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Effect of Garlic on Vancomycin-Resistant Enterococci

There is great concern about the worldwide increase in antibiotic resistance, especially of gram-positive bacteria such as vancomycin-resistant enterococci (VRE). As garlic, especially the thiosulfinate allicin, has been known for its antibacterial activity against facultative aerobic bacteria (2), the antibacterial effect of garlic alone and in combination with vancomycin on VRE was studied.

Fourteen clinical isolates of VRE (MIC > 8 μg/ml), one vancomycin-sensitive isolate, and three reference strains (BM4147, V583, and ATCC 29212) were studied. Fresh Spanish garlic was peeled, mashed, filtered, and freeze-dried. Allicin was kindly supplied by L. D. Lawson. The interaction between garlic, allicin, and vancomycin, measured as fractional inhibitory concentration (FIC), was determined by the checkerboard titration method (3). Dilutions of garlic ranged from 63 to 8,000 μg/ml, dilutions of allicin ranged from 1 to 64 μg/ml, and dilutions of vancomycin ranged from 0.06 to 128 μg/ml. The bactericidal effects of the combination of garlic and vancomycin with the lowest FICs on VRE strains BM4147 and V583 were determined with killing curves (3). One hundred thousand CFU of each microorganism per ml was inoculated in separate tubes with garlic (1,000 to 2,000 μg/ml), vancomycin (8 μg/ml), and the combination and incubated at 37°C. Samples were taken for a bacterial count at 0, 2, 4, 8, and 24 h. In addition, the influence of cysteine and β-mercaptoethanol on the combination of vancomycin and garlic was studied. A growth control was always included. All experiments were performed twice.

TABLE 1. Effects of garlic, allicin, and vancomycin on VRE

Strain	sp.	MIC (μg/ml)			FIC[a]	
		Vanco[b]	Garlic	Allicin	Garlic	Allicin
ATCC 29212	*E. faecalis*	4	4,000	32	0.53	0.53
F346	*E. faecium*	1	4,000	32	0.53	0.53
BM4147	*E. faecium*	256	8,000	64	0.28	0.38
V583	*E. faecalis*[c]	32	8,000	64	0.38	0.31
KH2V	*E. durans*	64	8,000	64	0.27	0.28
KH5V	*E. faecium*	64	8,000	64	0.25	0.27
KH16V	*E. faecium*	128	8,000	64	0.25	0.28
KH32V	*E. durans*	64	4,000	32	0.52	0.31
KS19V	*E. faecium*	128	8,000	64	0.27	0.27
KS31V	*E. faecium*	128	8,000	64	0.27	0.27
KS32V	*E. faecium*	128	4,000	64	0.28	0.26
KS36V	*E. durans*	128	8,000	64	0.26	0.27
F7	*E. faecium*	256	8,000	64	0.26	0.26
F16	*E. faecium*	128	8,000	64	0.25	0.27
F29	*E. faecium*	256	8,000	64	0.25	0.28
F52	*E. faecium*	64	8,000	64	0.27	0.28
F163	*E. faecium*	32	8,000	64	0.28	0.28
F199	*E. faecium*	256	8,000	64	0.26	0.28

[a] For combinations with vancomycin.
[b] Vanco, vancomycin.
[c] *vanB* genotype, all other VRE strains possess the *vanA* genotype.

The MIC of vancomycin for VRE decreased from 32 to 256 μg/ml without garlic to 0.5 to 16 μg/ml in the presence of garlic (1,000 to 2,000 μg/ml) or allicin (8 to 16 μg/ml). The FICs (<0.5) indicated a synergistic effect between the compounds tested on all VRE except KH32V and the vancomycin-sensitive ATCC 29212 and F346 (Table 1). Killing curves showed a bacteriostatic effect of the combination of garlic and vancomycin: bacterial counts remained 10^5 CFU/ml for 24 h.

In the presence of garlic, vancomycin, and cysteine (0.1 or 0.01%) or β-mercaptoethanol (0.01 or 0.001%), bacterial growth increased from 10^5 CFU/ml at 0 h to 10^8 CFU/ml at 24 h.

The data show an antibacterial bacteriostatic effect of garlic and allicin on VRE. In addition, inhibitory synergism between these compounds was observed. The MICs of garlic corresponded to only one clove of garlic in an empty stomach. Findings with allicin (MIC and FIC) confirmed a major contribution of this thiosulfinate to the antibacterial effect of garlic. SH groups in allicin can theoretically form disulfide bonds with SH groups in bacterial enzymes or nutrients (4, 5). By binding to enzymes located on transposon Tn*1546* encoding vancomycin resistance (1), garlic (i.e., allicin) may inhibit their activity and thereby enhance the susceptibility of VRE to vancomycin. The inhibition of the synergistic effect by cysteine (which interacts with allicin via the sulfhydryl group) and β-mercaptoethanol (which breaks disulfide bonds) suggests a role of the formation of disulfide bonds. Further research regarding the application and mechanisms of the synergistic effects may be warranted.

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