

Supplementary Information

**Antimicrobial spine bone cement with caffeic acid
phenethyl ester for controlled release formulation and
in vivo biological assessments**

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Table S1. Composition ratios of antibiotic/antimicrobial PMMA bone cements.

Components	Contents (g)
Powder (20g)	
Methylmethacrylate methacrylate copolymer (PMMA)	13.4
Zirconium dioxide (ZrO ₂)	6.0
Benzoyl peroxide (BPO)	0.6
Liquid (8.5g)	
Methylmethacrylate monomer (MMA)	8.245
N, N-dimethyl-p-toludine (DMPT)	0.255
Antibiotic/antimicrobial agents	
Caffeic acid phenethyl ester (CAPE, 20-80 mM)	0.048 – 0.242
Gentamicin (GM, 10 mM)	0.049

Table S2. Macroscopic observations on implantation sites in rabbits

Implantation	Category	Animal No.												
		M1			M2			M3			M4			
		1 ^a	2	3	1	2	3	1	2	3	1	2	3	
Test	Inflammation	0	0	0	-	0	0	0	0	0	0	-	0	0
	Encapsulation	0	0	0	-	0	0	0	0	0	0	-	0	0
	Hemorrhage	0	0	0	-	0	0	0	0	0	0	-	0	0
	Necrosis	0	0	0	-	0	0	0	0	0	0	-	0	0
	Discoloration	0	0	0	-	0	0	0	0	0	0	-	0	0
	Total	0	0	0	-	0	0	0	0	0	0	-	0	0
	Mean(T/5)	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0
	Average Mean Score	0.0			0.0			0.0			0.0			
Control	Inflammation	0	0	0	-	0	0	0	0	0	0	-	0	0
	Encapsulation	0	0	0	-	0	0	0	0	0	0	-	0	0
	Hemorrhage	0	0	0	-	0	0	0	0	0	0	-	0	0
	Necrosis	0	0	0	-	0	0	0	0	0	0	-	0	0
	Discoloration	0	0	0	-	0	0	0	0	0	0	-	0	0
	Total	0	0	0	-	0	0	0	0	0	0	-	0	0
	Mean(T/5)	0.0	0.0	0.0	-	0.0	0.0	0.0	0.0	0.0	0.0	-	0.0	0.0
	Average Mean Score	0.0			0.0			0.0			0.0			

a : Tissue implantation site

* Mean Animal Score (Sum of Average Mean Score / # of Site)

: Test = '0.0', Control = '0.0'

Table S3. Microscopic observations on implantation sites in rabbits

Implantation	Category	Animal No.											
		M1			M2			M3			M4		
		1 ^a	2	3	1	2	3	1	2	3	1	2	3
Test	Inflammation												
	Polymorphonuclear												
	Leukocyte	0	0	0	-	0	0	0	0	0	-	0	0
	Plasma cells	0	0	0	-	0	0	0	0	0	-	0	0
	Macrophages	0	0	0	-	0	0	0	0	0	-	0	0
	Giant cells	0	0	0	-	0	0	0	0	0	-	0	0
	Necrosis	0	0	0	-	0	0	0	0	0	-	0	0
	Neovascularisation	0	0	0	-	0	0	0	0	0	-	0	0
	Fibrosis	0	0	0	-	0	0	0	0	0	-	0	0
	Fatty infiltrate	0	0	0	-	0	0	0	0	0	-	0	0
	Traumatic necrosis	0	0	0	-	0	0	0	0	0	-	0	0
	Foreign debris	0	0	0	-	0	0	0	0	0	-	0	0
	No. sites examined		3			2			3			2	
	Control	Inflammation											
Polymorphonuclear													
Leukocyte		0	0	0	-	0	0	0	0	0	-	0	0
Plasma cells		0	0	0	-	0	0	0	0	0	-	0	0
Macrophages		0	0	0	-	0	0	0	0	0	-	0	0
Giant cells		0	0	0	-	0	0	0	0	0	-	0	0
Necrosis		0	0	0	-	0	0	0	0	0	-	0	0
Neovascularisation		0	0	0	-	0	0	0	0	0	-	0	0
Fibrosis		0	0	0	-	0	0	0	0	0	-	0	0
Fatty infiltrate		0	0	0	-	0	0	0	0	0	-	0	0
Traumatic necrosis		0	0	0	-	0	0	0	0	0	-	0	0
Foreign debris		0	0	0	-	0	0	0	0	0	-	0	0
No. sites examined			3			2			3			2	
Average^b								0.0					

a : Tissue implantation site

b: Average = Test (Group Total Score / # of Site) – Control (Group Total Score / # of Site)

* **Bioreactivity Rating = ‘ 0.00 ’ {Average (Test – Control)}**

Fig. S1. (a) Cumulative release profiles and (b) burst release profiles of GM- and CAPE-loaded bone cements during 25 h. (○: 10 mM GM-, ●: 20 mM CAPE-, ▼: 30 mM CAPE-, ▲: 50 mM CAPE-, ■: 70 mM CAPE-, and ◆: 80 mM CAPE- loaded bone cements)

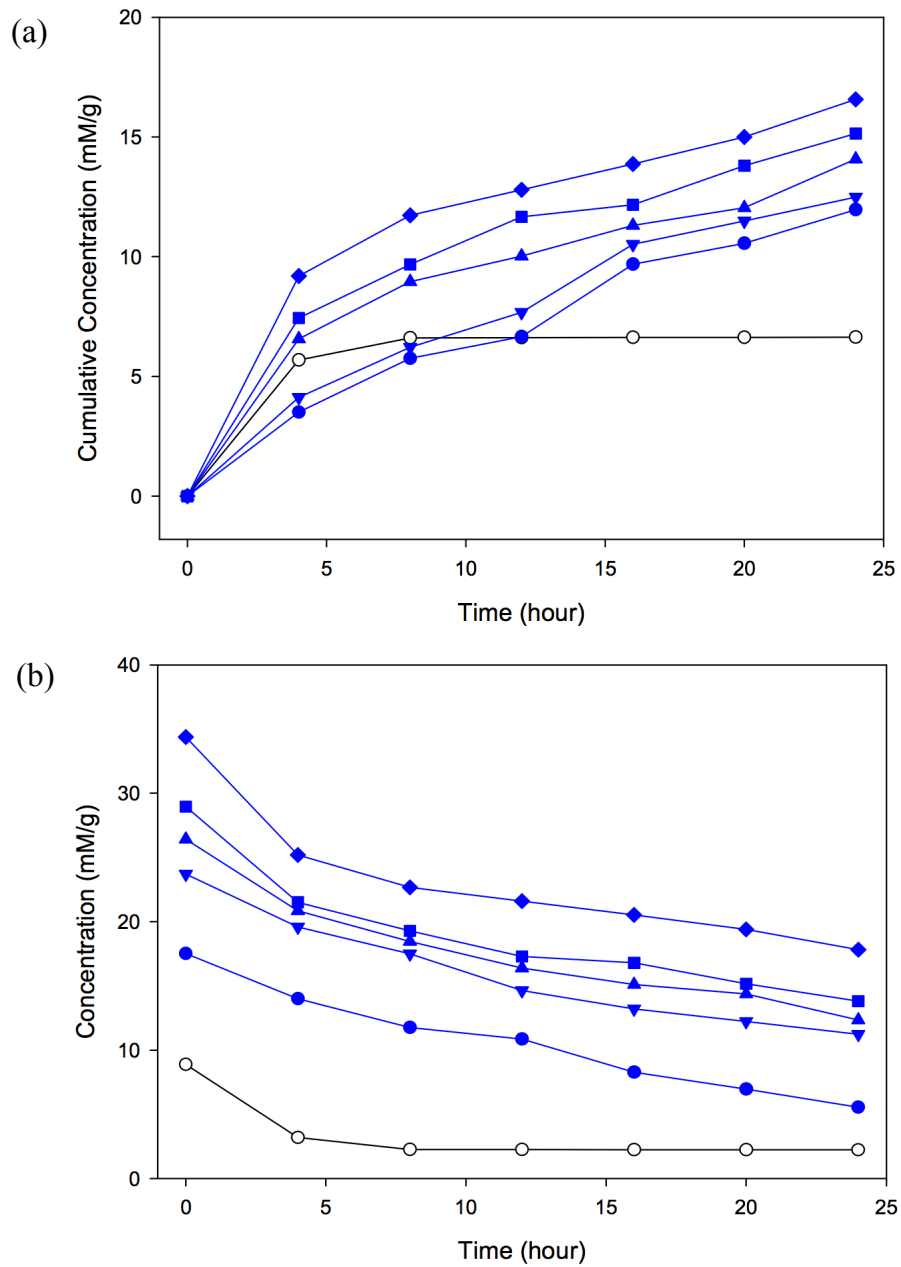


Fig. S2. (a) Histology diagrams with hematoxylin-eosin staining of control and test articles on implantation sites in rabbits, and (b) fluorescent microscopic images

