Proc Indian Natn Sci Acad **80** No. 5 December 2014 pp. 1045-1054

DOI: 10.16943/ptinsa/2014/v80i5/47972

Review Article

Major Sulphur Compounds in Plants and their Role in Human Nutrition and Health – An Overview

R PRASAD
Indian Agricultural Research Institute, New Delhi 110 012, India

(Received on 15 October 2014; Accepted on 22 October 2014)

Major sulphur compounds in plants include amino acids methionine and cysteine, vitamins thiamine and biotin and others of value from the viewpoint of human health, such as aliin (a precursor of alicin), glucisinolates (GSL), glutathione (GSH) and methylsulfonylmethane (MSM). Of these, methionine and thymine are essential nutrients and humans must obtain these from plant foods. Although cysteine is not an essential amino acid, its derivative - acetylcystein or N-acetylesystein - is used for the treatment of paracetamol toxicity, mucolytic (mucus dissolving) therapy, acute renal failure and psychiatric disorders. In recent years, the plant food that has received most attention is garlic, responsible for the production of alicin, which is credited for preventing cardiovascular disorders. Similarly, vegetables from the family *Brassicae*, such as, broccoli, cabbage and turnip rape have gained attention due to the presence of glucosinolates, which are reported to be useful in curing cancer. Glutathionate (GSH) pool is important in preventing diseases where increased oxidative stresses are implicated or where there is protein-energy malnutrition seen as a secondary manifestation, such as in AIDS, cancer, burns, chronic digestive diseases and alcoholism. Methylsulfonylmethane (MSM) is used for treating arthritis. Since plants obtain their sulphur from soil, adequate sulphur fertilization can play an important role in producing plant products with higher amounts of S-compounds, but there have been very few agronomic studies on this subject. The main objective of this review is to emphasize the need for such studies in India, especially in view of the fact that about 42% soils are deficient in sulphur.

Key Words: Methionine; Alicin; N-acetylesystein; Glucisinolate (GSL); Glutathionate (GSH); Methylsulfonylmethane (MSM); Garlic; Broccoli; Cabbage; Turnip Rape; Rapeseed

Introduction

Sulphur is an essential element for plants as well as humans. The primary source of S for human beings are the sulphur containing amino acids (SAAs) methionine and cysteine obtained from plant products in diet. The animal products in diet also owe this to plants , because the animals obtain S from these two amino acids present in grasses, fodder and feeds. This is due to the fact that biosynthesis of organic S compounds takes place only in plants and bacteria (Parcell, 2002). In addition to SAAs, plant products also contain S containing vitamins thiamin and biotin, some odorous compounds and several other compounds, which are important from the viewpoint of human nutrition and health.

Plants in turn obtain S from soil and adequate supply of available S is a must for successful production of agricultural and horticultural crops. Deficiency of sulphur in soils is global and has been reported from China (Messick and Fan, 2007), Europe (Messick, 2003), USA (Rehm, 2005), Canada (Solberg *et al*., 2006) and India (Singh, 2001; Tandon, 2011). In Asia, the recent rise in sulphur deficiency in soils is due to introduction of high yielding hybrids and varieties of crops and intensive cropping systems, such as 'rice-wheat' and increased use of non-sulphur

**Author for Correspondence: E-mail: rajuma36@gmail.com*

high analysis nitrogen and phosphorus fertilizers (Prasad, 2005). There is also reduced contribution of atmospheric sulphur due to national and international agreements for reducing industrial sulphur dioxide production (Zhao *et al*., 1999). In India, nearly half of the cultivated soils are deficient in available S and good yield responses to S application have been reported (Singh, 2001; Biswas *et al*., 2004; Tandon, 2011). Most of the agronomic studies in India are restricted to yield increase and S uptake by crops. It has been reported that limited availability of sulphur in soils may lead to synthesis and accumulation of S-poor proteins (Zhao *et al*., 1999; Flaete *et al*., 2005). No reports are available in India on the varietal differences and effect of agronomic management on SAAs and other S containing compounds in plants. This review focuses the attention for the need of such research.

Sulphur Containing Amino Acids (SAAs)

About 70% of sulphur in plants is present as amino acids. Of the two SAAs making up different proteins, methionine is considered essential (along with lysine, leucine, isoleucine, histidine, phenylalanine, threonine, tryptophan and valine), while cysteine (along with alanine, arginine, glycine, aspartic acid, glutamic acid, glutamine, proline, serine, tyrosine, asparagine, and sclenocysteine) is considered a non-essential for humans (Furst and Stehle, 2004). Humans cannot synthesize essential amino acids and these must be obtained through diet. The recommended daily allowance (RDA) (mg/kg/day) for SAAs (methionine+cysteine) is 58 for 3-4-month infants, 27 for 2-year-old, 22 for 10-12-year-old and 13 for adults (Parcell, 2002). Information on average content of some amino acids in plant foods is presented in Table 1.

(a) Methionine

As already stated, methionine is an essential amino acid that cannot be synthesized by humans and must be obtained through diet. Beans, soybean and sesame in plants and of course animal foods including eggs are the main source of methionine. Methionine is an intermediate in the biosynthesis of cysteine, carritine, taurine, lecithin and phospholipids. Methionine can reduce acetaldehyde levels after alcohol ingestion and can thus lower lever-damaging effects of alcohol (Tabakoff *et al*., 1989). As a methyl-donor, methionine helps prevent fatty liver disease and eventual cirrhosis of the lever (Richmond, 1986). Methionine is also reported to be effective in the treatment of Parkinson's disease (Smythies and Hasley, 1984) and acute pancreatitis (Uden *et al*., 1990). However, excessive methionine consumption can be harmful. Restricting methionine consumption is reported to increase life span in some animals (Alleyene, 2009). Methionine restriction can also inhibit aging related disease processes (Richie *et al*., 1994) and colour carcinogenesis in rats (Komninou, 2006).

An important metabolite of methionine is S-adenosylmethionine (SAMe), which is involved in many metabolic processes in human body (Chiang *et al*., 1996). Human body in general produces all SAMe that it needs, however, shortage of methionine or cofactors folate and choline required for the production of SAMe can lead to its shortage. Deficiency of SAMe can lead to depression (Reynolds *et al*., 1984). SaMe supplements are used for curing depression (Kagan *et al*., 1990) and for treating osteoarthritis (diPadova, 1987).

Table 1: Average amino acid content (mg/g protein) in some plant foods

Plant food	Lysine	SAAs	Threonine	Tryptophan
Legumes	64±10	25±3	38±3	12±4
Cereals	31±10	37±5	32±4	12±4
Nuts & Seeds	45±14	44±17	36±3	17±3
Fruits	45±12	27±6	29±7	11±2

Adapted from: Young and Pellet (1994)

Methionine is the precursor of ethylene, which is responsible for fruit ripening, an important physiological process in plants from the viewpoint of human nutrition. The fruits which ripen due to ethylene are known as climactric and include mango, guava, banana, apple, pear, peach, apricot, avocado cantaloupe, fig, kiwi fruit, tomato etc. (Kader, 1999). The non-climactric fruits include berries, cherry, grapes, limes, oranges etc. Ripening makes fruits sweeter (by conversion of starch into sugar by amylases), softer (by reducing the amount of pectin by enzymes such as polygalacturonase), less tart (by conversion of acids to neutral molecules by kinases , fragrant (by conversion of a large number of organic molecules to volatile aromatic compounds) and red to yellow in colour (by destruction of chlorophyll) (Medicott and Thompson, 1985; Bashir and Abu-Goukh, 2003; Prasanna *et al*., 2007; Duana *et al*., 2008). Russian scientist Dimitry Neljibou was the first to point out the role of ethylene in ripening and Gane (1934) was the first to report the biosynthesis of ethylene by plants. It was later found that ethylene in plants is formed from the Cu^{+}-catalyzed breakdown of methionine (Lieberman and Kunishi, 1965). The bulk of the fruit industry handles (harvest, transport and storage) climactric fruits, in which ripening can be controlled by concentration and exposure to ethylene (Ritenour *et al*., 1999; Chomchelow *et al*., 2002; Dang *et al*., 2006). In India, a plastic cover is placed over unripe fruits and calcium carbide is placed in open containers in strategic positions. Moisture from the air reacts with calcium carbide and produces ethylene. However, industrial grade calcium carbide contains traces of arsenic and phosphorus, which can be toxic to children (Hakan, 2007).

(b) Cysteine

Cysteine plays important roles as an extracellular reducing agent, a critical substrate for protein synthesis and the rate limiting precursor of glutathione and taurine (Kleinman and Richie, 2000). In baking industry, higher cysteine residues in wheat flour produce a more extensible and pliable dough due to disulphide bonds leading to better quality bread (Alary and Kobrechel, 1987). Based on studies on mice, it has been shown that Se-methylselenocystein can serve as a therapeutic agent which disrupts androgen receptor signaling for prostate cancer (Pinto *et al*., 2007).

Acetylcystein (or N-acetylcystein), a derivative of cysteine is manufactured and sold as a pharmaceutical drug and nutritional supplement and is on the WHO's list of essential medicines needed in a basic health system (WHO 2013). It has several medicinal uses, which include:

(i) Treatment of paracetamol (acetaminophen) overdose or toxicity (Green *et al.* 2013),

(ii) Mucolytic (mucous-dissolving) therapy as an adjuvant in respiratory conditions with excessive and/or thick mucus production as in bronchitis, tuberculosis, pneumonia etc. (Stey *et al.* 2000),

(iii) Prevention of radio contrast-induced nephropathy (a form of acute renal failure) (Tapel *et al.* 2000),

(iv) Prevention of progressive interstitial lung disease (Poole and Black, 2011),

(v) Treatment of psychiatric disorders (Bark *et al.* 2013).

(c) Sulphur Fertilization and S Concentration, S:N Ratio and SAAs in Grain

Sulphur fertilization generally results in increased S concentration in grain. Ercoli *et al*. (2011) reported that S concentration in wheat grain increased from 1.4 to 1.6 g kg^{-1} due to an application of 120 kg S ha^{-1}. Similarly Shivay *et al.* (2014) reported that S concentration in rice grain increased from 1.2 to 1.6 g kg^{-1} with an application 45 kg S ha^{-1}. Increased S concentration leads to a decrease in N:S ratio. Coyle and McAleese (1970) reported that N:S ratio in wheat grain declined from 11-28 to 10-17 and from 26-28 to 8-10 in barley grain due to sulphur fertilization. Lerner *et al*. (2006) also observed that S fertilization caused significant changes in N: S ratio in wheat.

Shivay *et al.* (2014) found that application of 45 kg S ha^{-1} reduced N:S ratio from 9.77 to 7.79 in rice grain. A reduced N:S ratio in grain suggests an increase in SAAs. Josefsson (1970) found that S fertilization increasd S-containing amino acids in rapeseed. Jarvan *et al*. (2008) reported an increase in cysteine and methionine content in wheat grain due to S fertilization (Table 2).

Sulphur-Containng Vitamins

Thiamine (or thiamin or Vit B_1) and biotin (or Vit H or Coenzyme R) are two sulphur containing amino acids.

(a) Thiamine

Thiamin is one of the components of vitamin B complex. It is water-soluble. Thiamine pyrophosphate or thiamin diphosphate is a coenzyme involved in the catabolism of sugars and amino acids. Thiamin is involved in the biosynthesis of neuro-transmitter acetylcholine and γ-aminobutyric acid (GABA). It is on the list of WHO essential medicines needed in the basic health system (WHO 2013).

Just like essential amino acids, only plants, bacteria and fungi can synthesize thiamine and humans must obtain it from the food that they eat. Cereal grains are the most important source of thiamine. In cereal grains, thiamine is concentrated in the outer layer and germ, which are generally removed in the refining process. In USA and Australia, the processed wheat flour must be enriched with thiamine nitrate. Yeast and yeast extract are the most highly concentrated source of thiamine. Leavened (bakery made) wheat bread is therefore richer in thiamine than unleavened bread (*Indian chapati*). The RDA for thiamine is 1.4 mg.

Human nervous system is particularly sensitive to thiamine deficiency and well known syndromes caused by this deficiency include beriberi (Mahan and Escott-Stump, 2000; Shils *et al*., 2006; Spinazzi *et al*., 2010), Wernicke-Korsokof syndrome (alcohol abuse syndrome) (Harper, 1979; Krill, 1996) and optic neuropathy (bilateral visual loss, impaired colour perception) (Spinazzi *et al*., 2010).

(b) Biotin

Biotin is a coenzyme involved in the synthesis of fatty acids, isoleucine and valine and in gluconeogenesis. In humans, intestinal bacteria produce enough biotin and therefore there is no RDA for it, although pregnant females may need biotin supplement. Leafy green vegetables are a good source of biotin. Biotin is considered to be involved in strengthening of hair and nails and a large number of commercial formulations are marketed for this purpose although scientific proofs based on well-planned studies for it are lacking (http://en.wikipedia.org/wiki/Biotin).

Alliin, Allicin and Diallyldisulfide

(a) Alliin

Alliin a sulfoxide, is a derivative of cysteine and is natural constituent of fresh garlic and a precursor of allicin (Iberi, 1990).

Table 2: Effect of sulphur fertilization on amino acid composition in wheat grain[1]

Fertilizer (kg ha^{-1})	Grain (t ha^{-1})	Protein (%)	Amino acid in grain (g kg^{-1})			
			Cystein	Threonine	Methionine	Lysine
0 (control)	4.58	11.1	2.35(21.2)[2]	2.82(25.4)	1.77(15.9)	3.28(29.5)
100 N	5.08	13.9	2.23(16.0)	2.74(19.7)	1.26(9.1)	3.13(22.5)
100 N +10 S	5.88	13.4	2.91(21.7)	3.40(25.4)	1.98(14.8)	3.65(27.5)
LSD (0.05)	0.32	0.4	0.31	0.16	0.19	0.23

1. Data for 2005 trial at Saku; 2. Figures in parentheses are g kg^{-1} protein; Adapted from Jarvan *et al*. (2008)

(b) Allicin

Allicin is produced from alliin with the help of enzyme allinase when fresh garlic is chopped or crushed. Alliin and allinase are kept in separate compartments of the cell and react only when the compartments are broken. Allicin is responsible for the fresh aroma of fresh garlic (Kourounakis and Rekka, 1991), is unstable and soon changes into a series of sulfur compounds including diallyldisulfide. Allicin provides protection to the garlic plants from insect pests.

Allicin has anti-bacterial (Cutler and Wilson, 2004), anti-viral (Block, 2010) and anti-protozoal (Salama *et al*., 2014) properties. It is reported to reduce fat deposition (Eliat *et al*., 1995; Abramovitz *et al*., 1999), cholesterol absorption (Nijjar *et al*., 2010) and blood pressure (Silagy and Neil, 2003; Elkayam *et al*., 2003). It has also anti-inflammatory and anti-oxidant properties (Banerjee *et al*., 2001; Bautista *et al*., 2005). Raw garlic, powdered garlic supplements and aged garlic supplements are equally efficacious (Choudhary and Tomer, 2013).

(c) Effect of Fertilizers

Mirzaei *et al*. (2007) reported that garlic clones differed significantly in their allicin content, which varied from 0.05 to 5.64 mg g^{-1}, but the effects of organic and chemical fertilizers were not significantly different.

(d) Dially-Disulfide

Dially-disulfide (DADS) is derived from garlic and few other genera of *Alliaceae*. In highly diluted forms, DADS is used as a flavoring agent and improves the taste of meat, vegetables and fruits. It is also an environmentally benign nematicide (Block, 2010). Some of the benefits of garlic, such as prevention of colorectal cancer (Milner, 2003; Jo *et al*., 2008) are due to DADS. However, DADS is a skin irritant and an allergen (Horn, 2003).

Glucisinolates (GSLs)

Glucosinolates (GSLs) are natural pungent secondary metabolites in plants of family Brassicae, such as, mustard, cabbage, broccoli, horse radish etc. GSLs are derived from glucose and amino acids and are water-soluble. The so-called aliphatic GSLs are derived mainly from methionine, but also from alanine, leucine, isoleucine and valine, while aromatic GSLs, such as glucobrassicin, are derived from tryptophan. So far, about 132 GSLs have been reported. When the plant material is cut, chewed or crushed, the enzyme myrocinase cleaves off glucose from GSLs in the presence of water and releases isothiocynates (commonly known as mustard oil), thiocyantes and nitriles (Glawisching *et al*., 2003), which are responsible for pungency and defence mechanism against insect pests (Wittstock *et al*., 2004). In the plants, the enzyme myrocinase and GSLs are kept in separate compartments but come in contact when the plant tissue is cut or crushed. Some GSLs are toxic (mainly as goitrogens) to humans and animals at high doses. However, recently GSLs have been reported to be involved in mitigating cancer ((Beecher, 1994; Williamson *et al*., 1998; Das *et al*., 2000; Hayes *et al*., 2008) and consumption of large amounts of vegetables especially broccoli, Brussels sprout and cabbage is being encouraged.

(a) Effects of Frtilizers

Staley *et al*. (2010) reported that GSLs in cabbage (*Brassica oleracea* var capitata) were three times when grown on organic manure than when it was grown on chemical fertilizers. He also reported that the content of glubrassicin was much more than sinigrin. Pradhan *et al*. (2007) reported that cabbage grown with human urine had as much GSLs as obtained with inorganic fertilizers; total GSLs were about 3.07 to 3.69 µmoles g^{-1} DM.

Nartis (2011) found that application of fertilizer nitrogen in 2 or 3 split applications produced more GSLs in winter turnip rape (*Brassica rapa* L). The amount of total GSLs in 6 cultivars studied ranged from 10.6 to 18.7µmoles g^{-1} DM. Zhao *et al*. (1993) observed that nitrogen application decreased GSL content in seeds of double row (*Brassica napus* L) in the absence of S but increased it when adequate S was applied along with nitrogen. Josefsson (1970) and Schung (1989) also reported that S fertilization increased GSLs in rapeseed (*Brassica napus* L). As regards vegetable turnip rape (*Brassica rapa* L), Kim *et al*. (2001) observed that application of lower doses of N with adequate S fertilization increased GSL concentration in edible portion; total GSL content varied from 28 to 80 µmoles g^{-1} DM and gluconapin and glucobrassicanapin were the main GSLs, which were also responsible for the bitterness.

In broccoli (*Brassica oleracea* var italica), Naquib *et al*. (2011) found that application of 50% nitrogen as chicken manure and the rest 50% as chemical fertilizer gave a GSL concentration 71.34 µmoles g^{-1} DM in florets as compared to only 48.7 µmoles g^{-1} DM obtained with 100% chemical fertilizer. Perez-Ballibrea *et al.* (2010) found that sulphur fertilization increased GSLs in broccoli sprouts during germination. Avilla *et al.* (2013) obtained no effect of selenium application on GSLs in broccoli.

Glutathione (GSH)

Glutathione (GSH) is an important antioxidant in plants, animals, fungi and some bacteria preventing damage to important cellular components caused by reactive oxygen species such as free radicals and peroxides (Pompella *et al*., 2003). It is a tripeptide of γ-glutamine, cysteine and glycine (Huxtable, 1986). GSH pool is important in diseases where increased oxidative stresses are implicated or where there is protein-energy malnutrition seen as a secondary manifestation, such as in AIDS, cancer, burns, chronic digestive diseases and alcoholism (Bray and Taylor, 1993).

It is not an essential nutrient and needed amounts are generally synthesized in the human body. However, it is possible to raise GSH levels in blood by daily consumption through GSL supplements (Richie *et al*., 2014) including those containing cysteine (Bray and Taylor, 1993). GSH has a role in iron metabolism (Kumar *et al*., 2011). The concentration of GSH in must (freshly pressed grape pulp that contains the skins, seeds, and stems of the fruit) determines the browning effect during the production of white wine (Jacques *et al*., 2011).

Methylsulfonylmethane (MSM)

Methylsulfonylmethane (MSM) (an oxidation product of dimethylsulfone) is found in fruits, corn, tomatoes, tea, coffee, alfalfa, human and, bovine milk and in human urine (Richmond, 1986). About 4-11 mg day^{-1} is excreted in human urine (Williams *et al*., 1966). MSM contains 34% S. The concentration of sulfur in arthritic cartilage is about one-third of normal cartilage and therefore MSM is being used for treating arthritis (Parcell, 2000). MSM is also reported to reduce the duration of chiropractic (treatment and prevention of mechanical disorders of the musco-skeletal system, especially the spine) visits for treating athletic injuries. MSM is also used for treating hyperacidity, parasites, constipation and allergies and for immunomodulation (Parcell, 2000).

Epilogue

The year 2013 marked the 50^{th} anniversary of the commencement of a yield revolution in wheat that ushered the Green Revolution in 1968 and assured food-security in India (Swaminathan, 2013). Higher and higher grain yield of food grains has been the goal of most plant breeding and agronomic research in the country and nutritional quality of the farm produce received only little attention. However, increasing global interest in nutraceuticals as supportive or alternative medicine in view of the undesirable side effects of chemotherapy has focused attention of the content of such compounds in farm food products (Choudhary and Tomar, 2013). Sulphur compounds in farm food products, especially from the plants of *Brassicae* and *Alliaceae* families deserve special attention. However, most agricultural universities and institutions do not have departments of food and nutrition and such studies have not been possible. It is high time that such facilities are created in agricultural universities and institutes. Until such additional facilities are developed, the Indian National Science Academy may consider organizing group discussions of scientists from the disciplines of agriculture, nutrition, pharmacy and medicine to draw out a joint program of creating such data in India. Such information has become more so important in view of the fact that compositional details have now become essential for marketing farm food products in the international trade.

References

Abramovitz D, Gavri S, Harats D, Levkovitz H, Mirelman D, Miron T, Eliat-Adar S, RobinkovA, Wilchek M, Eldar M and Vered Z (1999) Allicin-induced decrease in formation of fatty streaks (atherosclerosis) in mice fed a cholesterol rich diet. *Coronary Artery Dis* **10** 515-519

Alary R and Kobrechel K (1987) The sulphhydryl plus disulfide content in the proteins of durum wheat and its relationship with the cooking quality of pasta. *J Sci Food Agric* **39** 130-136

Alleyene R (2009) Vegetarian low protein diet could be key to long life. *The Telegraph (London),* December 3 (http://www.telegraph.co.uk/health/healthnews/6710896/Vegetarian-low-protein-diet-could-be-key-to-long-life.html)

Avilla F W, Faquin V, Yang Y, Ramos S J, Guillheme L R, Thannhauser T W and Li L (2013) Assessment of anti-cancer compounds Se-methylselenocystein and glucosinolates in Se-biofortified broccoli (*B oleracea* varitalica) sprouts and florets. *J Agric Food Chem* **61** 6206-6213

Banerjee S K, Mukherjee P K and Maulik S K (2001) Garlic as an anti-oxidant: the good, the bad and the ugly. *Phtotherapy Res* **17** 97-106

Bashir H A and Abu-Goukh A A (2003) Compositional changes during guava fruit ripening. *Food Chem* **80** 557-563

Bark M, Malhi G S, Gay L J and Dean O M (2013) The promise of N-acetylcystein in neuropsychiatry. *Trends Pharmacol Sci* **34**167-177

Bautista D M, Movahed P, Hinman A, Axelsson H E, Sterner O, Hogestatt E D, Julius D, Jordt S E and Zygmunt P M. (2005) Pungent products from garlic activate sensory ion channel TRPAI. *Proc Natn Acad Sci, USA* **102** 12248-12252

Beecher C (1994) Cancer preventive properties of varieties of *Brassica oleracea*: a review. *Am J Clin Nutr* **59** 1166-1170

Biswas B C, Sarkar M C, Tanwar S P S, Das S and Kalwe S P (2004) Sulphur deficiency in soils and crop responses to fertilizer sulphur in India. *Fertiliser News* **49** 13-33

Block E (2010) *Garlic and Other Alliums: The lore and the Science*. Royal Society of Chemistry, Cambridge

Bray T M and Taylor C G (1993) Tissue glutathione, nutrition and oxidative stress. *Canadian J Physiol Pharmacol* **71** 746-751

Chiang P K, Gordon R K and Tal J, Zeng G C, Doctor B P, Pardhasarathi K and McCann P P (1996) S-adenosylmethionine and methylation *FASEB J* **10** 471-480

Chomchelow S, El Assi N M, Sargent S A and Brecht J K (2002) Fruit maturity and timing of ethylenetreatment affects storage performance of green tomatoes at chilling and non-chilling temperatures. *Hor Technology* **12**(1) 104-114

Choudhary M and Tomar V (2013) Cardioprotective effect of nutraceuticals-the emerging evidence. *Proc Indian Natn Sci Acad* **79**(4) (Special Issue B) 985-996

Coyle E A and McAleese D M (1970) Aspects of sulphur uptake and distribution in cereals. In: *Sulphur in Agriculture*, pp 158-176 Ann Foras Taluntais, Dublin

Cutler R R and Wilson P (2004) Antibacterial activity of a new, stable, aqueous extract of allicin. against methicillian-resistant *Staphylococcus aureus*. *Brit J Biomed Sci* **61**(2) 71-74

Dang K T H, Singh Z and Tan S C (2006) Influence of maturity stage at harvest and ethylene application on colour and quality of controlled atmosphere-stored mango fruit. *Acta Hort* **768** 209-216

Das S, Tyagi A K and Kaur H (2000) Cancer modulation by glucisinolates: a review. *Curr Sci* **79**(12) 1665-1670

diPadova(1987) S-adenosylmethionine in the treatment of osteoarthritis. *Am J Med* **83** 60-65

Duana X, Guiping Cheng G and Jiang Y (2008) Modification of pectin polysachharides during ripening of post-harvest banana fruit. *Food Chem* **80**(4) 557-563

Eliat S, Oestraicher Y, Robinkow D, Ohad D, Mirelman D, Ballar A, Eldar M and Vared D (1995) Alteration of lipid profile in hyperlipidemic rabbits by allicin, an active constituent of garlic. *Coronary Artey Dis* **6**(12) 985-990

Elkayam A, Mirelman D, Peleg E, Wilchek T, Miron A, Robinkov M, Oron-Herman M and Rosenthal T. (2003) The effects of allicin on weight in fructose induced hyperinsulenemic, hyperlipidemic, hypersensitive rats. *Am J Hypertens* **16**(12) 1053-1056

Ercoli L, Lulli L, Aduini I, Mariotti M and Mason A (2011) Durum wheat grain yield and quality as affected by sulphur rate under Mediterranean conditions. *Euopean J Agron* **35** 63-70

Flaete N E S, Hollung K, Ruud L, Sogn T, Faergestad E, Skarpeid H J, Magnus E and Uhlen A K (2005) Combined nitrogen and sulphur fertilization and its effect on wheat quality and protein composition measured by SE-FPLC and proteomics. *J Cereal Sci* **41**(3) 357-369

Furst P and Stehele P (2004) What are essential elements needed for the amino acids required in humans *J Nutr* **134**(6 Suppl) 1558S-1565S

Gane R (1934) Production of ethylene by some fruits. *Nature* (London) **134** 1008

Glawisching E, Mikkelsen M D and Halkier B A (2003) Glucosinolates: biosynthesis and metabolism. In: Sulphur in Plants (Abrol YP and Ahmed A, eds) 145-162, Kluwer Academic Pub., Dordrecht

Green J L, Mead K J, Reynolds K M and Albert D (2013) Oral and intraveinousacetylcystein for treatment of acetaminophen toxicity: A systematic review and meta-analysis.*West J Emerg Med* **3** 218-226

Hakan P M (2007) Calcium carbide poisoning in food in childhood. *J Emerg Med* **32**(2) 179-180

Harper C (1979) Wernicke's encephalopathy, a more common disease than realized (a neuropathological study of 51 cases) *J Neurol Neurosurg Psych* **42**(3) 226-231

Hayes J D, Kelleher M O and Eggleston I M (2008) The cancer chemopreventive actions of phytochemicals derived from glucosinolates. *European J Nutr* **47** (Suppl 2) 73-88

Horn T D (2003) *Dermatology* Vol 2. Elsevier Health Sciences, New York.

Huxtable R (1986) *Biochemistry of Sulphur*. Plenum Press, New York pp. 64-316.

Iberi B (1990) Quantitative determination of alliin and allicin from garlic by HPLC. *Planta Med* **56**(5) 320-326

Jacques R, Cheynier V, Souquet J and Moutounet M (1991) Influence of must composition on phenolic oxidation kinetics. *J Sci Food Agric* **57**(1) 55-63

Jarvan M, Edesi L, Adamson A, Lukme L and Akk A (2008) The effect of sulphur fertilization on yield quality of protein and baking quality of winter wheat. *Agronomy Res* **6**(2) 459-469

Jo H J, Song J D, Kim K M, Cho Y H, Kim H K and Park Y C (2008) Diallyldisulfide induces reversible G2/M phase arrest on a p53-independent mechanism in humans colon cancer HCT-116 cells. *Oncology Repts* **19**(1) 275-280

Josefsson E (1970) Glucosinolate content and amino acid composition of rapeseed (*Brassica napus* L) meal as affected by sulfur and nitrogen nutrition. *J Sci Food Agric* **21** 98-103

Kader A A (1999) Fruit maturity, ripening and quality relationships. *Acta Hort* **485** 203-208

Kagan B L, Sultzer D L, Rosenlicht N and Gerner R M (1990) Oral S-adenosylmethionine in depression: a randomized double blind placebo-controlled trial. *Am J Psychiatry* **147** 591-595

Kim S J, Ishida M, Matsuo T, Watanabe M and Watanabe Y (2001) Separation and identification of glucosinolates of vegetable turnip rape by LC/APCI-MS and comparison of their content in ten cultivars of turnip rape (*Brassica napus* L) *Soil Sci Plant Nutr* **47** 167-177

Kleinman W A and Richie Jr J P (2000) Status of glutathione and other thiols and disulphides in human plasma. *Biochem Pharmacol* **60** 19-29

Komninou D, Lentzinger Y, Reddy B S and Richie Jr J P. (2006) Methionine restriction inhibits colour carcinogenesis. *Nutrition & Cancer* **54**(2) 202-208

Kourounakis P N and Rekka E A (1991) Effect of active oxygen species of alliin and *Allium sativum* (garlic) powder. *Res Commun Chem Pathol Pharmacol* **74**(2) 249-252

Krill J J (1996) Neuropathology of thiamine deficiency disorders. *Metab Brain Dis* **11**(1) 9-17

Kumar C, Igbaria A and Toledano M B (2011) Glutathione revisited; a vital function in iron metabolism and ancillary role in thiol-redox control. *EMBO J* **30** 2044-2056

Lerner S E, Seghezzo M L, Molfese E R, Ponzio N R, Cogliatti M and Rogers W J (2006) Nitrogen and sulphur effects on grain composition, industrial quality and end use in durum wheat *J Cereal Sci* **42** 2-11

Lieberman M and Konishi A (1965) Ethylene production from methionine. *Biochem J* **97**(2) 449-459

Mahan L K and Escott-Stump S (eds) (2000) Kraus's Food Nutrition & Dietary Therapy, 19th ed,,W B Saunders Company, Philadelphia

Medicott A P and Thompson A K (1985) Analysis of sugars and organic acids in ripening mango fruits (*Mangiferaindica* L var. Keitt) by high performance liquid chromatography. *J Sci Food Agric* **36** 561-566

Messick D L (2003) Sulphur fertilizers-A global perspective. Proc TSI-FAI-IFA Workshop on Sulphur In Balanced Fertilization (Sarkar MC, Biswas BC, Das S, Kalwe SP, Maity SK,eds), The Fertiliser Association of India, New Delhi, 1-7

Messick D L and Fan M X (2007) Sulphur in balanced fertilization in China. *In,Proc TSI-FAI IFA Workshop on Sulphur.* In: *Balanced Fertilization* MC Sarkar, B C Biswas, S Das, S Dev (eds), The Fertiliser Association of India, New Delhi, 1-12

Milner J A (2006) Preclinical perspectives on garlic and cancer. *J Nutr* **136** (3Suppl) 827S-831S

Mirzaei R, Liaghati H and Mahdavi DamghariA (2007) Evaluating yield quantity and quality of garlics affected by different farming systems and garlic clones. *Pakistan J Biol Sci* **10** 2219-2224

Naquib A M, El-Baz F K, Salama Z A, Hanna H A, Ali H E and Gaafar A A (2012) Enhancement of phenolics, flavanoida and glucosinolates of broccoli (*Brassica oleracea* var italca) as anti-oxidants in response to organic and bio-organic fertilizers. *J Saudi Soc Agric Sci* **11**(2) 135-142

Narits L (2011) Effect of top fertilizing on raw protein and glucsinolate content of winter turnip rape. *Agron Res* **9** (Special Issue II) 451-454

Nijjar P S, Burke C M, Bloesch A and Rofer D J (2010) Role of dietary supplements in lowering low-density lipoprotein cholesterol: A review. *J Clin Lipidol* **4** 248-258

Parcell S (2002) Sulfur in human nutrition and application in medicine. *Alternative Med Rev* **7** 22-44

Perez-Ballibrea S, Moreno D A and Garcia-Viquera C (2010) Glucosinolates in broccoli (*Brassica oleracea* var italica) sprouts during germination. *J Food Sci* **75**(8) C 673-677

Pinto J T, Sinha R, Papp K, Facompare N C, Desai D and El-Bayoumy K (2007) Differential effects of naturally occurring and synthetic organoselenium compounds on biomarkers in androgen responsive and androgen independent human prostate carcinoma cells. *Int J Cancer* **120** 1410-1417

Pompella A, Visvikis A, Paolicchi A, Tata V and Casini A F (2003) The changing faces of, glutathione -A cellular protagonist. *Biochem Pharmacol* **66**(8)1499-1503

Pool J and Black P N (2011) Oral mucolytic drugs for exacerbations of chronic obstructive pulmonary disease: systematic review. *Brit Med J* **322** 1271-1274

Pradhan S K, Nerg A, Sjoblom A, Holopainen J K and Heinonen-Tanski H (2007) Use of human urine fertilizer in cultivation of cabbage (*Brassica oleracea* var capitata) –impact on chemical, microbial and flavor quality. *J Agric Food Chem* **55** 8657-8663

Prasad R (2005) Rice-wheat cropping system. *Adv Agron* **86** 255-339

Prasanna V, Prabha T N and Tharnathan R N (2007) Fruit ripening phenomena-an overview. *Crit Rev Food Sci Nutr* **47**(1) 1-19

Rehm G (2005) Sulphur management for corn grown with conservation tillage. *Soil Sci Am J* **69** 709-717

Reynolds E H, Carney M W and Toone B K (1984) Methylation and mood. *Lancet* **2** 196-198

Richie Jr J P, Lentzinger Y, Parthasarathy S, Malloy V, Orentreich N and Zimmerman J A (1994) Methionine restriction increases blood glutathione and longevity in F334 rats. *FASEB J* **8** 1302-1307

Richie Jr J P, Nichenametla S, Neidig W, Calcagnotto A, Haley J S, Shell T D and Muscat J E (2014) Randomized controlled trial of oral glutathione supplementation on body stores of glutathione. *European J Nutr* May 5 (epub ahead of publication)

Richmond V L (1986) Incorporation of methylsulfonylmethane sulfur into guinea pig serum protein. *Life Sci* **39** 263-268

Ritenour M A, Crisoto C H, Garner D T, Cheng G W and Zaffoli P J (1999) Temperature, length of cold storage and maturity influences the ripening rate of ethylene pre-conditioned kiwi fruit. *Postharvest Biol Tech* **15** 107-115

Salama A A, Aboulalia M, Terkawi MA, Mousa A, El-Sify A, Allaam M, Zaghawa A, Yokoyama N and Igarashi I (2014) Inhibitory effect of allicin on the growth of *Babesia* and *Theileriaequi* parasites. *Parasitology Res* **113**(1) 275-283

Schung E (1989) Double row oilseed rape in West Germany, sulfur nutrition and glucosinolatelevel. *Aspects Appl Biol* **23** 67-82

Shils M E, Shike M, Ross A C, Caballero B and Cousins R J (eds.) (2006) Modern Nutrition in Health and Disease, 10th ed, Lippincott Williams & Wilkins, Baltimore

Shivay Y S, Prasad R and Pal M (2014) Effect of levels and sources of sulphur on yield, sulphur and concentration and uptake and S-use efficiency in Basmati rice. *Communications Soil Sci Plant Anal* 001-12 (on line)

Silagy C A and Neil, H A (2003) A meta-analysis of the effect of garlic on blood pressure. *Am J Hypertens* **12**(4) 463-468

Singh M V (2001) Importance of sulphur in balanced fertilizer use in India. *Fertiliser News* **46**(10) 13-35

Smythies J R and Hasley J H (1984) Treatment of Parkinson's disease with L-methionine. *South Med J* **77** 1577

Solberg E D, Malhi S S, Nyborg M, Henrique B and Gill K S (2006) Crop responses to elemental Sulphur and sulphate S sources on sulphur deficient soils in Parkland region of Alberta and Saskatchewan. *J Plant Nutr* **30** 321-333

Spinazzi M, Angelini C and Patrini C (2010) Subacute sensory ataxia and optic neuropathy with thiamne deficiency. *Nature Rev Neurology* **6** 288-293

Staley J T, Stewart-Jones A, Pope T W, Wright DT, Leather S R, Hadley P, Rossiler J T, van Emden H F and Poppy G M (2010)Varying responses of herbivores to altered plant chemistry under organic and conventional treatments. *Proc Royal Soc B* **227** 779-786

Stey C, Steura J, Bachmann S, Medici T C and Tramer M R (2000) The effect of oral N-acetyl-cysteine in chronic bronchitis- a quantitative systematic review. *European Respir J* **16**(2) 253-262

Swaminathan M S (2013) Genesis and growth of revolution in India: lessons for shaping our agricultural destiny. *Agric Res* **2**(3) 183-188

Tabakoff B, Ercksson C J and von Wartburg J P (1989) Methionine lowers circulating levels of acetaldehyde after ethanol ingestion. *Alcohol Clin Exp Res* **13** 164-171

Tandon H L S (2011) Sulphur in Soils, Crops and Fertilizers. Fertilizer Development and Consultation Organization (FDCO), New Delhi.

Tapel M, van der Giet M, Schwarzfeld C, Laufer U, Liermann D and Zidek W (2000) Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcystein. *New England J Med* **343**(2) 180-184

Uden S, Bilton D and Nathan L (1990) Antitoxidant therapy for recurrent pancreatitis: placebo-controlled trial. *Aliment Pharmacol Ther* **4** 357-371

WHO (2013) Modal List of Essential Medicines, World Health Organization. October 2013

Williams K I, Burstein S H and Layne D S (1966) Dimethylsulfone: isolation from human urine. *Archives Biochem Biophys* **113** 251-252

Williamson G, Faulkner K and Plumb G W (1998) Glucosinolates and phenolics as anti-oxidants from plant foods. *European J Cancer Prevention* **7** 17-21

Wittstock U, Agerbirk N, Stauber E J, Olsen C E, Hippler M, Mitche-Olds T, Gershenzon J and Vogel H (2004) Successful herbivore attack due to metabolic diversion of a plant chemical defense. *Proc Natn Acad Sci, USA* **101**(14) 4859-4864

Young V R and Pellet P L (1994) Plant proteins in relation to human proteins and amino acid nutrition *Am J Clin Nutr* **59** (Suppl) 1203S-1212S

Zhao F L, Evans E J, Bilsborrow P E and Syers J K (1993) Influence of sulfur and nitrogen on seed quality of low glucosinolate rape (*Brassica nsapus* L). *J Sci Food Agric* **63** 29-37

Zhao FJ, Hawksford M J and McGarth S P (1999) Sulphur assimilation and effects on yield and quality of wheat. *J Cereal Sci* **30**(1) 1-17.