Garlic in the Marine Aquarium:
How it may work against Marine Ich

Diallyl thiosulfinate activity against *Cryptocaryon irritans* infestations of marine fish

by Horge Cortes-Jorge Jr. , 12/31/00.

I. The Pungent Rosebud

Garlic has received a noticeable amount of attention in the Westernized portion of the marine-aquarium hobby the past three years, though in truth garlic has been incorporated in tonics and feed for domesticated fish for decades in Asia (pers.obs., author). The hobby is now fairly garnished with anecdotes about the efficacy or futility of garlic treatments, which have been applied against diverse infections and infestations of marine fish.

It is naturally difficult to gauge the overall value of garlic therapy for diseased fish, given that the diseases treated vary as widely as the dosage and the delivery vehicle. Nevertheless, a quick review of hobbyist claims on internet discussion boards reveals a mostly-favorable assessment by those who've used it to treat parasitic infestations, particularly cryptocaryosis, also known by the epithet "Marine Ich". That disease is authored by the ciliate protozoan parasite *Cryptocaryon irritans*, and it is upon that disease that much of the proceeding discussion dwells.

A thorough description of the life cycle of *C. irritans* is beyond the scope of this article, and indeed might generate some contention on its own. Suffice to say that a free swimming form, or tomite, locates a host fish, and proceeds to attach to and anchor/burrow into the host as a trophont. In time the fattened trophont forms a 'cyst', called a tomont, in which many young tomites begin development, this tomont may 'hatch' either on the fish, or detach to fall to the substrate and release the little tomites.

I hope here to help point towards clues to why garlic might work, in particular against cryptocaryosis. Also why, under certain circumstances, it might not.

II. Clove Med?

Allicin, a.k.a. Diallyl thiosulfinate (or Diallyl disulphide-oxide), has been identified as the chief active pharmaceutical ingredient in garlic (*Allium sativum*). Allicin is a broad-spectrum agent against both Gram+ and Gram- bacteria (Cavallito, 1944; Adetumbi & Lau, 1983; Ankri & Mirelman, 1999) with a scope of applicability about as wide as penicillin's, though less potent.

Allicin also works against at least some viruses (Weber et.al., 1992), and some parasitic protozoans (Lun et.al., 1994; Ankri et.al., 1997) Lastly, some of its rapid-breakdown products, ajoene in particular, possess considerable anti-fungal properties (Yoshida et. al.,1987). Of course, garlic also yields other active compounds, and they too have some pharmaceutical value, but are said to be decidedly less potent than the chief active

ingredient.

Allicin is naturally produced when garlic is damaged or crushed, allowing the release and inter-reaction of two substances, the non-protein amino acid alliin and the enzyme alliinase (Krest & Keusgen, 1999). In that sense, allicin is an all-around defense of the garlic plant, manufactured fresh, right where trauma to the plant occurs and where the threat of invasion or infection is imminent. Not surprisingly, it reportedly has insect repellent properties as well.

Allicin further has a remarkable ability to permeate living tissue (Miron et.al., 2000). That is why it is hard to get garlic's smell off your skin after contact with the raw material --it really digs in, penetrating tissue with comparative ease, and this has implications on its potency.

Hobbyist attention presently seems to center on garlic's value as therapy versus infestations of *C. irritans*, and so I shall get right to such a scenario, focusing on allicin as the active ingerdient of garlic.

III. Allicin Wonderland

In a parasitic protozoan infestation similar to "Marine Ich",there are usually two major insults to the fish's physiology:

1) the gross tissue damage committed by the protozoans themselves;
2) and the secondary infections that crash the party.

The applicability of such a broad-spectrum antiseptic as contained in garlic towards fending off secondary infections should be obvious, so I will set aside such secondary infections at this point.

Allicin has been observed to suppress the efficacy of cysteine proteinase and alcohol dehydrogenase, two tissue-demolition agents produced by another protozoan parasite, *Entamoeba histolytica*, (Ankri et.al., 1997), and one can easily extrapolate how garlic medication might limit the invasive and predatory damage caused **directly** by *C. irritans*.

Yet what generates as much (if not more) speculation is not the ability of garlic to restrict damage, but rather garlic's apparent ability to **deliver** damage to the parasites themselves - with numerous claims of outright detachment of *C .irritans* trophonts (the burrowing protozoans) and tomonts (the "egg cysts") as a result.

The aforementioned ability of allicin to permeate tissue and mucus enables it to invest an afflicted area thoroughly with its partially sulfurous chemical signature. The potential is there to mask the chemical cues that enable a parasite's recognition of the host, potentially confusing the invader and further suppressing the havoc it wreaks. This means garlic therapy can benefit even uninfested fish, allowing them to escape detection by host-hunting *C. irritans* tomites

Definitely, allicin brings outright chemical assault to the parasite. In one test, allicin's cytotoxicity fell heavily against the parasitic protozoans *Trypanosoma spp*. and *Giardia lamblia* in concentrations that were well within the tolerance of sample-host fibroblasts (Lun et.al., 1994). The same penetrating power that ensures thorough investiture of the contested tissue, with protective and camouflaging agents, can also ensure thorough delivery of allicin's antagonism to --indeed, into-- invading parasites.

Lastly (though certainly, other properties may yet be discovered), allicin is said to

reinforce the cues for cellular apoptosis, the mechanism of programmed cell-death (Thatte et.al., 2000). An innate mechanism such as apoptosis, guided with care, has the potential to severely limit the spread of say, cancer, by motivating cancerous cells to quickly self-terminate before they can multiply. If such a 'scorched earth' defense can be triggered by an infestation episode and be guided/reinforced by allicin, then yet another way may be revealed how garlic hinders both the ability of parasites to feed on host tissue and any opportunity for secondary infections to spread.

To recap, allicin can:
1) Hamper the chemicals used by parasitic protozoans to destroy host tissue
2) Fend off opportunistic secondary infections
3) Camouflage host tissue against recognition by the parasite
4) Directly damage the parasite

If this all sounds too good to be true, there are most assuredly vast wrinkles to the fabric woven thus far.

IV. The Catch

There are, admittedly, problems to allicin use.
Allicin is described as an unstable and highly reactive substance. Granted, some of its more stable breakdown products and siblings are not without pharmaceutical properties, but they are apparently of a lesser order of significance in garlic's overall value.

If the chief active ingredient is unstable and highly reactive, then commercial garlic-based products, by virtue of the various preparation processes they undergo, have lessened ability to yield allicin. To wit, judicious re-hydration of some dried garlic products can reinitiate the alliin-plus-alliinase synthesis of allicin, but much of those two reactive components will have already been expended in the course of industrial processing. Anyway, whether using processed or fresh garlic, the clock is running from the moment garlic is crushed to the moment its active ingredients are finally delivered to the host's afflicted parts, and there is no shortage of neutralizing substances barring the way.

It is at this point useful to take a step back and consider how garlic in any form is presently being used in marine aquaristics: either it is fed to the fish or added straight to the water.

There are two big problems with feeding garlic to fish.
First is the way that an acidic (pH 3 or lower) environment like, say, in the gastric cavity, can irreversibly neutralize alliinase (Lawson & Hughes, 1992). Without that enzyme, no allicin can be formed in such an acidic stomach no matter how much alliin might be ingested. Certainly, better information on the chemistry of gastric juices in fish would be useful.

Second, presuming some allicin does form, and it travels out from the gut into the bloodstream, allicin’s sheer reactiveness would seem to prevent it from getting past the vigilance of the liver, let alone past hostile interaction with blood itself, which results first in reduction of hemoglobin to methemoglobin, the latter incapable of oxygen transport to cells and organs ("brown blood disease" in fishes) --and second in neutralization of the allicin (Freeman et.al.,1995). In one experiment, substantial damage to a rat’s liver cells was sustained at the concentrations of allicin required for some of it to get past (Egen-Schwind et.al., 1992). A better understanding of fish blood and fish liver reactivity (as opposed to those of humans and the more common lab animals) towards allicin would be very useful, but the available data nevertheless suggests --at first glance-- that orally is not

the way to administer allicin.

Indeed, much literature points towards topical application as being effective, and oral administration as futile. So, why do we have numerous relations of success from hobbyists, after oral administration of garlic?

Obviously, the aquatic environment presents additional challenges to topical administration --but the gastric and hemic barriers remain to confound oral administration. How to overcome those barriers? How to explain the success stories?

Mastication by a fish cannot be so thorough as to deliver a fine garlic puree to the stomach (otherwise, many gut surveys in the field would be pointless), and thus stomach acids cannot thoroughly neutralize all enzyme before some allicin is synthesized. Garlic is at that point effective against at least gastrointestinal parasites and infections.

Let us assume that some allicin in the belly of the beast might then somehow proceed outward, and this is usually imagined as being through the blood vessels lining the gastrointestinal wall. The reactive, neutralizing embrace of both blood and liver has already been mentioned, but there are perhaps two ways to defeat those barriers and explain the 'success stories'.

First, the quantity of garlic fed might be massive enough to produce sufficient allicin to overwhelm the blood-and-liver barricade. Liver and hemoglobin damage be damned, some allicin thus reaches the infested tissue.

Second, and more elegantly, a backdoor of sorts is made obvious by recognizing that allicin formation begins even before digestion (indeed it should start even before acquisition and mastication). Already-formed allicin can rapidly permeate through tissue outward from the mouth and pharynx as the morsel travels to the stomach, or even along the dermal mucus of the fish from the mouth outward.

By traversing tissue and mucus on its own rather than relying on the circulatory system alone for transportation, allicin may avoid more massive, neutralizing exposure to liver or blood. Even from the gut, allicin has some opportunity to travel though tissue rather than blood vessels exclusively. It thus might reach afflicted tissue without concentrated damage to host blood and liver, nor depletion of itself arising from such contact. Obviously, the less tissue there is to traverse, the better, and relatively small-bodied creatures like most marine ornamental fish have it pretty good in this regard.

Ingested allicin bypassing or overwhelming the hemoglobin barricade, and reaching the afflicted area, is thus at least theoretically possible (setting aside any resulting damage to the host).

An important point is that it is not only allicin that is in play. While allicin's chemical siblings and children, born of the same garlic, may be less potent, they are more stable. Even if allicin formation is restricted to the gastric cavity, and even if its transport is restricted to blood vessels, and yes, even if no allicin gets past the liver... its breakdown products may remain drifting in the bloodstream, and by themselves may effect (at the barest minimum) the camouflaging of host tissue described earlier.

Now, if oral administration can somehow be effective, how about administration by broadcast of garlic extract to the water? It certainly at first blush seems more akin to the so-called “correct" method of delivery: topical application. But there is the obvious problem of dilution, and the thick biological soup that passes for tank water waiting to once again,

neutralize any allicin. Conceptually, this is much the same barricade that hemoglobin presented to ingested allicin in the preceding paragraphs.

You can again either overwhelm this barrier via massive dosage, with the risk of impact this time on microorganisms throughout the aquarium, or, you bypass contact with the water.

It has been suggested that oily-vehicle garlic preparations may better preserve any active ingredients against dilution AND water-borne neutralizing agencies, long enough for the vehicle and payload to come in random contact with more receptive, afflicted tissue. However, the trouble with oily vehicles is specific gravity: the payload in such vehicles can remain bobbing on the surface of the water, reducing the probability of delivery to the afflicted fish. It is here worth noting that oil-macerated garlic was found to yield a lesser amount of total thiosulfinate, and scant allicin, compared to ordinarily-crushed garlic (Yoshida et.a.l,1999). In the aquatic context, rather than protecting garlic's potency, oil tends to incarcerate it.

On the merits of the above scenarios, it would seem that oral administration has a better chance of delivering the payload to the target. Both oral administration and direct broadcast into the water run the risk of an overdose producing significant collateral damage, but oral administration tends to limit any such 'friendly fire' to the fish being treated, rather than potentially affecting the biology of the whole aquarium.

We have to focus on the fact that we are comparing oral and topical administration of allicin from the simple points of view of efficiency and reduced risk of collateral damage. One method may prove more 'efficient' at delivering allicin, but by default increases the risk of accidental overdose! This seemingly brings us to a question that clinicians really ought to answer: what is the correct dosage?

There may be an impulse to seize upon Lun et.al. (1994) and wring out of their data a correct dosage of garlic. The 1994 study obtained the effective concentrations of allicin needed to reduce a parasitic protozoan metabolism by 50% (IC50). The figures yielded were <5.5micrograms/ml for diverse *Trypanosoma spp*., 14micrograms/ml for *Giardia lamblia*, and 59 micrograms/ml for *Entamoeba histolytica*. The IC50 for the host fibroblasts (from *Homo sapiens* and *Mastomys natalensis* --an African Soft-Furred Rat) was at about 25 micrograms/ml. These values are derived from in vitro conditions, and involve rather exotic host species (from a reef aquarist's point of view), and so they are of limited value in bringing us any closer to a marine-aquarium standard prescription formula like "X milligrams of garlic medication per Y grams of patient tissue, over Z days".

Such a practical result (defining correct dosage) was not our objective here. Rather, it was to examine the possible pathways towards the claimed efficacy of garlic treatments against cryptocaryosis. I focused mostly on just one of garlic's active ingredients, allicin, based on the prominence assigned it in cited references spanning half a century.
My goal was, simply, to try better arm the ongoing discussions with theory, basic principle, and occasional hard data.

V. Capitulation

We know that the chief active ingredient in garlic is allicin, and we know many of the pathogens that it (and its derivatives/siblings) can be effective against, including bacteria, viruses, fungi, and parasites.

Focusing on cases of cryptocaryosis, I have noted how allicin fends off secondary infection and restrains certain chemicals that parasitic protozoans use to damage host tissue.
I have noted how easily allicin permeates living tissue, and have suggested how allicin might render host tissue unrecognizable to parasites. Furthermore, I have noted how allicin directly attacks protozoan parasites.

Examination has been made of some limitations and complications attending the use of allicin, beginning with its instability and potential to harm the patient's circulatory system. I have described some of the many barriers both within the patient's body and without, and considerable verbiage was let loose (and the author thanks the reader for their patience) in the course of exploring how such barriers might be overcome.

Lastly, the assessment has been made, that while research focused on terrestrial models suggests that topical application of allicin is best, an aquatic model bearing inherent risk of immediate dilution/neutralization seems to shift favor to oral administration of garlic pharmaceuticals to afflicted fish.

It is certainly my prayer that the foregoing has at least opened up some aspects of garlic therapy for further inquiry, and to aid in ongoing hobbyist discussion of garlic's merits. But I would be the first to point out that any such discussion is hampered by the lack of clinical studies specifically grounded in marine aquaristics.

The past few years have seen an increase in research into garlic's pharmaceutical potential, the accumulation of earlier research having attained sufficient mass to support more detailed inquiry and experimentation. Commercial interests, and the incentives they offer, incline most of the research towards relevance in the profitable arena of **human** health issues.

Marine-context applications of garlic-based pharmaceuticals are naturally **not** the center of focus for much research.

Ironically, there is left at least one sizeable source of information on garlic treatments specifically grounded in the context of marine aquaristics: those very stories, those anecdotes of experiences with garlic, that beggared explanation and motivated this article in the first place. In their present forms, such anecdotes avoid utility as data . What is keenly missed is a heightened ability to intelligently and systematically observe, describe, record, and share such experiences among all marine aquarists. Otherwise all this potential data, from so many informal and individual trials of garlic and its derivatives, goes largely to waste.
Hopefully, this discussion, even if partially, avoids such a fate.

VI. References and Further Reading

Adetumbi MA, Lau BH. Allium sativum (garlic)--a natural antibiotic. *Med Hypotheses* 1983 Nov;12(3):227-37

Agarwal KC. Therapeutic actions of garlic constituents. *Med Res Rev* 1996 Jan;16(1):111-24

Ankri S, Mirelman D. Antimicrobial properties of allicin from garlic. *Microbes Infect* 1999 Feb;1(2):125-129

Ankri S, Miron T, Rabinkov A, Wilchek M, Mirelman D. Allicin from garlic strongly inhibits cysteine proteinases and cytopathic effects of Entamoeba histolytica. *Antimicrob Agents Chemother* 1997 Oct;41(10):2286-8

Cavallito, C. J. and Bailey, J. H. (1944). Allicin, the antibacterial principle of *Allium sativum*. I. Isolation, physical properties and antimicrobial action, J. Amer. Chem. Soc., 66, 1950-1951.

Cavallito, C. J., Buck, J. S. and Suter, C. M. (1944). Allicin, the antibacterial principles *of Allium sativim*. II. Determination of the chemical structure, J. Am. Chem. Soc., 66, 1952-1954.

Egen-Schwind C., Eckard R. and Kemper F.H. Metabolism of Garlic Constituents in the Isolated Perfused Rat Liver. Planta Medica, 58: 301-305, 1992

Feldberg RS, Chang SC, Kotik AN, Nadler M, Neuwirth Z, Sundstrom DC, Thompson NH. In vitro mechanism of inhibition of bacterial cell growth by allicin. *Antimicrob Agents Chemother* 1988 Dec;32(12):1763-8

Freeman F. and Kodera Y. Garlic Chemistry: Stability of S-(2-propenyl)-2-propene-1-sulfinothioate(Allicin) in Blood, Solvents, and Simulated Physiological Fluids. Journal of Agriculture and Food Chemistry, 43: 2332-2338,1995

Krest I, Keusgen M. Stabilization and pharmaceutical use of alliinase. *Pharmazie* 1999 Apr;54(4):289-93

Krest I, Keusgen M. Quality of herbal remedies from Allium sativum: differences between alliinase from garlic powder and fresh garlic. *Planta Medica* 1999 Mar;65(2):139-43

Lawson L.D. and Hughes B.G. Characterization of the Formation of Allicin and other Thiosulfinates from Garlic. *Planta Medica*, 58: 345-350, 1992

Lun ZR, Burri C, Menzinger M, Kaminsky R. Antiparasitic activity of diallyl trisulfide (Dasuansu) on human and animal pathogenic protozoa (Trypanosoma sp., Entamoeba histolytica and Giardia lamblia) in vitro. *Ann Soc Belg Med Trop* 1994 Mar;74(1):51-9

Mayeux PR, Agrawal KC, Tou JS, King BT, Lippton HL, Hyman AL, Kadowitz PJ, McNamara DB. The pharmacological effects of allicin, a constituent of garlic oil. *Agents Actions* 1988 Aug;25(1-2):182-90

Miron T, Rabinkov A, Mirelman D, Wilchek M, Weiner L The mode of action of allicin: its ready permeability through phospholipid membranes may contribute to its biological activity. *Biochim Biophys Acta* 2000 Jan 15;1463(1):20-30

Rabinkov A, Wilchek M, Mirelman D. Alliinase (alliin lyase) from garlic (Alliium sativum) is glycosylated at ASN146 and forms a complex with a garlic mannose-specific lectin. *Glycoconj J* 1995 Oct;12(5):690-8

Rabinkov A, Miron T, Konstantinovski L, Wilchek M, Mirelman D, Weiner L. The mode of action of allicin: trapping of radicals and interaction with thiol containing proteins. *Biochim Biophys Acta* 1998 Feb 2;1379(2):233-44

Scharfenberg K, Wagner R, Wagner KG The cytotoxic effect of ajoene, a natural product from garlic, investigated with different cell lines. *Cancer Lett* 1990 Sep;53(2-3):103-8

Stoll, A. and Seebeck, E. (1951). Chemical investigation of alliin, the specific principle of garlic, Adv. Enzymol., 11, 377-400.

Stoll, A. and Seebeck, E. (1948). Uber Alliin, die genuine Muttersubstanz des Knoblauchols. 1. Mitteilung uber *Allium* Substanzen, Helv. Chim Acta, 31, 189-210

Thatte U, Bagadey S, Dahanukar S "Modulation of programmed cell death by medicinal plants." *Cell Mol Biol (Noisy-le-grand)* 2000 Feb;46(1):199-214

Uchida Y, Takahashi T, Sato N. [The characteristics of the antibacterial activity of garlic]. *Jpn J Antibiot* 1975 Aug;28(4):638-42

Weber ND, Andersen DO, North JA, Murray BK, Lawson LD, Hughes BG. In vitro virucidal effects of Allium sativum (garlic) extract and compounds. *Planta Med* 1992 Oct;58(5):417-23

Yoshida S, Kasuga S, Hayashi N, Ushiroguchi T, Matsuura H, Nakagawa S. Antifungal activity of ajoene derived from garlic. *Appl Environ Microbiol* 1987 Mar;53(3):615-7

Yoshida H, Katsuzaki H, Ohta R, Ishikawa K, Fukuda H, Fujino T, Suzuki A. Antimicrobial activity of the thiosulfinates isolated from oil-macerated garlic extract. *Biosci Biotechnol Biochem* 1999 Mar;63(3):591-4

http://www.reefs.org/ , [Various discussion board threads], 1999-2000

http://www.aqualink.com/ , [Various discussion board threads], 1999-2000

http://www.thereeftank.com/ , [Various discussion board threads], 2000

http://www.reefcentral.com/, [Various discussion board threads], 2000

VII. Acknowledgements

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----------end of article----------

The author welcomes comments and queries.

It is late and my head is light as I type this. I did say I would welcome queries, so, to forestall repetitive responses to such e-mail, here is a short FAQ rundown ;-)

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Q: Horge, you use a lot of scientific gobbledygook in your writing, are you a marine biologist? Maybe a pharmacologist?
A: A Marine Biologist? Uhrmmm... I eat like a marine, and can smell like a biologist, but... did you say pharmacologist? I DO have first-hand knowledge about certain ...pharmaceuticals.

Q: Right. Horge, can you just provide us with your credentials, then?
A: Credentials?? Uhmmm... how about "I have no police record"? ...No, wait. Lemme double-check on that...

Q: Horge, then why do you write such bandwidth-consuming ...'stuff'?
A: To show off. I'm only faking it, ...but it makes me a babe-magnet!

Q: Dear Horge, I now wish to have you killed, where do you live?
A: The Philippines has thousands upon thousands of kilometers of coral-blessed coastline. I'd be snorkeling some part of that every HOUR if I could help it, getting my free fish, free live rock ---look! There's a glowing, lavender *Acropora reclinata* just sitting there!...haha, all those poor overseas saps, paying CASH for this stuff...

Q: So Horge, ...any ...last ...words?
A: Apart from future articles? Well, I post regularly on the discussion board at http://www.thereeftank.com/ and urge everyone to eat a well-balanced diet, bathe and brush regularly, and be nice to one another.

...oh, and "Horge Cortes-Jorge" is mostly a pseudonym, so good luck hunting me down :-)

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Bersa Thunder Chapterhouse,