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A REVIEW ON CHEMICAL AND MEDICINAL ASPECTS OF ALLIUM SATIVUM

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Apart from its popularity as spice, particularly in the Mediterranean region, garlic (*Allium sativum*) has been used from ancient times in India and China in folk medicine. Many of the properties ascribed to it in folk medicine have been confirmed by modern scientific researches and it is now certain that garlic possesses many useful medicinal properties.[1] It is good as antiseptic and antispasmodic agent and effective in bronchial and asthmatic complaints. It is also stimulant, carminative, antirheumatic, anthelmintic, and alterative. If given in sufficient doses, it is invaluable remedy for the treatment of pneumonia. As resolvent, the garlic is applied to indolent tumors. Garlic oil capsules are very effective to protect the body from the attacks of bacteria. It is also used as a blood pressure depressant and recently garlic has gained importance due to the above property.

In view of its medicinal importance, extensive research is being carried out in Pakistan and other countries to find out the active constituents responsible for curing various diseases, specially blood pressure. In this article a review is given of the chemical, clinical, pharmacological and technical research carried out so far on *Allium sativum*.

Chemical Constituents. Two varieties of garlic of Peru have the following analytical results[2]: water, 78.79–79.04, fat 0.95–1.25, proteins 3.14–3.17, total sugars 3.94–4.26, cellulose 1.36–1.37, pectin 2.21–3.20, mucilage 9.97–10.33, allyl isothiocyanate 2.64–2.76, total ash 0.722–0.782, acid soluble ash 0.476–0.518, Na and K 0.1008–0.1565, Fe 0.00033–0.00047, Ca 0.02235–0.04805, P 0.05924–0.0616, S 0.0560–0.0615% vit B 25 γ and vit C 0.0291–0.09819 mg/100 g of garlic.

Kominato isolated a biologically active thioglycoside from garlic.[3] This compound was identified as R.CH—$CH.CH_2$.S $C_6H_8O_6$,0.5 ca, in which 'R' was a peptide containing a new amino acid, and carbohydrate part was calcium fructuronate. Its aglycon showed some sterilization effects for *E. coli*. The glycosides of garlic are hydrolysed by enzyme to allyl disulfide, allyl propyl disulfide, allyl trisulfide and vinyl sulfide.[4] Garlic also contains alliinase—a lyoenzyme, which splits alliine into allicin, pyruvic acid and ammonia.[5] Bulbs[6] of garlic contain a substance R CH_2 N(CHO). CMe : C—(S S CH_2 CH : CH_2) CH_2. CH_2 OH (R = 2-CH_3-4-NH_2-S-pyrimidyl) which has vit B, like activity. Matsukawa and his coworker[7] isolated allithiamine from garlic, a compound formed by the action of vit B_1 and the component of garlic. The structure of allithiamine is similar to aneurin disulfide. Passage[8] of nitrogen through crushed garlic and bubbling the effluent gas through mercuric chloride solution, gave a ppt, m 200°C(dec), which was identified as $(CH_2:CH.CH_2)_2.SO$. If the above operation is performed at dry ice temperature, the volatile products are not the same as obtained by steam-distillation. The products obtained by the low temperature operation are more biologically active than those obtained at higher temperature. Green leaves[9] of garlic contain (i) fructose, (ii) glucose, (iii) arabinose, (iv) sucrose, (v) maltose and (vi) fructan. Intermediate portion of garlic plant contains fructose, glucose, arabinose, sucrose, maltose, four fructose oligosaccharides and fructan, whereas bulbs contain (i), (ii), (iii), (iv), (v), (vi) and more than five fructose oligosaccharides. Garlic is quite rich in sulphur and alliine content. Total sulphur and alliine in four Mexican varieties are as follows:[10] morado chileno 4.558, 13.813, morado criollo 2.915, 7.469, blanco italiano 2.446, 8.138 and blanco campeche 1.571, 5.095 g/kg respectively. Indian[11] garlic contains 0.13–0.21% essential oils (org. sulfides). Garlic also contains thiamine 133γ%.[12]

Garlic contains many peptides.[13] out of which at least nine have been isolated by ion exchange chromatography. These are γ-glutamyl phenyl alanine, γ-glutamyl-*S*-methyl cysteine, γ-glutamyl-*S*-β-carboxy-β-methyl ethyl cysteinlyglycine, γ-glutamyl-*S*-allyl cysteine and γ-glutamyl-*S*-propyl cysteine. As to free amino acids,[14] garlic bulbs contain leucine, methionine, (*S*)-propyl-L-cysteine and (–)-(*S*)-propenyl-L-cysteine. The leaves of three varieties of garlic of Crimea[15] contained up to 85 mg% vit C, while the bulbs only 7–8 mg %. Fresh bulbs contain 22–29% sugar, 3% inulin and 37–43.5% dry substance. Fresh juice of Indian garlic[16] contains up to 35.25% water soluble sugars. Garlic also contains high content of selenium 9.3 γ/100 g on wet basis[17] and manganese, 20.0 mg/kg on dry basis.[17,18]

Gas chromatographic analysis[19] of the essential oil of garlic showed the presence of $(CH_2:CH.CH_2)S_2$, Me_2S_2, $(CH_2:CH.CH_2)_2S$, Me_2S_3 and $(CH_2:CH.CH_2)S_3$. Hoerhammer[20] detected *S*-methyl cysteine, *S*-allyl cysteine, *S*-Me, *S*-Et, *S*-allyl and *S*-butyl derivatives of cysteine sulfoxide, *S*-ethyl-L-cysteine sulfoxide and *S*-butyl-L-cysteine sulfoxide. Recently Bernhard[21] has detected the occurance of various other sulfur compounds namely methyl-n-propyl disulfide, methyl allyl disulfide, di-n-propyl disulfide, n-propyl allyl disulfide, and nine isomers of dipropenyl disulfide, methyl-l-propenyl, n-propnyl-l-propenyl and allyl-l-propenyl disulfides in different species of *allium* including *A. sativum*.

As Blood Pressure Depressant. From experiments on both animals and humans, Debray and Loeper[22] found that garlic tincture causes a decided drop in blood pressure in cases of hypertension. Piotrowski[23] achieved similar results after his experiments on the use of garlic as blood pressure depressant on about a hundred patients. In 40% cases he obtained a drop of 20 mm in blood pressure after about a week-treatment. The subjective symptoms dizziness, angina-like pains, headaches and backaches began to disappear in 3–5 days after garlic treatment began. Petkov[24] recently studied the clinical and pharmacological effects obtained with garlic. The addition of extract of garlic in cholesterol feeding experiments on rabbits (52–82 days) slightly influenced severe forms of experimental hyper-cholesteremia (923.80–558.53 mg %). In actual blood pressure studies in cats, I. V injection of 0.05 g/kg of garlic extract (corresponding to 0.20 g of garlic) exerted a hypotensive effect (50 mm). In chronic studies in dogs with experimentally induced hypertension, garlic reduced their systolic arterial pressure. In clinical studies on 114 patients having hypertension and atherosclerosis, garlic caused a marked improvement in the systolic (8–33 mm) and diastolic arterial tension (4–20 mm).

Anticancerous Properties

Garlic was found useful in the treatment of tumors by Romanyuk.[25] He studied the action of the antibiotics(I) of garlic with cathepsin(II) from human and animal tumors. He found that the activity of the liver cathepsin increases in a malignant growth. The antibiotic of garlic(I) retard the activity of liver cathepsin(II) in animals suffering from malignant growth. The garlic antibiotic also inhibits somewhat the cathepsin of malignant tumors of humans.

Weisberger and Pensky[26] injected cancerous cells into mice which produced a rapid cancerous growth and death in 16 days. When the cancerous cells were treated with garlic extract and injected into mice, no deaths occured amongst the animals for a period of six months. Kroening[27] also confirmed the above findings by feeding fresh garlic to female mice, which completely inhibited the development of mammary tumors in them.

Other Clinical Uses

A deodorised garlic carminative is prepared[28] by converting the diallyl sulfide in garlic to allyl bromide by the action of bromine on the crushed bulbs in alkaline solution. Thus to a mixture of 10 lb crushed garlic bulbs, 25 ml 8% methanol and 20 methanol is added 0.4 lb bromine during half an hour. The mixture is allowed to stand for four hours, dried and powdered.

An emulsion of naphthalene ointment with phytocides of garlic and onion showed a high effectiveness in treatment of eye burns.[29] The relatively nonvolatile hydrocarbons retard the evaporation of the phytocides and stabilize the formulation. The emulsion causes a rapid epithelization of cornea with a resultant slight surface opacity. Garlic has been proved useful in lip and mouth diseases, and Sergaiev and Leonov[30] have reported treatment of 194 cases of such disorders. In their experiments, Garlic-paste was applied to the effected parts and retained from 8–12 hr. Complete healing was observed in over 90% of such disorders as leukoplakia (white spots), hyperkeratosis (a horny-swelling) and fissures and ulcers of the lip.

In workers suffering from chronic lead poisoning,[31] garlic had a beneficial prophylactic action, erythrocyte concentration improved and the urinary porphyrin content went from 109 $\pm$ 6.2 to15 $\pm$ 2.2 γ%. A Bulgarian drug Satal (a preparation of *A. sativum*) was examined clinically in 106 healthy people, working with lead. The oral daily administration of Satal improved the symptoms of chronic lead poisoning; the high porphyrins level in urine and basophilic granulations in erythrocytes. The preparation also normalised the elevated blood pressure of the majority of workers. The efficacy of the preparation is due to the high content of sulphur compounds.

Garlic contains blood anticoagulant constituents,[32] which was verified by studying the effect of sodium, potassium, ammonium and magnesium bromides, pyridoxine and garlic extract on blood coagulation by a coagulographic technique. Sodium bromide and potassium bromide shortened the coagulation period. Garlic extract made blood noncoagulable in 18% of the cases for 75 min, but it became normal after 24 hr. Chung[33] and his coworkers actually isolated the blood anticoagulant constituent, although its structure could not be identified. The sodium salt of this anticoagulant component of garlic contains 18.7% phosphorus, 15.7% sodium, 0.2% nitrogen and some inositol. The inositol–phosphorus–sodium ratio is 1:6:6.7, indicating the possible presence of phytic acid. This constituent is toxic to mice and rabbits. ($L.D_{50}$ in mice was 222 mg/kg). Intravenous injection of 70 mg of anticoagulant constituent into rabbits caused death with muscular hyperactivity. The sodium salt of the above has a hypocalcemic effect both *in vitro* and *in vivo*.

Garlic contains an active component called gastroenteric allichalon which has some sedative action. Damrau and Ferguson[34] has found by X-ray studies that the sedative action is due to a delaying effect upon excessive motor activity of the stomach and of intestines.

Garlic and root bark of *Ficus religiosa* were found to exhibit sufficient hypoglycaemic activity.[35] Sun-dried bulbs of garlic and the thoroughly dried root bark of *Ficus religiosa* were extracted with various solvents. Only water soluble extract of *Ficus* and ether extract of garlic were active. The extracts were administered to albino rabbits weighing 2 kg each with fasting 18 hr blood sugar levels of 100–125 mg/100 ml. Garlic was 58.88% and *Ficus* was 75.9% active as compared to 100 activity of tolbutamide.

Garlic exhibits some antiinflammatory activity. Allisatin prepared from garlic and in doses of 200 mg/100 g/day was screened by Prasad and his cowerkers,[36] for antiinflammatory activity against arthritis induced by formalin and against granulo-

mapouch in rats. Betamethasone (50 γ /100 g/day) was used as the reference compound. Allisatin reduced the foot val. vecrosis of the feet and tenderness following formalin injection, but to a lesser extent as compared to betamethasone. It does not effect granulation pouch.

Antibacterial and Antifungal Properties

Numerous workers have observed that garlic juice exhibit strong antibacterial and antifungal properties and due to these properties, garlic juice is effective against various diseases. Rao[37] and his coworkers have prepared an extract of garlic with alcohol and after the removal of alcohol and purification, an oil was obtained which is antibacterial against typical Gram–positive, Gram–negative bacteria and has also antifungal properties. It is stable in the presence of blood. Szymova[38] has observed that garlic juice inhibits the growth and respiration of *Candida albicans*, *Trichophyton carebriforme* and *T. granulosum*. It is postulated that the antibacterial and antifungal property of garlic juice is due to the inhibition of succinic dehydrogenase via the inactivation of thiol group.

Leskinov[39] claimed that garlic extract can be useful in a number of fungal diseases, after observing the effect of garlic juice on the control of geotrichoid cultures. Fungicidal action was further proved by Dubova[40] who exposed mould-cultures in agar-mash to garlic gratings juice and found that garlic juice is fungicidal at higher concentration. Datta[41] and his coworkers isolated two active factors, allistatin I and allistatin II from garlic. Both are active against *Staphylococcus* and *Escherishiacoli*. The bacterio-static activity is of the order of 1:50,000 when tested by dilution method against *Staphylococcus*. The active principle[42] was found to be $CH_2{=}CH.CH_2S(:O)\text{-}S\text{-}CH_2.CH{=}CH_2$ which is extremely sensitive and polymerises easily. Due to its bacteriocidal action, it was found useful in curing various diseases.[43] Solutions of phytocides of garlic and onion were tried clinically for throat spraying in angina. Hyperemia of the glottic region was rapidly reduced and the drop in body temperature was accelerated. The results were much more satisfactory than penicillin therapy. Experiments with treatment of grippe by peroral route (alcoholic-zz-aqueous extracts of the plants) gave results that compared well with sulfa therapy; even 1:2000 solutions were effective. Favourable results were reported in the treatment of diseases like sciatica, chronic colitis, gastritis and whooping cough.

Pharmacological Properties

Water and organic solvent extracts of garlic have been thoroughly studied and both were found to posses useful properties. Tempel[44] noted the effect of two water soluble fractions of garlic and two synthetic poly sulfides resembling those in garlic oil, and checked atheromatus changes in rabbits fed with cholesterol. Only the synthetic polysulfides significantly reduced atheromatus changes in the aorta. Their protective action appears to be independent of the total cholesterol in blood and organs. Administration of garlic juice to guinea pigs effected the calcium titer of blood.[45] After daily administration of garlic juice for three weeks the blood calcium titer was 2–3 times normal. After two-months' continued administration it returned to normal. The calcium content of bone ash and teeth increased during the two month period while the phosphorus pentoxide diminished in the first three weeks and returned to normal after 2 months.

Enrique[46] has observed that the alcoholic extract of *A. sativum*-bulbs contained three pharmacologically active constituents. One, chloroform–soluble fraction, had an antiseptic action, a slightly atonic effect on isolated frog heart, a slightly hypertensive effect on etherised cats, and a paralysing effect on isolated rabbit intestine. The other, chloroform-insoluble fraction, had no antiseptic effect, no action on isolated frog heart, but a strong hypertensive effect on etherised cats and atonic effect on isolated rabbit intestine. The third, alcoholic extract, when given by stomach tube to carries and rats, produced no consistent visceral damage. Tagiev[47] studied the effect of plant antibiotic on infected wounds of 30 rabbits. After treatment of the wounds with the phytocides of garlic and essential oils of thuja and other plants, the RNA and DNA contents in the experimental animals were increased while in control animals these RNA and DNA did not increase. Bacterial cultures in different media of *pseudomonas* (*seanthomonas*) *malyacearum*, *Fusarium vasinfectum*, *Verticillium dahliae* and *Rhizoctonia* were observed[48] for the zones of inhibition produced in petri-dishes by using fresh and dry garlic extract. All the cultures were inhibited. Rudat[49] observed that garlic and horse radish (*Armoracia lapathifolia*) produced a most desirable inhibitory action on Gram–negative germs of the typhoid-paratyphoid–enteritis group. Use of daily[50] (10 mg) garlic oil prevented beriberi even when thiamine deficient diets were fed and also produced recovery from beriberi. The oral administration of garlic oil (10,100 and 200 mg/daily) to healthy humans did not effect the number of erythrocytes but anemia was caused by the injection of large doses of garlic oil.[51]

Garlic increases the excretion of urinary 17-keto steroids, which was observed by Velazquez and coworkers.[52] They injected alcoholic and ethyl acetate extract of garlic into rabbits and found that the ethyl acetate extract of the lower portion of garlic gave the highest excretion. This behaviour is opposite to that of cortisone and similar to that of carticotropin (ACTH) and it is suggested that garlic, like ACTH, stimulates secretion of those harmones which are transformed in metabolism to 17-keto steroids. Tinao[53] and his coworker experimented with alcoholic extract of garlic and found that it increases amplitude and frequency of uterine contractions and slightly increased uterine muscle tone. Garlic extracts also reinforced the uterine-stimulating action of estradiol and inhibited the sedative action of large doses of the same, resulting in a greater uterine contraction than initially and counteracted the paralysing effect on

uterine contractions of sodium glycerophosphate. Petkov[54] studied the influence of garlic on the dynamics of resorption, distribution and elimination of radioactive isotopos introduced into the organism. Garlic extract accelerates the excretion of isotopic gold ^{198}(Au) and reduces considerably its accumulation, probably due to other chemical interaction between the gold from the colloidal macromol and the chemically active sulfur derivatives of garlic on the one hand and its activating effect on the reticuloendothelium on the other. The experiments were performed on rats.

Miscellaneous Properties

Animal Diseases. Catar[55] studied the effect of the volatile fractions of aqueous and alcoholic extracts of seven different plants on the tick, which is the carrier of encephalitis. The best results were obtained with garlic and lemon peel. The ticks stopped increasing in 20–25 min and dried after 30–35 min showing a striking repellant effect.

Garlic is used in a preparation for treatment of foot and mouth disease in cattle.[56] It is prepared by extracting finely comminuted garlic (3–13 parts by weight with 40-45%, ethanol (65–75 parts) for 26-36 hr at slightly elevated or reduced temperature and adding lemon juice (15–30 parts) and anethole (2 parts by weight) to the filtered extract. The mixture is again filtered after standing for 8–18 hr. Garlic mixed[57] with some aureomycin and cress seed improved the growth rate and feed efficiency of leghorn chicks.

Effect of Plant Hormones

Very little research has been done on the effect of plant hormones on garlic. The only auxin tried on garlic was gibberellic acid.[58] A 100 p.p.m. gibberellic acid solution was applied with an atomizer to the tips of the youngest leaves of garlic at weekly intervals for weeks. A highly significant difference was observed in favour of treated plants in respect of size, weight of bulbs and length of foliage. Bulbs of the treated plants developed 27 days earlier and matured 4 days earlier than the controls. Zink[59] studied the physiological changes during the growth of garlic. He observed that weight of fresh plant increased in early period while its dry weight continued to increase until harvest. The percentage of nitrogen, phosphorus, potassium and sodium in whole plants on a dry weight basis tended to decreasing during the major period of growth. The magnesium level remained nearly constant and the calcium content increased during the growth of the crop.

Antioxidant Properties

Like onion, marjoram, and green chillies, garlic had also antioxidant property and is used as an antioxidant in ghee. Dhar[60] dialyzed garlic with alcohol and petroleum ether soluble portion of the dialyzate exhibited high antioxidant property as determined by the peroxide values of the products by the swift stability test. Marjoram and garlic[61] restrain the development of all characteristic indexes of rancidity (acidity, peroxides, iodine No. etc.). Garlic retained its antioxidant properties for half year after harvesting.

Pesticidal Properties

Californian[62] entomologists Amonkar and Reeves proved that garlic is an effective pesticide. They used a crude methanolic extract of commercially available dehydrated garlic, called instant minced garlic and a more refined form obtained from freshly reconstituted dehydrated garlic by steam-distillation. Both of these were tested against larvae of a number of mosquitoes including *Culexpeus*, *C. tarsalis*, *Aedes aegypti*, *A. triseriatus* and *A. nigromaculis*. In addition to these mosquitoes field collected larvae of highly insecticide-resistant strains of *A. nigromaculis* from Tulare and Kern counties in California were also exposed with all five species of laboratory bred larvae. A 100% mortality was obtained with the crude methanolic extract of garlic at concentrations of 200 p.p.m. and above. At 100 p.p.m. mortality of 98% or more was obtained in four of the five species. Better results were achieved with the steam-distilled oil fraction of garlic. Extensive tests indicated that a concentration of about 20 p.p.m. would give the same results, except for the field collected highly insecticide resistant larvae, which require 30 p.p.m. for 100% mortality. Bioassays indicated that the active principle responsible for the larvicidal activity is present in the oil of garlic, and that the more refined oil fraction is twelve and a half times as potent as the crude methanolic extract. Further work on the isolation of pure active principle and a study of its pathological effects on mosquito larvae is still under investigation by these authors. Since there is considerable difference in the amounts of active principle in garlic obtained from different sources they recommend that strains of garlic with high activity should be selectively bred.

Chemistry and Technology of Garlic Powder

Due to the importance of garlic in unani, ayurvedic and allopathic systems and also its great use as a condiment, Pruthi[63] and his coworkers have considered it worthwhile to study the effect of heat, moisture, storage etc. on the quality and medicinal properties of garlic. According to their findings, the outer papery skins of bulbs and peels or skins of cloves had no antibacterial action and had negligible amounts of sulphur compounds. The critical temperature for the dehydration of garlic is 60°C, beyond which most of the pungency and antibacterial activity is lost. Sulphuring and sulphitation of garlic prior to dehydration improved the colour of the garlic powder but they reduced its flavour and completely destroyed its antibacterial activity. The application of l-ascorbic acid had no beneficial effect on the retention of antibacterial activity and flavour of garlic powder.

Freeze-drying and vaccum-shelf drying produced slightly better coloured product as compared to those obtained by hot-air drying and sun-drying. There was, however, no significant difference in the retention of flavour and antibacterial activity. Garlic powder should be stored at low temperature and in hermetically sealed tin (cans) or air-tight bottles in order to preserve its antibacterial activity, pungency etc. Komissarov[64] and his coworkers have studied the changes in the carbohydrate of garlic during a 6-month storage under cold (0–4°C) and warm (18–22°) conditions. Under warm conditions the inulin content decreased to 25% of the initial value, disaccharides decrease to 10% and monosaccharides decrease to 0% of their initial values respectively. Under cold conditions, the decrease in the three carbohydrates are much less than under warm storage. Pnoznick[65] and his coworkers have prepared garlic concentrate which has a strong, uniform and stable fresh garlic flavour. Fresh garlic bulbs (without roots and skins) are washed, ground to ≤ 0.04 in particle size, mixed with cellulase 35, pectinase or anylase, maintained at 120°F, cooled to 70°F and spray-dried either to a concentrated juice or powder. Brockman[66] and his coworkers have prepared garlic condiment which is free from bad flavour. They mixed garlic with citrus fruit juice to prevent the breakdown of allicin. Thus reconstituted lemon juice 2 fl oz, water 1 fl oz, sugar 1.4 oz and sodium benzoate 0.45 g, were thoroughly mixed, 3 cloves garlic added to it and mixing continued till the slurry gets uniform. A storable garlic composition was manufactured by Bruner.[67] He added sorbic or ascorbic acid in an amount up to 0.5% by weight of garlic. The comminuted mixture is then dried at 70–80°C in an inert atmosphere until the mixture is still soft. While still warm, oils, emulsifiers etc. may be added to obtain the desired consistency.

Conclusion

Garlic is mainly used as a condiment and also as medicine due to its antibacterial, antifungal and blood pressure depressant properties. The constituents responsible for antibacterial property have been isolated and identified, but those responsible for blood pressure depressant property have not been isolated so far. It is hoped that the extensive research being carried out on this aspect may reveal the above constituents. In most of the countries, garlic is used in powder form and after frying. So far only fresh garlic or its extract has been investigated for its beneficial properties but no work has been done to find out whether garlic after drying or after cooking retain the above properties. It will be worthwhile to investigate the above aspects. Also it will be more fruitful to introduce preparations like garlic condiment in syrup form which will retain all the useful properties of garlic and also eliminate unnecessary expenses on drying.

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