GARLIC THE WONDER ADJUVANT IN MEDICINAL FIELD

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ABSTRACT

Plant derived compounds are drawing attention in curing and treating variety of ailment and diseases. This increase in popularity of natural products has renewed interest in garlic, which has been used by human for centuries. It has been found that garlic pulp contains more than 200 chemical compounds and numerous garlic molecules can still be explored, extracted, synthesized and optimized. As in market various preparations of garlic are available which include tablets made from dried and powdered clove, oils and liquid extracts however, it would also be interesting to explore the effect of different forms of garlic extract on standard drug therapy especially when used as an adjuvant therapy. In this review a report on the pharmaceutical preparation which has used extracted compounds from garlic or its derivatives as a main constituent is compiled, so that it could be useful to increase our knowledge about the therapeutic effect of garlic and could improve our future experimental and chemical plans. We performed a systematic review of literature using term garlic. In this report a comprehensive investigation has been conducted on garlic which includes various scientific aspects about it by which researchers from various disciplines could be directed to put efforts toward discovering the benefits of garlic on human health. Garlic and its extracts had a wide range of applications even against resistant organisms to serve as powerful anti-microbial agent. Therefore, research is needed to refine the pathophysiological mechanisms of action of garlic and its utility in the treatment of various diseases by developing more stable and suitable formulations. The development of Garlic as a commercial anti-biotic has come to a halt. Although its efficiency is scientifically proven, it has only been used as a dietary supplement or traditional medicine.

Keywords: *Ailment, clove, garlic, treatment, utlity.*

INTRODUCTION

Garlic is famous as allium, da-suan, la-suan, rustic treacle, stinking rose, poor man's treacle, nectar of the gods, camphor of the poor and also known by other common names like Rasonam, Lasan, Vellulli, Vallai-pundu, Seer, Ullippoondu, Maharu (1) is a bulbous herb having botanical name-Allium sativum belongs to family Lillaceae (2) is a native to central Asia and northeastern Iran. Garlic had been used by some civilizations against the bad evils, in ancient times and also as a therapeutic medicinal plant in many other places. It has considered as a traditional medicinal herb based on the experiences passes from generation to generation whose description is available in Rig-veda 41 and some old existing corpus also support its uses in Chinese, Egyptian, French and Ayurvedic medicine (3, 4). Throughout history, worldwide garlic has been using both as a spice and medicine (5). Now day garlic has attracted more attention as a modern medicine due to its broad-spectrum therapeutic effect with minimal toxicity (6).

CHEMICAL CONSTITUENTS OF GARLIC

Garlic has more than 500 species in 30 genera (7), is a good source of anti-oxidants and contains at least 33 sulfur compounds, several enzymes, vitamin B, flavonoids and certain minerals (8). Garlic contains 17 amino acids e.i. lysine, histidine, arginine, aspartic acid, threonine, glutamine, proline, glycine, alanine, cysteine, valine, methionine, isoleucine, leucine, tryptophan, serine and phenylalanine (9). Garlic's pungent odor and many of its medicinal effects (10) are due to presence of high concentration of sulfur compounds than any other *Allium* species. Allicin (diallyl thiosulfinate or diallyldisulfide) is the most biologically active compounds in garlic and Alliin (S-allylcysteine sulfoxide) is the most abundant sulfur compound which is a colorless, odorless and water-soluble compound which is present at 10 and 30 mg/g in fresh and dry garlic, respectively (11, 12).

Garlic and onion contain, Allicin ($C_6H_{10}OS_2$) which is a volatile compound. Alliin (L-(+)-S-Allyl cystein sulfoxide) is an amino acid which, under the action of the alliinase enzyme, converts to allyl sulfenic acid (2-propene sulfenic acid), an unstable and highly reactive compound at room temperature (13). Then, two allyl sulfenic acid molecules condense spontaneously to form allicin with the elimination of water molecule (Figure-1).

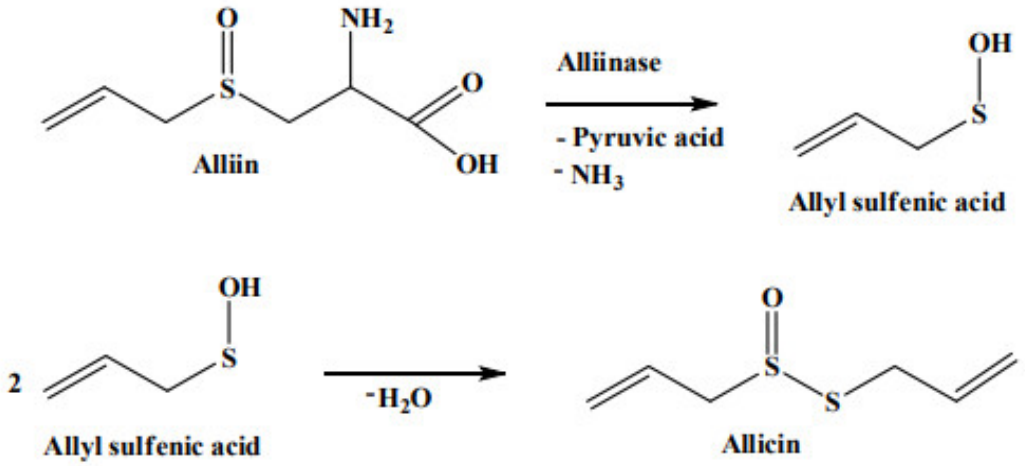


Figure 1. Synthesis of Allicin

Allicin decomposes in the presence of air and water producing mainly "diallyl disulfides" (responsible for the characteristic odor of garlic). This same degradation process occurs in the body, and it is associated with the characteristic odor in breath after garlic ingestion (13).

Table 1. Chemical constituents found in garlic bulb (14, 15)

S. No	Compound	Amount (ppm)	S. No	Compound	Amount (ppm)
1	1,2-Dimercaptocyclopentane	2.4	33	Fiber	7000-39,000
2	1,3- Dithiane	0.08-3	34	Glutamic acid	8050-19,320
3	2-Vinyl-4H-1,2-dithiin	2-29	35	Glycine	2000-4800

S. No	Compound	Amount (ppm)	S. No	Compound	Amount (ppm)
4	3,5-Diethyl-1,2,4-trithiolane	0.15-43	36	Histidine	1130-2712
5	3-Vinyl-4H-1,2-Dithiin	0.34-10.65	37	Iron	15-129
6	Alanine	1320-31,168	38	Isobutyl-isothiocyanate	0.14 - 25
7	Allicin	1500-27,800	39	Isolucine	2170-5208
8	Allin	5000-10,000	40	Leucine	3050 -7392
9	Allyl – propyl – disulfide	36 – 216	41	Lysine	2730 - 6552
10	Aluminium	52	42	Magnesium	240-1210
11	Aniline	10	43	Manganese	5.4-15.3
12	Arginine	6340– 15, 216	44	Methyl-allyl-disulfide	6-104
13	Ascorbic acid	100 – 788	45	Methyl-allyl-sulfide	0.5-4.6
14	Aspartic acid	4890– 11,736	46	Methyl-allyl-trisulfide	6-279
15	Beta-carotene	0.17	47	Methyl-propyl-disulfide	0.03-0.66
16	Biotin	22	48	Niacin	4-17
17	Boron	3 – 6	49	Nickel	1.5-1.7
18	Caffeic acid	20	50	Nicotinic acid	4.8
19	Calcium	180 – 4947	51	P-coumaric acid	58
20	Carbohydrates	274000-851000	52	Phenylalanine	1830 - 4392
21	Chromium	2.5 – 15	53	Phosphorus	880 - 5220
22	Cobalt	0.5 – 100	54	Potassium	3730-13,669
23	Copper	4.8 – 9.7	55	Proline	1000-2400
24	Cystine	650 – 1560	56	Propenethiol	1-41
25	Diallyl-disulfide	16 – 613	57	Protein	35,000-179,000
26	Diallylsulfide	2 – 99	58	Protodegalactotigonin	10
27	Diallyl-trisulfide	10 – 1061	59	Protoeruboside-B	100
28	Dimethyl-difuran	5 – 30	60	Quercetin	200
29	Dimethyl-disulfide	0.6 – 2.5	61	Riboflavin	0.5-3
30	Dimethyl-trisulfide	0.8-19	62	Scordinine-A-1	67-30,000
31	Fat	2000-12,000	63	Scordinine-A-2	250-8000
32	Ferulic acid	27	64	Scordinine-B	800

EFFECT OF GARLIC'S FORM ON ITS ACTIVE CONSTITUENT

Traditionally, Garlic was used in its raw form, but now days it is also used in heated, dehydrated and aged, form. Heat is used for dehydrating the plant to form garlic powder but at high temperatures alliinase is deactivated and hence cannot react with alliin to form allicin (16). This explains why cooked garlic has a mellower flavor than raw garlic. Only freshly crushed garlic has hydrogen sulfide, which is suspected to have significant cardio-protective effects as a vasodilator (17).

Allicin content can be retained in the powder to some extent if the cloves are frozen before being pulverized; acetone removes the water and alliin and alliinase remain separate yet intact until water is added, at formation point of allicin. Alliinase is not destroyed during dehydration process of forming

powder in comparison to heat by which more than half of the alliin is lost. Alliinase is deactivated by the acidic environment of the stomach. It has also concluded that when dehydrated garlic powder is exposed to simulations of the gastrointestinal fluids the production of allicin is decreased by 99% presumably due to the lack of allinase. This is further matter of research that dehydrated garlic powder when taken in a capsule with an enteric coating whether it is protected or not from stomach acid. These studies also show that manipulating garlic's form leads to changes in the active constituents and could lead to data inconsistencies in studies (18, 19).

USES OF GARLIC

Therapeutic uses (20)

Traditionally, it has been employed to treat: infections, wounds, diarrhea, rheumatism, heart diseases and diabetes.

Experimentally, it has been shown to exert: anti-lipidemic, anti-hypertension, anti-neoplastic, anti-bacterial, immune-stimulant and hypoglycemic actions.

Clinically, it has been evaluated to treat number of conditions including: hypertension, hypercholesterolemia, intermittent claudication, diabetes, rheumatoid arthritis, common cold, arteriosclerosis and cancer (20).

Garlic, from crushed to capsules, is consumed throughout the world, despite the widespread use of garlic for various purposes, the increasing craze on health maintenance and use of natural/ herbal products, garlic is being used for variety of formulations in various forms such fresh garlic, garlic oil, extracts of garlic or its chemical constituents (21). Furthermore, garlic has pharmaceutical effects and used to cure vast conditions including blood pressure, cholesterol (22, 23) and cancer (24, 25). Moreover, garlic is also used as hepato-protective (20, 26), anti-protozoal (27, 28), anti-viral (29, 30), anti-oxidant (31), anti-microbial (20, 32) and anti-fungal. Further, it is also used to treat wounds (33), diabetes (34), asthma, arthritis, sciatica, lumbago, backache, bronchitis, chronic fever, tuberculosis, rhinitis, malaria, obstinate skin disease including leprosy, leukoderma, discoloration of the skin and itches, indigestion, colic pain, enlargement of spleen, piles, fistula, fracture of bone, gout, urinary diseases, kidney stone, anemia, jaundice, epilepsy, cataract and night blindness. Garlic products are used as sources of medicine in many ways in human beings in their day-to-day life (35, 36).

Table 2. The medicinal spectra of garlic compounds (37)

Pharmacological activity	Chemical compounds of garlic contributed activity	Pharmacological activity	Chemical compounds of garlic contributed activity
• Anticoagulant	Ajoene	• Antiparasitic	Allicin-alliin
• Antihypertensive	Selenium germanium	• Antibiotic	Allicin-alliin
• Antimicrobial	Selenium germanium	• Antimycotic	Allicin-alliin, Ajoene
• Antiviral	Allicin- Ajoene	• Hypolipemic	Diallyl disulfide
• Antioxidants	Selenium, germanium	• Antiaging	Selenium, diallyl disulfide
• Antitumour	Selenium, germanium	• Humoural immunity	Germanium allicin
• Detoxification of heavy metals	Selenium allyl mercaptan germination	• Vitamins	Thiamine, vitamins A and C
• Natural killer cell activity and other kind of cell mediated immunity • Anti-inflammatory activity • Hepatoprotective activity • Digestive system protection	Selenium, germanium Ethyl linoleate, garlic 14-kDa protein, allicin Garlic oil, DADS and LAFGE DADS, DAS and allicin	• Complement activity • Modulating immune system • Cardiovascular protection • Anti-cancer activity • Anti-diabetic activity	Magnisium, calcium Polysaccharides, garlic oil Polyphenols, S-1-propylenecysteine, alliin and allyl methyl sulfide Lipid bioactive compounds, allicin, DATS and Z-ajoene LAFGE and garlic oil

DOSAGE

A commercial garlic product should provide a daily dose equal to at least 4000 mg (one to two cloves) of fresh garlic. The cloves may be diced and mixed with wildflower honey for palatability. This dosage translates to at least 10 mg alliin or a total allicin potential of 4000 ug. In dried form this would be 300 mg of garlic powder tablet (standardized to 1.3 percent alliin or 0.6 percent allicin yield) two to three times per day or 7.2 g of aged garlic extract per day. In tincture form

from fresh bulb as a 1:2 in 95 % alcohol, the dosage can be 40 drops up to six times per day (38).

TYPES OF GARLIC FORMULATION

1. *Antiacne garlic gel*: It was developed and evaluated for the anti-acne activity containing garlic juice against *P. acnes* to facilitate topical usage (39).
2. *Sustained release tablet: Allium Sativum* tablets were formulated by wet granulation using acacia, and gelatin in order to enhance efficacy and improve patient compliance (40).
3. *Garlic Extracts:* Extracts are the preparations of crude drugs which contain all constituents which are soluble in the solvent. The following extracts have been prepared -
   A. *Garlic extract for skin care*: The physiological effects of a formulation containing garlic extract as compared to the base formulation on skin care were compared. In conclusion, the garlic formulation had high inhibitory activities for tyrosinase and elastase, thus suggesting that garlic may have beneficial properties as a material for cosmeceuticals (41).
   B. *Aqueous extract of garlic* as a pessary*: It* was formulated using the pouring method and cocoa butter as a base (42).
   C. *Pharmaceutical formulation of garlic and turmeric dried crude extract and their synergistic anti-fungal activity:* The effectiveness of these natural products towards *Candida albicans* causes Candidiasis (fungal infection) was identified towards their pharmacological and toxicity aspects. The agar disc diffusion method was used to study the anti-fungal activity of their ethanolic extracts. As delivery agents, cream and gel formulations demonstrated good stability test results. Furthermore, both plants showed synergistic effects (43).
4. *Garlic Oil Preparations:*
   A. *Garlic essential oil nanoemulsion:* The nanoemulsion of garlic essential oil by ultrasonic emulsification was developed and the results showed that it can be used for developing natural nano acaricide (44, 45).
   B. *Garlic oil nanoparticles with enhanced anti-microbial activities:* Garlic oil (GO) colloidal nano-particles (NPs) were prepared by combining GO with poly lactic-co-glycolic acid (PLGA) polymer by single emulsion/solvent evaporation (SE/SE) method with 70-80% of more anti-bacterial activity compared with GO in bulk form (46).
   C. *Formulation, development and evaluation from garlic oil macerate:* Ajoene is one of the active constituents of garlic is highly unstable, it remains stable only in oil macerate form. For this garlic oil is obtained by two methods steam distillation and cold maceration by this its antibacterial as well as anti-fungal properties can be preserved (47).
   D. *Anti-fungal soap of garlic oil:* The formulated soap of garlic oil is typically effective against athlete's foot and jock itch (48).
   E. *Preparation methods for monodispersed garlic oil microspheres in water using the microemulsion technique and their use as anti-microbial:* The purpose of the present work is to develop and evaluate an oil-free microemulsion system. Microemulsions were prepared with ethoxylated hydrogenated castor (Cremophor RH40) as surfactant, n-butanol (or ethanol) as co-surfactant, oleic acid-containing garlic oil as oil phase, and ultrapure water as water phase. In addition, the anti-microbial activity (*in vitro)* against *Escherichia coli* and *Staphylococcus aureus* was assessed. The experimental results show that a stable microemulsion region can be obtained when the mass ratio of surfactant to co-surfactant is respectively, 1:1, 2:1 and 3:1 especially when the mixture surfactants of RH40/n-butanol 2/1 (w/w) is used in the microemulsion formulation. The area of o/w microemulsion region is 0.089 with the particle size 13.29 to 13.85nm and garlic oil encapsulation efficiency 99.5%. The prepared microemulsion solution exhibit remarkable anti-bacterial activity against *S. aureus* (49).
5. *A novel microparticulate formulation with Allicin in situ synthesis:* Spray drying was used to obtain a powder that releases allicin (Alliin and alliinase, served as precursors for allicin production, and were encapsulated separately into microspheres) and the in situ synthesized allicin was made available under safe and reproducible conditions for pulmonary application (50).
6. *Formulation Savings: Liquid Extracts in Replacement of Dry Powders? Garlic and Onion Powder:* Liquid garlic and onion extracts can offer as much as 40 to 80 percent savings over dehydrated powders. Because liquid extracts are more concentrated than powders, they allow for significantly lower usage rates and can also provide additional savings by reducing inventory, shipping and quality testing (51).
7. *Garlic: A natural antibiotic as liquid and cream formulations:* It has been found that allicin has potent activity against vancomycin-resistant enterococci (VRE) *in vitro.* In another study, it has been found that allicin liquid and cream formulations were highly potent against clinical isolates of methicillin-resistant *staphylococcus aureus* (MRSA) (52).
8. *Anti-oxidant potential of garlic and turmeric mixture (Traditional Indonesian formulation):* The combination of anti-oxidant activity of garlic bulb water extract and turmeric ethanol extract had been examined *in vitro* using DPPH (2,2-diphenyl-1-picrylhydrazyl) method and activity of the extract and its combination had been examined using lipid peroxidation method *in vitro* and in Swiss Webster female rats *ex vivo* which showed higher anti-oxidant activity *in vitro* compared to each extract, but in *ex-vivo* study showed similar effect (53).
9. *Garlic extract versus cryotherapy in the treatment of male genital warts:* The aim of this clinical study was to compare the garlic extract effect with cryotherapy in the treatment of male genital warts (54).

10. *Formulation of garlic oil-in-water Nanoemulsion: antimicrobial and physicochemical aspects:* In this work, a nanoemulsion containing garlic essential oil (GEO) was formulated to cover and protect the volatile compounds of GEO and it has been found that the formulated nanoemulsions had a stronger effect against Gram-positive bacterium (*Staphylococcus aureus*) than Gram-negative bacterium (*Escherichia coli*) (55).
11. *Development and assessment of stable formulations containing two herbal anti-microbials: Allium sativum L. and Eruca sativa miller seed oils:* Emulsions of both oils were prepared by the bottle method using water, Tween 80 and Span 80 and were evaluated for creaming index (CI), droplet size, and turbidity to determine rHLB. Utilizing determined rHLB, creams were formulated using a combination of two surfactants, Span 60: Brij 58 (1:2.333) at three different concentrations (2, 4 and 6%) (56).
12. Garlic oil: It is a volatile oil (essential oil) derived from garlic. It is usually prepared using steam distillation, and can also be produced via distillation using ether. It is used in cooking and as a seasoning, a nutritional supplement, and also as an insecticide. Steam-distilled garlic oil has around 900 times the strength of fresh garlic and around 200 times the strength of dehydrated garlic (57).
13. *Formulation and Evaluation of odour-free garlic powder:* A gastro retentive floating matrix tablet (FMT) from garlic powder (GP) was prepared using wet granulation technique and non-enteric film coating was applied to mask GP odor (58).
14. *Herbal Anti-dandruff Shampoo Containing Garlic Loaded Solid Lipid Nanoparticles:* These were formulated by using garlic as an anti-fungal agent. The ALL - SLNs (allicin - solid lipid nanoparticles) were formulated by hot homogenization method and evaluated by using different parameter. It is more effective for the treatment of dandruff on scalp and hair with no side effect (59).
15. *Garlic powder is an herbal formulation used in ayurvedic system of medicine for the treatment of platelets aggregation:* The interaction of garlic with heparin has been studied in influence to platelets aggregation effect of standard drug in various parameters. No significant toxicity was observed during toxicity study (60).
16. *Efficacy of new EC (emulsifiable concentrate) formulation derived from garlic creeper (Adenocalymma alliaceum Miers.) against anthracnose and stem end rot diseases of mango:* Different leaf extracts of Garlic creeper (Adenocalymma alliaceum Miers.) using water and solvents were prepared and they were screened for their anti-fungal activity against Colletotricum gloeosporioides Penz. and Botryodiplodia theobromae Pat. causal agents of mango post harvest diseases viz., anthracnose and stem end rot respectively. The extract was partially purified and formulated as ADENOCAL 60 EC for the management of post harvest diseases of mango fruits (61).
17. *Formulation and evaluation of herbal ointment for Antimicrobial activity:* The present work is to formulate and evaluate the ointment of garlic bulb extract for anti-microbial activity. The benzene extract was prepared by the Soxhalation method. The formulation shows more zone of inhibition against *Bacillus subtilis* (62).
18. *Formulation, development and evaluation of cream containing natural essential oils having mosquito repellent property:* A mosquito repellent cream naturally obtained from medicinal plants instead of commonly available synthetic insecticides and repellents such as N-Diethyl-3-methylbenzamide (DEET), which are carcinogenic and non-eco-friendly. Essential oils of Tulsi, Clove, Garlic, Kapoor kacheri and Lemongrass were used in the cream formulation and evaluated for various parameters. It was concluded that the formulated mosquito repellent cream using essential oil is natural, safe, effective, usable for the skin and stable too (63).
19. *Aqueous preparation of Allium Sativa (garlic) on erythrocyte osmotic fragility in Wistar rats: in vivo and in vitro studies:* The effects of garlic on the osmotic fragility of red blood cells in albino rats were assessed *in vivo* and *in vitro*. In the *in vivo* studies, five albino rats weighing between 150-200 g composed each of three study groups. Group A were administered 150 mg/Kg body weight aqueous garlic preparation; Group B 75 mg/Kg body weight aqueous garlic and 75 mg/Kg body weight garlic preparations and Group C served as the control and were administered distilled water. The treatment regimens were orally administered thrice a week, for a period of four weeks by gavages. The *in vitro* erythrocyte osmotic fragility was also evaluated in 12 Wistar rats that were not pre-treated with garlic. The same observation was made in the *in vitro.* It is concluded that garlic increases the osmotic fragility of red blood cells in albino rats (64).
20. *Garlic used as an additive in pesticides:* Many people have expressed concerns about the harmful effects of chemical pesticides and show interest in organic farm products. Thus, to address these concerns there is a need to reduce the use of chemical pesticides and supplement with relatively lesser toxic like natural additives such as garlic (Allium sativum) and hot pepper (Capsicum frutescens) which exhibit synergistic effects on the neem product. Studies also reveal some relatively great effectiveness when these extracts are mixed with or applied alternatively with bio-pesticides such as *Bacillus thuringiensis* (Bt) (65).
21. *Formulation of garlic capsules:* Garlic gelatin capsules were prepared, they are used as a preventative for age-related vascular changes, for the treatment of arteriosclerosis, colds, coughs, fevers, high blood pressure, high cholesterol, infections, intestinal parasites, inflammation of the mouth, inflammation of the pharynx, and for those with a tendency towards infection. They are effective as a supportive to dietary measures for elevated lipid levels in the blood. They are useful as an anti-bacterial and anti-infection agent also helps to reduce cough, flu, and respiratory ailments (66).

CONCLUSION

Garlic and its extracts had a wide range of applications even against resistant organisms to serve as powerful anti-microbial agent. Therefore, research is needed to refine the pathophysiological mechanisms of action of garlic and its utility in treatment of various diseases by developing more stable and suitable formulations. The development of Garlic as a commercial anti-biotic has come to a halt. Although its efficiency is scientifically proven, it has only been used as dietary supplement or traditional medicine. In this report a comprehensive investigation has been conducted on garlic which includes various scientific aspects about it by which researchers from various disciplines could be directed to put efforts toward discovering the benefits of garlic on human health.

CONFLICT OF INTERESTS

The authors declare no conflicts of interest.

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None.

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