Phytochemicals and Potential Biological Activities of *Allium sativum* Linn.

Shailendra Suryawanshi Sanjay, Darshan KN, Radhakrishna DB, Rakesh MN, Sameed Kabbinavar and Dr. Zaranappa

Abstract

Medicinal plant belongs to the earliest known health care products that have been used by the mankind. Over three-quarter of the world population rely on the use of traditional medicines for their primary health care needs and they are regarded as alternative to synthetic drugs because of local availability, eco-friendly nature and lower prices and playing an important role in majority of countries for providing health care to large section of population. Many Indian plants have been quoted to be useful as medicinal agents as they are effective with fewer side effects and are also inexpensive. *Allium sativum* Linn is among the oldest of all cultivated plants which belongs to the family Liliaceae and traditionally used as spice and flavoring agent for foods. Phytochemically it composed of carbohydrates, proteins, lipids, amino acids, minerals, vitamins, fibers and organosulphur compounds. Due to presence of wide range of phytochemicals it has potential biological activities such as antiviral, anticancer activity, antibacterial, antifungal, antiparasitic, antidiabetic, anti-inflammatory, antioxidant, radio protective, hepatoprotective, cardio protective, hypolipidemic, diuretic and digestive activity and used to treat variety of diseases and disorders. Hence *Allium sativum* Linn. Containing products were used as sources of medicines in many ways in human beings in their today life. In the present work literature survey has been done on its pharmacognostic, phytochemical and pharmacological aspects and were reviewed briefly.

Keywords: *Allium sativum*, Liliaceae, Garlic, Anticancer Activity, Hepatoprotective, Medicinal Plant, Phytochemicals.

Introduction

Medicinal plant belongs to the earliest known health care products that have been used by the mankind. Over three-quarter of the world population rely on the use of traditional medicines for their primary health care needs and they are regarded as alternative to synthetic drugs because of local availability, eco-friendly nature and lower prices and playing an important role in majority of countries for providing health care to large section of population \[1\]. Many Indian plants have been quoted to be useful as medicinal agents as they are effective with fewer side effects and are also inexpensive. *Allium sativum* Linn. Commonly known as garlic is among the oldest of all cultivated plants and traditionally used as spice and flavoring agent in food preparations. It is one of the most widely researched medicinal plant \[2, 3\] with 22 therapeutic formulations that mention garlic as an effective remedy for a variety of ailments including heart problems, headache, bites, worms and tumors \[4\]. Chemically it composed of wide variety of chemicals which includes carbohydrates, proteins, lipids, amino acids, minerals, vitamins, fibers and organosulphur compounds. Due to presence of wide range of phytochemicals it has potential biological activities such as antiviral, anticancer activity, antibacterial, antifungal, antiparasitic, antidiabetic, anti-inflammatory, antioxidant, radio protective, hepatoprotective, cardio protective, hypolipidemic, diuretic and digestive activity. Pictures of garlic were showed in Figure 1 \[9\]. Many research work has been done on the garlic and were published in many journals, literatures, articles, books and publications and were reviewed thoroughly and presented in this review work. It includes botanical description, Unani description, Ayurvedic description, pharmacognostic description, phytochemistry, biological activities, chemical modification, clinical and toxicological studies, dosage forms and adverse effects were reviewed in detail as follows.

**Correspondence**

Shailendra Suryawanshi Sanjay
Department of Pharmaceutical Chemistry Government College of Pharmacy, RGUHS, Bengaluru, India

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Shailendra Suryawanshi Sanjay, Department of Pharmaceutical Chemistry Government College of Pharmacy, RGUHS, Bengaluru, India

Darshan KN, Department of Pharmaceutical Chemistry Government College of Pharmacy, RGUHS, Bengaluru, India

Radhakrishna DB, Department of Pharmaceutics, Government College of Pharmacy, RGUHS, Bengaluru, India

Rakesh MN, Department of Pharmaceutics, Government College of Pharmacy, RGUHS, Bengaluru, India

Zaranappa, Department of Pharmaceutical Chemistry Government College of Pharmacy, RGUHS, Bengaluru, India
Botanical Description
Allium sativum is further divided into two subspecies namely, Allium sativum var. sativum and Allium sativum var. ophioscorodon, known as soft neck garlic and hard neck garlic respectively. Both varieties are composed of an underground bulb made up of cloves, which are prophylls enclosed by dry membranous skins and held together by a basal plate. Various parts of the plant include bulb, leaves, flowers, fruits and seeds. Bulbs are rounded, composed of up to about 15 smaller bulblets known as cloves. Cloves and bulbs are covered by a whitish or pinkish tunic (papery coat). Leaves are four to twelve long, sword-shaped leaves attached to an underground stem. Flowers are borne in a dense, spherical cluster on a spike (flower stalk) up to 25 cm long. The young flower head is enclosed in a long beaked pair of enclosing bracts, which become papery and split to reveal the flowers. Individual flower stalks arise from a common point. Flowers are greenish-white or pinkish with six perianth segments (sepals and petals) about 3 mm long. Bulbils, which resemble tiny cloves, are often interspersed among the flowers. Fruits are usually abort before developing.
to a stage at which fertilization could take place. Seeds are not usually produced in the wild but have been produced under laboratory conditions[9].

Pharmacognostic Description
The microscopic and macroscopic study of the herb has been described as follows[7, 8].

Macroscopically, garlic occurs as a sub-globular, compound bulb greyish white having 8-20 cloves, surrounded by 3-5 whitish, papery, membraneous scales. The cloves are attached to a flattened, circular, woody axis with numerous thin, wiry roots on the underside and short, sub-cylindrical outgrowths on the upper surface. Each cloves is ovoid, 3-4 sided, surrounded by two papery scale leaves, the outer one whitish and loose, the inner one pink and adherent, easily separated from the solid portion of the clove. The papery scale leaves enclose two whitish, fleshy scales. The inner one is thinner and smaller than the outer. The odour is strongly alliaceous and the taste is persistently pungent alliaceous.

Microscopically, the cloves shows a number of concentric bulblets, each bulblet consisting of an outer scale, an epidermis, a ground tissue and a layer of lower epidermal cells. Dry scales consist of 2-3 layers of cells rectangular in appearance but with broadly angular slant end walls. These cells consist of plenty of rhomboid crystals of calcium oxalate. The upper epidermal cells next to the scale layer consist of rectangular to cubical cells of one layer next to which there are inter-spaced many vascular bundles each of which consists of xylem, and phloem arranged alternately. The lower epidermis consists of cubical cells which are much smaller than the upper epidermal cells.

Powdered Microscopy, of garlic showed fragments of parenchymatous cells. The cells are filled with rhomboid crystals of calcium oxalate and starch grains. Fragments of vessels are also seen. The histochemical tests on the powder of garlic with different chemical reagents have been done. It appears dark brown and light brown on treatment with concentrated sulphuric acid and nitric acid, respectively. The elemental analysis on the ash of garlic with the help of atomic absorption spectrometer shows the presence of sodium, potassium, calcium, magnesium, zinc, manganese, iron, copper and nickel[9].

Habit and Habitat: A hardy perennial herb, cultivated all over India[10].

The scientific classification, Unani description, Ayurvedic description and vernacular names of Allium sativum Linn. were presented in Table 1,2,3,4.

### Table 1: Scientific classification of Allium sativum Linn.

<table>
<thead>
<tr>
<th>Kingdom</th>
<th>Plantae</th>
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<tr>
<td>Subkingdom</td>
<td>Tracheobionta</td>
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<tr>
<td>Superdivision</td>
<td>Spermatophyta</td>
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<tr>
<td>Division</td>
<td>Magnoliophyta</td>
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<tr>
<td>Class</td>
<td>Equisetopsida</td>
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<td>Magnoliidae</td>
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<tr>
<td>Family</td>
<td>Amaryllidaceae</td>
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<td>Genus</td>
<td>Allium</td>
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Phytochemistry of Allium sativum Linn.
Chemical analysis of garlic revealed the presence of carbohydrates, amino acids, vitamins, enzymes, pigments, pectin and sulphur containing compounds. Sulphur compounds are main chemicals present in the garlic and this organosulphur compounds are responsible for alliaceous odour, taste smell and also for its biological effects. The composition of various nutrients present in A. sativum Linn. were given in Table 5.

Carbohydrate Analysis: Carbohydrates analysed in garlic bulbs were include reducing sugars, sucrose, starch and dextrin. Soluble polysaccharides are obtained from hydrolysis with sulphuric acids give mannose and fructose[11, 12].

Amino Acids Analysis: Cysteine, histidine and lysine are the major amino acids found in the garlic, also presence of other amino acids such as alanine, arginine, aspartic acid, asparagine, leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan and valine were reported. Bublis also contains above all amino acids except tryptophan and valine [13, 14].

Lipid Components Analysis: Lipid analysis of garlic showed that 0.6% of total lipid present in it. Fractionation study by using column chromatography showed that it contains neutral lipids, glycolipids and phospholipids. Palmitic acid, oleic acid, linoleic acid, linolenic acid, capric acid, lauric acid, myristic and stearic acids are the fatty acids present in the total lipids and fractionated lipids [15].

Nutrient Composition of Garlic: it includes carbohydrates, lipids, and proteins, minerals such as calcium, phosphorus,
iron, manganese, magnesium and zinc. Total fibre, uronic acids, tannins, phytic acid were reported. It was reported that nutrient elements were present in higher amount in top and roots of garlic during bulb development and level of decreased in the tops during the bulb development. Bulb contains higher percentage of reducing and non-reducing sugars and proteins than other organs of plant [16].

Ionic Components of Garlic: It also contains Iodine and Fluorine in composition of 0.88 and 5.0 ppm. Fluoride, calcium and phosphorus content in uncooked were quantitatively reported. Oxalic acid, calcium and phosphorus in bulb were also reported quantitatively [17, 18].

Analysis of Garlic Skin: Garlic skin showed the presence of proteins, unsaponifiable lipids, total sterols, lignin, pectin, arabinose, xylose, rhamnose, glucose and galactose. Chromatographic analysis of acid hydrolysate of the pectin indicated the presence of mo0-, di, tri and tetra-galacturonic acids and small amount of arabinose and rhamnose [19].

Sulfur Compound: This are the main chemical constituents responsible for Allium sativum taste, smell, and likely for its biological effects. When a garlic clove is intact, glutamylcysteins are the primary sulfur components [20]. These are hydrolyzed to form alliin. When garlic is crushed by chewing,opping, etc., the alliin promptly reacts with the enzyme alliinase to form allicin; after 30 seconds the reaction is 97% complete. Allicin is a diallyl thiosulfinate that accounts for 70-80% of the thiosulfinates present in Allium sativum [21]. Allicin is also highly unstable and quickly decomposes to yield sulfur compounds when oxidized such as diallyl sulfide (DAS), diallyl disulfide (DADS), diallyltrisulfide (DATS), ajoene, and hydrogen sulfide [22].

Allicin is one of the major organosulphur compound present in the garlic which is formed by its precursor Alliniby crushing. Some other products are also formed by enzymatic action and secondary reactions. The presence of alliinase was essential for the generation of allicin from the allin, which was studied by thermal stability of alliinase and enzymatic regeneration of flavor in odourless garlic powder study. Stability study of allicin and allin in aqueous extracts of garlic and in dehydrated garlic powder during storage at different temperature was studied and results showed that allicin in the aqueous extract of garlic lost its antibacterial effect during storage. Allin, in aqueous extract as well as in dehydrated garlic powder remains stable during the storage over long period [23, 24]. Chemical structures [25] of garlic components were showed in Fig 2,3,4.

Cell Culture Analysis: Unorganized white callus cell culture and organized green callus culture study revealed that total five amino acid precursors which includes methionyl-, propyl- and allyl cysteine sulphoxide and two unidentified ninhydrin-positive compounds. All the five precursors were hydrolysable by alliinlyase to yield pyruvic acid [26].

Biological/ Pharmacological Activities
Garlic has attracted greater attention for its biological activities due to presence of alkyl sulphides. Due to its biological active component Allicin and its derivative, garlic has been used as a medicine to cure a wide range of diseases and conditions.

Antiviral Activity
Tsai et al., have observed that garlic showed significant antiviral activities against various types of virus such as coxsackie virus species, herpes simplex virus types 1and 2, influenza B, Para influenza virus type 3, vaccinia virus, vesicular stomatitis virus, human immunodeficiency virus type 1 and human rhinovirus type 2. The antiviral activity was due to the presence of Ajoene, Allicin, Ally methyl thiosulfinate and methyl allyl thiosulfinate. Several laboratory
tests have showed that garlic is an effectual treatment for both the influenza B virus and herpes simplex virus [27]. Josling et al., have reported a double blind placebo controlled study with significant antiviral effect against common cold virus [28].

**Anti-cancer Activity**

Pendbhaje et al., have studied anticancer effect of garlic. Garlic extracts has ability to inhibit the development of cancer cells in the presence of known tumor promoters and Sulphurous components present in garlic [29]. Sadhaba et al., have reported anticancer effect of garlic and garlic oil when topically applied during the initiation phase of Ba P induced skin carcinogenesis in random breed adult female Swiss albino mice of two different subs trains, showed a decline in the number of tumor bearing mice [30]. Amagase et al., have noticed that garlic is used to prevent various types of cancer comprising colon cancer, rectal cancer, stomach cancer, breast cancer, prostate cancer, prostate cancer and bladder cancer, and lung cancer [31]. Powolny et al., concluded that organosulphur compounds of garlic act by arresting the cell cycle of cancerous cells [32]. Dirsch et al., found that ajoene prompted apoptosis in cancerous cells due to peroxide production [33]. Tsai et al., reviewed animal and cell studies and found an inverse correlation between consumption of garlic and presence of cancerous cells, suggesting it has anticancer effects [34].

**Antibacterial Activity**

Garlic acts a broad spectrum antibiotic effect, as it killing a wide variety of bacteria, and hence used as antibacterial agent. This property belongs to the presence of garlic constituent Allicin when whether taken internally or applied topically [35].

**Antifungal Activity**

Ledezma et al., reported antifungal effect of Ajoene [36], Shams-Ghahfarokhi et al., observed that Garlic has been shown to inhibit growth of fungal diseases as equally as the drug ketoconazole, when tested on the fungi Malassezia furfur, Candida albicans, Aspergillus, Cryptococcus and other Candida species [37]. Lemar et al., have reported that use of intravenous garlic to treat fatal and rare fungal infection of the brain called Cryptococcus meningitis. In the report, the Chinese compared the effectiveness of the garlic with standard medical treatment which involved a very toxic antibiotic called Amphotericin B. The study revealed that, intravenous garlic was more effective than the drug and at toxic regardless of its dosage [38]. Sabitha et al., A study found that Candida colonies were substantially reduced in mice that had been treated using liquid garlic extract. Garlic oil can be used to treat ringworm, skin parasites and warts if it is applied externally [39].

**Antiprotozoal Activity**

Reuter et al., Garlic is effective in treating intestinal parasites has been known for a long time. An extract of garlic was effective against a host of protozoa such as Opalina ranarum, Opalinumidicita, Balantidium entozoon, Entamaeba histolytica, Trypanosoma, Leishmania, Leptomonas and Crithidia [40].

**Antiparasitic Activity**

Kalyesa et al., have reported medical treatments for intestinal diseases is an alcoholic extract of crushed garlic cloves. Allicin exhibits anti-parasitic activity against major human intestinal parasites such as Entamaeba histolytica, Ascaris lumbricoides and Giardia lambilia [41]. Mirelman et al., have reported antiparasitic activity of Allicin against Entamaeba histolytica [42]. Ankri et al., have found that at lower concentrations allicin inhibited 90% the virulence of trophozoites of E. histolytica [43].

**Molluscicidal Activity**

Singh et al., have reported that water extracts if the bulb of garlic have a high molluscicidal activity against the snail Lymnaea acuminata. The activity was dose dependent and also time dependent [44].

**Miticidal activity**

Dakhshinkar et al., have studied that local application of crude extract of garlic and sweet oil 1:10 (v/v) showed miticidal effect against ear mange mites of rabbits [45].

**Insecticidal Effect**

The various extracts of garlic was showed good insecticidal activity against Culexpeus, Aedes aegypti, A. sierrensis, Anophelles larvae, Calicine larvae, Musca domestica, Trogoderma grunarium, Simukiumindiculum, Culex fatigans, Pentalonia nigronervosa f. caladii, Dysercus cingulatus, Anopheles stephensi, Aphroarea modicella [46].

**Anthelmintic Activity**

The garlic extract of the bulbs showed moderate in vitro activity against human Ascaris lumbricoides, extract of garlic cloves showed nematicidal activity against Meloidogyn incognita [47].

**Antirickettial**

Kumar et al., have reported anti rickettial effect of garlic extract on Coxliella burnetti [48].

**Anti- Diabetic Activity**

Most of the studies showed that garlic can reduce blood glucose level in diabetic mice rats and rabbits. Eidi et al., have evaluated oral administration of garlic extract for 14 days on the level of serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine, in normal and streptozotocin-induced diabetic rats. Administrations of the garlic extract significantly decreased serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine, aspartate amino transferase and alanine aminotransferase levels, while increased serum insulin in diabetic rats but not in normal rats [49]. Brahmacari et al., have reported hypoglycemic effect study in rabbits. The ethyl ether extract of dried cloves of garlic found to exhibit hypoglycemic effect on oral administration of extract in fasting rabbits [50]. Mathew et al., have reported hypoglycemic effect of Allicin in rabbits. Allicin was obtained from garlic and given orally showed, hypoglycemic action comparable to tolbutamide in rabbits with mild alloxan-diabetes [51].

**Antihypertensive Activity**

Silagy et al., have observed garlic extracts has a significant reduction in systolic blood pressure (SBP) and in diastolic blood pressure (DBP) and act as anti-hypertensive [52].

**Anti-inflammatory Effect**

Bhakuni et al., studied anti-inflammatory effect of ethanolic extract of bulbs of garlic in rats and it was observed that ethanolic extract of garlic showed good anti-inflammatory effect [53].

**Wound Healing Activity**

Jalali et al., have studied chicken dorsum skin excise on wound assay to investigate the influence of different concentrations of
aged garlic solution on wound healing. Gross, histopathology, scanning electron microscopy and computer-based three-dimensional image probing techniques were utilized to determine the effects of garlic on wound healing [64].

**Antiarthritic effect**
Shah *et al.*, have reported antiarthritic effect of borax, a vitamin mineral formulation and garlic oil against formaldehyde induced arthritis in rats [59].

**Antifertility**
Tewari *et al.*, have reported antifertility effect of garlic in female albino rats. The juice obtained from the bulbs of garlic at a dose of 150mg/100g body weight for 5 days revealed good oestrogenic activity in albino rats [58].

**Antimutagenic Effect**
Soudamini *et al.*, have performed a study in which, garlic extract at a concentration of 50 and 25 mg/plate inhibited the mutagenicity produced by direct acting mutagens such as N-methyl-N-nitro-N-nitrosoguanidine and sodium azide using the *Salmonella* strains [57].

**Anti-Clastogenic Activity**
Roy Choudhury *et al.*, have reported anti-clastogenic activity of fresh garlic in albino mice. Administration of single dose of fresh garlic orally in the diet of male Swiss albino mice for 30 days along with sodium arsenite was found to reduce the clastogenic effect of the toxicant [58].

**Antioxidative and Radio protective Effects**
Borek *et al.*, reported that aged garlic extract and its various constituents have proven an array of antioxidant and radioprotective effects in studies. They have been shown to protect white blood cells from radiation damage, liver cells from lipid peroxidation and vascular endothelial cells from oxidant injury and enhance antioxidant enzyme systems in cells [59].

**Hepatoprotective Activity**
It has been reported that aged garlic extract have liver protective effects. Singh *et al.*, have studied hepatoprotective effect of garlic oil against acetaminophen-induced hepatotoxicity in rats. Study was carried out by administrating 5% and 10% garlic oil intraperitoneally in acetaminophen induced hepatotoxicity in rats. It was observed that garlic oil has good hepatoprotective effect with prevention of formation of thiobarbituric acid reactive substances [60].

**Cardio protective Activity**
Borek *et al.*, have studied Garlic is well reported to scavenge oxidants, increase superoxide dismutase, catalase, glutathione peroxidase, and glutathione levels, as well as inhibit lipid peroxidation and inflammatory prostaglandins and also reduces cholesterol synthesis by inhibiting 3-hydroxy-3-methylglutaryl-CoA and found to be cardio protective [61].

**Alzheimer’ Disease Protective Activity**
Chauhan *et al.*, have reported Alzheimer’ Disease protecting ability of aged garlic extract on APP processing and tau phosphorylation in Alzheimer’ transgenic model [62].

**Hypolipidemic Effect**
The hypolipidemic activity of garlic has been studied in animals and man these studies indicate that different fractions of garlic such as garlic juice, an aqueous extract, an ethanolic extract and essential oil fraction have ability to lower down serum cholesterol levels. Study has been done on hypocholesterolaemic effect of garlic in normal rats. The control drug used was onion. The alcoholic extract of garlic and one clove bulb were given in doses equivalent to 5 g of crude drug per kg body weight, while that of onion was equivalent to 10 g of crude drug per kg body weight orally once daily for 7 days and results showed that one clove garlic possessed significant hypocholesterolaemic activity. Biochemical study on combined effect of garlic and ginger in adult male rats with different groups namely normal, group fed with garlic, group fed with ginger and group fed with combination of garlic and ginger have been reported and the results revealed significant decrease in serum cholesterol level in all the three groups except normal and it was concluded that combination of garlic and ginger showed more significant decrease in the serum cholesterol level. Hypocholesterolaemic effect of the essential oil, the residue after the removal of essential oil and of defatted garlic powder in rats fed on atherogenic diet were reported. The study showed that essential oil and the defatted garlic powder causes lowering in serum and liver cholesterol level. Study also concluded that the lipid lowering effect is due to the presence of polysulphides present in the essential oils. Hypolipidaemic activity of AL-6, a crystalline fraction obtained from *A. satium* in white rats and house rats showed significant depletion of total cholesterol, phospholipid, triglyceride and non-esterified fatty acids was observed. Garlic juice and essential oil obtained from the garlic has an ability to protect myocardial necrosis [63].

**Diuretic and Digestive Activity**
Ali *et al.*, have reported that garlic acts as a diuretic and helps to remove body liquids. It may act as a very useful resource in case of rheumatism, gout, arthritis, hidropesia, edemas. It eases digestion by stimulating the liver, the gall bladder and the pancreas [64].

**Haematological Effects**
Jain *et al.*, have studied effect of oral feeding of garlic (1 g capsule containing whole dehydrated powder) on some haemato logical parameters in rabbits. Study concluded that there were no appreciable changes in the haemogram. But it slightly depressed the WBC count and bleeding time in rabbits [65].

**Chemical Modifications**
When garlic is manipulated to produce alternate forms, the unstable sulfur compounds react and hence alter active chemical constituents. It is important to note that these changes in chemistry can alter the bioavailability of the compounds. Traditionally garlic used in its raw form, but now a days it is heated, dehydrated, and aged, but only freshly crushed garlic can also be aged by soaking it in aqueous ethanol and then extracting and concentrating essential compounds. When alliin is dissolved in oils, the major compound in the final product is S-Allylcysteine (SAC) while ajoene, the most stable component of garlic, is also present [66].

**Clinical Studies**
There was great spurt of interest amongst the scientific community, specially between 1970-1990 regarding the hypolipidemic activity of garlic. Several centres in the country
conducted clinical trials with garlic or its essential oil in normal healthy volunteers. Along with this, clinical trials of garlic and its product on fibrinolytic activities, ischemic heart disease, hypoglycemic, antiarhythmic activities [69].

Toxicological Studies
In rats fed garlic extract (2ml/100 g body weight intragastrically for 10 days), a significant rise in urea and D-aspartate aminotransferase and inhibition of alkaline phosphatase in serum were observed. The liver showed histopathological changes. Garlic oil feeding (10 mg/100 g body weight intragastrically) after 24 hr fasting was found to be lethal Comparable allergenic hypersensitivity on the fingertips of housewives in the form of contact dermatitis was observed with fresh garlic juice and garlic extract, which was reported by [69].

Adverse Effects of Garlic
- Main adverse effect commonly associated with garlic intake breath odor
- Nausea and vomiting are other major adverse effects
- Juice obtained from bulb of garlic is potent and can act as a strong emetic when exceeds acute dose.
- Topical application may cause garlic burns and anaphylaxis
- Rare garlic allergy has been attributed to the protein allinase, which has induced immunoglobulin E (IgE) mediated hypersensitivity responses from skin.

Conclusion
The present review on phytochemicals and potential biological activities of *Allium sativum* Linn. Concluded that *Allium sativum* has wide range of active constituents which includes carbohydrates, proteins, lipids, amino acids, minerals, vitamins, fibers and organosulfur compounds and because of this it has diverse biological activities such as antiviral, anticancer activity, antibacterial, antifungal, antiparasitic, antidiabetic, anti-inflammatory, antioxidant, radio protective, hepatoprotective, cardio protective, hypolipidemic, diuretic and digestive activity. Many ayurvedic marketed formulations containing garlic are available in market and used to treat many serious diseases and disorders due to its beneficial medicinal value.

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