

ALLISURE®

Summary of Product Characteristics

NAME OF THE ACTIVE MATERIAL

Allisure is Allicin powder with a 100% allicin yield

1a PRODUCT IDENTIFICATIONS

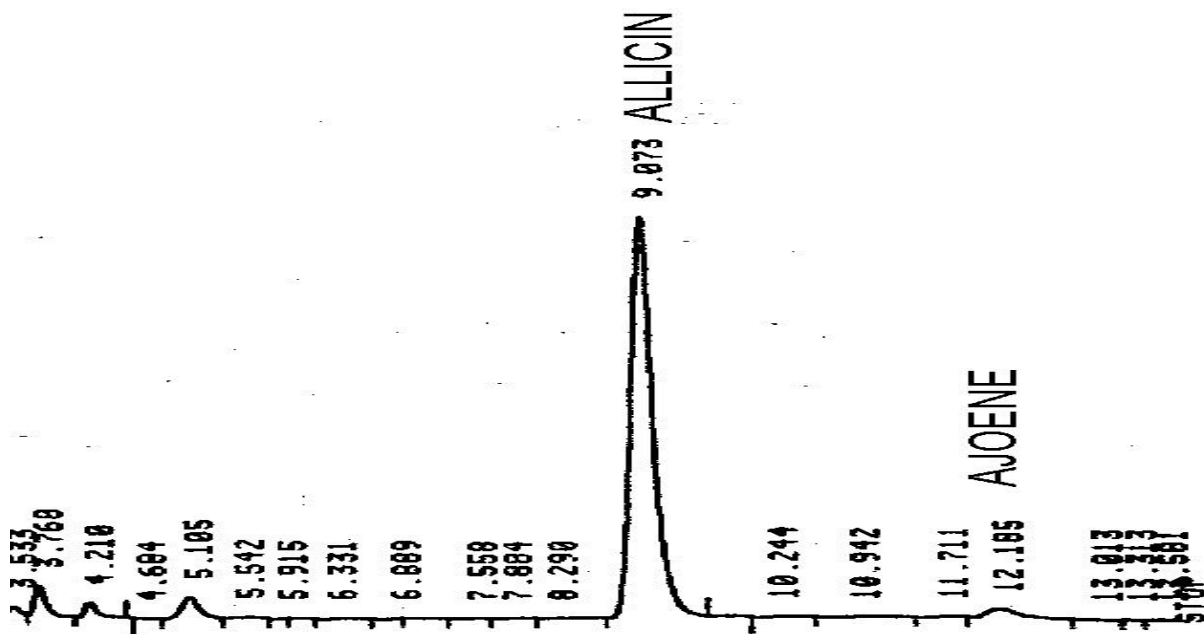
Allisure powder is the main active ingredient in the following branded products

ALLIMAX, WEISSIN, GARCIN, ALLI-C, ALLIFORCE, ALLIFORCE EXTRA, DETOXAL 21, KNOFLOX ALLIMAX, ALLIPRO, LIFESPICE.

QUALITATIVE AND QUANTITATIVE COMPOSITION

Capsules contain Allisure as the active agent which is made up from Non-genetically modified maltodextrin and gum acacia.

2a. HPLC determination of active component allicin in Allisure powder

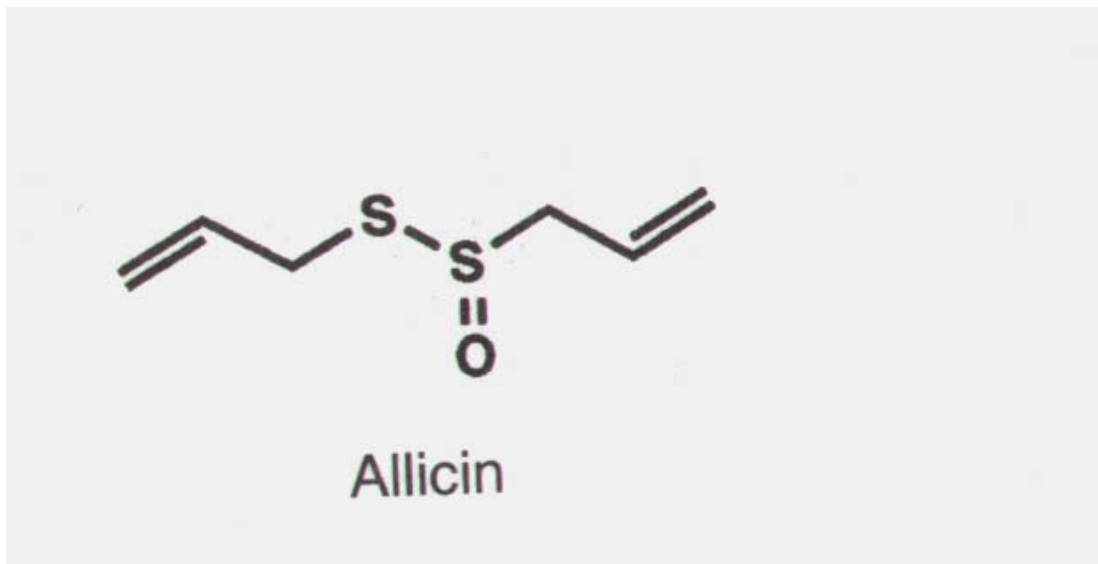


2b SHELF LIFE AND STORAGE

Allisure powder has a shelf life of 30 months. Even after this time period independent tests have shown that at 36 months the powder is still able to kill MRSA (methicillin resistant staphylococcus aureus)

Provided the product is kept boxed its shelf life will extend to past 36 months

CHEMICAL STRUCTURE



The sulphur - sulphur and sulphur - oxygen bonds are responsible for many of the beneficial properties associated with allicin. Although similar to the penicillin structure these bonds are very reactive and in fresh garlic they break down very quickly into a series of thiosulphinate components.

MANUFACTURING PROCESS – TECHNOLOGY PROCESS

Allsure powder™ is the result of a patented process, which produces purified allicin liquid. It is the first health food supplement to provide a 100% allicin yield, the key active ingredient of fresh garlic.

Garlic is harvested from the Pederonas area near Valencia in Spain however much of this garlic is destined for supermarkets and convenience stores throughout the UK. We are very selective in that only the best quality bulbs are picked for production of Allisure powder. All the garlic under 50mm wide is immediately rejected as too small. Any that has begun to sprout, or is in any way damaged, is removed by the ladies in the pack house.

Once the bulbs have been selected (approximately 5kg per 1 million capsules) some of the batch are analysed for alliin content using HPLC and Mass Spectrometry. Once this has been done the garlic is crushed in our special glass apparatus where extra alliin from the same garlic is also added. As the allicin begins to form it is physically removed from the reaction chamber by flooding the system with water. All through this phase the temperature is carefully controlled to within 0.1 degrees C (this increases the yield of allicin liquid) and the whole system is kept at constant pressure. The resultant allicin liquid is analysed by HPLC and immediately frozen for transport to the spray dryer.

At the spray drying house the liquid is carefully added to a reaction vessel along with non GM maltodextrin where it enters the spray dryer. The resultant powder is Allisure which is then tested microbiologically against an MRSA bacteria and HPLC. The powder is then filled into capsules for distribution around the world.

We have seen that Allisure is made from fresh, raw garlic heads that are specifically selected to ensure that they contain a significant enzyme activity (allinase enzyme). Garlic heads are split into cloves, which are left unpeeled and then subjected to filtration, controlled temperature and pressure extraction and a flood reaction process designed to produce stabilized liquid allicin dissolved in water. No chemical solvents are used. The alliin amino acid in fresh garlic is subjected to complete conversion by the allinase enzyme and to ensure a large volume of active agent is harvested. Allicin is quickly removed from the reaction system as it competes with and will destroy the enzyme allinase. The volume of active agent produced is directly related to the enzymatic concentration and activity.

CLINICAL PARTICULARS

ALLISURE® has demonstrated significant antibacterial, antifungal, larvicidal and antiviral properties. The material has also shown an ability to reduce cholesterol and blood pressure as well as increasing CD4-T cell count significantly.

5.1 Antibacterial, antifungal, antiviral and larvicidal properties

Allicin, one of the active principles of freshly crushed garlic homogenates, has a variety of antimicrobial activities. Allicin in its pure form was found to exhibit i) antibacterial activity against a wide range of Gram-negative and Gram-positive bacteria, including multidrug-resistant enterotoxigenic strains of *Escherichia coli*

ii) antifungal activity, particularly against *Candida albicans*

iii) antiparasitic activity, including some major human intestinal protozoan parasites such as *Entamoeba histolytica* and *Giardia lamblia* and iv) antiviral activity. The main antimicrobial effect of allicin is due to its chemical reaction with thiol groups of various enzymes, e.g. alcohol dehydrogenase, thioredoxin reductase, and RNA polymerase, which can affect essential metabolism of cysteine proteinase activity involved in the virulence of *E. histolytica*.

1. Introduction

Garlic is one of the edible plants, which has generated a lot of interest throughout human history as a medicinal panacea. Wide ranges of microorganisms including bacteria, fungi, protozoa and viruses have been shown to be sensitive to crushed garlic preparations. Moreover, garlic has been reported to reduce blood lipids and to have anticancer effects. Chemical analyses of garlic cloves have revealed an unusual concentration of sulfur-containing compounds (1–3%) [1, 2].

Analysis of steam distillations of crushed garlic cloves performed over a century ago showed a variety of allyl sulfides. However, it was not until 1944 that Cavallito and his colleague's [3] isolated and identified the component responsible for the remarkable antibacterial activity of crushed garlic cloves. The compound turned out to be an oxygenated sulfur compound, which they termed allicin, from the Latin name of the garlic plant, *Allium sativum*. Pure allicin is a volatile molecule that is poorly miscible in aqueous solutions and which has the typical odor of freshly crushed garlic [4]. Final proof of the chemical structure of allicin came in 1947, when it was shown that allicin could be easily synthesized by mild oxidation of diallyl disulfide [2]. The debate on the presence of allicin in crushed cloves versus its absence in odorless intact cloves was resolved after Stoll and Seebeck [5] isolated, identified, and synthesized an oxygenated sulfur amino acid that is present in large quantities in garlic cloves and which they named alliin (*figure 1*). Alliin was found to be the stable precursor that is converted to allicin by the action of an enzyme termed allinase, which is also present in the cloves [6]. Only one isomer of alliin ((+)-S-allyl-L-cysteine-sulfoxide) was found to be present, which in itself had no antimicrobial activity. Numerous investigators studied the amounts of alliin and allicin present in different strains of garlic. Considerable variations have been reported, ranging from 2.8 to 7.7 mg/gram found in Romanian red [2].

The transformation of alliin into the biologically active allicin molecule upon crushing of a garlic clove is extremely rapid, being complete in seconds. The

enzyme responsible for the lysis is alliinase, or alliin-lyase (E.C.4.4.1 4), a pyridoxal 3-phosphate-dependent glycoprotein consisting of two subunits 17, 81. Alliinase is present in unusually high amounts in garlic cloves: at least 10% of the total protein content (10 mg/g fresh weight).

The gene coding for the enzyme has been cloned, and upon translation, found to consist of 448 amino acids with a protein molecular mass of 51.45 kDa and together with a carbohydrate content of 5.5-6%, gives 55000 kDa [7, 8]. Alliinase has 10 cysteine residues, all of them in S-S bridges, and their reduction, or the removal of the pyridoxal coenzyme factor, renders the enzyme inactive. Expression of a recombinant alliinase has been achieved in the baculovirus system, and although protein yields were impressive, the enzymatic activity was very poor due to difficulties with folding of the protein (Mirelman *et al.*, unpublished results). Moreover, in the clove, alliinase is found closely associated with a lectin [9]. The site of linkage of the carbohydrate moieties of alliinase has been identified at Asp 146 [9]. Significant homology has been reported between the garlic and onion alliinases, although alliin was not detected in the latter species.

Garlic cloves are odour-free until crushed. Cross-section studies have indicated that the substrate alliin and the enzyme alliinase are located in different compartments [2, 6]. This unique organization suggests that it is designed as a potential defense mechanism against microbial pathogens of the soil. Invasion of the cloves by fungi and other soil pathogens begins by destroying the membrane, which encloses the compartments that contain the enzyme and the substrate. This causes the interaction between alliin and alliinase that rapidly produces allicin and which in turn inactivates the invader. The reactive allicin molecules produced have a very short half-life, as they react with many of the surrounding proteins, including the alliinase enzyme, and making it into a quasi-suicidal enzyme. This very efficient organization ensures that the clove defense mechanism is only activated in a very small location and for a short period of time, whereas the rest of the alliin and allinase remain preserved in their respective compartments and are available for interaction in case of subsequent microbial attacks. Moreover, since massive generation of allicin could also be toxic for the plant tissues and enzymes, its very limited production and short-lived reactivity, which is confined to the area where the microbial attack takes place, minimizes any potential self-damage to the plant.

2. Antibacterial activity of allicin

The antibacterial properties of crushed garlic have been known for a long time. (see table 1). Various garlic preparations have been shown to exhibit a wide spectrum of antibacterial activity against Gram-negative and Gram-positive bacteria including species of *Escherichia*, *Salmonella*, *Staphylococcus*, *Streptococcus*, *Klebsiella*, *Proteus*, *Bacillus*, and *Clostridium*. Even acid-fast bacteria such as *Mycobacterium tuberculosis* are sensitive to garlic [10]. Garlic extracts are also effective against *Helicobacter pylori*, the cause of gastric ulcers [11]. Garlic extracts can also prevent the formation of *Staphylococcus* enterotoxins A, B, and C1 and also thermonuclease [12]. On the other hand, it seems that garlic is not effective against toxin formation of *Clostridium botulinum* [13].

Cavallito and Bailey [4] were the first to demonstrate that the antibacterial action of garlic is mainly due to allicin [3]. The sensitivity of various bacterial and clinical isolates to pure preparations of allicin [14] is very significant. As shown in *table I* (Mirelman *et al.*, unpublished results) the antibacterial effect of allicin is of a broad spectrum. In most cases the 50% lethal dose concentrations were somewhat higher than those required for some of the newer antibiotics.

Interestingly, various bacterial strains resistant to antibiotics such as methicillin resistant *Staphylococcus aureus* as well as other multidrug-resistant enterotoxigenic strains of *Escherichia coli*, *Enterococcus*, *Shigella dysenteriae*, *S. flexneri*, and *S. sonnei* cells were all found to be sensitive to allicin. Allicin also had an in vivo antibacterial activity against *S. flexneri* Y when tested in the rabbit model of experimental shigellosis [15].

On the other hand, other bacterial strains such as the mucoid strains of *Pseudomonas aeruginosa*, *Streptococcus β hemolyticus* and *Enterococcus faecium* were found to be resistant to the action of allicin. The reasons for this resistance are unclear. It is assumed that hydrophilic capsular or mucoid layers prevent the penetration of the allicin into the bacteria, but this has to be studied more in depth.

Table 1. Sensitivity of various bacterial species to allicin.

Bacterial Strain	Allicin Concentration (LD ₅₀ µg/ml)	Comments
Escherichia coli	15	Sensitive to antibiotics
Escherichia coli	15	Multidrug resistant MDR
Staphylococcus aureus	12	Sensitive
Staphylococcus aureus	12	Methicillin resistant
Streptococcus progenies	3	Sensitive
Streptococcus β hemolyticus	>100	Clinical MDR strain
Proteus marbles	15	Sensitive
Proteus mirabilis	>30	Clinical MDR strain
Pseudomonas aeruginosa	15	Sensitive to cefprozil
Pseudomonas aeruginosa	>100	MDR mucoid strain
Acinetobacter baumannii	15	Clinical isolate
Klebsiella pneumoniae	8	Clinical isolate
Enterococcus faecium	>100	Clinical MDR strain

3. Antifungal activity of allicin

Garlic extracts also have a strong antifungal effect and inhibit the formation of mycotoxins like the aflatoxin of *Aspergillus parasiticus* [17]. Allicin was assumed to be the main component responsible for the inhibition of fungal growth. A concentrated garlic extract containing 34% allicin, 44% total thiosulfinates, and 20% vinyldithiols possessed potent in vitro fungistatic and fungicidal activity against three different isolates of *Cryptococcus neoformans*. The minimum inhibitory concentration of the concentrated garlic extract against 1×10^5 organisms of *C. neoformans* ranged from 6 to 12 $\mu\text{g/mL}$. In addition, in vitro synergistic fungistatic activity with amphotericin B was demonstrated against all isolates of *C. neoformans* [18]. Pure allicin was found to have a high anticandidal activity with a minimum inhibitory concentration of 7 $\mu\text{g/mL}$ [19]. Yamada and Azuma [20] report that pure allicin was effective in vitro against species of *Candida*, *Cryptococcus*, *Trichophyton*, *Epidermphyton*, and *Microsporium* at low concentration (minimal inhibitory concentrations of allicin was between 1.57 and 6.25 $\mu\text{g/mL}$). Allicin inhibits both germination of spores and growth of hyphae [20]. The sensitivities of various clinically important yeasts to a pure preparation of allicin were determined and found to be very significant (*table II*) (Mirelman *et al.*, unpublished results). The mode of action of allicin on the fungal cell has not yet been elucidated but it is assumed to function on thiol enzymes as in other microorganisms (see below).

4. Antiparasitic properties of allicin

The antiparasitic effects of freshly crushed garlic were known by many ancient cultures. Albert Schweizer used to treat people suffering from dysentery or intestinal worms with freshly crushed garlic. One of the traditional Chinese medical treatments for intestinal diseases is an alcoholic extract of crushed garlic cloves. Several years ago we found out that *Entamoeba histolytica*, the human intestinal protozoan parasite, is very sensitive to allicin, as only 30 $\mu\text{g/mL}$ of allicin totally inhibits the growth of amoeba cultures [21]. More recently we have found that at lower concentrations (5 $\mu\text{g/mL}$), allicin inhibited by 90% the virulence of trophozoites of *E. histolytica* as determined by their inability to destroy monolayers of tissue-cultured mammalian cells in vitro [22].

Allicin (30 $\mu\text{g/mL}$) also very efficiently inhibited the growth of other protozoan parasites such as *Giardia lamblia*, *Leishmania major*, *Leptomonas colosoma*, and *Crithidia fasciculata* (Mirelman *et al.*, unpublished results). Some allicin toxicity towards tissue-cultured mammalian cells was observed at concentrations above 100 μM [22]. Interestingly however, at these high allicin concentrations no damage to the mammalian cells was seen if the incubations were done in the presence of amoebic trophozoites, suggesting that the affinity of the allicin molecules is towards the parasite targets. The reason for microbial cells' higher sensitivity to allicin than that of mammalian cells is that most of the microbial cells do not have, or have very small amounts of, glutathione (or its equivalent thiol molecules such as trypanothione) and thus lack the ability to reactivate the essential SH-enzymes that are thiolated by allicin (see below section 6).

Table II Effect of allicin on various fungal pathogens

Fungal strain	Allicin concentration MIC ($\mu\text{g/mL}$)	Comments
Candida albicans	0.3	
Candida albicans	0.8	Clinical isolates
Candida neoformans	0.3	
Candida parapsilosis	0.15	
Candida tropicalis	0.3	
Candida krusei	0.3	
Torulopsis glabrata	0.3	
Torulopsis glabrata	1.9	Clinical isolates

5. Antiviral activity of allicin

Fresh garlic extracts in which allicin is known to be the main active component have been shown to have *in vitro* and *in vivo* antiviral activity. Among the viruses, which are sensitive to garlic extracts are the human cytomegalovirus, influenza B, herpes simplex virus type 1, herpes simplex virus type 2, parainfluenza virus type 3, vaccinia virus, vesicular stomatitis virus, and human rhinovirus type 2 [23]. The allicin condensation product, ajoene, seems to have in general more antiviral activity than allicin. Ajoene was found to block the integrin-dependent processes in a human immunodeficiency virus-infected cell system [24]. Interestingly, there are some viruses like the garlic plant virus X which are resistant to the antiviral effects of garlic extracts [25].

Most recently a double blind placebo controlled study has shown significant protection from the common cold virus. Conducted by The Garlic Centre and published in *Advances in Therapy* this is the first serious work to show both prevention, treatment and reduction of re-infection benefits from taking Allisure once daily [16].

6. Mechanism of action of allicin

Inhibition of certain thiol-containing enzymes in the microorganisms by the rapid reaction of thiosulfinates with thiol groups was assumed to be the main mechanism involved in the antibiotic effect [3]. Recently, we have studied the mechanism of action of pure allicin molecules with thiol groups in more detail [14]. This study confirmed the ability of allicin to react with a model thiol compound (L-cysteine) to form the S-thiolation product S-allylmercaptocysteine. The identification of the thiolation product was proven by nuclear magnetic resonance as well as by mass spectroscopy.

The main antimicrobial effect of allicin is due to its interaction with important thiol-containing enzymes. In the amoeba parasite, allicin was found to strongly inhibit the cysteine proteinases, alcohol dehydrogenases [22], as well as the thioredoxin reductases (Ankri *et al.*, unpublished results) which are critical for

maintaining the correct redox state within the parasite. Inhibition of these enzymes was observed at rather low concentrations (<10 µg/mL). Allicin also irreversibly inhibited the well known thiol-protease papain, the NADP⁺-dependent alcohol dehydrogenase from *Thermoanaerobium brockii*, and the NAD⁺-dependent alcohol dehydrogenase from horse liver. Interestingly, all three enzymes could be reactivated with thiol-containing compounds such as DTT, mercaptoethanol and glutathione [14]. At concentrations that are at least a log higher (> 100 µg/mL), allicin was also found to be toxic to tissue-cultured mammalian cells [22]. As mentioned above, the significant difference in sensitivity between the microbial and mammalian cells may be explained by the much higher concentrations of glutathione that the mammalian cells possess.

Allicin also specifically inhibits other bacterial enzymes such as the acetyl-CoA-forming system, consisting of acetate kinase and phosphotransacetyl-CoA synthetase [26]. The inhibition is noncovalent and reversible. (¹⁴C) acetate incorporation into fatty acids of isolated plastids was inhibited by allicin with a 50% inhibitory concentration (I₅₀ value) lower than 10 mM. Furthermore, allicin at bacteriostatic concentrations (0.2 to 0.5 mM) was found to partially inhibit, in *Salmonella typhimurium*, the DNA and protein synthesis, but the effect on RNA synthesis was immediate, suggesting that this could be a primary target of allicin action [27]. *E. coli* RNA polymerase, in its alpha-subunit, contains a single sulfhydryl group which was shown to react with the monomercuric derivative of fluorescein, a specific reagent for thiol groups (fluorescein monomercuracetate) [28]. This suggests that RNA polymerase could also be a target for allicin.

The condensation product of allicin, ajoene, which has a similar oxygenated sulfur group, has been shown to inhibit the proliferation of *Trypanosoma cruzi*, possibly by inhibition of phosphatidylcholine biosynthesis [29]. Ajoene was also recently shown to inhibit phosphatidylcholine biosynthesis in the human pathogenic fungus *Paracoccidioides brasiliensis* [30]. The inhibition capacities shown for ajoene clearly suggest that additional microbe-specific enzymes may also be targets for allicin.

It is reasonable to conclude, therefore, that the broad-spectrum antimicrobial effects of allicin (and ajoene) are due to the multiple inhibitory effects they may have on various thiol-dependent enzymatic systems. It is difficult at this stage to state, which are the more lethal targets. It could very well be that the effect of allicin may be at different levels. Some enzymes such as the thiol proteases, which cause severe damage to the host tissues, may be inhibited at the lowest concentrations.

At low concentrations the inhibition of these enzymes may not be lethal, but sufficient to block the microbe's virulence. At slightly higher concentrations other enzymes such as the dehydrogenases or thioredoxin reductases may be affected, and even partial inhibition of these enzymes could be lethal for the microorganism.

All the above descriptions on the wide range of biological activities that allicin has been found to have should have propelled this molecule into becoming a prime candidate for therapeutic use. Recently it has been possible to patent the manufacture of allicin in commercial grade quantities. This is not the first time that economic considerations will prevent a natural compound with superb medicinal properties to reach those patients that could most benefit from it. Allicin will therefore find a readily appreciative audience amongst those who purchase over the counter "medications" for a wide variety of conditions.

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5.2 Antiviral activity of ALLISURE™

Common Cold Prevention and Treatment

A double blind placebo controlled survey comparing an allicin containing garlic supplement [ALLISURE] with a placebo

Background

The Common Cold is the most widespread viral infection in the World today. It is estimated that most people will suffer 2 to 5 colds per year. Over 200 different viruses cause infection and cold symptoms, the most common of which are the Rhinoviruses which account for 30-40% of adult colds. Re-infection is also very prevalent because of this wide variety of infectious viruses.¹

Currently only a few publications exist to show the activity of garlic against viral infections.^{2,3} Hanley & Fenwick⁴ (1985) report that during an influenza epidemic, the former Soviet Union once imported over 500 tons of garlic cloves for the acute treatment of the disease. Among the viruses that are sensitive to garlic extracts are the human cytomegalovirus, human rhinovirus type 2, herpes simplex type 1 and 2 and influenza B virus. Evidence points towards allicin and its condensation product ajoene as the main components in garlic responsible for this antiviral activity. Recently ALLISURE Liquid and Capsules have been shown to be effective against Herpes Simplex type 1 and Molluscum Contagiosum viral infections.⁵

Traditionally many consumers take garlic supplements as a preventative measure and many report never getting a cold or symptoms associated with viral replication.

A "cure" for the common cold would significantly reduce the number of working days lost each year due to the classic symptoms of infection which include tiredness, headaches, a runny nose, sneezing, coughing, watery eyes and feeling unable to concentrate. Prevention is always better than simply treating symptoms and this survey is designed to see if a unique garlic supplement can prevent volunteers from getting a cold.

Although many garlic supplements are available in the UK, there is a wide variation in the type of supplement and an inadequate definition of active constituents within these health food products. However increasing evidence has shown that certain types of supplement may have significant beneficial properties, provided that the universally recognised active constituent (allicin) is made available to the body. We chose a new type of garlic supplement that only contains stabilised allicin. A literature review conducted by The Garlic Centre shows that the proposed anti-viral activity of garlic is almost certainly due to allicin and possibly a breakdown sulphur constituent known as ajoene. ALLISURE is the only supplement that actually claims to contain allicin as a starting material.

Study Objectives

1. To measure the number of colds recorded in each group as indicated by the scoring system detailed below. One group randomised to take ONE ALLISURE Capsule every day and one group randomised to take ONE PLACEBO Capsule every day for a period of 3 months.
2. As volunteers report an infection the period of time taken to full recovery will be monitored in each group.

Methodology

Following recruitment via PR in two daily Newspapers 144 participants were selected. A diary was designed for each volunteer to record progress over a 3-month period (90 days). Volunteers were asked to record general well being on a scale of 1 to 5 every day throughout the study period.

Symptom Measurement Scale

5 = Well no problems

4 = Quite well but the occasional sneeze no disruption to normal routine

3 = Can feel a cold coming on – some minor symptoms

2 = Feeling low and beginning to exhibit symptoms

1 = Full cold symptoms e.g. Headache, sneezing, runny nose, tiredness

If a cold developed then each volunteer was asked to note the number and variety of symptoms presented, the day they begin to recover and the day they felt completely better.

The 144 volunteers were split into 2 groups (sex, age and garlic consumption matched – see Table 1 Volunteer Demographics).

	ACTIVE	PLACEBO
Number of patients	73	73
Males	32	29
Females	41	44
Average age	52	53
Previously taken a garlic supplement	11	10

Table 1 Volunteer Demographics

Volunteers were then randomised, using a simple random number generator and assigned to the ACTIVE (Zero) or PLACEBO (One) group. Each volunteer was then instructed to take ONE CAPSULE every day with his or her main meal. This instruction follows the manufacturer's recommendation for taking a garlic supplement. Randomisation codes were kept securely at the Garlic Centre and were not broken until all the diaries had been returned.

The Garlic Centre contacted volunteers every 2 weeks to ensure that the capsules were being taken correctly and that the diary was completed daily.

Diary Analysis

Following return of the diaries the number of colds experienced by volunteers was counted. A cold is defined as a score of 3 which then proceeds to a score of 2 or 1 and some symptoms are experienced.

The duration of symptoms was taken as the number of days with a recorded score of 2 or 1 leading to an average recovery time ending with a score of 4 or 5 taken across all recorded colds.

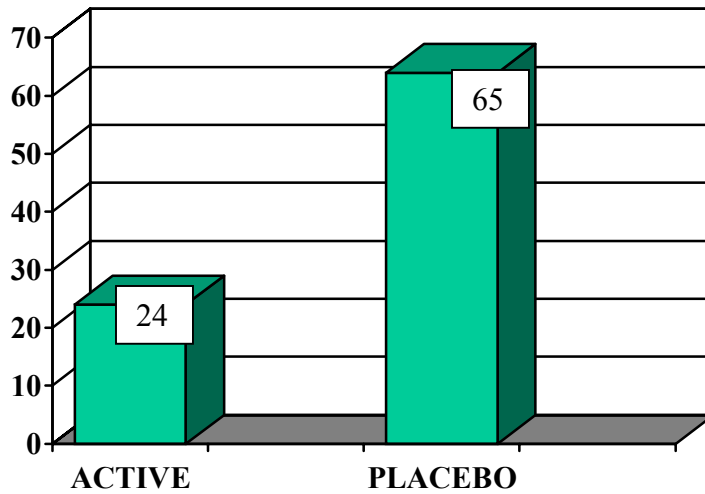
Results

The number of colds experienced in each group is shown in Figure 1 and the number of infected days and average number of days to a recovery is shown in Figure 2

The number of colds in the ACTIVE Group was 24 and the number of colds in the PLACEBO Group was 65. This result is highly statistically significant in favour of using ALLISURE as a cold prevention remedy. $p < 0.0001$

Figure 1 Number of colds suffered in each group

The average number of days needed to recover in the PLACEBO Group was 5.63 days (366 days of infection / number of colds) whereas in the ACTIVE Group this figure was 4.63 days (111 days of infection / number of colds). $p < 0.0001$



The number of volunteers experiencing more than 1 full cold throughout the survey period was much higher in the PLACEBO group as shown in Figure 3. A total of 16 volunteers became re-infected whilst taking PLACEBO as compared to only 2 volunteers taking the ACTIVE.

Diary Comments and Withdrawals

Volunteers were also asked to record ANY other factors that concerned them over the course of this study. Comments about the acceptability of taking capsules, side effects, smell and anything that might warrant a discontinuation of treatment, volunteers were encouraged to report these events in their diaries and to telephone The Garlic Centre if further advice was required.

Figure 2 Infected days and recovery period

TREATMENT	COLDS	INFECTED DAYS	RECOVERY PERIOD
One capsule per day with food			
ACTIVE (ALLISURE)	24	111	1.56
PLACEBO	65	366	5.06

There were a total of 4 withdrawals 3 from the ACTIVE group and 1 from the PLACEBO group. One from the ACTIVE group was withdrawn because the volunteer continued to take another garlic supplement. One from the ACTIVE group developed Gout and was advised to discontinue.

Figure 3 Frequency of re-infection

Volunteers experiencing more than 1 cold Throughout the survey period	
ACTIVE	2 (Two)
PLACEBO	16 (Sixteen)

One from the ACTIVE group developed an itchy rash below the knees, which faded away after stopping the treatment.

The PLACEBO volunteer developed severe headaches and was advised to stop taking the capsules.

A total of 5 volunteers noticed a "smell" whilst burping after taking capsules. Four were taking ACTIVE and 1 was taking PLACEBO. However it is not clear if they took capsules in accordance with the instructions (i.e. with their main meal).

Several volunteers taking ACTIVE reported feeling much more alert and generally healthier even though close contacts around them were falling ill. Several volunteers taking ACTIVE took them on holiday and reported avoiding a stomach upset and not getting bitten by mosquitoes.

Conclusions

This survey is the first one to follow a double blind placebo controlled design in the area of viral disease prevention using a garlic supplement. The results are overwhelmingly in favour of **ALLISURE** as a disease prevention measure. Also in the treatment of troublesome symptoms such as a sneezing, cough and a runny nose, volunteers taking **ALLISURE** recover faster. Furthermore our data indicates a faster reduction in symptoms and recovery to full fitness. Volunteers taking the active prevention were also less likely to become re-infected from other viral strains indicating a general improvement in the immune system.

Another important point to note is that volunteers in the **ALLISURE** group took the manufacturers recommended daily dose of 1 capsule per day indicated in the commercially available product. Many other studies published on garlic supplements, for numerous applications over the last 10 years, have often used double or triple the actual dose available in retail outlets.

This approach may represent not only a "cure" for the common cold but it clearly shows that effective prevention of infection and re-infection may be gained from taking **ALLISURE** on a daily basis throughout the year. The overall potential savings to National Industrial Output by preventing workers from taking sick leave is enormous. This product clearly exhibits excellent antiviral activity and further work is recommended to determine the nature and method of viral destruction.

References:

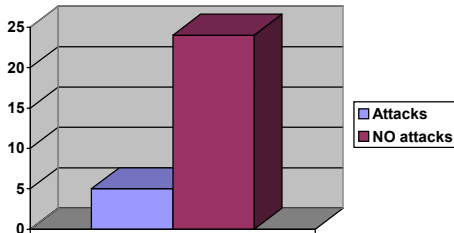
1. R Eccles Common Cold Centre Cardiff.
2. Koch and Lawson in Garlic – The Science and Therapeutic Application of Allium Sativum L and related species: Williams & Wilkins 1996.
3. Ankri & Mirelman, Microbes and Infection 2, 1999, 125-129
4. Hanley & Fenwick, Journal of Plant Foods 6; 211-238: 1985
5. Data on file at The Garlic Centre

6. Anti-histamine activity

A Pilot Investigation into the use of Allisure for the treatment of HAY FEVER (SEASONAL ALLERGIC RHINITIS) was carried out in 2002.

The survey was designed to determine whether a unique garlic supplement that contains only stabilized allicin could prevent the classic Hay fever attack from occurring amongst volunteers who have suffered for some years. The extract Allisure was chosen for study as it is the only product that claims to contain allicin as a starting material. Using a simple 5 point scoring system to grade the severity of any hay fever attacks we found that the overall **AVERAGE SCORE** was 3.95 indicating that Allisure was able to control hay fever very well. **Over 80% of volunteers reported a significant reduction in the number of challenges throughout the study period, Only 2 volunteers needed to resort to drug treatment for an attack**

- **The overall AVERAGE SCORE was 3.95 indicating that Allisure was able to control hay fever very well**
- **Over 80% of volunteers reported a significant reduction in the number of challenges throughout the study period**
- **Only 2 volunteers needed to resort to drug treatment for an attack**



- **Most volunteers were impressed with the treatment and claimed that their hay fever was “much better” controlled with Allisure**
- **Volunteers reported far fewer symptoms than they expected with big reductions in “sore eyes” “runny nose” “itching at the back of the throat” “sneezing” and “tiredness”**
- **Everyone found Allisure easy to take and did not report any side effects. There were no reports of smell whilst taking this product**

Generally the volunteers reported that Allisure was easy to take and actually rather effective. Although the treatment did not work for everyone and some comments indicated that the “season” was finishing most volunteers were extremely positive and included observations that previous drug treatment had never really removed all symptoms whereas Allisure did. People were more able to go about their normal daily routine without interruption from troublesome symptoms. One gentleman reported being able to play golf 3 times a week without any problems – apart from the golf! Another young lady was able to sit out on fresh mown lawn for the first time since her hay fever symptoms developed in her teens. Other unsolicited comments included volunteers being able to mix and socialise without worrying about running nose and streaming eyes.

So this pilot investigation shows clearly that allixin based supplements do show an ability to prevent allergic reaction to pollen and may indeed offer a safe and natural alternative to pharmaceutical preparations, Clearly the treatment should be started as early as possible and continued throughout the season. Further work should be done to ascertain the exact degree of efficacy and how Allisure compares with a chemical alternative. But for many people this represents a real chance to reduce the number of compromises that hay fever sufferers have to make each year. The full paper can be reviewed at www.bjcp.co.uk

7. METHOD OF ADMINISTRATION

Allisure Capsules contain allixin powder and are adapted for oral administration. It is recommended that they should be taken with food to minimise any risk of a smell developing.

However it is perfectly acceptable to break open the capsules and consume the powder by placing it onto or into food during preparation.

7. UNDESIRABLE EFFECTS

The incidence of side effects whilst taking ALLISURE is extremely low. Very few people report an odour whilst taking the product. Sensitivity can occur very infrequently and a rash is the most obvious sign. Any untoward side effects stop once the product is discontinued. Since ALLISURE is made from fresh garlic it can be seen to have a safety record dating back thousands of years and is unlikely to cause any problems. Always follow the recommendations stated on the packaging for taking ALLISURE capsules.

8. PREGNANCY AND LACTATION

There is no reason why ALLISURE should not be taken during pregnancy – indeed it may actually be beneficial to the fetus. Further information is available at <http://www3.mistral.co.uk/garlic>

9. USE IN CHILDREN

Generally supplements are not recommended for children under the age of 7 years. However, provided the recommended daily dose is not exceeded ALLISURE™ can be safely taken by children aged 7 and over.

10. PHARMACOLOGICAL/PHARMACOKINETIC PROPERTIES

The allicin powder that makes up ALLISURE™ is slightly acidic and as such it prefers the acid environment found in the human stomach. Since ALLISURE™ does not contain any alliin or alliinase enzyme it is impossible for the stomach acid to inactivate the allicin absorption. Therefore a genuine 100% yield is guaranteed from each dose of ALLISURE™. All other garlic supplements rely on your body being able to produce allicin and many are imperfectly protected against attack from stomach acid. Any acid contact will completely and irreversibly inactivate alliinase enzyme making production of allicin impossible.

Once absorbed, ALLISURE™ breaks down as predicted empirically to form a series of thiosulphinates compounds. None of these components can be easily measured or even detected in blood at present, although radiolabeling of allicin has been performed to confirm the expected breakdown components. One extremely beneficial component formed is ajoene and this has also demonstrated significant antiviral properties.

11. PHARMACEUTICAL PARTICULARS

The active agent is allicin. Each capsule contains 300 mg of allicin powder.

11.1 List of excipients

Non genetically modified maltodextrin from maize, gum acacia, silica.

12. MARKETING DETAIL HOLDER

Allicin International Limited, Half House, Military Road, Rye, East Sussex TN31 7NY. United Kingdom.

13. DATE OF FIRST AUTHORISATION

24th April 2000

14. COUNTRIES THAT MARKET ALLISURE PRODUCTS

United Kingdom, Republic of Ireland, Norway, Canada, Denmark, Holland, Belgium, USA, Japan, Hong Kong, Greenland, Iceland, Faroe Islands.

15. LEGAL CATEGORY (United Kingdom)

Health Food Supplement

16. DATE OF LAST REVISION

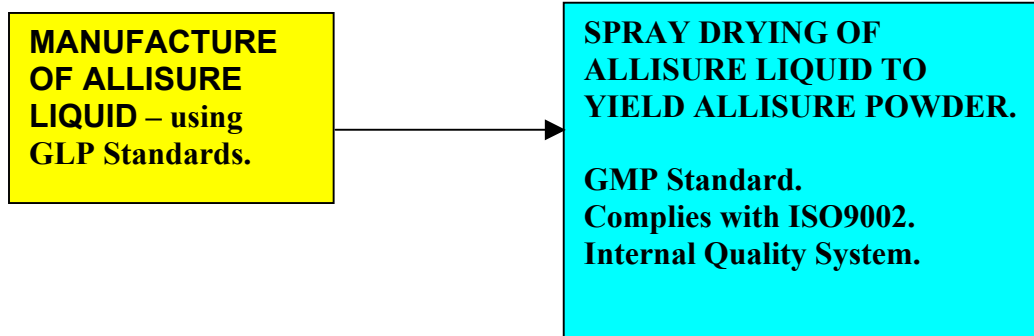
This document was updated in September 2003

SMPC/9/03/PDJ

AXIL Half House, Military Road, Rye, East Sussex, TN31 7NY, UK

- Phone: +44 (0) 1797 227959 • Fax: +44 (0) 1797 223404
- Email: info@allimax.com • website: www.allimax.com

Process flow chart for the manufacture of ALLISURE POWDER



Certificate of Analysis available from Allimax.US

Yeasts – nil
Molds – nil
Salmonella – nil
E. Coli - nil

Prepared by AXIL for Allimax.US 510 W. Erie Street Unit 2202 Chicago IL60610

MANUFACTURING PROCESS – TECHNOLOGY PROCESS

Allsure powder TM is the result of a patented process, which produces purified allicin liquid. It is the first health food supplement to provide a 100% allicin yield, the key active ingredient of fresh garlic.

Garlic is harvested from the Pederonas area near Valencia in Spain where much of this garlic is destined for supermarkets and convenience stores throughout the UK. We are very selective in that only the best quality bulbs are picked for production of Allisure powder. All the garlic under 50mm wide is immediately rejected as too small. Any that has begun to sprout, or is in any way damaged, is removed by the ladies in the pack house.

Once the bulbs have been selected (approximately 2.5kg per 1 million capsules) some of the batch are analysed for alliin content using HPLC and Mass Spectrometry. Once this has been done the garlic is crushed in our special glass apparatus where extra alliin from the same garlic is also added. As the allicin begins to form it is physically removed from the reaction chamber by flooding the system with water. All through this phase the temperature is carefully controlled to within 0.1 degrees C (this increases the yield of allicin liquid) and the whole system is kept at constant pressure. The resultant allicin liquid is analysed by HPLC and immediately frozen for transport to the spray dryer.

At the spray drying house the liquid is carefully added to a reaction vessel along with non GM maltodextrin and gum acacia, where it enters the spray dryer. The resultant powder is Allisure, which is then tested microbiologically against an MRSA bacteria, an HPLC analysis is performed as well as a taste assessment. The powder is then filled into capsules for distribution around the world.

We have seen that Allisure is made from fresh, raw garlic heads that are specifically selected to ensure that they contain a significant enzyme activity (allinase enzyme). Garlic heads are split into cloves, which are left unpeeled and

then subjected to filtration, controlled temperature and pressure extraction and a flood reaction process designed to produce stabilized liquid alliin dissolved in water. No chemical solvents are used. The alliin amino acid in fresh garlic is subjected to complete conversion by the alliinase enzyme and to ensure a large volume of active agent is harvested. Alliin is quickly removed from the reaction system as it competes with and will destroy the enzyme alliinase. The volume of active agent produced is directly related to the enzymatic concentration and activity.

Both the manufacturing process and the application of alliin liquid, powder and crème formulations are protected by PCT Patents filed across the World. The cover all the major areas where we have proven activity from using our patented alliin.

MATERIAL SAFETY DATA SHEET

ALLISURE POWDER® (Stabilised powdered alliin)

1. Chemical name: ALLICIN Nominal Concentration 300 ppm alliin

Contact:
Allimax.US
510 W Erie Street #2202
CHICAGO
Illinois 60610
USA
Telephone 312-640-2926
email info@allimax.us

2. Product Identification ALLISURE POWDER®

Chemical name: thio-2-propene-1-sulfinic- acid S-allyl-ester

Tariff Number: 3302.10.90

CAS Number: 539-86-6

Formula: C₆H₁₀OS₂

3. Hazard Identification Non hazardous

4. First Aid Procedures

Inhalation: Remove to fresh air and seek medical attention if necessary

Skin Contact: Wash with soap and water. Remove contaminated clothing. If irritation persists or tissue damage is evident, seek medical advice.

Eye Contact: Immediately flush eyes with plenty of water, or saline solution for at least 10 minutes. Seek medical advice

Ingestion: Rinse mouth with water. Give water to drink. Obtain medical advice. Do not induce vomiting.

5. Physical and Chemical Properties **Appearance: Off white powder**

Colour: **Colorless**

Odor/Taste: **Fresh crushed garlic**

Density @ 25C **0.998 to 1.002**

Safety and toxicological data exists for garlic. Allicin is produced by a natural substrate flood reaction and is classified as natural.

No restrictions on transport of ALLISURE POWDER® by land, sea, or air.

Batch number: CPC2001/13740 - Analysis: 14/6/03/5 BB 04/05

TESTIMONIALS

David from New York City has been HIV for 10 years and has had full blown AIDS for 2 years. He picked up a serious infection and used large doses of allicin powder capsules to get rid of this infection.

As someone who has had full-blown AIDS for over two years, I can attest to the strength and promise of allicin powder capsules. For a quick example, I was experiencing diarrhoea about once every day or two – and then I started taking the capsules. Since I started using them, I have not had diarrhoea ONCE. I have been using Allisure® powder for about two months now.

More dramatically, when I received my first shipment in the mail, I had been sick for three days with a viral infection and had been feeling worse each day. On the third day, I was really quite miserable and ill, especially realizing, this illness could go on for two or three weeks – or worse. I started taking my first capsule toward the end of that third day, and two days later (Superbowl Sunday evening in the U.S), I was sitting up, eating a Pizza, and enjoying watching television. I was surprised that I felt so much better in such a relatively short (48 hours) period of time. By the end of the third day I felt like I was basically over my viral infection, and that the “bug” had been killed. Naturally, I was not back to full vigor just yet, but each day, on Allisure capsules, I felt stronger, healthier and more vigorous. I was back to my full strength and vigor in about ten days, which is about what it would be for anyone. I was astounded at the healing power that allicin apparently contains. I feel like allicin will, in time, prove itself to be, essentially an “immune system in pill form”, seemingly without any drawbacks, side effects etc. The potential for improved health for humankind could – based on my own personal experience – be enormous, truly staggering.

If allicin could offer this kind of powerful help to someone in my condition, what could it do for people with normal immune systems? Since I’ve started using this product, I have not experienced any other abnormal health problems at all, and I’m not taking any other medicines. I’m now beginning to think that I may be able to “get my life back”, return to work etc. This – as opposed to thinking that my days were more or less “numbered”! I now once again do things that I enjoy – with confidence – for I no longer feel afraid to over-exert myself physically, etc. My life has, relatively speaking, “gone back to normal”. I consider allicin powder capsules to be a medical miracle.

Then a few weeks later David sent me another letter:

More good news – after years of having “borderline-high” blood pressure, my last visit to the doctor tells me my blood pressure is “good”! At first I thought, “How could that be possible? Why would my blood pressure suddenly be so different?” I think it’s the allicin. I can’t think of any other change in my life that might have lowered my blood pressure to such a degree.

Testimonial

Mr KL from Birmingham, Alabama says he started using the liquid as a treatment for Athletes Foot back in February 2002 and continues to take allicin powder capsules each day. The results are different to those of other treatments in that it does not dry out the skin but kills the infected tissue. Therefore, the incidence of cracking between the toes is virtually eliminated. The overall time scale is slightly slower than pharmaceutical drugs but it certainly keeps the complaint at bay. Interestingly it has not returned in over 9 months, which is very unusual as I often get recurrent infections. I find the capsules are easy to take and do not make me smell!

Drug resistant Streptococcus

In the country of Norway a young Mother of 2 children went into hospital for her third child. She was due to have a cesarian section and everything went according to plan and a bonny baby boy was born. Unfortunately, Camilla picked up an infection. This is a pretty common thing to happen, not just in Norway but in just about every country in the world. Camilla had a drug resistant streptococcus and after she was discharged from the hospital her wound failed to heal for several months and she had a systemic infection that made her tired, washed out and unable to look after her new baby or the family. Things got worse, so much so that her husband xxxxx had to take time off work to look after her and the family. Camilla was given successive courses of antibiotics but for months and months she could not get rid of the infection.

Camilla was desparate, she was ill and couldn't bond with her new baby, then one day she read in her newspaper about a new product that kills bacteria – it was a natural plant extract that came from fresh garlic and was called Weissin (the name chosen in Norway for allicin powder products). She contacted the supplier and they told her how to get the product. Camilla took 10 capsules per day, every day for 4 weeks and to her delight she began to feel better, she had already stopped taking the antibiotics and in less than a month the regular specimens she had to provide for the hospital came back negative – no bacterial infection. No bacteria found in her throat, her underarms or her vagina. She was clear, healthy and cured!

So the allicin had completely destroyed a multi drug resistant Streptococcus bacterial infection, Camilla was happy and able to bond with her new baby for the first time since he was born, Her husband was able to return to work and life could at last return to normal.

Drug resistant Acinetobacter baumannii

Acinetobacter infection causes a serious respiratory infection, it is difficult to breathe and to constantly bring up a type of sputum. Recently a middle-aged man who we shall call John was admitted to a London UK teaching hospital – one of the most famous in the world. John was very ill and he was prescribed a number of oral and intravenous antibiotics but nothing worked. The Consultant microbiologist in charge recommended the use of an experimental antibiotic, this was also ineffective. So he decided to use allicin powder capsules (this was because he had already experimented with allicin in the laboratory and seen it kill multi-drug resistant tuberculosis

John was given 10 allicin capsules a day for 2 weeks. Gradually the infection began to respond and to everyone's delight John had made a full recovery and walked out of the hospital 3 weeks after starting treatment with allicin.

Testimonial use

Thrush is the most common form of candida, affecting three out of four women in the UK, and eight out of ten women in the USA, at some time in their lives. One woman tells us what living with candida is really like, and shares advice on managing the condition.

American Jane Jones, 35, lives in Kent, England and has struggled to manage recurring candida infections since her teens.

The first time I got thrush I was only 15 and had no idea what it was. I had a white vaginal discharge and terrible itching – I thought it must be something to do with my periods, or that I'd caught something from a toilet seat. I kept it to myself for a few months until it became really bad. I finally broke down in tears and told my mum, who took me to a male gynaecologist. It was an awful experience, as he seemed to think I was sexually active – which I wasn't. It made me feel dirty. As I now know, although thrush can be transferred to a sexual partner, it's not necessarily caused by sex but by an overgrowth of the candida fungus in the system.

After that first time, the thrush kept on coming back. My mum took me to a couple of female doctors who prescribed the same standard medication, which was Monostat 7 (I was living in America at the time). This was effective at first, but I think I became immune after a while, as I had to take it so often. The doctors also gave me the same advice: don't wear tight jeans, tights or synthetic underwear, avoid perfumed bathing products that can irritate the vagina and always use protection if you are sexually active. The treatments were very focused on the vagina and on curing the symptoms. Nobody ever mentioned dealing with candida throughout the entire body.

A few years later many of the medications I was using became available over the counter so I didn't have to keep going to the doctor and it became easier to self-treat the condition. But the thrush still kept coming back, so I never felt free of it. I remember getting it badly when I was at university. The discomfort and itching were sometimes so severe I thought I'd go mad. I used to scratch myself until it hurt because the pain was better than the itching. I didn't confide in anyone about it. In a way I tried to pretend it wasn't there. I was shy around boys, and the boys didn't help my confidence. Whenever I had an outbreak I felt embarrassed and ashamed, even though there was nothing to be ashamed of. But psychologically it does get you down – you start to feel as if it's somehow your fault.

After university I went to live in London and then got married. During this time I started to feel generally tired and unwell. I was still having thrush all the time, but didn't relate the two – my doctor thought I might have glandular fever. I was reading up on the subject at the time and learnt that candida overgrowth can have more widespread effects on the system, from bloating to chronic fatigue and digestive problems. I started to think that maybe I didn't simply have vaginal thrush; perhaps there was something going on in my whole body. I realised that when the candida is really bad I don't just have thrush – I feel ill, tired and slow, like I can't think straight. One of the worst things is having no energy. I'm usually quite energetic, so feeling so tired for much of the time is very frustrating.

At this time of my life I was so unhappy that I let the candida get me down. It was as though thrush was taking over my body, and I didn't feel like myself any more. I also thought the treatment I'd been having was simply addressing the symptoms of the problem, rather than the root causes, and that's why it kept coming back.

I decided to consult a nutritional therapist, who suggested I follow a strict anti-yeast diet. I was advised to avoid all fungi and products with fermented ingredients, such as bread, cheese and alcohol. At the same time I was, I was also taking a probiotic supplement, acidophilus, to help maintain my body's "good" bacteria and keep the candida in check, and natural supplements such as garlic. My diet was something that I knew I could control and it was great to be able to do something practical, even though it was quite hard to stick to. I had to cut out all sugar, which feeds the fungi, so even seemingly "healthy" food such as fruit was out, as well as things you wouldn't think of, such as peanuts, as they contain a naturally occurring fungus.

I followed the diet for three months and it helped tremendously. I was symptom-free for about four years. Over that period, I gradually returned to eating normally – enjoying fruit, chocolate and sugary foods. I carried on taking acidophilus tablets regularly but I almost forgot about the candida. Then, about

two years ago, I went through a stressful time, took two courses of antibiotics and within a couple of months, started to get thrush again. (I now know it can also be associated with stress, low immunity and using antibiotics, which can disrupt the balance of natural flora in the body.) I used Canesten* cream and pessaries or Diflucan** tablets and it cleared up. But it started to come back more regularly, and became so frequent I went to my GP to check my symptoms weren't connected to anything more serious.

I was tested for diabetes and liver disease, which can both be characterised by recurrent thrush, but fortunately I didn't have either. I cut fruit and sugary foods from my diet again and started taking allicin powder capsules and vitamin C. I'd read about the curative anti-fungal properties of allicin in a book on garlic and found out that *Candida albicans* was one of the most sensitive species. I started on 6 capsules a day for about 4 weeks. At the same time I even tried aromatherapy, which is quite controversial as the treatment involves douching with essential oils and thrush sufferers are normally advised to avoid anything that may cause irritation. But I felt I had nothing to lose. Everything I've tried has had some kind of positive effect, though nothing has managed to keep candida away for good until recently. It has now been 12 months since I started on allicin capsules and I now take just one a day – this seems to prevent the infection from returning, my life is now much more settled and I feel fit and healthy for the first time in years.

Testimonial

Deborah's wounds are on her spine. One close to the top, which is approx. 2cm by 1.5cm this is overgranulated and weeps. The other is approx. 0.75cm by 0.5cm and near her waistline this is overgranulated but only weeps a little. She had a major spinal operation two years ago and although she has had antibiotics through a Hickman line and a wash-out so far nothing has worked. She has been on oral antibiotics and creams for several months but nothing has been able to shift the infection (its called MRSA). The only option now available to her via the hospital is to have all the metalwork removed. As you can imagine she does not want to go back into hospital nor does she want the metalwork removed. We would be very grateful if you could produce a cream and some capsules for her. If you require any further information we can speak to the District Nurses on Saturday. They dress her wounds then whilst I do them during the week.

Just a few weeks later

Dear Peter

I had not been in touch as mum said she had emailed you. I don't think she wanted to get carried away, but the news is very exciting - I no longer have any infection in my back and it is all thanks to the treatments you so generously suggested. Having had these two wounds on my back weeping for 2 years

I don't know quite how to thank you and hope that I get the opportunity to thank you in person at some point. I will also be telling anyone who may benefit from Allicin how miraculous it is.

I am going to the hospital on Thursday. I am not sure if my consultant can quite believe what has happened, as he, along with some of my district nurses, are not too happy about the thought of using alternative remedies. When I think how many courses of antibiotics I have been instructed to take in the last 2 years and how many biopsies came back positive for MRSA, I am not surprised that the medical staff cannot believe it!

The new scented cream sounds great, although I have plenty at the minute. I am running out of capsules, but know where I can buy them.

Thank you once again for all you have done. You saved me from another horrendous operation. Maybe I can repay you in some way. For instance, if it would be of any benefit, I could write something about my experience with MRSA and how Allicin cured it, if that might help promote the product - just a thought.

Yours eternally grateful

Deborah

Earlier this year I was told by our doctor that our daughter was suffering from Molluscum Contagiosum, a condition of the skin which causes wart-like spots which eventually (over a period of months or even years) turn into large and painful pustules which eventually burst, sometimes leaving behind a scar or pit. She was five years old at the time and we had first noticed some spots when she was only two. Gradually, over this time, they had spread from her trunk and arms to her legs, and particularly between her legs and around the genital area.

They were causing her a great deal of discomfort and embarrassment and it was most distressing to hear from the doctor that there was absolutely no treatment for them as they were caused by a virus. We were told that although painful and unsightly, they were otherwise totally harmless and that they would disappear eventually.

When I heard, through a friend, that it may be possible to treat them with garlic, I decided that anything was worth a try. Apparently, garlic has anti-viral properties (among many other benefits including anti-bacterial and anti-fungal). Through the Garlic Information Centre, we were given a bottle of pure allicin liquid (a component of fresh garlic most associated with healing properties) and told to apply it to our daughter's spots twice a day with a cotton bud.

After only three days there was a noticeable improvement, and after a week the spots had completely gone. We were absolutely thrilled and could hardly believe that allicin had worked so effectively and so quickly!

I know from talking to other parents that Molluscum Contagiosum is common in young children and that it seems to be particularly rife at the moment, not just in my area, but countrywide. I would thoroughly recommend trying this treatment. It can do no harm and may work for others as it has for us!

Claudia Macpherson

Allicin from fresh Garlic Nature's Original Antimicrobial

The Englishman's Doctor (Harrington, 1609)

"Garlic then have power to save from death Bear with it though it maketh unsavory breath And scorn not garlic like some that think It maketh men wink and drink and stink"

A rich history

Garlic is one of the edible plants, which has generated a lot of interest throughout human history as a medicinal panacea. A wide range of microorganisms including, bacteria, fungi, protozoa and viruses have been shown to be sensitive to crushed garlic preparations. Moreover, garlic has been reported to reduce blood lipids and to have anticancer effects. Chemical analyses of garlic cloves have revealed an unusual concentration of sulfur-containing compounds (1–3%) [1,2]. A quick search of the medical database at the National Library of Medicine in the USA reveals that garlic is top of the league for published research papers that cover a wide variety of disease conditions, the most prevalent of which are its significant antimicrobial properties.

National Library of Medicine

Research papers on popular herbal supplements since published since 1963

Garlic 1600

Ginseng 1550

Hypericum 650

Ginkgo 855

Tea Tree 103

Analysis of steam distillations of crushed garlic cloves performed over a century ago showed a variety of allyl sulfides. However, it was not until 1944 that Cavallito and his colleagues [3] isolated and identified the component responsible for the remarkable antibacterial activity of crushed garlic cloves. The compound turned out to be an oxygenated sulfur molecule, which they termed allicin, from the Latin name of the garlic plant, *Allium sativum*.

The debate on the presence of allicin in crushed cloves versus its absence in odourless intact cloves was resolved after Stoll and Seebeck [5] isolated, identified, and synthesized an oxygenated sulfur amino acid that is present in large quantities in garlic cloves and which they named alliin (*figure 1*). Alliin was found to be the stable precursor that is converted to allicin by the action of an enzyme termed allinase, which is also present in the cloves [6].

The transformation of alliin into the biologically active allicin molecule upon crushing of a garlic clove is extremely rapid, being complete in seconds. The enzyme responsible for this conversion is allinase, which is present in unusually large amounts in garlic cloves: at least 10% of the total protein content (10 mg/g fresh weight).

Garlic cloves are odor-free until crushed or processed when garlic supplements are manufactured and cross-section studies have indicated that the substrate alliin and the enzyme allinase are located in different compartments [2, 6]. This unique organization suggests that it is designed as a potential defense mechanism against microbial pathogens in the soil. Invasion of the cloves by fungi and other soil pathogens causes the interaction between alliin and allinase that rapidly produces allicin and which in turn inactivates the invader. The reactive allicin molecules produced have a very short half-life, as they react with many of the surrounding proteins, including the allinase enzyme, making it into a quasi-suicidal enzyme.

This very efficient organization ensures that the clove defense mechanism is only activated in a very small location and for a short period of time, whereas the rest of the alliin and allinase remain preserved in their respective compartments and are available for interaction in case of subsequent microbial attacks.

Cardiovascular properties

Successful clinical use of garlic for treating elevated blood pressure and arteriosclerosis has been known since the early part of this century. It has been reported that regular garlic intake causes both a prolonged lowering of hypertension and an improved sense of well-being in patients. As early as 1928, definite blood pressure decreases were achieved as well as increases in productive heart power with garlic therapy, not only in older patients, but also in younger hypertonic patients.

Type of supplement	Fresh garlic source declared on pack	Process to manufacture supplement	Allicin potential	Published blinded clinical data
Garlic Oil	No	Steam distillation	No	No
Aged Garlic	No	Aged over 2 years	No	Some
Garlic Macerates	No	Crushed and dried Some		No
Garlic powder	Sometimes	Cloves chopped and dried under pressure and temperature control	Yes (Stomach acid protection needed)	Yes
Allicin powder extract	No	Specialised patented extraction process produces allicin liquid that is spray dried Product	is allicin	Yes

Table 1 Types of garlic supplement found on Healthfood Store shelves

It is also well established that garlic extracts, in particular the powders can show a significant anti-cholesterol activity. A 12 week study comparing the effect of standardised garlic powder tablets (900mg daily) with that of bezafibrate (600mg daily), one of the most commonly prescribed blood lipid-lowering drugs until the advent of the statins, has also been conducted. The multi-centre, double-blind study was performed with 94 patients having cholesterol and/or triglyceride vales exceeding 250mg/dL. After 4 weeks of treatment, the decreases in cholesterol, LDL cholesterol, and triglyceride levels were all statistically highly significant, and there were no differences between the effects of garlic and bezafibrate. HDL cholesterol values in the course of 4 weeks also increased significantly, again without any differences between the two regimens [14].

Antibacterial activity of allicin

The antibacterial properties of crushed garlic have been known for a long time. Various garlic preparations have been shown to exhibit a wide spectrum of antibacterial activity against Gram-negative and Gram-positive bacteria including species of *Escherichia*, *Salmonella*, *Staphylococcus*, *Streptococcus*, *Klebsiella*,

Proteus, *Bacillus*, and *Clostridium*. Even acid-fast bacteria such as *Mycobacterium tuberculosis* are sensitive to garlic [10]. Garlic extracts are also effective against *Helicobacter pylori* the cause of gastric ulcers [11]. Garlic extracts can also prevent the formation of *Staphylococcus* enterotoxins A, B, and C1 and also thermonuclease [12]. Cavalito and Bailey [4] were the first to demonstrate that the antibacterial action of garlic is mainly due to allicin [3]. The sensitivity of various bacterial and clinical isolates to pure preparations of allicin [14] is very significant. As shown in *table 2*, the antibacterial effect of allicin is of a broad spectrum. In most cases the 50% lethal dose concentrations were somewhat higher than those required for some of the newer antibiotics. Interestingly, various bacterial strains resistant to antibiotics such as methicillin resistant *Staphylococcus aureus* as well as other multidrug-resistant enterotoxigenic strains of *Escherichia coli*, *Enterococcus*, *Shigella dysenteriae*, *S. flexneri*, and *S. sonnei* cells were all found to be sensitive to allicin.

Bacterial Strain	Allicin Concentration (LD50 µg/ml)	Comments
<i>Escherichia coli</i>	15	Sensitive to antibiotics
<i>Escherichia coli</i>	15	Multidrug resistant MDR
<i>Staphylococcus aureus</i>	12	Sensitive
<i>Staphylococcus aureus</i>	12	Methicillin resistant
<i>Streptococcus pyogenes</i>	3	Sensitive
<i>Streptococcus</i> â <i>hemolyticus</i>	>100	Clinical MDR strain
<i>Proteus mirabilis</i>	15	Sensitive
<i>Proteus mirabilis</i>	>30	Clinical MDR strain
<i>Pseudomonas aeruginosa</i>	15	Sensitive to cefprozil
<i>Pseudomonas aeruginosa</i>	>100	MDR mucoid strain
<i>Acinetobacter baumannii</i>	15	Clinical isolate
<i>Klebsiella pneumoniae</i>	8	Clinical isolate

Table 2 Bacterial species sensitivity to aqueous garlic extracts containing allicin

Most recently the University of East London have shown that aqueous extracts of allicin when formulated into a simple cream are able to kill vast swathes of the so called "superbug" MRSA (methicillin resistant *Staphylococcus aureus*). This nasty bacterium is forever changing its structure and developing resistance to many pharmaceutical antibiotics. This may have a significant effect on people who suffer from skin diseases such as eczema and acne as this bacterium is 6 to 7 times more likely to colonise these patients.

Methicillin resistant *Staphylococcus aureus* with plain aqueous cream

Methicillin resistant *Staphylococcus aureus* with allicin cream added (Allimax cream) showing a large zone of inhibition

Immunomodulatory Effects

There is a growing body of evidence that garlic may have significant enhancing effects on the immune system. While most of the work has been conducted on animals or in vitro, the human studies that have been conducted are encouraging.

Preliminary studies in humans, using an alliin standardised garlic powder preparation, have demonstrated positive effects on immunoreactions and phagocytosis. In geriatric subjects, the administration of 600mg garlic powder per day for 3 months induced significant ($p < 0.01$) increases in the percentage of phagocytosing peripheral granulocytes and monocytes when tested ex vivo for their ability to engulf *Escherichia coli* bacteria. The cell counts of lymphocyte cell sub-populations were also increased. Another human study was conducted with an unrefined garlic extract (5-10 g/day) which was given to AIDS patients. For the seven patients who completed the 12-week study, there was a major increase in the percent natural killer cell activity from a seriously low mean value of $5 \pm 4\%$ to a more normal mean value of $36 \pm 15\%$ [16].

The biological activity of allicin extracted from fresh garlic is thought to be related to a combination of factors:

1. its activity as an antioxidant
2. its ability to attack the sulphur (SH) groups in enzymes and proteins and modify their activities and
3. its ability to rapidly penetrate into cells through the cell membranes.

Laboratory Studies

Allicin has a number of beneficial properties, which could act together to enhance the bodies response to disease. Published laboratory studies (3) have found that allicin:

- Enhances the activity of phagocytic cells
- Enhances the activity of natural killer cells
- Inhibits the growth of pathogenic micro-organisms
- Inhibits the growth of certain cancer cells

One of the main problems with laboratory studies has been the purity of the extracts used, only recently has a purified, natural, stable extract of allicin

become available for testing. Recent studies in our own laboratory have confirmed the antibacterial activity of this purified allicin extract against a number of different bacteria including multiply antibiotic resistant *Staphylococcus aureus* (MRSA). Clinical trials with this substance are currently underway.

Clinical Trials

In the USA, trials in AIDS patients have demonstrated enhancement of natural killer cell activity using garlic extracts and Chinese studies with viral infections in bone marrow transplant patients have demonstrated a “potent antiviral activity”. Human population studies have shown that regular intake reduces the risk of oesophageal, stomach and colon cancer. This was thought to be due to the antioxidant effect of allicin in reducing the formation of carcinogenic compounds in the gastro-intestinal tract. A double blind placebo controlled survey using a 100% allicin yielding supplement has reported that allicin can reduce the occurrence of the common cold and the number of days needed to recover from symptoms [17].

Garlic has the potential to assist the immune system in a number of different ways, stimulating immune cells, killing pathogens and detoxifying carcinogens. Although the compound can be obtained directly from fresh garlic bulbs, one would have to regularly eat large amounts of cooked garlic to obtain any beneficial effect and few of us can eat large amounts of raw garlic. This leaves us with liquids and powders. Given the importance of the agent, any garlic liquids or powders should give an indication of the amount of allicin available from the product; many do not.

Contraindications

Taking too much garlic can hinder blood clotting and it would be sensible for people already on anticoagulants or those about to undergo surgery to advise their medical team before starting therapy with ANY garlic supplement but contrary to popular belief it is not a contra-indication. Garlic can also cause reactions in people who are allergic.

The identity of the active compounds for the effects thus far observed on the immune system with garlic and garlic products is far from conclusive. Since both allicin-derived garlic oils as well garlic extracts not containing allicin are effective *in vivo* at moderate doses, it appears that both allicin and other unidentified compounds are responsible for the effects. Both types of compounds may be important to the overall effects of garlic, since the immune system involves several types of cell, each of which may be affected differently, as has been indicated in the *in vitro* studies.

The future of garlic research – its anticancer activity

A very important epidemiological (prospective cohort) study for Americans has recently been published in which the intake of 127 foods (including 44 vegetables and fruits) was determined in 41,387 women (ages 55-69) followed

by a five-year monitoring of colon cancer incidence [18]. The most striking result of this "Iowa Women's Health Study" was the finding that garlic was the only food which showed a statistically significant association with decreased colon cancer risk. For cancers anywhere in the colon, the modest consumption of one or more servings of garlic (fresh or powdered) per week resulted in a 35% lower risk, while a 50% lower risk was found for cancer of the distal colon. Both a critique of this study and a good reply by the authors have been published hence one could predict that the future is bright the future is garlic.