Status and trends of nutraceuticals from onion and onion by-products: A critical review

Muhammad Sajid Arshad1*, Muhammad Sohaib2, Muhammad Nadeem3, Farhan Saeed1, Ali Imran1, Ahsan Javed1, Zaid Amjad1 and Syeda Mamoona Batool1

Abstract: The pivotal roles of vegetables are predominantly important for health due to availability of minerals, vitamins, phytochemicals and antioxidants. These foods and food products those are prepared from such kind of material having natural origin have great importance due to their versatile nature. Onion importance is greatly increasing and now it has become second most medicinal and horticultural crop after tomatoes. It has multiple functional compounds including organosulphur, anthocyanins, flavonoids, quercetin, kaempferol and polyphenols. Antibacterial, anti-inflammatory and antioxidant properties are the various diverse functions of onions, which have sound effects on human health. Fructo-oligosaccharides are present in abundant quantity in it due to which the growth of potentially harmful bacteria in the colon is retarded by the oligomers thus reducing the risk of emerging tumors in the colon and also initiates the growth of healthy bifidobacterium. In the nutshell, the onion and onion by-products have a lot of bioactive compounds against certain metabolic disorders.

Keywords: onion; anthocyanins; flavonoids; quercetin; kaempferol; polyphenols

1. Introduction
Onion (Allium cepa L.) is the main crop grown all over the world especially in the Asia. It belongs to the family, Amaryllidaceae, and the genus, Allium. Alliums are perennial herbs having bulbous and scented underground stems. This genus includes garlic, shallot, chives, leeks, and even a non-edible species grown only for its showy flower (Mollavali et al., 2016). The common garden onions are in the species, A. cepa. There are various varieties of onion each with their own unique flavor, ranging from mildly sweet to very strong i.e. red, yellow, white and green. It can be eaten fried, dried, raw, cooked or roasted. They are usually used to flavor salads, spreads, stir-fry, dips, soups and other dishes (van Wyk, 2014). Since ancient times in various cultures, onions on every continent have been growing in their natural habitat. Dates back to 3500 BC, onions were one of the only some foods that did not

ABOUT THE AUTHOR
Muhammad Sajid Arshad is Assistant Professor at Department of Food Science, Government College University, Faisalabad, Pakistan. He has published a number of research and review articles related to his research area in high repute Journals.

PUBLIC INTEREST STATEMENT
Onion and onion by-products have vital role against certain ailments due to the presence of bioactive compounds present in it. Before people did not use the by-products but now the concept of value addition is very popular. Pharmaceutically onion possesses many characteristics like anti-inflammatory, antioxidant and antibacterial properties. In decreasing pro-inflammatory diseases the effectiveness of onion is rooted in its nature as modulators of metabolism.
spoil during the winter seasons. Ancestors in Asia have become familiar with its stability and started to grow as a food. Swenson (2008) reported that the ancient Egyptians worshipped the onion, having faith in its spherical shape and concentric rings that represented eternity. Pakistan being an agricultural country, is producing onion as a major agricultural crop. The annual world production of onion is about 55 million tonnes and Pakistan ranked 8th in onion production with an area of 147.6 thousand hectares and production of 1,939.6 thousand tonnes (Mushtaq et al., 2013). Swenson (2008) proposed that in the mountainous areas of Pakistan, Tajikistan, Northern Iran and Afghanistan the bulb onion (A. cepa L.) has been domesticated and cultivated thousands of years ago. Allium species (onion bulbs and fresh shoots) are grown for the production of seeds, sets and as fresh shoots for green salad in open, sunny and dry mountain slopes of these countries. Onions vary in color, size, firmness, pungency shape, stiffness of outer neck and dry skins and may be consumed as uncooked or pickled (Akhtar, 2015).

Short-day and long-day onions are two major types being cultivated all over Pakistan. On the other hand, a third group named as an intermediary day length type is expressed between these two major groups. White and Zellner (2008) described that the onions which require 11–12 h to bulb are placed under short-day type category whereas those require more than 14 h to bulb are categorized as long day type of onions.

The chemical composition of onions for moisture, carbohydrate, total sugar, vitamin-C, Ca, P and K ranged from (82.99 and 82.77%), (14.146 and 14.772%), (4.74 and 2.32%), (6.5 and 5.7 mg), (46.9 and 25.7 mg), (50.6 and 30.3 mg) and (140 and 129 mg), respectively. Likewise, Bhattacharjee et al. (2013) revealed the level of protein and fat as (2.62 and 1.489%) and (0.4%) with other trace elements. Major components of commercially important volatile compounds of onion includes 3,5-Diethyl-1,2,4-trithionale and Propyl 1-propenyl disulphide (Farkaas, Hradsky, & Kovac, 1992). Whereas, amongst non-volatile components Sitosterol, Gitogenin, Oleanolic acid, Amyrin and Diosgenin are abundantly present (Ismailov & Aliev, 1974).

2. Onions and health interactions
Onion is the main component of condiments used in all households around the year. Small bulbs of onions are pickled in vinegar and are used for making various seasonings, sauces and soups. Onion is a spice with characteristic flavor and aroma as well as having pronounced medicinal importance such as rich in carbohydrates, phosphorus and calcium. Lee and Mitchell (2011) and Suleria, Butt, Anjum, Soeed, and Khalid (2013) have reported high levels of ACSOs (alk (en) yl cysteine sulfoxides) present in Allium plants. Onions are being used since primeval times as a traditional medicine. By having rich photochemistry, these reduce the peril of cardiovascular diseases, diabetes, cancer and atherosclerosis (Cazzola, Camerotto, & Cestara, 2011; Suleria et al., 2013).

3. Role of onion as antioxidant
BHT (butylated hydroxytoluene) and BHA (butylated hydroxyanisole) are synthetic antioxidants which are needed to be exchanged with natural antioxidants, as several studies showed that a number of synthetic antioxidants were toxic and carcinogenic (Che Othman et al., 2011). Antioxidant compounds (flavonoids and phenolics), have protective effects against different degenerative pathologies are present in high amount in onions (Pérez-Gregorio, Regueiro, González-Barreiro, Rial-Otero, & Simal-Gándara, 2011; Siddiq, Roidoung, Sogi, & Dolan, 2013). Onion consider as a good antioxidant additive for food due to Cysteine derivatives (Ostrowska et al., 2004), enhancing its usability as in ethnomedicine and as functional food (Tram Ngoc et al., 2005). Chemical spoilage, resulting in deterioration or rancidity of the texture, flavor color, nutritional quality and safety of foods is caused by the oxidation (Antolovich, Prenzler, Patsalides, McDonald, & Robards, 2002). Flavonoid extractability is increased during onion processing. Nemeth and Piskula (2007) reported that enzymes released from disrupted plant tissue causes deglycosylation, and after ingestion, due to β-glucosidases of microbial origin and those of the consumer’s body.
4. Disparity in antioxidant activity
Onion antioxidant activity is reduced after cooking, so onion is efficient in its raw form (Ali, Thomson, & Afzal, 2000). Yang, Meyers, van der Heide, and Liu (2004) reported that various kinds of onions were found which differ in their characteristics, with maximum in vitro tumor cell inhibition as well as highest total antioxidant activities seen in the onion variety Western Yellow and in shallots. The synthesis of amino acid and its transformation to leukotrienes and pro-inflammatory prostaglandins is inhibited by cepaene and thiosulphinate content present in onion (Ali et al., 2000). Cao, Sofic, and Prior (1996) suggest that many vegetables, fruits, and tea’s antioxidant activity have been studied, which pointed out that the presence of vitamin C, β-carotene and flavonoids shows the antioxidant activity of these plant foods (Bors & Soran, 1987; Gey, 1990; Willett, 1994). Cao et al. (1996) studied two members of Allium family are also known to have antioxidant activity, which are Garlic bulb and onion (Yang, Yasaei, & Page, 1993).

There is little information available about the antioxidant activity of other members of the allium family; however, antioxidant capacities of Garlic and onion bulbs have been investigated briefly. For the antioxidant activity of garlic bulb, Allicin which is a scavenger of peroxy radicals was responsible (Zakarova et al., 2014). Thiosulfimates and allicin configuration in allium members and garlic have been studied shows allicin is absent in onion and rich in thiosulfimates compounds which play a key role in onion antioxidant activity (Block, Naganathan, Putman, & Zhao, 1992; Lawson, Wood, & Hughes, 1991).

5. Onion and onion by products as antimicrobial and antifungal
Significant amounts of phenolic-rich by-products are being produced in food processing industries, which could be important natural sources of antioxidants. Roldán, Sánchez-Moreno, de Ancos, and Cano (2008) reported that we should worried about the production of large quantities of industrial onion wastage and its disposal. Stabilizing and processing onion wastes (surpluses and residues of onion) could symbolize advantages (Roldán et al., 2008). Literature shows that onions contain the powerful antioxidants, sulfur and other numerous phenolic compounds which provoke great interests and holds anti-bacterial and anti-fungal activities (Onyeoziri, Romanus, & Onyekachukwu, 2016).

Onion and onion by-product has high amount of antioxidants which makes it a good free radical scavenging ability. So, it has good anti-inflammatory and anti-mutagenic properties. Lipid peroxidation was found to be inhibited in rat liver microcosms and also found to effectively scavenge superoxide onions (Krishnakanth & Lokesh, 1993; Reddy & Lokesh, 1992). The antioxidant power of onion by product has also been confirmed in applications where extracts of onion by product was added to meat products. Fresh, frozen and precooked pork patties were further tested to check the ant oxidative effectiveness of onion by product extract. By the inclusion of onion by product extract, the shelf life of all products was enhanced which was determined by TBA value (Cao et al., 2013).

Onion by product has strong antibacterial. Active constituents of onion by product restrict the growth of Streptococci, Staphylococci, Proteus sp., Escherichia coli and Salmonella in vitro studies (Janes, Nannapaneni, & Johnson, 1999). Meena (1998) reported that at ambient temperatures fresh onion by product juice showed inhibitory action against S. cerevisiae, A. niger, Mycoderma spp. and L. acidophilus at 4, 10, 12 and 14% respectively.

In vitro and in vivo onion showed effective antioxidant activity (Jackson et al., 2002). Volatile oils (allicin, ajoene and alliin) consisting of sulphur, carbohydrates (sucrose, glucose), amino acids like methionine, glutamine, cysteine and isoleucine, minerals (selenium, zinc, germanium), bioflavonoids like cyanidin and quercetin and allilstatin I and allilstatin II, A, E and C vitamins, enzymes (mircynase, peroxidase and allilinase), and niacin, B vitamins and beta carotene fall in >20 is a plant0 components present in onion (Gulsen & Ayaz, 2010). Onion lowers glycaemia and cholesterol and kills parasites, fungus, bacteria and has the ability to protect liver and contains antitumor agents. Onion has the ability of protecting human body against various illnesses with more than 200 chemical substances present in its body. For protection against infections and free radicals onion should
be consumed as fresh (Ayaz & Alpsoy, 2007). Harris (2001) reported that onion has a wide range of actions; not only as antiprotozoal, antifungal, antibacterial and antiviral, but also has positive effects on the immune systems and cardiovascular.

6. Anthocyanins as antioxidant in onion

There is little information regarding absolute amount of anthocyanins in red onions. Ferreres, Gil, and Tomás-Barberán (1999) and Clifford (2000) reported that up to 250 mg/kg anthocyanins present in red onion. Nevertheless, it is not sure that this amount relates only to the edible part or to the whole onion bulb. It is also reported that the analysis performed on dry skins shows that values extending from a minimum (109/100 g) to a maximum (219/100 g) (Donner, Gao, & Mazza, 1997; Fossen, Andersen, Øvstedal, Pedersen, & Raknes, 1996). Flavonoids occur in a variety of complex conjugates with sugars, so sugars are very substantial for anthocyanin biosynthesis, but data about this stuff is still controversial (Harborne & Mabry, 2013). In the context of a survey aimed on the typical Italian varieties characterization, produced in some areas of southern Italy and was investigated. Tropea red onion is known for its crispness and sweetness that is why it is consumed uncooked which preserve the flavonoid compounds (Gennaro et al., 2002; Ioku et al., 2001).

7. Onion as disease preventive

Antioxidants hunt free radicals and are related to minimize the risk of cancer and cardiovascular diseases. Stajner and Varga (2003) reported that A. cepa L. has antispasmodic, hypoglycaemic, antimicrobial, hypotensive, antiasthmatic, anticholesterolaemic, anticancer, and antioxidant properties. In onions polyphenols, anthocyanins, quercetin, kaempferol, flavonoids and their glycosides have been reported (Ashwini, Balaganesh, Balamurugan, Murugan, & Sathishkumar, 2013). The studies proposed that fruits and vegetables have a defensive action against coronary heart disease and cancer. Much attention has been given for lowering the oxidative stress prompted by chronic diseases (Crozierm et al., 2000). Furthermore, Allium species are strongly resistant to diseases produced by nematodes. Onion is very helpful against free radicles and cancer due to antioxidant activity and antibacterial activity. It also consists of some terpenoids, carotenoids, flavonoids, vitamins, phytoestrogens and minerals etc. (Calucci, Pinzino, Zandomeneghi, & Capocchi, 2003).

8. Phytochemical synthesis

Pasteurized Recas product contained 721 mg/100 g quercetin of dry weight whereas frozen Recas paste contain highest total quercetin content of 4,431 mg/100 g of dry weight i.e. 4%. Major products of lipid oxidation are free radicals which implicated over 100 important diseases including atherosclerosis, cancer, arthritis (Hajhashemi, Vaseghi, Pourfarzam, & Abdollahi, 2010). Taste and toxicity both are undesired which are formed by the oxidation of unsaturated fatty acids (Benkeblia, 2005). The total quercetin concentration in onion is from traces in white varieties to 2.5–3 mmol/kg of fresh weight in red varieties. There are four predominant forms of Q in onions exists in: Q3G (quercetin-3-O-glucoside), Q3,4′G (quercetin-3,4-di-O-glucoside), Q aglycone, Q4′G (quercetin-4-O-glucoside), and many forms of monoglucoside and diglucoside conjugates in lesser amounts have been reported (Wiczkowski, Nemeth, Bucin’ski, & Piskula, 2003).

Among fruits and vegetables, onion rated maximum in quercetin (Q) content (Ko, Cheigh, Cho, & Chung, 2011). Lombard, Peffley, Geoffriau, Thompson, and Herring (2005) reported that bulb type and color vary the concentration of (Q) in onions and quercetin is spread typically in the outer rings and skins. Mainly aglycones are the end result of food processing but glycosylated, flavonols and other flavonoids are present in fresh vegetables (Rohn, Buchner, Driemel, Rauser, & Kroh, 2007). In onions secondary metabolites occur in two main classes; flavonoids and organosulfur compounds having beneficial health effects and methods of biosynthetic pathways and action are rather changed.

El-Hadidy, Mossa, and Habashy (2014) reported that by inhibiting lipoxygenase and cyclooxygenase enzymes the organosulfur compounds are thought to have anti-allergic, anti-thrombotic, antimicrobial and anti-inflammatory activity. Probably, the compounds work through sulfur-oxygen or
sulfur-sulfur bonds. When onion cell walls is disrupted and cut these compounds are produced. El-Hadidy et al. (2014) depicted that via S-alk (en)yl cysteine sulphoxides (ACSOs) Sulfenic acids are produced by Allinase enzymes which reposition to numerous compounds such as, cepoenes and thiosulfimates. Flavonoids comprise aromatic rings held together by a C$_7$ unit. The subclass of flavonoid is determined by the rate of C$_7$ unit oxidization such as anthocyanins, flavonols, and flavanones. Chalcone formation starts the Flavonoid biosynthesis by chalcone synthase from coumaroyl CoA and malonyl CoA, which is a derive form of amino acid phenylalanine. Flavanone is being isomerized by the chalcone. The formation of each flavonoid subclass is catalyzed by specific enzymes; Kaempferol and quercetin, in the flavonol subclass they are considered main flavonoids. The extent of hydroxylation differentiates them from one another. These compounds are associated with the beneficial health property which reduce various kinds of cancer and are believed to have anti-oxidative activity as well as metal ion chelation and risk of coronary heart disease and lipid peroxidation inhibition (El-Hadidy et al., 2014).

Singh et al. (2009) reported that many biologically active phyto-molecules are extracted from onions which include anthocyanins, thiosulfinates, flavonoids and phenolic acids. Prakash, Singh, and Upadhyay (2007) reported that dry peel of onion (consider as a waste product) contain major flavonoids which includes quercetin glycoside which is an effective antioxidants against oxidative stress. Patricia et al. (2005) reported that vegetables and fruits are excellent sources of antioxidant phytochemicals, such as terpenoids vitamins C and E, flavonoids, vegetable pigments carotenoids, glutathione, and polyphenolics, by defending against cellular damage due to their ability to reduce oxygen-derived free radicals by donating electron, inhibit lipooxygenases and chelate to redox-active metals (Dimitrios, 2006). Free hydroxyl and peroxy radicals can be scavenged by flavonoids, on the other hand, they may extract iron ions as metal-chelating agents and reduce the superoxide-driven Fenton reaction (Suh, Lee, Cho, Kim, & Chung, 1999).

Flavonoids and flavonols are present in high levels in Allium vegetables. Flavonoid ranges from <0.03 to >1 g/kg in the edible portions of Allium vegetables. Higher levels of flavonoids 2 ± 10 g/kg are present in onion skins rather than the edible portion. The most significant flavonoids were quercetin aglycone, quercetin diglucoside and quercetin 40-glucoside and kaempferol monoglucoside or isorhamnetin monoglycoside in some cases (Leighton et al., 1992). After onion processing, a huge amount of onion skins remains useless regardless onion skin contains higher levels of flavonoids. Nuutila, Puupponen-Pimiä, Aarni, and Oksman-Caldentey (2003) reported that onion skin extracts have an anti-oxidative activity.

9. Anticancer effect
Onion consumption has inhibitory action on human carcinoma which has been broadly researched. Excess uses of onions lower the risk for carcinoma (Corzomartinez, Corzo, & Villamiel, 2007). In those individuals who have the consumption of onion is more, they had a 50% reduced risk of cancers of the alimentary, stomach and respiratory tracts (Turati, Rossi, Pelucchi, Levi, & La Vecchia, 2015). Renal and colon carcinogenesis are inhibited by organosulfur compounds such as S-methylcysteine (SMC), diallyl disulfide (DDS), and S-allylcysteine (SAC) (Fukushima, Takada, Hori, & Wanibuchi, 1997; Hatano, Jimenez, & Wargovich, 1996). Allium vegetable consumption may have a strong effect for the prevention of stomach cancer. Stomach cancer may be reduce with high consumption of onions >0.5 onion/day. In China the risk of stomach cancer was decreased by consuming allium vegetables such as onion, Chinese chives and Welsh onion more than 1 time/week (Gao, Takezaki, Ding, Li, & Tajima, 1999). The risk of Helicobacter pylori infection, which causes stomach cancer by ulcer formation, may be decreased by higher intake of allium vegetables. Abourehab, Khaled, Sarhan, and Ahmed (2015) reported that quercetin not only increase the cure level of ulcers with the help of free radical scavenging, but also restrict the induction of gastric mucosal injury.

Dorant, van den Brandt, Goldbohm, and Sturmans (1996) reported that the risk of lung cancer was also be analyzed through stomach carcinoma risk. Dorant, Van Din Brandt, and Goldbohm (1994) reported that those who intake higher onion will have a mild risk of lung cancer. In the onions consumption it was
found that the quantity and/or dietary absorption of flavonoids compounds and organosulfur were insufficient to produce effective results. Hence, it can be concluded that onions intake have inhibitory effect on lung carcinoma risk, but the levels needed are feasible to consume is unknown.

It is reported that tobacco smoking is major cause of urinary bladder cancer in humans (Malaveille et al., 1996). Malaveille et al. (1996, 1998) reported that human urine have dietary phenols which have an ant mutagenic effect on a known tobacco-smoke correlated carcinogen. Extraction of phenols from urine was shown to have same effects as Extracted from wine and onions, resulting that after ingestion, flavonoids have the ability to protect against tobacco carcinogens which may cause through vegetable. By in vivo and in vitro analysis the impact of onion phytochemicals can be studied on colon cancer. Hatono et al. (1996) reported that from garlic, organosulfur compound such as S-allylcysteine (SAC) was shown to hinder the precursors of colon cancer when administered orally to rats. Cancer formation has been inversely related with antioxidant activity (Newmark, 1996).

Higher intake (>16 times/week) of onions showed a significant decrease in risk of breast cancer (Challier, Pernau, & Viel, 1998; Levi, La Vecchia, Gulie, & Negri, 1993). Rodgers and Grant (1998) reported that cytotoxic carcinogenic compounds can be deactivated by enhancing the role of reductase enzyme, on the cells of breast cancer quercetin may have a substantial anti-proliferative effect. Quercetin in vitro study showed to have anti-proliferative effect on ovarian carcinoma cells, major cause of death in women from cancer (Shen, Herenyiova, & Weber, 1999). Rzymowska, Gawron, Pawlikowska-Pawlega, Jakubowicz-Gil, and Wojcierowski (1999) suggested that in the signal transduction pathway dose-dependent inhibition of kinase activity was found as the mode of protective action. The risk of brain cancer was positively related to salt preserved foods and inversely associated with vegetable consumption (Guo, Linet, Chow, Li, & Blot, 1994). High consumption of onions has a strong inverse relationship to cancer risk. Both Hu et al. (1999) and Guo et al. (1994) postulated that the risk of brain cancer may be associated with N-nitroso compounds (NOCs) from salted foods (Shenoy & Choughuley, 1992).

Like ROS (reactive oxygen species), RNS (reactive nitrogen species) causes oxidative damage to tissues, cellular proteins and DNA (Juurlink & Paterson, 1998). Increased risk of brain cancer was associated with (NOCs) as described by Guo et al. (1996) and Hu et al. (1999). Strong oxidant in brain, peroxynitrate has been decreased due to quercetin by hunting superoxide anions (Shutenko et al., 1999). Shenoy and Choughuley (1992) reported that researchers on N-nitroso compound formation proposed that sulphur compounds present in onion juice were the causative agents in the observed inhibition of nitrosation reactions. Sulphydryl compounds show specific inhibitory effects. Hence, onions containing both sulphur and flavonoids compounds may decrease nitrosamine formation risk and in cancer development and also possible cellular damage.

10. Bioactivity of onion and onion by-products
In a number of agro-food residues, the regaining of bioactive polyphenolic phytochemicals is one of the higher value options. In Europe A. cepa is commonly cultivated horticultural crop and production on annual basis is more than 5 million tons. Schieber, Stintzing, and Carle (2001) reported that on an annual basis, 450,000 tons by-products of onion are produced during consumption and processing. Biodegradable substances are mainly present in these waste materials, excess in fibre and polyphenols. Outer, non-edible dry layer of onions bulbs contain a wide-range of polyphenolic components which are removed before processing (Ly et al., 2005; Ramos et al., 2006). As these substances are absent in bulb scales, but they characterize oxidation products of its quercetin and glucosides. Ly et al. (2005) and Ramos et al. (2006) reported that phenolic compounds present in onion and onion by-products possessed strong antioxidant activity in vitro and have anti-platelet properties.

The vast research related to exploitation of agro-food waste materials in which the major field of concern is the extraction of polyphenols with its functional properties is just because of the day by day increasing knowledge of health relevant potential of polyphenolic phytochemicals and its major role
as food antioxidant (Schieber et al., 2001). In this concern, usage of wide range of residual sources for the recovery of natural antioxidants has been under investigation (Balasundram, Sundram, & Samman, 2006; Moure et al., 2001). In this finding, water/ethanol mixtures were investigated by non-toxic means in extraction process. For maximum recovery of total flavonol, solvent composition was kept at the optimum level. In onions, polyphenols and fructo-oligosaccharides (FOS) are good sources of bioactive compounds. Onions by-products were characterized to develop as a possibly bioactive food ingredient. The main subject of our study was to find the safety and the effects on health of by-product of onion were shared by either of two derived fractions, a fraction containing mainly materials of cell wall and an extract containing the onion polyphenols and FOS. We studied here about feeding these products to rats and their signs on gut environment, protective enzymes potential toxicity. A diet containing control feed balanced in carbohydrate were fed to rats during 4 weeks. Anaemia is caused by the onion extracts and onion by-products in rodents as expected for Allium products. Including genotoxicity no other toxicity was detected. When extract of onion were fed to rats, the activities of glutathione peroxidase (GPx1) and Glutathione reductase (GR) in erythrocytes was increased. Hepatic gene expression of 5-aminolevulinate synthase, NADPH, Gpx1, Gr and catalase: quinone oxidoreductase does not altered when onion is fed in any groups. By contrast, when rats given the onion residue the catalytic subunit gene expression of gamma-glutamylcysteine ligase was up regulated. The insoluble and soluble fractions as well as by-products of onion had prebiotic effects which was verified by increased butyrate production, changed gut micro biota enzyme activities and decreased pH. Roldán-Marín et al. (2009) suggested that in vivo, the by-products of onion may support antioxidative defense with no genotoxicity and change the functionality of the rat gut microbiota.

11. Antitumor effect
Craig (2010) reported that variety of sulfides rich in onion extracts, provide protection against tumor growth. Natural constituents of onion sodium, NPTS (n-propyl thiosulfate) and Two alk(en)yl thiosulfates induced hemolytic anemia as causative agents of onion. Antitumor effects of these compounds were studied by studying the beneficial functions of n-propyl thiosulfate (NPTS). Study shows that in vitro, propagation of three human tumorigenic cell lines HL-60, 293 and WiDr was inhibited. General, 2PTS as compared to NPTS have strong activity for inhibiting cell growth, not occur in WiDr cells as they are sensitive for both compounds. Oxidative damage and induced apoptosis caused by 2PTS and NPTS to HL-60 cells. Oxidative damage was approximately proportional to the extent of apoptosis and also to that of the cytotoxicity produced by these compounds. Chang, Yamato, Yamasaki, Ko, and Maede (2004) demonstrated that apoptosis induction is initiated by oxidative stress as the alk(en)yl thiosulfates have an antitumor effect.

Cell cultures of an epidermoid carcinoma cell line derived from HCPC-1 (hamster buccal pouch carcinoma) were performed by adding various onion extract concentrations in vitro studies. Concentration of onion extracts (25% and above) in culture media cause inhibition of tumor growth after 24 h of incubation. After incubating 4–10 days tumor proliferation was decreased. Niukian, Schwartz, and Shkla (1987) suggested that there-suits shown here give in vitro sign of the cytotoxic and inhibitory activity on an oral carcinoma cell line.

A bioflavonoid, quercetin, usually distributed in vegetables (onion) shows to have a chemoprotective role in cancer, through compound effects on signal transduction involved in angiogenesis and cell proliferation. The effects of quercetin supplementation (30 mg per day) were observed in the study, incorporated into a blackcurrant drink. For 14 days healthy male subjects aged between 33 and 64 years received either placebo or quercetin. At baseline Blood samples were taken and upon completion of the study and examined for full blood count, MMP-2(matrix metalloproteinase-2), TIMP-1 and -2 (tissue inhibitor of matrix metalloproteinase-1 and -2) plasma levels using ELISA techniques. For carrying out matrix metalloproteinase-2 and tissue inhibitor of matrix metalloproteinase-1 and -2 gene expression determinations, RNA was taken out from the RT–PCR (reverse transcriptase–polymerase chain reaction) and peripheral blood lymphocytes. In this study plasma protein levels of the healthy subjects or matrix metalloproteinase-2 or tissue inhibitor of matrix metalloproteinase-2 gene transcription was not changed by supplementation of the diet with quercetin. In this study the
plasma protein levels (311 ± 70 ng/ml and tissue inhibitor of matrix metalloproteinase-1 gene transcription at baseline to 183 ± 35 ng/ml post-supplementation, \( p < 0.05 \)) of the subjects were decreased following quercetin supplementation. This is an interesting result, the functions of tissue inhibitor of matrix metalloproteinase-1 in tumour progression has some disputes. Artificially increased tissue inhibitor of matrix metalloproteinase-1 levels decrease or prevent growth of tumour in certain model systems. Yet, high levels of tissue inhibitor of matrix metalloproteinase-1 have been associated with destructive diseases and poor diagnosis in patients with certain malignancies in other studies. Morrow, Fitzsimmons, Chopra, and McGlynn (2001) proposed that a potential role for the anti-tumour promoter quercetin as a dietary mediator of the carcinogenic cascade.

In a study using \( \text{CH}_2\text{C}_2\), crude thiosulfonates are isolated from \textit{Allium tuberosum} L. and then with silica gel column chromatography purified \( S \)-methyl 2-propene-1-thiosulfinate and \( S \)-methyl methanthiosulfinate from the crude thiosulfonates. Consequently, \textit{in vitro} as well as \textit{in vivo} the thiosulfonates were examined against antitumor activities and cytotoxicities against human cancer cells. Cancer cells in human have strong cytotoxicities, in the order of \( S \)-methyl methanthiosulfinate, crude thiosulfonates, and \( S \)-methyl 2-propene-1-thiosulfinate. For 7 days, when thiosulfonates consecutively administered at 10, 30, and 50 mg/kg ip, in mice, an increase in the life spans of mice occur that had been immunized with Sacoma-180 tumor cells. In MCF-7 cancer cells crude thiosulfonates also induces apoptosis. These results suggest that via apoptosis thiosulfonates from \textit{Allium tuberosum} L. prevent the propagation of cancer cells and have antitumor activities (Park et al., 2007).

12. Need for natural antioxidant

Synthetic antioxidants (BHA and BHT) are being restricted because of their carcinogenicity e.g. they cause liver swelling and influence liver enzyme activities. Thus there is a growing interest in search for natural antioxidants for the public perception. Spices and herbs contain high amounts of compounds capable of free radical scavenging activity (Dastmalchi et al., 2008; El-Ghorab et al., 2008). In this perspective, due to its natural high content of flavonoids and its widespread popularity all over the world, the onion is an interesting vegetable plant species (Griffiths, Trueman, Crowther, Thomas, & Smith, 2002).

Allium contains pharmaceutically interesting compounds that are mainly sulfur-based compounds. Tada, Hiroe, Kiyohara, and Suzuki (1988) reported that so far, antibacterial and nematicidal activities of these compounds against \textit{E. coli} and \textit{Bacillus} sp. have been already investigated. Growth of root of chrysanthemum cuttings was inhibited by Allelopathic substances present in Welsh onion roots (Choi, 1993). Havey (1995) suggested that Alliums have been historically maintained as open pollinated populations and the growth of edible Alliums are worldwide and are, traded, and consumed in many countries. Numerous scientific reports suggesting that onions and its relatives can be used to cure, to lessen, or avoid some of the health problems such as asthma, antibiosis, antidiabetic, cancer, cardiovascular diseases, and prebiotic effects. Onions and its relatives contains phenolic (Fossen, Pedersen, & Andersen, 1998), minerals with antioxidant capacity (Terry, Zayed, de Souza, & Tarun, 2000), sulfur compounds (Kubec, Svobodová, & Velišek, 2000), and polysaccharides with significant prebiotic properties (Biedrzycka & Bielecka, 2004).

Lanzotti (2006) proposed that researchers assessed the antioxidant and chemical properties of various types of onions and found high concentration of kaempferol, luteolin and quercetin. Tepe, Sokmen, Akpulat, and Sokmen (2005) studied methanol extracts of five different Allium species except \textit{A. cepa} red green, violet, and white Four onion scale color, compared antioxidant capacity and phenolic content, with no specified variety (Prakash et al., 2007). They suggested that kaempferol and quercetin contents are present in highest amount in red onion than other types of onion. Santas, Carbo, Gordon, and Almajano (2008) compared the polyphenol content and antioxidant. More recently, attention are diverted towards antioxidant content of onions because regular consumption of onions reduces the risk of cataract formation, inhibition of heart and vascular diseases by stopping lipid peroxidation (LPO), reduction in symptoms associated with osteoporosis (NOA), lowering of low density lipoprotein (LDL) cholesterol levels, many forms of cancer, ulcer development, and
neurodegenerative disorders (Kaneko & Baba, 1999; Kawai, Tomono, Katase, Ogawa, & Yano, 1999; Sanderson, McLauchlan, & Williamson, 1999; Shutenko et al., 1999). Generally flavonols occur in the edible vegetables, fruits and seeds (Herrmann, 1976, 1988), and their content may reach up to a few hundred mg/kg of fresh weight (Pierpoint, 1986). Häkkinen, Kärenlampi, Heinonen, Mykkänen, and Törrönen (1999) reported that Berries such as cranberry (Vaccinium oxycoccos and) bog whortleberry (Vaccinium uliginosum) contains 263 and 184 mg/kg fresh weight of total flavonols, respectively. Still, kale (Brassica oleracea L. cv. Alba DC.) and onions (A. cepa L.) considered as excellent dietary sources, as in total flavonols their content may reach 311 and 349 mg/kg fresh weight, respectively, determined as aglycons (Hertog, Hollman, & Katan, 1992).

An integral part of the human diet is flavonols which are consumed daily by humans and for the determination of flavonol levels few efforts have been made. Total flavonoids average intake on daily basis is about 1.0 g out of which 115 mg are, the share of flavonols and flavones (Kühnau, 1976). Intake of flavonoid vary from 2.6 to 68.2 mg daily and the quercetin percentage is 39 to 100% shown by “Seven Countries Study” (Hertog et al., 1995). From fourteen countries on seventeen volunteers showed that the main use of kaempferol and quercetin is 28 mg/day approximately (De Vries, Janssen, Hollman, van Staveren, & Katan, 1997). Quercetin concentration can be lowered in tomato and onion from 35 to 82% by microwave cooking, frying and boiling which are common domestic processes particularly in flavonoids (Price, Bacon, & Rhodes, 1997). It is reported that boiling and frying process show an overall loss of 25% in quercetin glucosides in case of onions and 4¢-glucoside and quercetin 3,4¢-diglucoside also show the lower level of 39% which is done by the boiling of about 25 min (Hirata, Shimoda, & Takahama, 1998). Kaempferol and quercetin level can be lowered from 39 to 64% in onion by blanching, respectively (Ewald, Fjelkner-Modig, Johansson, Sjöholm, & Åkesson, 1999). It can also be lowered in sweet potato leaves from 19 to 50% in myricetin and quercetin respectively (Chu, Chang, & Hsu, 2000). Pharmacological properties like anti-stress, anti-infection, immune enhancement potential and many more was also observed (Valko et al., 2007). In outer layer rather than purple, white and green varieties of onion the highest antioxidant and anti-oxidants activities in red onion and free radical scavenging activities (Prakash et al., 2007). The significance of onion is also significant by the major sources of antioxidant intake, both for specific class of flavonoids and the specific sulfur-containing compounds (Hertog, Feskens, Hollman, Katan, & Kromhout, 1993). Rather than red grape and blackberry the anthocyanin content of red onion is quite low (Clifford, 2000), with respect to flavonols their level is ~10% (Fuleki, 1971). At the same time both anthocyanins and flavonols intake is regarded as particularly healthy.

13. Conclusion
Onion and onion by-products have vital role against certain ailments due to the presence of bioactive compounds present in it. Before people did not use the by-products but now the concept of value addition is very popular. Pharmaceutically onion possesses many characteristics like anti-inflammatory, antioxidant and antibacterial properties. In decreasing pro-inflammatory diseases the effectiveness of onion is rooted in its nature as modulators of metabolism. The onion also consist of anthocyanin, flavonoids and rich source of phenolic compounds which act as antioxidant compounds. The antioxidant compounds help in control of oxidation. It is also used as condiment in different dishes. Onion has effective role against fungi and bacteria and increase the shelf life of food. It also has medicinal value and effective against different diseases. In nutshell, use of nutraceutical are better than to consume drugs against certain diseases.

Funding
The authors received no direct funding for this research.

Competing Interest
The authors declare no competing interests.

Author details
Muhammad Sajid Arshad1
E-mail: sajid_ft@yahoo.com
Muhammad Sohaib2
E-mail: ftsohaib@yahoo.com
Muhammad Nadeem3
E-mail: mnadeem11@gmail.com
Farhan Saeed1
E-mail: f.saeed@gcuf.edu.pk
Ali Imran1
E-mail: aliimran.ft@gmail.com

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