets *in vitro* (129, 130) by decreasing thromboxane synthesis (131). Both raw onion and its essential oil increased fibrinolysis in *ex-vivo* on rabbits and humans. An increase in coagulation time was also observed in rabbits (132). It has been reported that intragastric administration of the juice or an ether extract (100 mg/kg) of the onion inhibited allergen and platelet activating factor-induced allergic reactions, but not histamine or acetyl choline-induced allergenic responses in guinea pigs (43). Chloroform extract (20-80 mg/kg) inhibited allergen and platelet aggregation factor-induced bronchial obstruction in guinea pig (43). Thiosulfinates and cepaenes appeared to be the active constituents of onion (132). Inhibitory effects of garlic and onion extract on human platelet aggregation have been attributed to adenosine, allicin, allins, ajoene, polysulphides and vinyl di-thiines. Allicin is reported to inhibit human platelet aggregation *in vitro* without affecting cyclooxygenase or thromboxane-II synthase activity or cyclic AMP levels, possibly by influencing Ca^{2+} movements. Ajoene is reported to prevent loss of platelets and increase the rate of restoration

of platelet clotting activity. Moreover, ajoene can also inhibit adhesive interaction of human neutrophils and consequently effect *in vivo* super oxide anion formation. This is an illustration of antioxidant (free radical scavenging action) property of onion products (10). Quercetin exerts its beneficial effects on cardiovascular health by antioxidant and anti-inflammatory activities (133, 134). Lipid peroxidation is a self-propagating chain of highly reactive radicals that have drastic effects on membrane functions (96). Aldehydes derived from lipid peroxidation can diffuse within or escape from the cell and attack targets far away from the site of origin (135). LDL oxidation and endothelial cell damage is believed to be involved in the early development of atherosclerosis (94, 97). Researchers have found that the presence of quercetin significantly reduced LDL oxidation *in vitro* by various oxidases including 15-lipoxygenase, copper-ion, UV light, and linoleic acid hydroperoxide (94, 97, 100).

Stroke and coronary heart diseases can be caused by platelets in the blood, adhering to the walls of blood vessels in the heart or brain and aggregating to the point of obstruction (136). *In vivo* effects of onion (500 mg/kg) consumption in rats showed significant inhibition of serum thromboxane, an inducer of platelet aggregation (137). Low dose (50 mg/kg) showed little effect, but benefit was observed over long-term consumption. Boiled onions, even at the high dosage level, showed no effect, suggesting that effective compounds are thermolabile. Similarly, raw Welsh onion extracts were shown to have vasodilating effects on precontracted aortic rings while boiled extracts caused vasoconstriction and were purported to induce thromboxane synthesis (138). In a subsequent study it was found that oral administration of raw Welsh onion juice in rats prolonged bleeding time reduced platelet aggregation and increased cAMP level (138). However, boiled onion juice showed none of these effects. Again, change in thromboxane balance was thought to be the reason for the inhibition of platelet adhesion. Other researchers showed antiplatelet activity in rabbit plasma, but not in human plasma (136) and suggested that varietal differences may play a role. Goldman et al. (139) found that onions containing higher sulfur levels exhibited a greater antiplatelet effect than genotypes with low sulfur content. Janssen et al. (125) performed both *in vitro* and *in vivo* studies. 2500 μmol/L quercetin isolated from onions was shown to inhibit platelet aggregation by 95-97% *in vitro*. However 18 human subjects ingesting 114 mg quercetin/day showed no significant effects. Therefore, it was concluded that necessary concentration levels of quercetin for beneficial effects were too high to be obtained dietarily.

Cataract

The cataract, characterized by lens opacification has been shown to be instigated by oxidative stress, primarily from hydrogen peroxide (H_2O_2) (140). Quercetin is known to scavenge the free radical super oxide onion, a major *in vivo* source of H_2O_2 (96). Opacity induced in rat lenses by exposure to H_2O_2 was almost entirely reversed after incubation with 30 μM quercetin for 4 hours (91). Pretreatment of lenses with quercetin before oxidation was shown to provide 46% protection as compared to control. Further tests showed that the mode of action was not inactivation or removal of H_2O_2 by free radical scavenging, but that quercetin inhibited opacification by protecting modification of lens membrane channel proteins by an influx of Ca^{2+} and Na^{+} ions. Daily consumption of more than 500 ml of green tea, a large source of quercetin, was associated with decreased risk of cataract (141). It has been reported that the percentage of quercetin absorbed from onions is approximately twice that of tea (107). Therefore, high daily intake of onions may provide a nutritional benefit against the risk of cataract formation.

Fibrinolytic properties

The fibrinolytic activity of onion has been confirmed by Menon et al. (142) in people with fat-induced clotting of blood. Reduced blood fibrinolytic activity is a defect that promotes thrombus formation in atherosclerotic vessels. Agarwal et al. (143) have reported that cycloallin administration to post-myocardial infarction patients induced a significant increase in fibrinolysis after 15 h of medication. Butanol extract of the fresh bulbs, taken orally by adults, was active (144). The essential oil, administered by gastric intubation to male rabbits at a dose of 2.0 g/kg for 3 months, enhanced the fibrinolytic activity (77).

Immunosuppression

Inflammation is the part of the body's natural immune response to trauma. Thiosulfinates and capaenes responsible for the anti-inflammatory activities also cause inhibition of the immune response (43, 145). Quercetin also affects immunosuppression and has been shown to create a beneficial effect in aiding renal transplantation (57, 146). Quercetin was shown to suppress both immune and non-immune injury responses, the key risk factors in chronic graft loss. This showed promising application as it was noted that current drugs and treatments may worsen harmful, non-immunological reactions (ischemia, hypertension, and hyperlipidemia) to the transplant. Alternately, quercetin has been shown to prevent immunosuppression induced by UV exposure to mice (57).

Neuroprotective effect

Recently, it has been reported that administration of methanolic extract of outer scales and edible portion of *A. cepa* bulb to mice before cerebral ischemia and reperfusion exhibit significant neuroprotection by markedly reducing cerebral infarct size, significantly decreasing, increase in thiobarbituric acid reactive substances (TBARS) concentration in brain mitochondria and supernatant fractions and preventing global cerebral ischemia reduced impairment of short-term memory and motor incoordination (147).

Anti-inflammatory activity

The anti-inflammatory effect of quercetin on prostaglandins, leukotrienes, histamine release and subsequent antiasthmatic activity has been investigated (129). It has been reported that aqueous suspension of the fresh bulbs, administered by gastric intubation to rabbits at a concentration of 10.0% was active (148). Onion taken orally by adults at variable dosage levels was found to be anti-inflammatory. Ethanol (80%) extract of the bulb, administered by gastric intubation to male rats at a

dose of 100 mg/kg, was inactive against carrageenan-induced paw edema (149). Thiosulfinates and cepaenes in onion have been shown to possess anti-inflammatory properties (150). This action is related to inhibition of inflammatory cell influx by thiosulfinates and cepaenes.

Over-expression of pro-inflammatory enzymes such as inducible nitric oxide synthetase (NOS) and cyclooxygenase-II (COX-II) are observed in numerous human pathologies including cancer, cardiovascular and inflammatory diseases. Increased activity of inflammatory enzymes leads to the generation of pro-inflammatory mediators including nitric oxide (NO) and prostaglandins (PG). Endogenous production of NO and PG has a beneficial role in the maintenance of blood pressure, inflammation, wound healing and temperature regulation. However, overproduction leads to pathphysiological conditions such as the promotion of colon cancer, atherosclerosis, inflammatory bowel disorders, multiple sclerosis, Alzheimer's diseases and septic shock (1). Both NOS and COX-II protein expression are regulated by nuclear factor kappa B, a transcription factor activated by carcinogens, toxins and oxidative stress. To date, nuclear factor kappa B has been demonstrated to regulate the transcription of over 150 separate genes, many of which are involved in inflammation. Recent studies have shown that antioxidants can inhibit nuclear factor kappa B activation, and, thus reduce the symptoms of debilitating disease states. Indeed, when we consider the association between *Allium* vegetable consumption and reduced risk to cardiovascular diseases and cancers, may of the beneficial effects are perhaps due to the anti-inflammatory properties.

SUMMARY

The present review deals with the botanical, phytochemical, ethnopharmacological and pharmacological information on *Allium cepa* famous for its use as an important source of phytoconstituents and food flavour. An exhaustive survey of literature revealed the presence of flavonoids quercetin, kaempferol, myricetin, pigments such as anthocyanins; saponins, and organonosulphur compounds like cysteine derivatives non-volatile S-amino acids, S-alk(en)yl-substituted cysteine sulphoxides and their decomposition products such as thiosulfinates and polysulfides. Other constituents include alliinase enzyme (a glycoprotein), volatile oil, proteins, vitamins, etc. Research on flavonoids and sulphure compounds have gained a special attention in recent times as several of them have shown promising activities like antioxidant, antidiabetic**,** anti-inflammatory**,** anticancer, antimicrobial, antihyperlipidaemic, fibrinolytic**,** antiplatelet aggregation, immunomodulatory, anti-ischemic in cerebral stroke, etc. Keeping in view the traditional and alternative medicinal uses, phytochemical and pharmacological reports and low toxicity, *A. cepa* seems to hold great potential for in depth investigation for various biological activities, especially its effect on the central nervous systems and cardiovascular system. Recently, it has been reported that the methanolic extract of outer scales and edible portion of *A. cepa* exhibit significant neuroprotection in ischemia and reperfusion-induced cerebral injury (147). The authors are involved in bioactivity-directed-fractionation of this plant with a view to isolate bioactive fraction(s)/constituent(s).

REFERENCES

1. P. Rose, M. Whiteman, P.K. Moore and Z.Y.I. Zhun. Bioactive S-alk(en)yl cysteine sulphoxide metabolites in the genus *Allium*: The chemistry of potential therapeutic agents. *Nat Prod Rep.* **22:** 351-368 (2005).
2. G.R. Fenwick and A.B. Hanley. The genus *Allium*- part I. *Crit Rev Food Sci Nutr.* **22:** 199-271 (1985).
3. E. Strasburger, P. Sitte, E.W. Weiler, J.W. Kadereit, A. Bresinsky and C. Korner. *Gustav Fischer Verlag Stuttgart* (New York, 1978) 855.
4. K.R. Kirtikar and B.D. Basu. *Indian meditional plants*. Edi II, Vol IV (Lalit mohan basu, 1993) 2511-2513.
5. Anonymous, WHO *monographs on selected medicinal plants*, Vol I, (World Health Organization, Geneva, 1999) 5-15.
6. R. Hegnauer. *Chemotaxonomie der Pflanzen*, Vol II, (Birkhauser Verlag Basel, Stuttgart, 1963) 45.
7. R.M. Dahlgren, T. Clifford and P. Yeo. *The families of the monocotyledons* (Springer-Verlag, Berlin, Heidelberg, New York, 1985) 58.
8. G. Griffiths, L. Trueman, T. Crowther, B. Thomas and B. Smith. Onions- A global benefit to health. *Phytother Res.* **16:** 603-615 (2002).
9. FAOSTAT. *Agriculture data, Food balance sheets*, URL. http://apps.fao.org, 2002. Through, *EJEAF Chem.* **2:** 519-524 (2003).
10. M. Mazelis and L. Crews. Purification of alliin lyase of garlic*, Allium sativum* L. *Biochem J.* **108:** 725-730 (1968).
11. M. Mazelis and R.K. Creveling. Purification and properties of S-Alkyl-L-cysteine lysase from seedlings of *Acacia farnesiana* wild. *Biochem J.* **147:** 485-491 (1975).
12. L.P. Nock and M. Mazelis. The C-S lyases of higher plants. Direct comparision of the physical properties of homogeneous allinase of garlic (*Allium sativum*) and onion (*Allium cepa*). *Plant Physiol.* **85:** 1079-1083 (1987).
13. J. Landshuter, E.M. Lohmuller and K. Knobloch. Purification and characterization of a C-S-lyase from Ramson, and wild garlic, *Allium ursinum. Planta Med.* **60:** 343-347 (1994).
14. E.M. Lohmuller, J. Landshuter and K. Knobloch. On the isolation and characterization of a C-S-lyase preparation from Leek (*Allium porrum*). *Planta Med.* **60:** 337-342 (1994).
15. J.E. Lancaster and H.A. Collin. Presence of alliinase in isolated vacuoles and of alkyl cysteine sulphoxides in. the cytoplasm of bulbs of onion (*Allium cepa*). *Plant Sci Lett.* **22:** 169-176 (1981).
16. M.H. Brodnitz and J.V. Pascale. Thiopropanal S-Oxide: *A Lachrymatory Factor in Onions. J Agri Food Chem.* **19:** 269-272 (1971).
17. E. Steinegger, O. Sticher and R. Hansel. *Pharmakognosie, Phytopharmazie*, 6 (AuflSpringer Verlag, Berlin, Heidelberg, New York, 1999) 939.
18. W.M. Randle, J.E. Lancaster, M.L. Shaw, K.H. Sutton, R.L. Hay and M.L. Bussard. Quantifying onion flavour compounds responding to sulphur fertility-Sulphur increases levels of alk(en)yl cysteine sulphoxides and biosynthetic intermediates. *J Amer Soci Hort Sci.* **120:** 1075-1081 (1995).
19. W.M. Randle. Increasing nitrogen concentration in hydroponic solutions affects onion flavour and bulb quality. *J Amer Soci Hort Sci.* **125:** 254-259 (2000).
20. W.M. Randle and J.E. Lancaster. Sulphur compounds in *Allium*s in relation to flavour quality. In: H.D. Rabinowitch, and L. Currah ed. *Allium Crop Science: Recent Advances*. CAB International, Wallingford, UK; 329-356 (2002).
21. T.W. Coolong and W.M. Randle. Sulphur and nitrogen availability interact to affect the flavour biosynthetic pathway in onion. *J Amer Soci Hortic Sci.* **128:** 776-783 (2003).
22. K.T. Augusti. Therapeutic values of onion and garlic. *Ind J Exp Biol.* **34:** 634-640 (1996).
23. J.E. Lancaster, B.J. Callion and M.L. Shaw. The dynamics of the flavour precursors, the S-alk (en)yl-L-cysteine sulphoxides, during leaf blade and scale development in the onion (*Allium cepa*). *Physiologia Plantarum.* **66:** 293-297 (1986).
24. W. Breu. *Allium cepa* L. (onion) part 1. Chemistry and analysis. *Phytomed.* **3:** 293-306 (1996).

25. S. Imani, S. Tsuge, M. Tomotake, Y. Nagatome, H. Sawada and T. Nagata. An onion enzyme that makes the eyes water. *Nature*. **419:** 685 (2002).
26. A. Crozier, M.E.Z. Lean, M.S. Donald and C. Black. Quantitative analysis of the flavonoids content of commercial tomatoes, onion, lettuce and celery. *J Agri Food Chem*. **45:** 590-595 (1997).
27. J.B. Harborne. Nature, distribution and function of plant flavonoids: In V.E. Cody, Middleton, J.R. and J.B. Harborne ed. *Progress in Clinical and Biological Res,* Vol CCXIII. Alan R. Liss, New York. Through, *Texas J Agri Nat Reso*. **16:** 24-28 (2003).
28. A. Bilyk, P.L. Cooper and G.M. Sapers. Varietal differences in distribution of quercetin and kaempferol in onion (*Allium cepa* L.) tissues. *J Agri Food Chem*. **32:** 274-276 (1984).
29. M.J.C. Rhodes and K.R. Price. Analytical problems in the study of flavonoid compounds in onions. *Food Chem*. **57:** 113-117 (1996).
30. C.A. Rice-Evans, N.J. Miller, P.G. Bolwell, P.M. Bremley and J.B. Pridham. The relative antioxidant activities of plant-derived polyphenolic flavonoids. *Free Radi Res*. **22:** 375-383 (1995).
31. T. Leighton, C. Ginther, L. Fluss, W.K. Harter, J. Cansado and V. Notario. Molecular characterization of quercetin and quercetin glycosides in *Allium* vegetables phenolic compounds in food and their effects on health II. *ACS Symposium Series*. **507:** 220-238 (1992).
32. B. Patil, L. Pike and B. Hamilton. Changes in quercetin concentration in onion owing to location, growth stage and soil type. *New Phytol*. **130:** 349-355 (1995).
33. B.S. Patil and L.M. Pike. Distribution of quercetin contents in different rings various coloured onion (*Allium cepa* L.) cultivars. *J Hort Sci*. **70:** 643-650 (1995).
34. V. Lambard, E. Geoffriau and E. Peffley. Flavonoid quantification in onion (*Allium cepa* L.) by spectrophotometric and HPLC analyses. *Hort Sci*. **37:** 682-685 (2002).
35. V. Tsushida and M. Suzuki M. Content of flavonol glucosides and some properties of enzymes metabolizing the glucosides in onion. *Nippon Shokuhin Kougyo Gakkaishi*. **43:** 642-649 (1996).
36. S. Hirota, T. Shimoda and U. Takahama. Tissue and spatial distribution of flavonol and peroxidase in onion bulbs and stability of flavonol glucosides during boiling of the scales. *J Agri Food Chem*. **46:** 3497-3502 (1998).
37. U. Takahama and S. Hirota. Deglucosidation of quercetin glucosides to the aglycone and formation of antifungal agents by peroxidase dependent oxidation of quercetin on browning of onion scales. *Plant Cell Physiol*. **41:** 1021-1029 (2000).
38. G. Corea, E. Fattorosso and V. Lanzotti. Antispasmodic saponins from bulbs of red onon, *Allium cepa* L. Var. Tropea. *J Agri Food Chem*. **35:** 935-940 (2005).
39. G.J. Meriel, H. Jill, T. Angela, M. Jonothan, A. Brian and A.C. Hamish. Biosynthesis of the flavour precursors of onion and garlic. *J Exp Botany*. **55:** 1903-1918 (2004).
40. B.K. Watt and A.L. Merrill. *Composition of foods, raw, processed, prepared, Agricultural handbook No 8* (U.S. Department of Agriculture, Washington, 1963) 1056.
41. W. Dorsch. *Allium cepa* L. (onion) part 2: Chemistry, analysis and pharmacology. *Phytomed*. **3:** 391-397 (1996).
42. K.K. Sharma, R.K. Gupta, S. Gupta and K.C. Samuel. Antihyperglycemic effect of onion: Effect on fasting blood sugar and induced hyperglycemia in man. *Ind J medical Res*. **65:** 422-429 (1977).
43. W. Dorsch, J. Scharff, T. Bayer and H. Wagner. Antiasthmatic effects of onions: Prevention of platelet-activating factor induced bronchial hyper reactivity to histamine in guinea pigs by diphenylthiosulfinate. *Int Arch Aller Appl Immunol*. **88:** 228-230 (1989).
44. W. Dorsch and H. Wagner. New antiasthmatic drugs from traditional Medicines? *Int Arch Aller Appl Immunol*. **94:** 262-265 (1991).
45. P.T. Mathew and K.T. Augusti. Hypoglycemic effects of onion (*Allium cepa* Linn). On diabetes mellitus: a preliminary report. *Ind J physio Pharmacol*. **9:** 213-217 (1975).
46. Y. Kimura and K. Yamamoto. Cytological effect of chemicals on tumors. XXIII. Influence of crude extracts from Garlic and some related species on M.K.T sarcoma III. *Gann*. **55:** 325 (1964).
47. J.P. Perchellet, E.M. Perchellet and S. Belman. Inhibition of DMBA induced mouse skin tumorigenesis by garlic oil and inhibition of two tumor-promotion stages by garlic and onion oil. *Nutr Cancer*. **14:** 183-193 (1990).
48. S. Belman, A. Shellakumar, M.C. Bosland, K. Savarese and R.D. Tensen. Papilloma and carcinoma production in DMBA initiated, onion oil promoted mouse skin. *Nutr Cancer*. **4:** 141-148 (1990).
49. C.M. Gao, T. Takezaki, J.H. Ding, M.S. Li and K. Tajima. Protective effect of *Allium* vegetables against both esophageal and stomach cancer: A simultaneous casereferent study of a high-epidemic area in Jiangsu province, China. *Jpn J Cancer Res*. **90:** 614-621 (1999).
50. J. Hu, C. Vecchia, E. Negri, L. Chatenoud, C. Bosetti, X. Jia and R. Liu. Diet and brain cancer in adults: a case-control study in northeast China. *Int J Cancer*. **81:** 20-23 (1999).
51. E. Dorant, P.A. Van Den Breandt, R.A. Goldbohm and F. Sturmans. Consumption of onions and a reduced risk of stomach carcinoma. *Gastroenterology*. **110:** 12-20 (1996).
52. M. Hertog and M. Katan. Quercetin in foods, cardiovascular disease, and cancer. In: *Flavonoids in Health and Disease*; 447-467 (1998).
53. S. Hatono, A. Jimenez and M. Wargovich. Chemopreventive effect of S-allylcysteine and the relationship to the detoxification enzyme glutathione S-transferase. *Carcinogenesis*. **17:** 1041-1044 (1996).
54. S. Fukushima, N. Takada, T. Hori and H. Wanibuchi. Cancer prevention by organosulphur compounds from garlic and onion. *J Cell Biochem Supp*. **27:** 100-105 (1997).
55. M. Richter, R. Ebermann and B. Marian. Quercetin-induced apoptosis in colourectal tumor cells: possible role of EGF receptor signaling. *Nutr Cancer*. **34:** 88-99 (1999).
56. P. Miodini, L. Gioravanti, G. Di Fronzo and V. Cappelletti. The two phyto-oestogens genistein and quercetin exert different effects on oestrogen receptor function. *Br J Cancer*. **80:** 1150-1155 (1999).
57. P.A. Steerenberg, J. Garssen, P. Dortant, P.C. Hollman, G.M. Alink and M. Dekker. Protection of UV-induced suppression of skin contact hypersensitivity: A common feature of flavonoids after oral administration? *Photochem Photobiol*. **67:** 456-461 (1998).
58. S. Fukushima, N. Takada, H. Wanibuchi, T. Hori, W. Min and M. Ogawa. Suppression of chemical carcinogenesis by water-soluble organosulphur compounds. *J Nutr*. **131:** 1049s-1053s (2001).
59. C. Malaveille, A. Hautefeuille, B. Pignatelli, G. Talaska, P. Vineis and H. Bartsch. Dietary phenolics as anti-mutagens and inhibitory of tobacco related DNA adduction in the urothelium of smokers. *Carcinogenesis*. **17:** 2193-2200 (1996).
60. F. Levi, C. La Vecchia, C. Gulie and E. Negri. Dietary factors and breast cancer risk in Vaud, Switzerland. *Nutr Cancer*. **19:** 327-335 (1993).
61. B. Challier, J. Pernau and J. Viel. Garlic, onion and cereal fibre as protective for breast cancer: A French case study. *Europ J Epidemiol*. **14:** 739-774 (1998).
62. F. Shen, M. Herenyiova and G. Weber. Synergistic down-regulation of signal transduction and cytotoxicity by tiazofurin and quercetin in human ovarian carcinoma cells. *Life Sci*. **64:** 1869-1876 (1999).
63. W.D. Guo, M.S. Linet, W.H. Chow, J.Y. Li and W.J. Blot. Diet and serum markers in relation to primary brain tumor risk in China. *Nutr Cancer*. **22:** 143-150 (1994).
64. N.R. Shenoy, A.S. Choughuley. Inhibitory effect of diet related sulphydryl compounds in the formation of carcinogenic nitrosamines. *Cancer Lett*. **65:** 227-232 (1992).
65. A. Law, J. Wu, L.H. Zeng, T.W. Wu. Aortic endothelial cells damaged by a nitric oxide donor and protected by flavonoids. *Life Sci*. **64:** 199-204 (199).
66. Z. Shutenko, Y. Henry, E. Pinard, J. Seylaz, P. Potier and F. Berthet. Influence of the antioxidant quercetin *in vivo* on the level of nitric oxide determined by electron paramagnetic resonance in rat brain during global ischemia and reperfusion. *Biochem Pharmacol*. **57:** 199-208 (1999).
67. H.D. Brahmachari and K.T. Augusti. Effect of orally effective hypoglycemic agents from plants on alloxan-induced diabetes. *J Phar Pharmacol*. **14:** 617 (1962).
68. K.T. Augusti. Studies on the effects of a hypoglycemic principle from *Allium cepa L*.. *Ind J Med Res*. **1:** 1066-1071 (1973).
69. R.C. Jain, C.R. Vyas. Hypoglycemic action of onion on rabbits. *Br Med J*. **2:** 730 (1974).
70. B.O. Bever and G.R. Zahnd. Plant with oral hypoglycemic action. *Quart J Crude Drug Res*. **17:** 139-196 (1979).
71. E.T. Ashwah, R.M. EI-Allawy, F.S. EI-Hashimy and M.H. Ibrahim. The hypoglycemic activity of onion extracts "*Allium cepa*" influenced by adrenaline-induced hyperglycemia. *J Drug Res*. **13:** 61-68 (1981).

72. R. Roman-Ramos, J.L. Flores-Scaenz and F.J. Alarcon-aguilar. Anti-hyperglycemic effect of some edible plants. *J Ethnopharmacol.* **84:** 25-32 (1995).
73. C.G. Sheela and K.T Augusti. Antiperoxide effects of S-allyl cysteine sulphoxide isolated from *Allium sativum* Linn and gugulipid in cholesterol diet fed rats. *Ind J Exp Biol.* **33:** 337-341 (1995).
74. M. Lean, M. Noroozi, I. Kelly, J. Burns, D. Talwar and N. Satter. Dietary flavonoids protect diabetic human lymphocytes against oxidant damage to DNA. *Diabetes.* **48:** 176-178 (1999).
75. K. Kumari, B.M. Mathew and K.T. Augusti. Antidiabetic and hypolipidemic effects of S-Mehyl cysteine sulphoxide isolated from *Allium cepa* L. *Ind J Biochem Biophysics.* **32:** 49-54 (1995).
76. M.S. Karawya, S.M. Abde, M.M. EI-Olemy and N.M. Farrag. Diphenylamine, an antihyperglycemic agent from onion and tea. *J Natural Prod.* **47:** 775-780 (1984).
77. B. Hughes and L. Lawson. Antimicrobial effects of *Allium sativum* L. (garlic), *Allium ampeloprasum* L. (elephant garlic), and *Allium cepa* L. (onion), garlic compounds and commercial garlic supplement products. *Phytother Res.* **5:** 154-158 (1991).
78. D.E. Conner and L.R. Beuchat. Effects of essential oils from plants on growth of food spoilage yeasts. *J Food Sci.* **49:** 429-434 (1984).
79. A. Zohri, K. Abdel-Gawad and S. Saber. Antibacterial, antidermatophytic and antitioxigenic activities of onion (*Allium cepa*) oil. *Microbiol Res.* **150:** 167-172 (1995).
80. N. Didry, M. Pinkas and L. Dubreuil. Activite antibacterienne d'especes du genre *Allium*. *Pharmazie.* **42:** 687-688 (1987).
81. K. Arunachalam. Antimicrobial activity of garlic, onion, and honey. *Geobios.* **7:** 46-47 (1980).
82. J. Fan and J. Chen. Inhibition of aflatoxin producing fungi by Welsh onion extracts. *J Food Prote.* **62:** 414-417 (1999).
83. J. Kim. Anti-bacterial action of onion extracts against oral pathogenic bacteria. *Nihon Uni Sch Dent.* **39:** 136-141 (1997).
84. G.R. Gibson. Dietary modulation of the human gut microflora using prebiotics. *Br J Nutr.* **80:** S209-S212 (1998).
85. J. Yang, K.J. Meyers, J.V. Heide and R.H. Liu. Varietal differences in phenolic content and antioxidant and antiproliferative activities of onions. *J Agri Food Chem.* **52:** 6787-6793 (2004).
86. H. De Groot and U. Rauen. Tissue injury by reactive oxygen species and the protective effects of flavonoids. *Fundam Clin Pharmacol.* **12:** 249-255 (1998).
87. Y. Suzuki, I. Masashi, T. Segami and M. Ito. Antiulcer effects of antioxidant, quecetin, a-tocopherol, nifedipine and tetracycline in rats. *Jpn J Pharmacol.* **78:** 435-441 (1998).
88. H.J. Suh, J.M. Lee, J.S. Cho, Y.S. Kim and S.H.E Chaug. Radical scavenging compounds in onion skin. *Food Res Int.* **32:** 659-664 (1999).
89. A.M. Nuutila, R. Puupponen-Pimia, M. Aarni and K.M. Oksman-Caldentey. Comparison of antioxidant activities of onion and garlic extracts by inhibition of lipid peroxidation and radical scavenging activity. *Food Chem.* **81:** 485-493 (2003).
90. S. Kawaii, Y. Tomono, E. Katase, K. Ogawa and M. Yano. Anti-proliferative activity of flavonoids on several cancer cell lines. *Biosci Biotech Biochem.* **63:** 896-899 (1999).
91. J. Sanderson, W. Mclauchlin and G. Williamson. Quercetin inhibits hydrogen peroxide-induced oxidization of the rat lens. *Free Radi Biol Med.* **26:** 639-645 (1999).
92. L. Fremont, M.T. Gozzelino, M.P. Franchi and A. Linard. Dietary flavonoids reduce lipid peroxidation in rats fed polyunsaturated or monounsaturated fat diets. *J Nutr.* **128:** 1495-1502 (1998).
93. M. Aviram, M. Rosenblat, S. Billecke, J. Erogul, R. Sorenson and C.L. Bisgaier Human serum paraoxonase (PON1) is inactivated by oxidized low-density liporotein and preserved by antioxidants. *Free Radi Biol Med.* **26:** 892-904 (1999).
94. T. Kaneko and N. Baba. Protective effect of flavonoids on endothelial cells against linoleic acid hydroperoxide-induced toxicity. *Biosci Biotechnol Biochem.* **63:** 323-328 (1999).
95. D. Jurdi-Haldeman, J. Mac-Neil and D. Yared. Antioxidant activity of onion and garlic juices in stored cooked ground lamb. *J Food Prote.* **50:** 411-413 (1987).
96. B. Juurlink and P. Paterson. Review of oxidative stress in brain and spinal cord injury. *Spinal Cord Med.* **21:** 309-334 (1998).
97. E.L. Da Silva, T. Tsushida and J. Terao. Inhibition of mammalian 15-lipoxygenase-dependent lipoprotein by quercetin and quercetin monoglucosides. *Arch Biochem Biophy.* **49:** 313-320 (1998).
98. C. Yuting, Z. Rongliang, J. Zhongjian and J. Yong. Flavonoids as superoxide scavengers and antioxidants. *Free Radi Biol Medic.* **9:** 19-2 (1990).
99. P. Sestili, A. Guidarelli, M. Dacha and O. Cantoni. Quecetin prevents DNA single strand breakage and cytotoxicity caused by tert-butylhydroperoxide: Free radical scavenging versus iron chelating mechanism. *Free Radi Biol Med.* **25:** 196-200 (1998).
100. A. Negre-Salvayre and R. Salvayre. Quercetin prevents the cytotoxicity of oxidized LDL of lymphoid cell lines. *Free Radi Biol Med.* **12:** 101-106 (1992).
101. G.T. Mc-Anlis, J. Mc-Eneny, J. Pearce and I.S. Young. Absorption and antioxidant effects of quercetin from onions, in man. *Eur J Clin Nutr.* **53:** 92-96 (1999).
102. G. Gazzani, A. Papetti, M. Daglia, F. Berte and C. Gregotti. Protective activity of water-soluble components of some common diet vegetable on rat liver microsome and the effects of the thermal treatment. *J Agri Food Chem.* **46:** 4123-4127 (1998).
103. G. Gazzani, A. Papetti, G. Massolini and M. Daglia. Anti- and pro-oxidant activity of water-soluble components of some common diet vegetables and the effect of thermal treatment. *J Agri Food Chem.* **46:** 4118-4122 (1998).
104. M. Yin and W. Heng. Antioxidant activity of several *Allium* members. *J Agri Food Chem.* **46:** 4097-4101 (1998).
105. G. Block, B. Patterson and A. Subar. Fruit, vegetables, and cancer prevention: A review of the epidemiological evidence. *Nutr Cancer.* **18:** 1-29 (1992).
106. G. Cao, E. Sofic and R.L. Prior. Antioxidant capacity of tea and common vegetables. *J Agri Food Chem.* **44:** 3426-3431 (1996).
107. J.H.M. De Vries, P.C.H. Hollman, S. Meyboom , M.N.C.P. Buysman, P.L. Zock and W.A. Van Staveren. Plasma concentrations and urinary excretion of the antioxidant flavonoids quercetin and kaempferol as biomarkers for dietary intake. *Am J Clin Nutr.* **68:** 60-65(1998).
108. S. Widder S, S. Luentzel, T. Dittner and W. Pickenhagen. 3-Mercapto-2-methylpentan-1-ol, a new powerful aroma compound. *J Agri Food Chem.* **48:** 418-423 (2000).
109. P. Rose, S. Widder, J. Looft, W. Pickenhagen, C.N. Ong and M. Whiteman. Inhibition of peroxynitrite-mediated cellular toxicity, tyrosine nitration, and 1-antiproteinase inactivation by 3-mercapto-2-methylpentan-1-ol, a novel compound isolated from *Allium cepa. Biochem Biophysi Res Communications*. **302:** 397-402 (2003).
110. S. Lata, K.K. Saxena, V. Bhasin, R.S. Saxena, A. Kumar and N.K. Srivastava. Beneficial effects *Alliums sativa, Alliums cape,* and *Commiphora mukul* on experimental hyperlipidemia and atherosclerosis: A comparative evaluation. *J Postgra Medic.* **37:** 132-135 (1991).
111. G.S. Sainani, D.B. Desai and P. Sainine. Onion in prevention of atherosclerosis. *J Ind Medical Associ.* **71:** 109 (1978).
112. K.K. Sharma, N.K. Chowdhury and A.L. Sharma. Studies on hypocholesterolaemic activity of onion. II. Effect on serum cholesterol in rabbits maintained on high cholesterol diet. *Ind J Nutr. Diet.* **12:** 388-391 (1975).
113. I. Adamu, P.K. Joseph and K.T. Augusti. Hypolipidemic action of onion and garlic unsaturated oils in sucrose fed rats over a two-month period. *Expentia.* **38:** 899-901 (1982).
114. T.M. Vatsala, M. Singh and R.G. Murugesan. Effects of onion in induced atherosclerosis in rabbits: In Reduction of arterial lesions and lipid levels. *Artery.* **7:** 519-530 (1980).
115. A. Bobboi, K.T. Augusti and P.K. Joseph. Hypolipidemic effects of onion oil and garlic oil in ethanol-fed rats. *Ind J Biochem Biophys.* **21:** 211-21 (1984).
116. P. Ahluwalia and A. Mohindroo. Effect of oral ingestion of different fractions of *Allium cepa* on the blood and erythrocyte membrane lipids and certain membrane-bound enzymes in rats. *J Nutr Sci Vitaminol.* **35:** 155-161 (1989).
117. R.C. Jain and C.R. Vyas. Onion and Garlic in atherosclerotic heart disease. *Medikon.* **6:** 12-14 (1977).
118. K.K. Sharma and S.P. Sharma. Effect of onion on blood cholesterol, fibrinogen and fibrinolytic activity in normal subjects. *Ind J Pharmacol.* **8:** 231-233 (1976).

119. K.K. Sharma and S.P. Sharma. Effect of onion and garlic on serum cholesterol on normal subjects. *Mediscope*. **22:** 134-136 (1979).
120. Y. Itokawa, K. Inoue, S. Sasagawa and M. Fujiwara. Effect of S-methylcysteine sulphoxide, S-allylcysteine sulphoxide and related sulfur-containing amino acids on lipid metabolism of experimental hypercholesterolemic rats. *J Nutr*. **103:** 88-92 (1973).
121. K.T. Augusti and P.T. Mathew. Effect of long-term feeding of the aqueous extracts of onion (*Allium cepa* L.) and garlic (*Allium sativum* L.) on normal rats. *Ind J Medi Res*. **11:** 239-241 (1973).
122. B.F. Wilcox, P.K. Joseph and K.T. Augusti. Effects of allylpropyl disulphide isolated from *Allium cepa* Linn on high-fat fed rats. *Ind J Biochem Biophys*. **21:** 214-216 (1984).
123. D. Farya, I.A. Goji, P.K. Joseph and K.T. Augusti. Effects of garlic oil on streptozotocin-diabetic rats maintained on normal and high fat diets. *Ind J Biochem Biophys*. **23:** 24-27 (1986).
124. K. Kumari and B.C. Mathew. Antidiabetic and hypolipidemic effects of S-Mehyl cysteine sulphoxide isolated from *Allium cepa* L. *Ind J Biochem Biophys*. **32:** 49-54 (1995).
125. K. Janssen, R.P. Mensink, F.J.J. Cox, J.L. Harryvan, R. Hovenior and P.C.H. Hollman. Effects of the flavonoids quercetin and apigenin on hemostasis in healthy volunteers: results from an *in vitro* and a dietary supplement study. *Am J Clin Nutr*. **67:** 255-262 (1998).
126. K.C. Srivastava. Aqueous extracts of onion, garlic and ginger inhibit platelet aggregation and alter arachidonic acid metabolism. *Biomedica Biochimica Acta*. **43:** 335-346 (1984).
127. A.N. Makheja, J.Y. Vanderhoek and J.M. Bailey. Inhibition of platelet aggregation and thromboxane synthesis by onion and garlic. *Lancet*. **1:** 781 (1979).
128. T. Ariga and S. Oshiba. Effects of the essential oil components of garlic cloves on rabbit platelet aggregation. *Igakuto Seibutsugaku*. **102:** 169-174 (1981).
129. H. Weissenberger. Isolation and identification of the platelet aggregation inhibitor present in onion (*Allium cepa). FEBS Lett*. **26:** 105-108 (1972).
130. J.Y. Vanderhoek, A.N. Makheja and J.M. Bailey. Inhibition of fatty acid oxygenases by onion and garlic oils. Evidence for the mechanism by which these oils inhibit platelet aggregation. *Biochem Pharmacol*. **29:** 3169-3173 (1980).
131. A. Makheja and J. Baily. Antiplatelet constituents of garlic and onion. *Agents and Actions*. **29:** 360-363 (1990).
132. W. Breu and W. Dorsch. *Allium cepa* L. (Onion): Chemistry, analysis and pharmacology. In: H. Wagner, N.R. Farnsworth, ed. *Economic and Medicinal plants Research*, London, Academic Press; 115-147 (1994).
133. Anonymous. Quercetin. *Alter Med Revi*. **3:** 140-143 (1998).
134. M.K. Kuhlmann, G. Burkhardt, E. Horsch, M. Wagner and H. Kohler. Inhibition of oxidant-induced lipid peroxidation in cultured renal tubular epithelial cells (LLC-PK1) by quercetin. *Free Radi Res*. **29:** 451-460 (1998).
135. K. Uchida, M. Shiraishi, Y. Naito, Y. Torii, Y. Nakamura and T. Osawa. Activation of stress signaling pathways by the end of lipid peroxidation. *J Biol Chem*. **274:** 2234-2242 (1999).
136. M. Ali, T. Bordia and T. Mustafa. Effect of raw versus boiled aqueous extract of garlic and onion on platelet aggregation. *Prosta Leuko Esse Fatty Acids*. **60:** 43-47 (1999).
137. T. Bordia, N. Mohammed, M. Thompson and M. Ali. An evaluation of garlic and onion as antithrombotic agents. *Prosta Leuko Esse Fatty Acids*. **54:** 183-186 (1996).
138. J.H. Chen, S.J. Tsai and H. Chen. Welsh onion (*Allium fistulosum* L.) extracts alter vascular responses in rat aortae. *J Cardiovas Pharmacol*. **33:** 515-520 (1999).
139. I.L. Goldman, M. Kopelberg, J.E.P. Debaene and B.S. Schwartz. Antiplatelet activity in onion (*Allium cepa*) is sulfur dependent. *Thrombos Haemostas*. **76:** 450-452 (1996).
140. A. Spector. Oxidative stress-induces cataract. Mechanism of action. *FASEB J*. **9:** 1173-1182 (1995).
141. J.M. Robertson, A.P. Donner and J.R. Trevithick. A possible role for vitamin C and E in cataract prevention. *Am J Clin Nutr*. **53:** 346S-351S (1991).
142. I.S. Menon, R.Y. Kendal, H.A. Dewar and D.J. Newell. Effect of onions on blood fibrinolytic activity. *Br Med J*. **3:** 351-352 (1968).
143. R.K. Agarwal, H.A. Dewar, D.J Newell and B. Das. Controlled trial of the effect of cycloalliin on the fibrinolytic activity of venous blood. *Atherosclerosis*. **27:** 347-351 (1977).
144. I.S. Menon. Onion and blood fibrinolysis. *Ind Practi*. **32:** 72-76 (1979).
145. M. Chisty, R. Quddus, B. Islam and B. Khan. Effect of onion extract on immune response in rabbits. *Bangladesh Med Res. Counc Bull*. **22:** 81-85 (1996).
146. D.A. Shoskes. Effect of bioflavonoids quercetin and curcumin on ischemic renal injury. *Transplan*. **66:** 147-152 (1998).
147. R. Shri and K.S. Bora. Neuroprotective effect of methanolic extracts of *Allium cepa* L. on ischemia and reperfusion-induced cerebral injury. *Fitoterapia*. **79:** 86-96 (2008).
148. D.S. Vyas, R.P. Acharya, A.P. Dadhich, J.L. Godhwani and V.S. Purohit. Effect of *Allium cepa* (onion) on immune response in rats. *Ind J Physio Pharmacol*. **27:** 259-260 (1983).
149. I.A. Ross. *Meditional Plants of the World. Chemical constituents, traditional and modern Medicinal uses*, Vol II, (Humana press, Totowa, New Jersey, 2001) 1-35.
150. W. Dorsch, E. Schneider, T. Bayer, W. Breu and H. Wagner. Anti-inflammatory effects of onions: inhibition of chemotaxis of human polymorphonuclear leukocytes by thiosulfinates and cepaenes. *Int Arch Aller Appl Immunol*. **92:** 39-42 (1990).