SILVER-PMMA ANTIBACTERIAL BONE CEMENT

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The incorporation of antibiotics into methyl-methacrylate bone cements for prophylaxis or treatment of infection associated with implant surgery may entail increased risks of allergic reaction, mechanical failure or super-infection. Our experience with the antibacterial effects of silver ions (1) suggested that the addition of simple silver salts to bone cement might be an attractive alternative to organic moieties, offering maximum effectiveness at low concentrations with low risk.

To explore this, AgCl, Ag-AgCl (chloride silver powder), Ag_2O and Ag_2SO_4 were individually added to Simplex-P, Radiopaque Bone Cement and tested in vitro against Staphylococcus aureus, Pseudomonas aeruginosa and E. coli. The final concentrations of the salts chosen were 0%, 0.05%, 0.12%, 0.5%, and 1.0% by weight of dry powder, far lower than the 3-6% that has been found effective for conventional antibiotic additions. 10 mm diameter tablets, 3 mm thick, were formed from the mixtures and from plain cement and tested after cooling in B.H.I. agar plates inoculated with bacteria. Replicate tablets were bathed in normal saline at 37°C from 1 to 28 days, with constant changes, and then tested in S. aureus cultures to measure the persistence of the antibacterial effects with time. Rods were also formed from the 1.0% mixtures and controls for mechanical testing. Maximum compressive strengths were determined according to ASTM Standard Method D-695, using five specimens of each type.

INHIBITORY ZONE WIDTH (mm)

	*	0%	0.05%	0.1%	0.5%	1.0%
Ag-AgCl	S	0	0	0	0	1
	E	0	0	0	0	0.5
	P	0	0	0	0	0.5
AgCl	S	0	0	0	0.5	1.5
	E	0	0	0	0	0.5
	P	0	0	0	1.5	2.5
Ag_2O	S	0	0.5	1.3	4.0	5.0
	E	0	0	0.2	2.0	2.5
	P	0	0.5	3.0	6.0	6.0
Ag_2SO_4	S	0	0.7	0.7	1.8	2.5
	E	0	0.5	1.0	1.8	2.8
	P	0	2.0	2.0	3.0	3.5

TABLE 1: Inhibition zone width in BHI agar cultures for silver additions to Simplex-P as percent by weight of the dry powder portion of the mix.
* S=Staph. Aureus; E=E. coli; P=Pseudomonas aeruginosa.

Results, as determined by the width of inhibitory zones around the Ag-PMMA tablets, are shown in Table 1. All composites showed some inhibition; Ag2O seemed most effective and Ag-AgCl the least. It was noteworthy that the silver inhibition, as judged by zone size, is as good or better for Pseudomonas as for the other organisms. The inhibitory zones, while generally increasing with Ag concentration, were not linearly related to it.

Saline incubation generally reduced the inhibitory zone size in a few days, for all but Ag_2SO_4 whose effectiveness persisted for 21 days. At this time it appears that the ability of the Ag+ ion to be mobilized from the methacrylate is directly related to the aqueous solubility of the added salt. The use of a more porous material, such as Palacos cement, should also increase Ag+ mobilization. The compressive strengths of the highest concentration AgCl and Ag2O composites, stored at room conditions for one week, were not significantly different from identically handled control specimens ($P>0.1$). Variations seemed dependent rather on handling and porosity, etc., as might have been anticipated. Because of their density, the volume percent of silver salts added in these experiments is from 0.006% to 0.12%, 2-3 orders of magnitude below the levels of, say, gentamycin that has been added to bone cements.

In summary, the addition of ionized silver to methacrylate bone cement is an effective means of inhibiting bacteria in its vicinity, without loss of compressive strength and with some degree of persistence in vitro. Experience with silver shows that it has a broad spectrum of effectiveness at relatively low concentrations. It also is relatively non-toxic and non-allergenic and thus might be an ideal additive to implant materials in chronic applications. The biocompatibility and effectiveness of Ag-PMMA against infections in vivo are now under study.

1. T.J. Berger, et al., Antimicrob. Ag. And Chemother. 9, 357 (1976). J.A. Spadaro, et. al, Proc. O.R.S. 22, 112 (1976).

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