



# A natural new approach to treating MRSA

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## ALLIMED treats MRSA patients successfully

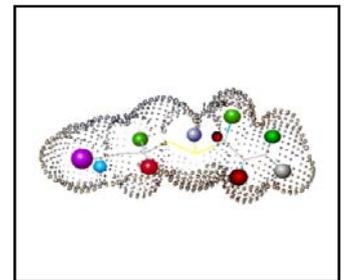
### How does Allicin work?

- Stabilised extract of Allicin confirmed by HPLC and Mass Spectroscopy
- Allicin kills MRSA
- Allicin kills multi-drug resistant strains of MRSA
- Allicin can penetrate cell membranes
- MIC's can be lower than 16 mg/l
- Weeping lesions are dried
- MRSA infection is removed
- Patients report improvement in 2-3 weeks
- All formulations well tolerated and free from side effects
- Previous antibiotic treatments had failed
- Research centres are needed for further studies
- Other problem species have been killed

Stabilised allicin has now been formulated into an active range of products called Allimed™. Powdercapsules, liquid, soap and cream presentations all show highly significant activity against multi-drug resistant organisms including MRSA. The mechanism of action of allicin may be due to inhibition of certain thiol-containing enzymes in the microorganisms by the rapid reaction of thiosulfonates with thiol groups. This was assumed to be the main mechanism involved in the antibiotic effect of allicin. Recent studies have suggested that the mechanism of action of Allicin may be its ability to react with a model thiol compound (L-cysteine) to form the S-thiolation product S-allylmercapto-cysteine.

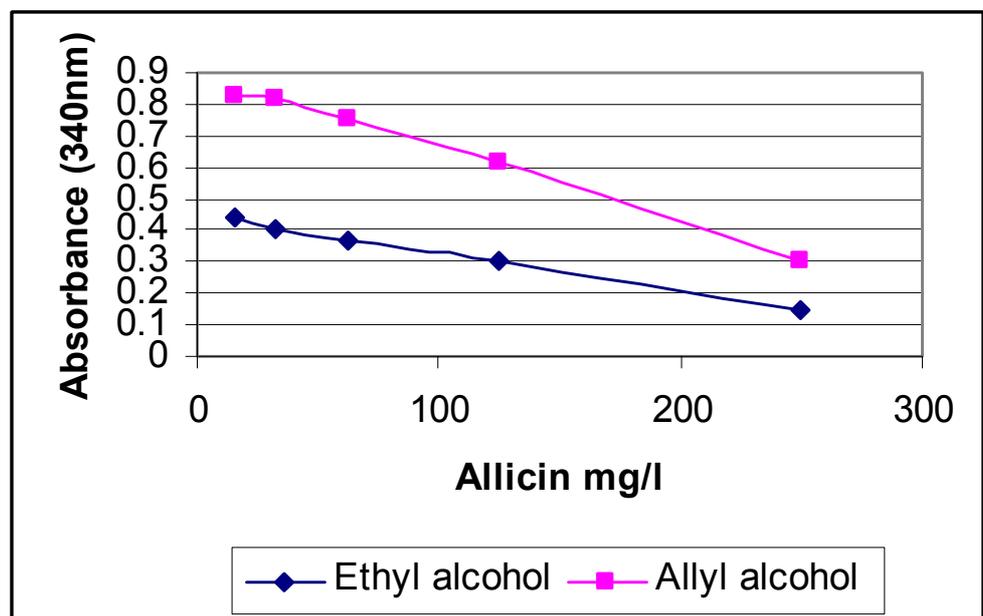
The identification of the thiolation product was proven by nuclear magnetic resonance as well as by mass spectroscopy. The main antimicrobial effect of allicin is due to its interaction with important thiol-containing enzymes. In the amoeba parasite, allicin was found to strongly inhibit the cysteine proteinases, alcohol dehydrogenases as well as the thioredoxin reductases (Ankri *et al.*, unpublished results) which are critical for maintaining the correct redox state within the parasite.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 mg/mL). Allicin also irreversibly inhibited the well known thiol-protease papain, the NADP<sup>+</sup> dependent alcohol dehydrogenase from *Thermoanaerobium brockii* and the NAD<sup>+</sup>

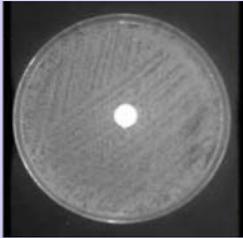
dependent alcohol dehydrogenase from horse liver. Figure A shows the effect of allicin on alcohol dehydrogenase activity using 2 different alcohol substrates. This indicates the level of alcohol dehydrogenase activity in the solution. There is a clear relationship between reduction in activity and increasing allicin concentration (mg/l). The concentration of enzyme used in the experiment remained constant.



The Allicin molecule is small and easily penetrates cell walls

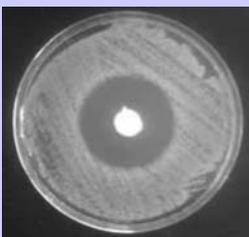
Figure 1: The effect of allicin on alcohol dehydrogenase activity using 2 different alcohol substrates. Absorbance is measured at 340nm





No zone was found when using mupirocin cream on at least 30% of MRSA strains tested

“Due to national publicity, patients with long standing infections requested treatment with Allimed™”



Large zones of inhibition are reported with 500ppm alliin as seen in Allimed Cream

**Inside Story Headline**

Alliin is recognised as the main bioactive agent from *Allium sativum* or garlic. This compound is highly active but generally unstable. Using a cold aqueous extraction method, we have obtained a novel extract of alliin (Allimed™) that we have reported is stable and highly active *in vitro* against methicillin resistant *Staphylococcus aureus* (MRSA). Due to national publicity of Allimed™, patients with long standing unresolved MRSA infections requested this agent for treatment. MRSA is commonly related to delayed closure for many chronic and acute wounds.

This is associated with high levels of bacteria in tissues but they can also close through toxin secretion. These toxins can cause local necrosis and disrupt the delicate balance of critical mediators such as cytokines and proteases necessary for healing progression. Alliin has been reported to have a strong SH-modifying and antioxidant properties. Alliin reacts very rapidly with free thiol groups, via a thiol-disulphide exchange reaction. The main antimicrobial effect of alliin may be due to its chemical reaction with thiol groups of various enzymes, e.g. alco-

hol dehydrogenase, thioredoxin reductase, and RNA polymerase. In previous work we have demonstrated that alliin is bactericidal against MRSA at concentrations of 128 to 256 ug/ml (Figure 2). We present initial findings from three patients who have completed a course of treatment. These courses consisted of Allimed™ capsules (450mg, 3 per day); spraying liquid Allimed™ (1000 ug ml<sup>-1</sup>) onto the affected areas once per day and applying Allimed™ Cream (500 ug ml<sup>-1</sup>) to the infected area once daily.

**Patients recruited**

Patients were screened, nasal and wound for MRSA prior and during treatment. All patients were nose and wound swab MRSA positive prior to treatment. All were over 60 years of age and had either major surgery or long term skin infections leading to the formation of ulcers infected by MRSA. Two of the MRSA infections were community acquired and one hospital acquired. The

strains isolated from each patient were tested *in vitro* against Allimed™ and all were susceptible. Patients reported an improvement in their condition after 2 and 6 weeks treatment and the infections resolved in 3 to 4 months, see figures 2 and 3. Although the timescales required for treatment may be longer than those nor-

mally required using antibiotics, the initial relief from weeping ulcers and pain was much quicker. It should be noted these the patients had been receiving unsuccessful treatment with antibiotics for months or years prior to treatment with Allimed™. A possible reason for the initial relief from symptoms could relate to the reported activity of alliin extracts to

**Figure 2**  
**Minimum Inhibitory and Minimum Bactericidal Concentrations (MIC/MBC) of Alliin against 30 Clinically Isolated strains of MRSA**

	MIC 16 mg/l	MIC 32 mg/l	TOTALS
MBC 128 mg/l	76%	12%	88%
MBC 256 mg/l	12%	0	12%
TOTALS	88%	12%	100%

## Reduced enzyme activity

neutralise bacterial exoenzymes *in vitro*. In initial studies we have demonstrated that even after brief exposure, allicin can reduce the activity of microbial enzymes. The activity of alcohol dehydrogenase in producing NADH from NAD<sup>+</sup> was reduced as the concentration of allicin in the solution increased (figure 1). The potential ability to reduce the activity of extracellular virulence factors account for the findings that patients got relief from their symptoms before the MRSA were fully removed from the lesion site.



**Figure 3:** Picture on the left shows weeping inflamed lesions (before allicin treatment). The picture on the right shows that the lesions have dried and are healing after 3 months treatment with Allimed™ capsules, liquid and cream. No side effects were reported by the patient.

## Chronic leg wound



**Figure 2:** Pictures of leg wounds before and after 2 months treatment using only Allimed™ capsules, liquid and cream formulations. The picture left shows a red inflamed weeping lesion before allicin treatment.

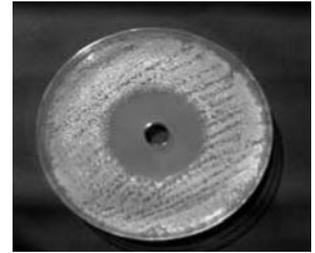


The picture left shows the inflammation has reduced and the lesion is healing. The patient reported a feeling of more energy and no side effects. Several other antibiotic courses had failed to show any degree of success

## Safety and toxicology confirm allicin is safe

Recent independently conducted safety and toxicological testing of Allicin powder and liquid extracts have confirmed safety of both presentations. Acute oral toxicity studies showed that a single dose of 2000 mg/kg had no adverse effects on Sprague Dawley rats.

Tests were conducted in Scottish laboratories. With millions of people already exposed to allicin the safety and side effect profile is generally favourable. Allimed™ can be safely added to almost any other pharmaceutical agent including Warfarin.



An average Zone of inhibition against MRSA observed with allicin liquid (Allimed™ Spray)

**“The initial relief from weeping ulcers and pain was much faster than recorded with pharmaceutical antibiotics”**

**“All patients are now free from MRSA infection”**

