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Medicinal properties of Persian Shallot

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ABSTRACT

Persian shallot (Allium hirtifolium), called as ''Mooseer'' in Iran belongs to Alliaceae family and is one of the important edible alliums in Iran. It is native and endemic of Iran and grows as a wild plant across the Zagross Mountains. In traditional medicine Persian shallot were recommended for the treatment of rheumatic and inflammatory disorders, gout, arthritis, diarrhea, stomach pain, psoriasis and hemorrhoid. Moreover, in modern medicine, Persian shallot has been reported to have a range of health benefits which include anticarcinogenic, hypoglycemic, hypolipidemic, antioxidant, antibiotic properties, kidney and liver protective effects. Here we review the medicinal properties of Persian shallot and its components on recent data obtained from previous studies.

Keywords: Persian Shallot, *Allium hirtifolium*, Anticancer properties, hypoglycemic effects.

INTRODUCTION

The use of Alliums by humans has a long history that can be traced back to the Egyptians. Olympic athletes were fed alliums to improve performance in track and field events and Europeans have treated blood clots in horses for centuries with alliums. The genus *Allium* includes more than 700 species which grow wild in the temperate, semi-arid and arid regions of the northern hemisphere and therefore, results a remarkable polymorphism [1].

The oldest citation of shallot (a cultivated variety derived from *A. cepa*) is found in the work of Fattorusso et al., who described six different types of alliums with their therapeutic uses, indicating shallot as the most important one [2]. Persian shallot (*Allium hirtifolium*), sometimes mistakenly named *Allium ascalonium* (common shallot), called as ''Mooseer'' in Iran belongs to Alliaceae family and is one of the important edible alliums in Iran. It is native and endemic of Iran and grows as a wild plant across the Zagross Mountains at high elevations of different provinces from Northwestern to Southern of Iran (Sanandaj, Kangavar, Siakhdarengoon, Sahneh, Ashtian, Dashtearzhan, Koohrang, Sepidan, Divandareh, Boroujerd, Khomein, Yasuj, Nahavand, Khansar, Harsin, Arak, Doshmanziare and Koohmaresorkhi) with the climate of very cold to moderate cold [3]. This exhibit a great diversity in form including

color, shape, dry matter content and pungency. This diversity is also reflected in the success of the species in adapting to a very wide range of environments. In this field a study has investigated morphological characteristics of Persian shallot include, mean bulb weight, clove number, plant height, leaf number, leaf width, leaf length, days-to-emergence and days-to-flowering [4].

Persian shallot (A. hirtifolium) is different from common shallot (A. ascalonicum) for many characteristics (Figure-1). Persian shallot is a wild, perennial, herbaceous and aromatic plant. It consists of a naked and erect scape with 80 to 120 cm height. The green leaves are linear and lanceolate with 20 to 30 cm length and it flower's color are red or violet [3]. Bulbs of common shallot are pear-shaped, reddish-brown skinned and clustered at the base of the plant and its clusters may contain as many as 15 bulbs [5]. In Persian shallot the storage tissue is bulb like, yellow, oval, white skinned and usually consists of a single main bulb or rarely of two bulbs, the weight of each bulb being 8–15 times of garlic clove. As mentioned Persian shallot is originated from cold mountains of Iran, but common shallot is originated from warm regions of west Asia [6]. The main difference in their propagation is that Persian shallot produces more seed than common shallot. However, the germination of Persian shallot seed faces certain problems such as the low germination percentage and velocity as well as the slow growth of the subsequent seeding. Such problems obstruct the use of seeds as a convenient way of propagation and prefer using bulbs [7].

Figure-1. Morphological differences of Persian shallot (above figures) and common shallot (below figures) in bulb, inflorescence and bush (From : (Etemadi et al., 2011 [7])).

Roots and bulbs of Persian shallot use after doing particular actions, change them to very slim fibers and superpose them in water way so take bitterness of bulb and dry them at sun and then use as nutritive condiment. Its powder give good taste to foods used as a tasty additive or spice for foods, particularly to souse's that hasn't good taste. Also its dried bulb slices are used as an additive to yogurt and also pickling mixtures [8].

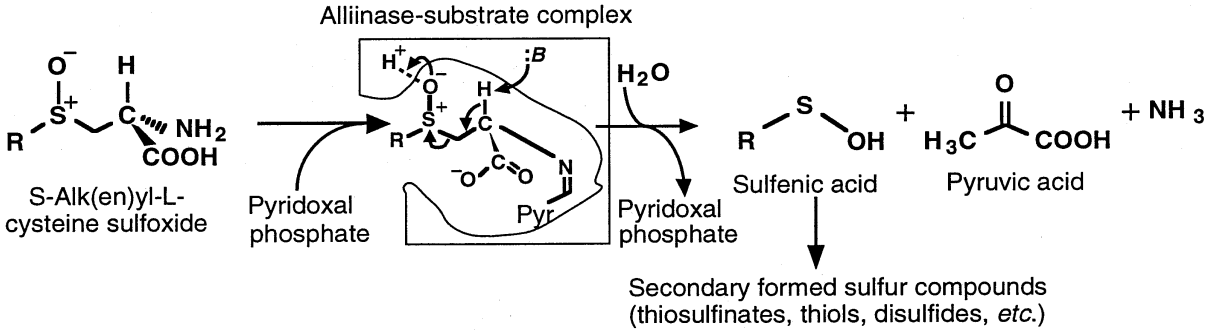
Persian shallot production in Iran falls into three broad product segments; bulbs for fresh market, dehydrated Persian shallot for food processing and green salad Persian shallots for fresh consumption. Although able to survive low moisture conditions, a good yield requires an adequate supply of water. A major advantage of Persian shallots as a crop is their storability. Plants, lifted at maturity and dried so that roots, shoots and skin are completely dry, keep well. The bulbs remain dormant at both low and high temperatures. Also its fresh or dried bulbs are exported to Persian Gulf (Khalij-e-Fars) countries [9].

In traditional medicine Persian shallot were recommended for the treatment of rheumatic and inflammatory disorders, gout, arthritis, diarrhea, stomach pain, psoriasis and hemorrhoid [7].

Since Persian shallot grows as a wild plant only in some mountains of Iran, there are some information on its medicinal properties so current study try to gathering the findings of previous investigation about medicinal properties of Persian shallot in a categorized cluster.

Persian shallot components (Figure-2)

The constituents of Allium are divided into two main groups: sulfur containing compounds and non-sulfur containing compounds. Most of the medicinal benefits of Allium such as reducing total plasma cholesterol, blood pressure and platelet aggregation are attributed to a sulfur compound known as allicin [10]. By analogy with garlic, allicin is flavor of Persian shallot, formed by the cleavage of S-alk(en)yl- L-cysteine sulphoxides by alliin alkyl-sulphenate-lyase (alliinase) (Scheme-1). In intact tissue the S-alk(en)yl- L-cysteine sulphoxides and alliinase are stored in separate cellular compartments [11]. Disruption of these compartments due to tissue damage (when the cloves are cut or crushed) results in alliinase hydrolysing the S-alk(en)yl- L-cysteine sulphoxides to give α-iminopropionic acid and a S-alk(en)yl cysteine sulphenic acid [12]. Simple correlation analysis showed a significant positive correlation between bulb weight and allicin content of Persian shallot (r = 0.40). Therefore, an increase in allicin content usually occurred with an increase in clove weight [4].



Scheme -1. Cleavage reaction of S-alk(en)yl-L-cysteine sulfoxide catalyzed by alliinase.(from:Manabe et al. Eur. J. Biochem. 1998).

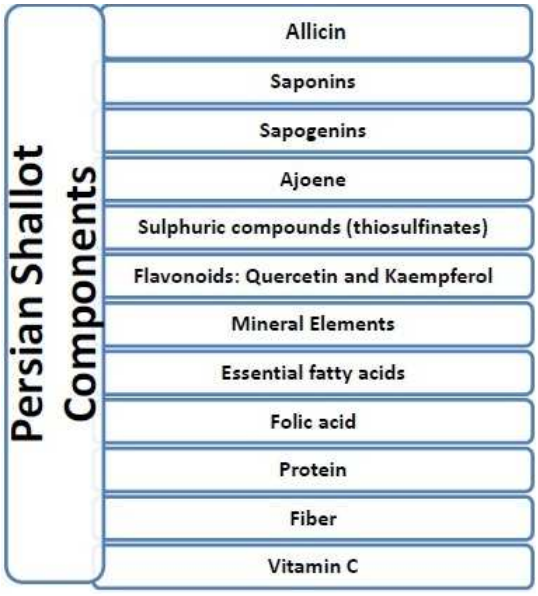


Figure-2. Some components found in Persian shallot.

Saponins, sapogenins, ajoene, sulphuric compounds (thiosulfinates) and flavonoids, including quercetin and kaempferol, are other components found in different species of *Allium* genus and likely Persian shallot (by further investigations) [13]. Flavonoids are potential antioxidants found in a wide range of foods but can be particularly rich in alliums like Persian shallot [14]. Quercetin in Persian shallot is other kind of flavonoids that can be absorbed in humans from dietary sources to sufficient levels to increase the overall antioxidant activity of the plasma. Interestingly, the greatest loss of flavonoids takes place when alliums are peeled. Cooking, frying or warm-holding

for up to 2 h had little effect on flavonoid content and it was concluded that alliums in ready-made dishes and home cooked food may be good dietary sources of these compounds [15].

It observed that the mean dry matter of Persian shallot is higher than other alliums except garlic. Also Persian shallot is rich in Cu as well as Zn and Mn elements. As linolenic acid and linoleic acid was higher in Persian shallot than common shallot and onion, so Persian shallot landraces are important in mineral elements and essential fatty acids content and are recommended for human nutrition [8]. Additionally Persian shallot overfilled of vitamin C, potassium, fiber, folic acid, calcium and iron and it could consider as good source of protein, so, it is very good vegetable for vegetarians [16].

Medicinal Properties (Figure-3)
Hypoglycemic and antioxidant properties

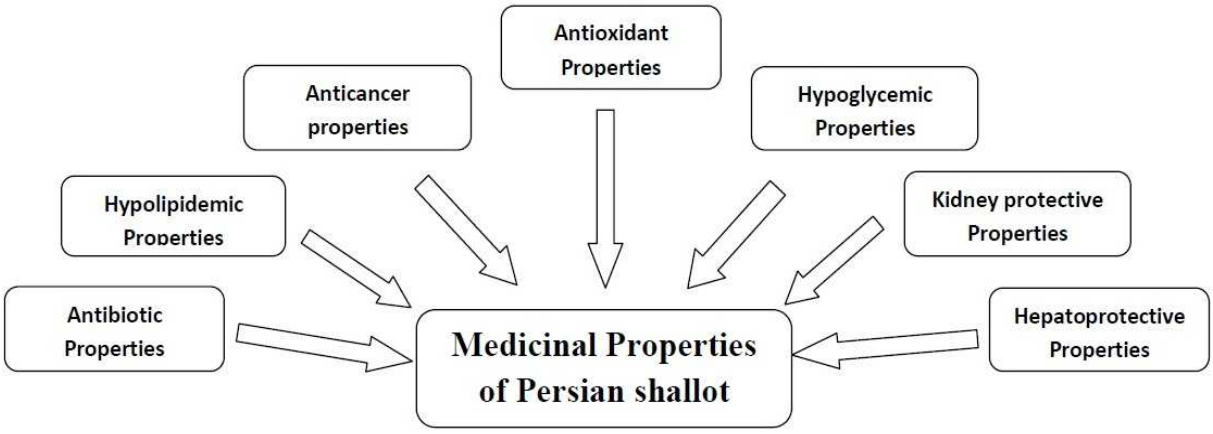


Figure-3. Medicinal Properties of Persian Shallot.

Recently there has been a growing interest in hypoglycemic agents from natural products, especially those derived from plants, because plant sources are usually considered to be safer, with fewer side effects than synthetic sources [17]. During aerobic metabolism cells are prone to oxidative damage initiated by reactive oxygen species (ROS) or free radicals. Plant cells contain a complex array of antioxidant components such as vitamin C, vitamin E, glutathione and phenolics (including flavonoids) which offer protection against cellular damage [18] Ingestion of such compounds may also offer direct chemoprotective roles in animal cells and help reduce oxidative stress. In addition, many of these compounds may also initiate the animal cells to produce their own chemical oxidative defense mechanisms such as induction of phase II drug metabolizing enzymes like glutathione-S-transferase and UDP-glucuronosyl transferase [19].

Our previous study has confirmed Persian shallot hypoglycemic effects [20]. The Persian shallot extract is a stronger hypoglycemic agent compared to garlic extract and it could be a useful supplemental remedy in diabetes. In our previous study Persian shallot reduces significantly FBS in diabetic rats ($P<0.05$). Different dose of Persian shallot administration induced mRNA expression levels of hepatic GCK and increase significantly GCK activity in diabetic rats. In addition, blood insulin concentrations were increased in Persian shallot treated groups. These results suggest that Persian shallot preserves and protects the pancreas by its strong antioxidative capacity. So it may be useful for preventing or delaying the development of diabetes and its complications [21] . Also Persian shallot had probably ability to accelerate the hepatic glucose metabolism may be via down-regulating the expression of the functional genes of PEPCK [20] (Hosseini-zijoud et al., 2012). The PEPCK is a key enzyme that control gluconeogenesis and glucose output from the liver and recently considered as a potential drug target in the treatment of diabetes mellitus [22].

In a study FBS was significantly lower (29.8% and 56.2%) in Persian shallot treated diabetic rats at 4th and 8th week as compared to untreated diabetics ($p<0.01$& $p<0.005$) [23], so oral administration of Persian shallot time-dependently has a significant hypoglycemic effect.

It was observed that Persian shallot extract reduced HbA1c level in diabetic rats too [20]. Increased glycation and accumulation of tissue AGEPs (Advance Glycated End Products) cause changes protein activity like hemoglubin via impairing its function and conformation. It also modifies protein half-life, immunogenicity and structural cross-link of protein structures. Considerable interests raised in inhibitors of glycation for their therapeutic potential. Antiglycation compounds may act as blockers carbonyl groups on reducing sugars, amadori products, and 3-deoxy-glucosones to inhibit formation of AGEPs. One can speculate Persian shallot may probably cleave AGEP cross-links, thus, leading diabetes complications [24].

Probably some of these hypoglycemic and antioxidant properties of Persian shallot are related to its content of phenolic and sulfur compounds [25]. Previous studies reported that the total content of phenolic and diallyl disulfide compounds in shallot extract were higher than garlic [8].

Treatment with Persian shallot extract can increases hormones T3 and insulin levels in diabetic rats. So we suppose maybe shallot increased insulin level and then insulin raised the T3 level [26]. The impact of thyroid hormones on glucose metabolism has been known for a long time. They up-regulate some of genes including GlUT-4 and phosphoglycerate kinase, involving glucose transport and glycolysis, thus, acting synergistically with insulin [27].
It could probably be stated that the extract of Persian shallot may provide a new therapeutic avenue against diabetes and diabetes-related complications. Overall, from the data obtained, treatment with Persian shallot extract produced a significant hypoglycemic effect. Moreover, further work is necessary to seek the active ingredients present in this extract having antidiabetic efficacy.

Kidney protective properties
The decrease in protein and albumin may be due to microproteinuria and albuminuria, which are important clinical markers of diabetic nephropathy and/or may be due to increased protein catabolism [28]. Treatment with Persian shallot increased albumin and protein in diabetic rats [20]. It has been established that insulin stimulates the incorporation of amino acids into proteins and this may reflect the albumin and total protein production which was happened in diabetic rats [29].

Also a significant elevation in serum creatinine, uric acid and urea levels is indicative for impaired renal function in diabetic animals. It was shown Persian shallot extract improved renal function, which was evident from the lowered serum uric acid, and creatinine levels in the rats treated with Persian shallot extract. The presence of polyphenols and flavonoids in Persian shallot extract might be responsible for the antioxidant nephroprotective activities and the reduction of serum uric acid and creatinine levels [20].

Hepatoprotective properties
Aminotransferases are considered as indicators of hepatocellular health. Previous investigations indicated that high levels of these enzymes associated with later development of diabetes.

Aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP) and lactate dehydrogenase (LD) enzymes are released into the circulation from the cytosol and subcellular organelles of hepatocytes once liver is injured or damaged and their activities increased in blood [30].

It is revealed that treating of rats with hydroalcoholic extract of Persian shallot could protect liver cells against oxidant effects of STZ, and it could consequently cause a significant reduction (dose dependent fashion) in serum concentration of ALP, ALT, AST and LD as compared to the diabetic control group [31]. Other study revealed that treating rats with hydroalcoholic extract of Persian shallot could protect liver cells against oxidant effects of alloxan, and it could consequently cause a significant reduction in serum concentration of ALP, ALT, and AST as compared with the diabetic control group [32].

The beneficial effect of Persian shallot extracts on reducing these enzymes in diabetic rats may be due to the antioxidant capacity of its antioxidant compounds like phenolic and sulfur compounds [31]. Polyphenolic compounds and flavonoids can protect the cells against emptying of reduced glutathione by increasing antioxidant enzymes capacity (such as catalase, superoxide dismutase and glutathione peroxidase). Furthermore, having antioxidant properties, these compounds are able to neutralize free radicals existing in the environment and prevent their destructive effects [25].

Hypolipidemic properties

In some studies hypolipidemic effect of Persian shallot components has been reported [20]. Exposure of human liver HepG2 cells to allicin and ajoene resulted in the concentration-dependent inhibition of cholesterol biosynthesis. At low concentration, both compounds inhibited the hydroxymethylglutaryl-(HMG)-CoA reductase, the enzyme at the start of the cholesterol biosynthetic pathway, while at higher concentration of both compounds, inhibition was observed at later steps in the pathway resulting in the accumulation of lanosterol, indicating inhibition of lanosterol 14 α-demethylase [33]. Recently, quercetin has also been shown to inhibit rat hepatic cholesterol biosynthesis in vitro [34]. Intake of dietary flavonols and flavones has been reported to be inversely associated with risk of cardiovascular disease in several epidemiological studies. Thus the antiplatelet activity of Alliums is considered to be a property of the organosuphur compounds [35].

Persian shallot including active sulphur compounds, to which its hypolopidemic effects may be associated. SH groups of sulphur compounds oxidize the lipid-synthesizing enzymes, and hence reduce or inhibit lipid synthesis. Moreover, these compounds oxidize NADPH to NADP, and since NADPH provides the hydrogen necessary during lipid synthesis stages, they inhibit lipid synthesis. Sulphur compounds also increase the activity of 7- alpha hydroxylase enzyme, and therefore increase the conversion of cholesterol into bile acids [36].

Hyperlipidemia is associated with diabetic state and this may possibly be due to uninhibited action of lipase [37]. Treatment of the induced-diabetic rats with Persian shallot extract led to reduced plasma triglycerides and LDL-C, while in presence of these extracts plasma HDL-C (insignificantly) level were increased. Since insulin inhibits adipose tissue hormone sensitive lipase and reduces lipolysis, the Persian shallot extract may correct the above mentioned disorders via mimicking insulin action. Also the decreasing levels of plasma triglycerides and LDL-C following the treatment with Persian shallot extract might be due to the stimulatory effects of Persian shallot extract on insulin secretion [20]. In other study there was a significant lower level of triglyceride, total- cholesterol and LDL-cholesterol in Persian shallot treated diabetic rats ($p<0.05$). On the other hand, although Persian shallot treatment did not cause a significant improvement in HDL-cholesterol level in treated diabetic group as compared to untreated diabetic group [23]. So oral administration of Persian shallot time-dependently improves lipid profile. However, whether such a benefit translates to the human diet in vivo awaits further study.

Anticancer properties

It is believed that the products resulting from the breakdown of alliin are responsible for the antiproliferative effects of Alliaceae family [38]. Persian shallot contains some useful biological secondary metabolites, which include allicin, S-allyl-cysteine, diallyldisulphide and diallyltrisulphide. Allicin have been reported in treatment of cancer. A study investigated the in vitro effects of chloroformic extract of Persian shallot and its allicin on the proliferation of HeLa (cervical cancer), MCF7 (human, caucasion, breast, adenocarcinoma) and L929 (mouse, C3H/An, connective) cell lines. While Hela and MCF-7 cells were sensitive to Persian shallot, the cell survival rate was almost unchanged in L929 cell line. It means that Persian shallot did not affect the normal L-929 cell; it only decreased cancer cells population. The ability of Persian shallot to preferentially suppress the growth of neoplastic over non neoplastic cells provides interesting possibilities for the development of new anticancer strategies in humans [11]. Several pieces of evidences suggested that allyl sulfides, found in processed Alliaceae family, possess anticancer properties as shown by their ability to suppress tumor proliferation in vitro [39]. Concentration and duration of the exposure to Persian shallot increased the anti-proliferative effects. Also anti- cancer effect was greater for chloroform-soluble than for water-soluble Persian shallot.

Other study investigated anti-microtubules activities of Persian shallot. Microtubules are vital in maintains of cell shape and cell division. It confirmed that Persian shallot and allicin can inhibit microtubule polymerization and also it can bind to tubulin as a ligand, it means that Persian shallot and allicin interferes with microtubule assembly by modifying SH groups in both α and β subunits, so it is a good alternative for cancer therapy [11].

Many organosulfur compounds, the major active principles in alliums, inhibit the proliferation of cancer cells, and some of them cause apoptosis in tumor cells of different tissue origin [40]. Hence, apoptosis could be a potential general mechanism providing a mechanistic basis for the anticarcinogenic activities of individual Persian shallot components. So we are investigating it and our results will be published soon.

Shrinkage, granulation of cytoplasm and detachment were observed in treated cells with chloroformic extract of Persian shallot and allicin. Particularly in higher concentrations of extract and allicin and longer period of incubation the number of colony forming cells was decreased [41].

These findings provided important insights into the use of Persian shallot as an additive to food or as a drug without any side effects. Further investigations were needed to elucidate subcellular mechanisms involved in the suppression of growth in tumor cell lines.

Antibiotic properties

Antimicrobial effects of three types of Persian shallot extract-fresh, dried and autoclaved extracts- were used and the results showed that fungal species were more sensitive to shallot extract than bacteria [42].

Previous in vitro studies have shown that the crude extract of the bulb of Persian shallot has antimicrobial properties against a variety of pathogenic bacteria [43]. After autoclaving, the crude aqueous extract of shallot, unlike onion and garlic, maintained its antimicrobial activity against both gram-negative and gram-positive pathogenic bacteria species (*Pseudomonas aeruginosa, Staphylococcus aureus, Listeria monocytogenes, Bacillus cereus, Serratia marcescens, Escherichia coli[44], Salmonella typhi, S. paratyphi A, Proteus mirabilis,* and *Shigella species*), with a minimum inhibitory concentration (MIC) ranging from 5 to 20 μg/mL [42].

Additionally, the crude extract showed fungistatic and fungicidal activity against pathogenic fungi (*Microsporum gypseum, Aureobasidium pullulans, Trichophyton mentagrophytes, T. rubrum, Fusarium oxysporum, Saccharomyces cerevisiae, Aspergillus niger, A. flavus, A. fumigatus,* and *Candida albicans*), with a MIC range of 0.15 to 20 mgμg/mL [44]. The active compound responsible for the antimicrobial properties is a flavonoid with the general formula $C_{14}H_8O_8$ and the proposed name of shallomin [42]. Therefore, this ancient plant is a potential source for the treatment of bacterial and fungal infections. Since the fungal pathogens are eukaryotes, the treatment may also affect the infected patients [45]. Hence as an alternative, cheap and affordable eco-friendly plant extracts may possibly be used for the treatment [46].

Persian shallot inhibits growth of T. vaginalis at low concentrations and in short times, therefore this plant has some antitrichomonas component(s). Persian shallot may contain sulfide components including allicin, ajoene and other organosulfides; accordingly antitrichomonas properties of this extract could be related to these components. It has been suggested that microbial cells are more affected than human cells because they do not have intracellular thiol content adequate to counterbalance the thiol oxidation by allicin and allicin-derived products. Ajoene has been shown to inhibit phosphatidylcholine synthesis in some protozoan [47].

Interestingly, comparison between alcoholic extract of Persian shallot and aqueous extract, showed that antifungal activity and anti-candidal activity of alcoholic extract was more than aqueous extract. This indicates that the active ingredients of Persian shallot against fungal and candida strains, dissolved better in methanol than water, and for prospective supplementary researches about antimicrobial properties of Persian shallot, it seem that alcoholic extract is more useful than aqueous extract [48].

Persian shallot killed larve of Rhabiditis sp. at high concentration. Therefore, this plant has some nematocide components. Parasitic cells are more sensitive than host cells to allicin and allicin-derived components [49]. Persian shallot maybe decrease the oxygen uptake, reduce the growth of the organism, inhibit the synthesis of lipids, proteins and nucleic acids and damage membranes [50].

The findings indicate that Persian shallot extract exerts antioxidant and antibacterial effects on vacuum-packaged rainbow trout during storage and increases its shelf life. Persian shallot extract delayed significantly ($p<0.05$) lipid oxidation in the treated sample, Furthermore, microbial spoilage decreased significantly ($p<0.05$) in the treated [51]. In other study significant increase in lactic acid bacteria counts in ileum and cecum of broiler chicken was shown by Persian shallot treated as compared to the control. In comparison to the control, Persian shallot treatment significantly decreased Enterobacteriaceae counts in ileum and cecum of broiler chicken. Moreover, protein, DNA and RNA contents were not affected by Persian shallot so Persian shallot might be useful additive instead of antibiotic growth promoters such as virginiamycin, considering performance and ileal microbial population of broilers [52].

In a study, inhibitory effect of Persian shallot hydroalcoholic extract on growth of Leishmania infantum was evaluated in vitro. The results prove inhibitory effect of Persian shallot hydroalcoholic extract (containing allicin, ajoene and other agents) on *Leishmania infantum*. For exact evaluation of Persian shallot antileishmanian properties, it is necessary to evaluate inhibitory effect of the plant hydroalcoholic extract in vivo [53].

Considering these findings about antimicrobial properties of Persian shallot, it looks promising that in future, it can obtain some effective antimicrobial agents with minimal side effects from Persian shallot extract, but in vivo studies for evaluation of pharmacokinetic effects of shallot are required.

Other medicinal properties

Many foods like Persian shallot can be enriched with fructan dietary fibers without any negative impact on the taste of the product. With an additional uptake of 10–15 g of fructans per day the recommended daily uptake of dietary fibers (30 g) could be reached. Fructans stimulate the growth of specific microorganisms in the colon (e.g. bifidobacteria, lactobacilli) with a general positive health effect [54]. Inulin (a type of fructan) rich in alliums like Persian shallot also improved blood lipid profiles and altered the colonic environment in a beneficial manner [55]. Depression of cutaneous inflammation and edema formation by topical application of alliums extracts have been reported and are likely to operate through suppression of prostanoid metabolism [56].

CONCLUSION

It could probably be stated that the extract of Persian shallot may provide a new therapeutic avenue against different diseases and their-related complications. Overall, from the data obtained, treatment with Persian shallot extract produced a significant useful medicinal effect. Moreover, further work is necessary to seek the active ingredients present in this extract having medicinal properties.

Certainly a systematic approach to evaluating the effects of various refinement practices on health benefits of Persian shallot is required in order to draw firm conclusions before policies on health issues and advice to the public can be formulated. Given the genetic diversity within Persian shallot, a detailed chemical profiling of their compositions is required in order to understand the range of variation which may exist and to identify further components which may offer enhanced health benefits. The ability to produce defined sulphur metabolites in vitro has exciting potential to aid in the systematic evaluation of their potential benefits to health.

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