Bone cement not weakened by cefuzonam powder

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We report tensile, shearing, and bending tests on bone cement to which cefuzonam sodium (Cosmosin®), a third generation cephalosporin, had been mixed. Mixing 3 g of cefuzonam sodium to 40 g of polymethyl methacrylate (PMMA) polymer did not diminish the strength of the bone cement in any of the tests. We speculated that this lack of influence was because the cefuzonam sodium powder used was in the form of relatively uniform-sized spheres and therefore did not become the origin of stress concentration within the cement.

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Kinoshita (1973) showed that the addition of 3 g of cephalothin sodium to bone cement reduced the compressive strength by 6.5 percent and the bending strength by 6 percent. Cephaloridin sodium similarly reduced the strength, but to a lesser degree. Takahashi (1986), on the other hand, reported that the addition of 5 g of amikacin sulfate had little affect on the strength of bone cement.

In this study, loading tests were performed on bone cement to which an antibiotic, cefuzonam sodium, had been mixed. We confirmed that there was no effect by adding this drug on the strength of the cement. These discrepancies seem to be due to a difference in the drug used, particularly in regard to the physical form of the drug powder.

Material and methods

Methods of kneading and polymerization

The bone cement was kneaded and polymerized under the following four conditions to simulate typical clinical use: (1) kneading and polymerization under 9.8×10^4 Pa (1 atm); (2) kneading under 9.8×10^4 Pa and polymerization under 1.96×10^6 (20 atms); (3) kneading under 4.9×10^4 Pa (0.5 atms) and polymerization under 9.8×10^4 Pa; and (4) kneading under 4.9×10^4 Pa and polymerization under 1.96×10^6 Pa; Kneading was carried out according to the instruction manual for the purchased bone cement (Surgical Simplex-P®). Briefly, 40 g of PMMA polymer powder was mixed with each 0, 1, 2, and 3 g of cefuzonam sodium in a stirrer (MixEvac Mixing system), and then 20 mL of MMA monomer was added and stirred. The prestirred nonpolymerized bone cement in the stirrer was placed in a desiccator for 5 min at 4 °C under 4.9×10^4 Pa to remove air bubbles by evacuation. Kneaded paste-like bone cement was then poured into an acrylic vessel and polymerized under either atmospheric or a higher pressure. The individual bone cement samples thus prepared were then coded as follows:

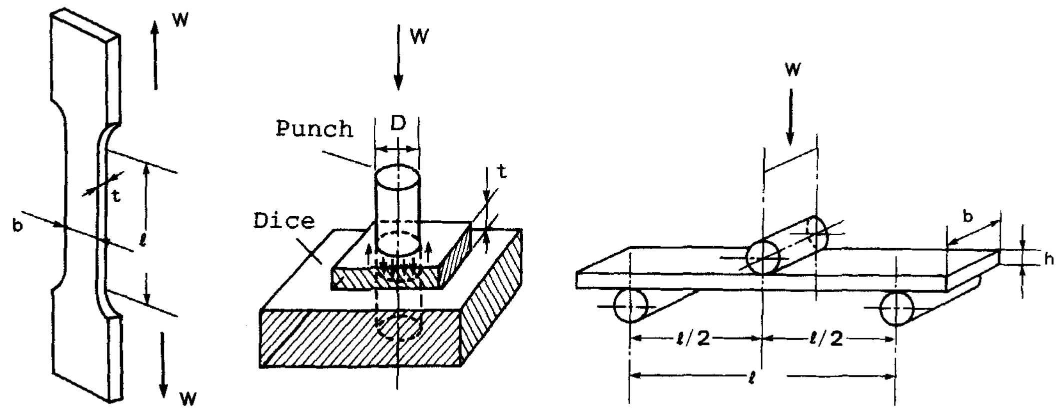
(An example of the code in this experiment)

0 – 1 – 2 – T

- T: Test methods
  - T Tension, S Shearing, B Bending
- 2: Amount of drug added (g)
  - (however, 0 means not contained.)
- 1: Polymerization conditions
  - 0 under 9.8×10^4 Pa
  - 1 under 1.96×10^6 Pa
- 0: Kneading conditions
  - 0 air bubbles not removed
  - 1 air bubbles removed by evacuation

Estimation of the porosity of the cement block

Blowholes contained in the bone cement are expected to seriously reduce the strength of the cement (Lidgren et al. 1987, Linden 1988, Wixson et al. 1987). The porosity (P) represents the percentage contamination by blowholes within the cement and is given by the equation $P = 1 - (\rho/\rho_0)$, where ρ



a. Tension test.
Tensile strength
$\sigma_T = W_{max} / (bt)$
l = 30 mm
b = 6 mm
t = 3 mm

b. Shearing test.
Shearing strength
$\sigma_S = W_{max} / (\pi Dt)$
D = 10 mm
t = 3 mm
JIS K-7214 (JIS 1985)

c. Bending test.
Bending strength. (ASTM 1989)
$\sigma_B = W_{max}\ (l/4)\ /\ (bh^2/6)$
l = 55 mm
b = 15 mm
h = 3 mm

Figure 1. Shapes of test specimen and schematic diagrams of three types of loading tests for PMMA bone cement.

and ρ_0 represent the density of the bone cement block and PMMA bone cement with no blowhole contamination, respectively. The value of P was calculated from the observed weight and volume of the block. The density of the PMMA bone cement was measured as described by Schreurs et al. (1988), and 1.290 g/cm^3 was used as the value of ρ_0. Because the amount of antibiotic added was small relative to that of PMMA polymer, its influence on the overall density was ignored, although the density of the drug is slightly greater than that of PMMA bone cement itself.

Loading tests

For the tension test, 10–12 dumbell-shaped specimens and for the shearing and bending tests, the same number of plate-shaped specimens were prepared from each cement block, respectively. Loading was done at a rate of 98 N/min, and the strength was calculated from the maximum load causing fracture using each equation (Figure 1).

Correction of strength for the porosity

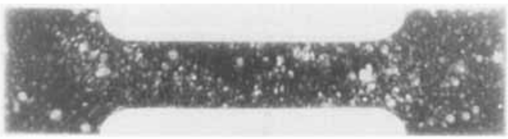
The influence of the porosity on the strength must be eliminated to quantitatively evaluate the effect of the added antibiotic alone. Actual measured strength of each bone cement was corrected for its porosity, and the strength at the same degree of porosity (standardized porosity) was calculated for each specimen using the equation $\sigma = \sigma_0 \exp(-\alpha P)$. Where σ_0 is the strength of the solid cement (P = 0 vol%), and α is a constant. Values σ_0 and α were determined from the relation between the actual measured strength and the porosity in four types of bone cement without antibiotic powder.

Statistics

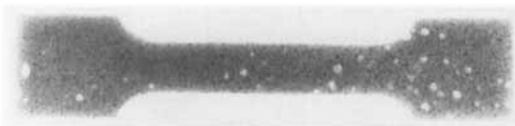
The statistical significance of the differences in strength between the antibiotic-free and antibiotic-containing cement was examined using the Wilcoxon rank sum test (software; STAX Kaihara 1985). The critical value for significance was set at the probability $P < 0.01$ or $P < 0.05$.

Fractographic observation of the ruptured surface

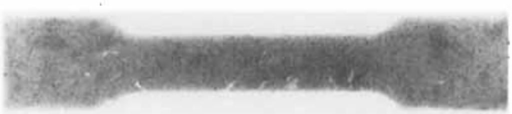
The ruptured surface, obtained after the tension test, was observed using a scanning electron microscope (JEOL JSM-820). The ruptured surface of the bone cement prepared with 40 g of PMMA powder mixed with 3 g of another antibiotic, cephalothin sodium (Keflin®), and polymerized with 20 mL of MMA monomer was also evaluated.



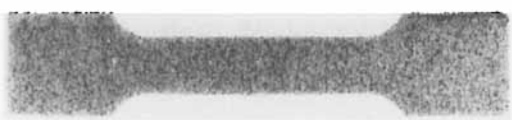
000T: not evacuated, polymerized under 1 atm.



010T: not evacuated, polymerized under 20 atms.



100T: evacuated, polymerized under 1 atm.



110T: evacuated, polymerized under 20 atms.

Figure 2. Soft radiographs of tension test specimens prepared under different polymerization conditions.

Table 1. Density and porosity of all the bone cement blocks

A	B	C	A	B	C
000T	1.11	13.8	100S	1.18	8.92
001T	1.02	20.6	101S	1.17	9.15
002T	1.19	7.98	102S	1.17	9.23
003T	1.11	14.0	103S	1.23	4.50
010T	1.20	7.29	110S	1.18	8.61
011T	1.17	9.38	111S	1.19	7.83
012T	1.19	7.52	112S	1.19	7.52
013T	1.18	8.37	113S	1.22	5.27
100T	1.23	4.88	000B	1.01	21.7
101T	1.17	9.30	001B	1.07	17.3
102T	1.16	10.2	002B	1.10	14.8
103T	1.16	10.2	003B	1.01	21.5
110T	1.20	6.90	010B	1.18	8.84
111T	1.19	7.44	011B	1.19	8.14
112T	1.21	6.51	012B	1.19	7.91
113T	1.22	5.58	013B	1.19	7.60
000S	1.00	22.3	100B	1.17	9.07
001S	1.08	16.6	101B	1.18	8.30
002S	1.09	15.3	102B	1.18	8.30
003S	1.03	20.0	103B	1.24	3.95
010S	1.17	9.15	110B	1.19	7.67
011S	1.17	9.46	111B	1.20	7.05
012S	1.17	9.54	112B	1.21	6.05
013S	1.19	8.14	113B	1.22	5.58

A Code No. of sample.
B Density, ρ (g/cm^3).
C Porosity, P (vol %).

Results

Soft x-ray photographs were taken leaving the distribution of the blowholes in the specimen used for the tension test (Figure 2). All the bone cement samples that were not evacuated, but polymerized under 9.8 $\times$ 10^4 Pa, displayed a high degree of porosity (OOOT). When the blowholes were removed by careful evacuation, on the other hand, the porosity was reduced to about 6 percent of the initial amount.

The density and porosity of all the bone cements tested were calculated (Table 1). The actual measured strength of each specimen was corrected, and the strength at the normalized porosity was estimated for each specimen (Table 2). The results of the statistical analysis are added in this table, in which the symbols * and ** indicate significant differences at $P < 0.01$ and $P < 0.05$, respectively.

The ruptured surfaces of the bone cements and antibiotic powders were observed (Figure 3).

Discussion

Porosity of bone cement

The porosity was found to be very susceptible to slight changes in the kneading procedure, indicating technical difficulties in kneading and in obtaining a standardized quality bone cement preparation. Several factors can be attributed to the formation of blowholes inside the bone cement (Lidgren et al. 1987, Linden 1988, and Wixson et al. 1987).

Strength of bone cement containing cefuzonam sodium

Only the specimen (O13S) showed a significant difference in shearing ($P < 0.01$). Although significant differences were noted in several cases ($P < 0.05$), the strength was found to be higher in some drug-containing cement samples, and therefore showed no consistent tendency. This inconsistency seemed to be due to other factors introduced by the correction for porosity. Unless the shape and distribution

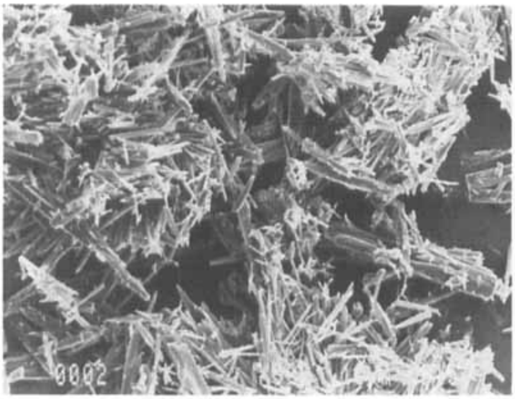
Table 2. Actual measured and corrected strengths of bone cements

A	B	C	D		E		F	G	H
			mean	± SD	mean	± SD			
000T	10	14.11	8.43	2.35	8.04	2.25	5.19	11.3	
001T	10		6.27	2.55	15.1	6.17	4.31	23.0	
002T	10		11.1	4.31	4.80	1.86	2.25	7.25	
003T	10		10.1	3.92	9.99	3.82	4.04	15.7	
010T	11	8.64	15.2	5.29	12.6	4.51	5.00	19.5	
011T	12		15.2	5.88	16.9	6.57	9.11	25.1	
012T	11		16.3	3.43	13.9	2.94	9.31	18.4	
013T	11		13.6	4.61	13.1	4.41	8.13	20.6	
100T	10	8.64	28.6	7.93	17.2	4.80	10.1	26.1	
101T	10		17.3	4.70	18.9	5.10	10.3	28.4	
102T	10		11.2	4.51	13.8	5.59	6.66	25.7	
103T	10		18.9	4.70	23.2	5.49	14.6	31.2	*
110T	11	6.61	25.3	7.06	26.3	7.25	15.7	38.1	
111T	11		16.9	3.92	18.9	4.41	11.3	25.6	
112T	10		18.9	7.35	18.6	7.34	8.92	32.5	
113T	10		18.6	6.95	16.2	5.98	7.84	26.5	
000S	11	18.55	33.3	4.51	36.4	5.00	32.1	46.3	
001S	11		38.4	3.04	36.8	2.84	27.2	45.3	
002S	11		33.5	5.10	31.2	4.80	30.0	40.5	
003S	11		43.0	1.86	44.5	1.96	28.0	45.2	
010S	11	9.07	46.6	2.35	46.7	2.35	42.2	51.3	
011S	11		43.1	1.86	45.5	1.86	41.7	48.9	
012S	11		43.6	1.86	44.1	1.96	40.8	47.0	
013S	11		42.8	1.86	41.9	1.86	39.2	46.7	**
100S	11	7.95	44.9	2.64	45.9	2.74	41.1	49.7	
101S	11		43.5	3.53	44.7	3.63	39.0	49.6	
102S	11		44.3	5.10	45.6	5.19	39.1	52.8	
103S	11		51.3	1.86	47.4	1.76	45.2	49.5	
110S	10	7.31	44.2	3.33	45.6	3.43	39.1	48.7	
111S	10		44.5	3.82	45.0	3.92	39.8	50.2	
112S	11		47.6	2.65	47.9	2.64	42.5	51.2	
113S	11		48.7	1.86	46.5	1.75	43.7	49.4	
000B	11	18.82	36.1	6.37	40.0	7.06	33.8	58.4	
001B	11		36.0	4.51	34.1	4.31	26.2	40.6	*
002B	10		47.8	5.00	37.1	4.31	27.2	40.1	
003B	11		35.2	20.0	38.7	21.9	17.9	99.9	
010B	11	8.12	65.5	9.31	68.2	9.60	50.9	82.9	
011B	11		62.3	9.21	62.3	9.31	47.1	75.7	
012B	11		57.5	8.62	57.0	8.53	51.6	68.8	
013B	11		61.4	5.88	60.3	5.78	50.2	68.8	
100B	11	7.40	53.5	15.9	56.8	16.9	34.0	88.5	
101B	11		60.8	9.51	62.8	9.80	48.9	81.7	
102B	11		57.9	10.5	59.8	10.9	48.9	75.6	
103B	12		73.7	6.17	65.1	5.39	58.7	70.6	
110B	11	6.59	57.6	13.5	59.8	14.1	43.5	84.1	
111B	10		63.7	9.60	64.8	9.80	53.2	79.5	
112B	12		64.6	11.4	63.4	11.2	47.2	78.8	
113B	12		69.8	7.06	67.2	6.76	52.7	75.1	

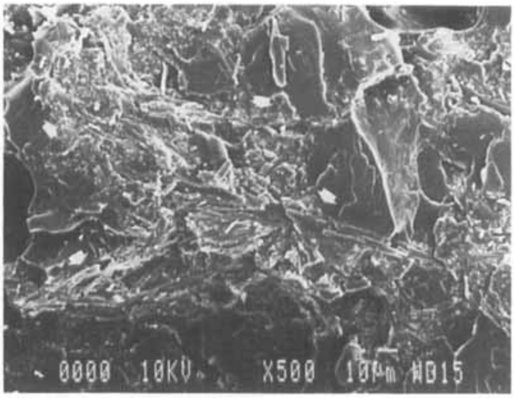
Corrected strength was calculated using the following equations:
Tensile strength $\sigma'_T = 53.12 \exp(-13.55 \times 10^{-2} P)$, (MPa)
Shearing strength $\sigma'_S = 55.27 \exp(-2.26 \times 10^{-2} P)$, (MPa)
Bending strength $\sigma'_B = 79.48 \exp(-3.60 \times 10^{-2} P)$, (MPa)

A Code No. of sample
B No. of test specimens
C Normalized porosity, P (vol%)
D Actual strength, σ (MPa)
E Corrected strength, σ' (MPa)
F Range, σ' min (MPa)
G Range, σ' max (MPa)
H Levels of significance
** $P < 0.01$
* $P < 0.05$

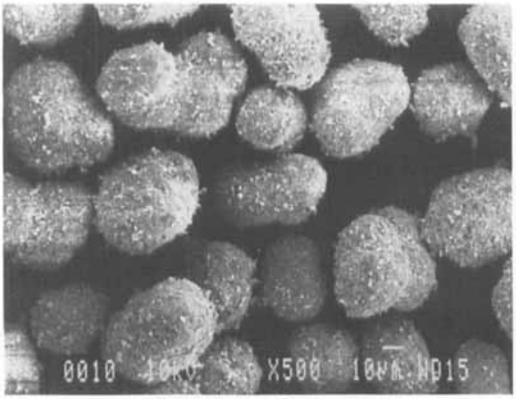
of blowholes is uniform inside the cement, the insignificance of porosity as regards overall strength does not hold, and interactions among blowholes cannot be ignored. This was supported by the finding that significant differences were more frequent in the bone cement samples kneaded under 1 atmosphere



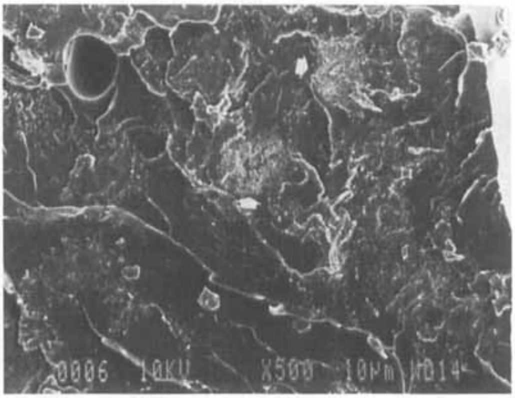
a. Cephalothin sodium (Keflin®) powder.



b. Ruptured surface of bone cement containing Keflin® powder.



c. Cefuzonam sodium (Cosmosin®) powder.



d. Ruptured surface of bone cement containing Cosmosin® powder.

Figure 3. The SEM image photographs of antibiotic particles and ruptured surfaces of bone cement containing antibiotic powder. Arrows show antibiotic particles.

of pressure. In fact, significant differences nearly disappeared when porosity was eliminated. These results indicate that the strength of bone cement is not affected by the addition of the antibiotic cefuzonam sodium if the amount added is less than 3 g per 40 g bone cement powder. Thus, the bone cement containing this amount of the drug is expected to maintain the intrinsic strength of PMMA bone cement in clinical practice.

Fractographic study of the ruptured surface

We also prepared a bone cement containing cephalothin sodium—which has been reported to reduce the strength of the bone cement (Kinoshita 1972)—and observed the ruptured surface of the cement. Cephalothin is a powder consisting of radially oriented needle-shaped crystals (Figure 3a). This structure was clearly retained even in the bone cement (Figure 3b). It was clearly observed that the cleavage occurred at the interface between the cephalothin crystals and the bone cement matrix. This would seem to imply poor adhesion between the crystals and the cement. Moreover, the tip of the needle crystalline structure of the drug may serve as the origin of stress concentration and hence greatly reduced the strength of the cement.

In contrast, cefuzonam sodium is a spherical powder consisting of 30–50 μm particles (Figure 3c). In the case of cefuzonam sodium-containing cement, the image of the ruptured surface did not show a clear boundary around each drug particle, and the fracture extended within the drug crystals (Figure 3d). Cefuzonam sodium powder has a granular structure formed by agglutination of fine crystals. Because of the structure of these particles, it is thought that MMA monomer molecules can penetrate within the powder to active good adhesion or mechanical bonding between the drug and the cement.

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