



# Mesoporous Silica Functionalised Composite Bone Cement for Effective Delivery of Antibiotics

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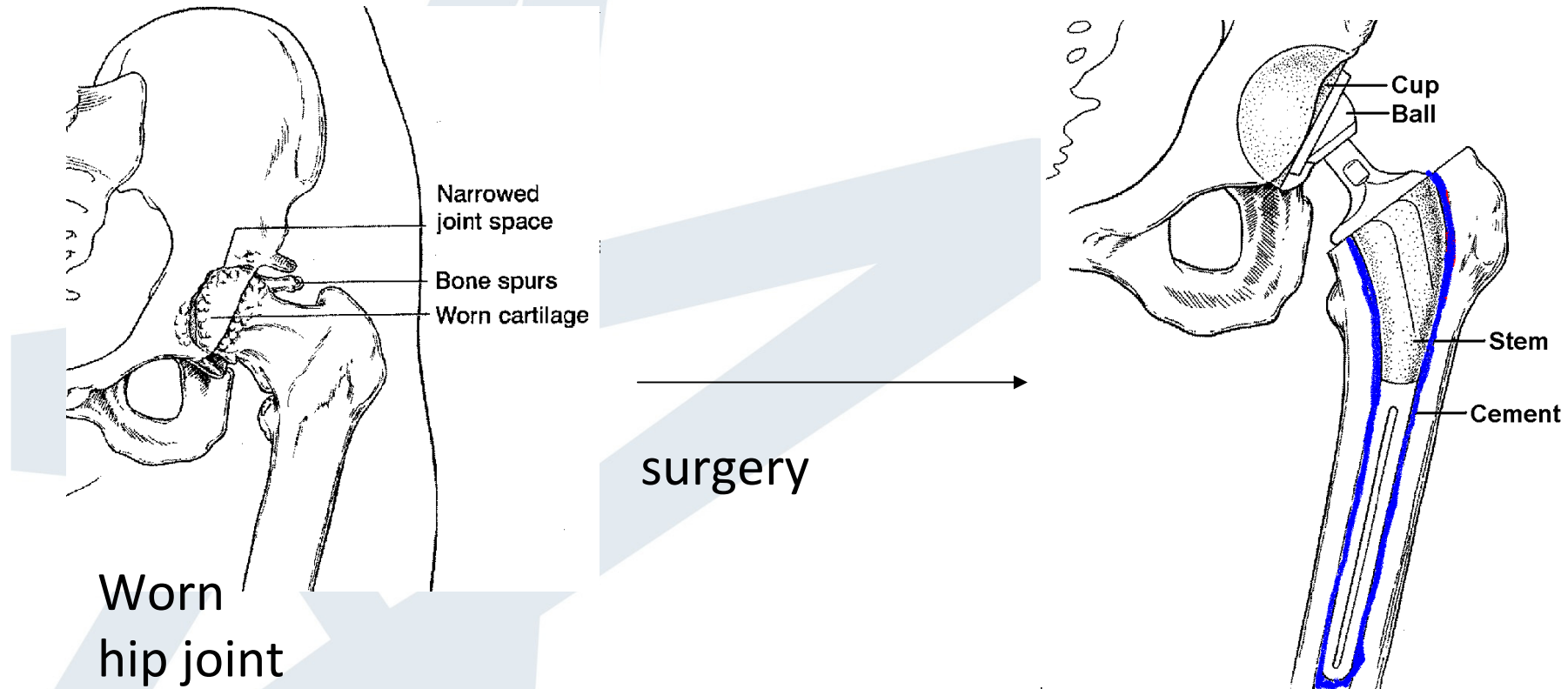
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# Function of Antibiotic-loaded Bone-cement



- Fix the metal part
- Release antibiotic to protect surrounding tissue

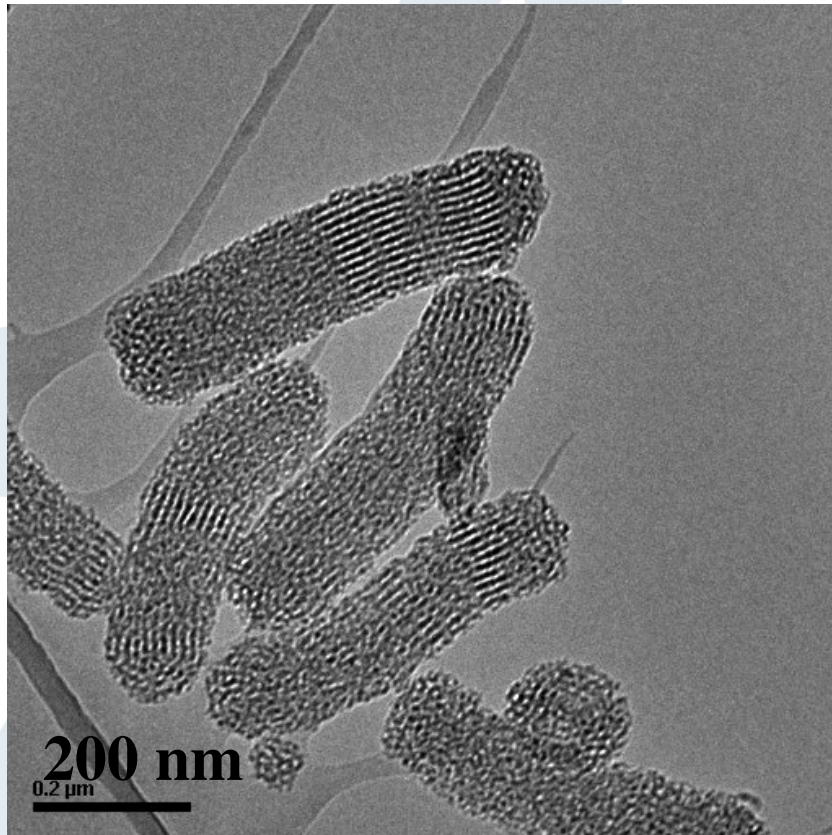
# Problem Faced

- “ Numerous studies about its (antibiotic-loaded acrylic bone cement) pharmacokinetic properties have demonstrated that **only a small part of the incorporated antibiotic amounts can be released**”<sup>1</sup>
- It is necessary to incorporate fillers to PMMA based bone cement without detriment of mechanical property
- “However, the **ideal filler** material and amount of filler are **yet to be established.**”<sup>1</sup>

<sup>1</sup> Gladius Lewis, Review: Properties of Antibiotic-Loaded Acrylic Bone Cements for Use in Cemented Arthroplasties: A State-of-the-Art Review, Journal of Biomedical Materials Research Part B: Applied Biomaterials, 89B: 558-574 (2009).

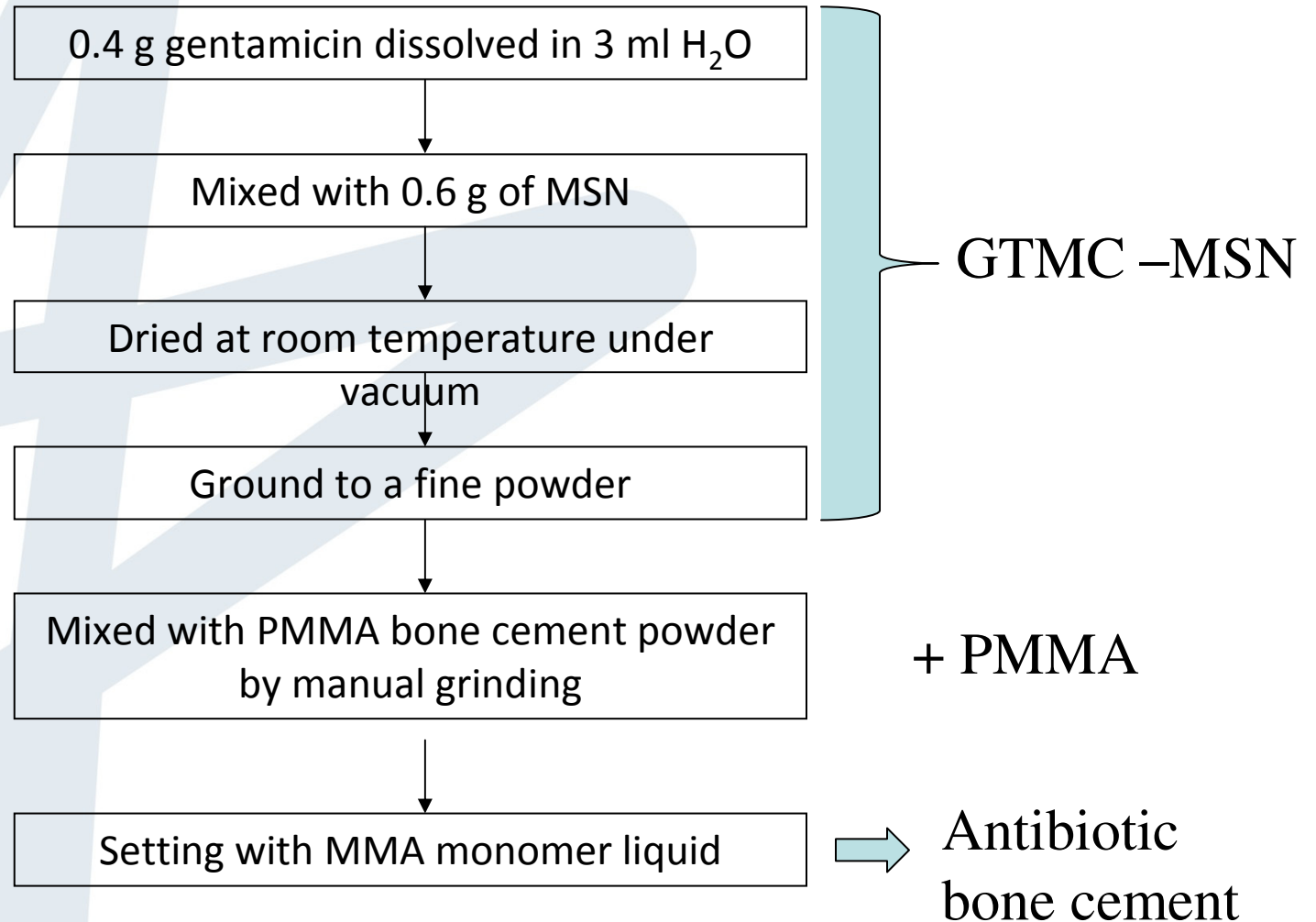
<sup>2</sup> Konstantinos Anagnostakos, Jens Kelm, Review: Enhancement of Antibiotic Elution From Acrylic Bone Cement, Journal of Biomedical Materials Research Part B: Applied Biomaterials, J Biomed Mater Res Part B: Appl Biomater 90B: 467–475 (2009),

# Mesoporous Silica Nanoparticles (MSN) as drug carriers/filler

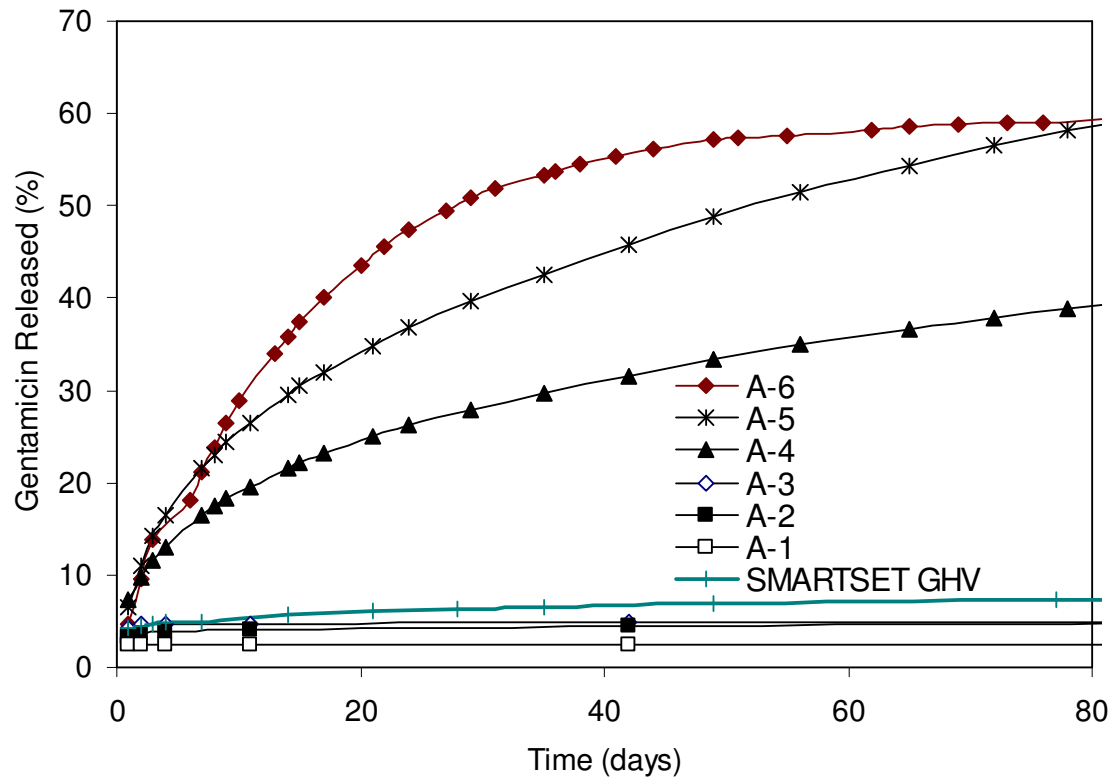


- Large specific surface areas ( $\sim 600 \text{ m}^2/\text{g}$ )
  - Large pore volume ( $\sim 1.0 \text{ cc/g}$ )
  - Uniform nanoporous channels
- ↓
- Large drug loading in nano encapsulation
  - The pores also provides diffusion channels for drug molecules to elute

# Formulation Method-A: 2-step Procedure



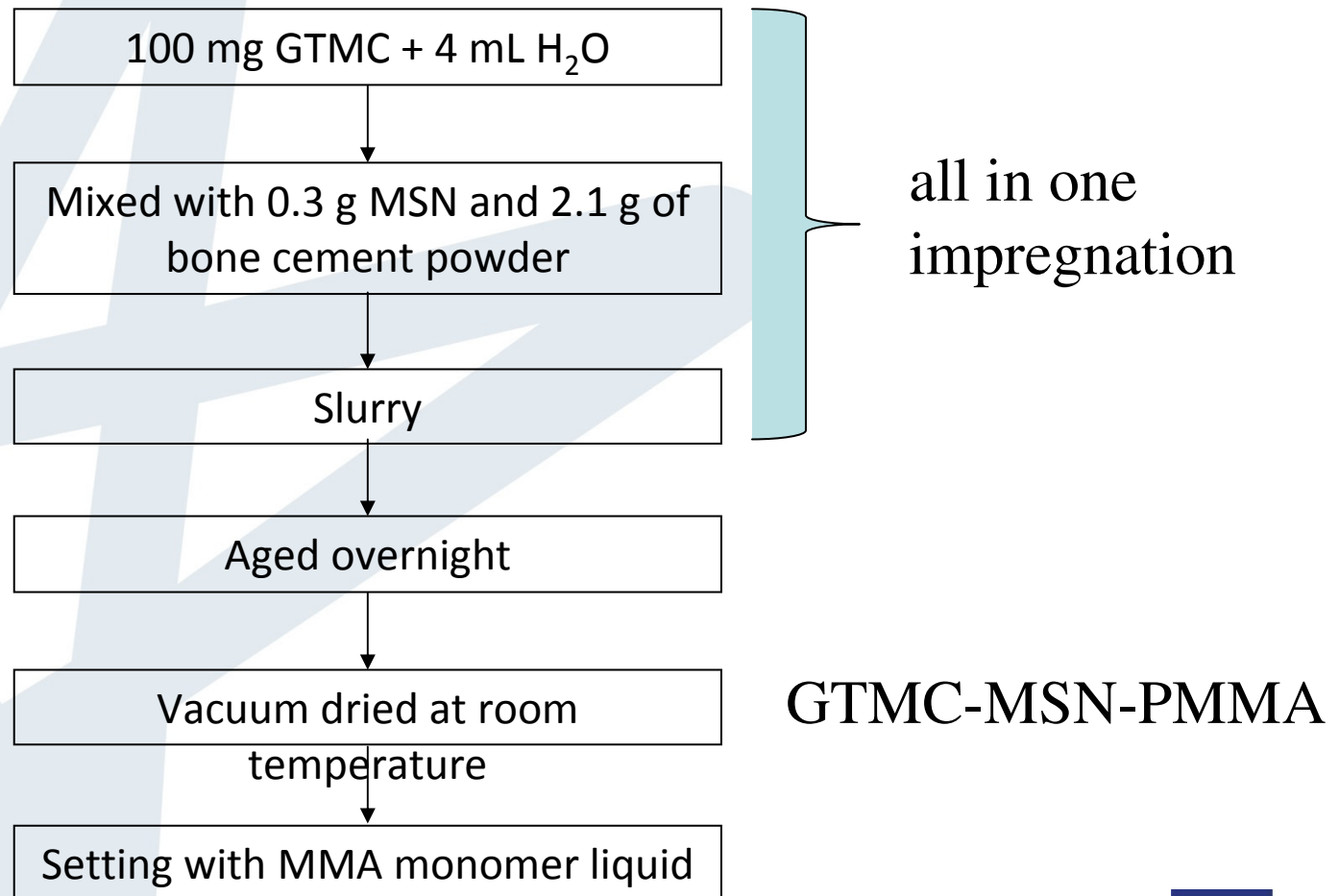
# Drug Release Profiles of Bone Cement



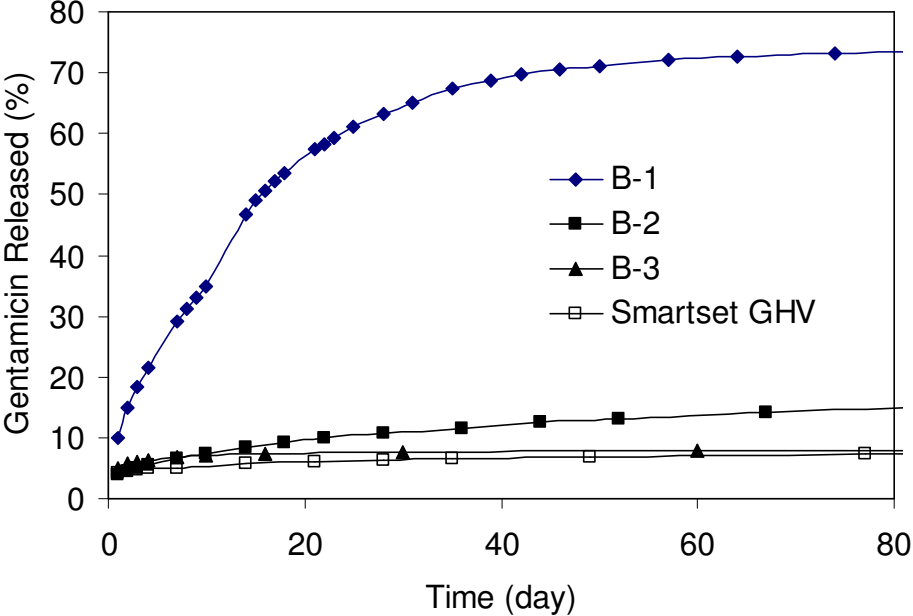
	MSN [wt.%]	Drug Loading [wt.%]
A-1	0	3.40
A-2	2.04	1.36
A-3	4.08	2.72
A-4	6.12	4.08
A-5	8.15	5.44
<b>A-6</b>	<b>10.19</b>	<b>6.79</b>

SMARTSET GHV is a gentamicin loaded commercial bone cement, 4.22wt% in powder and 2.87 wt% in final composition

# Formulation Method-B: one-step Method



# Drug Release Profiles of Bone Cement Prepared by Method B

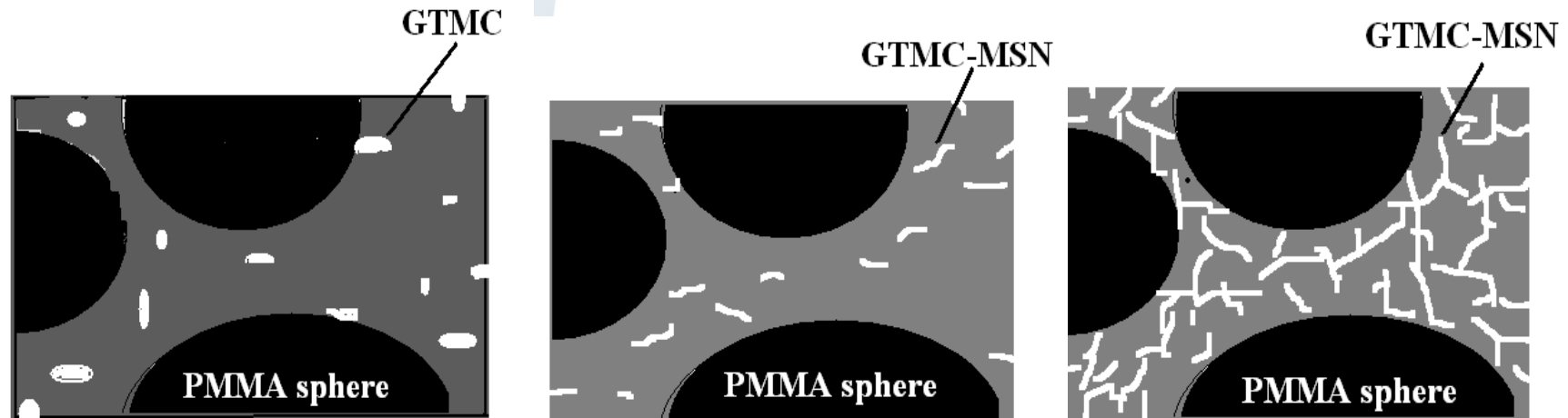


	MSN [wt.%]	Drug Loading [wt.%]
B-1	8.15	2.72
B-2	5.44	2.72
B-3	2.72	2.72

\*B-1 prepared by method-B exhibits best result for drug sustained release



# Scheme of Drug Release System



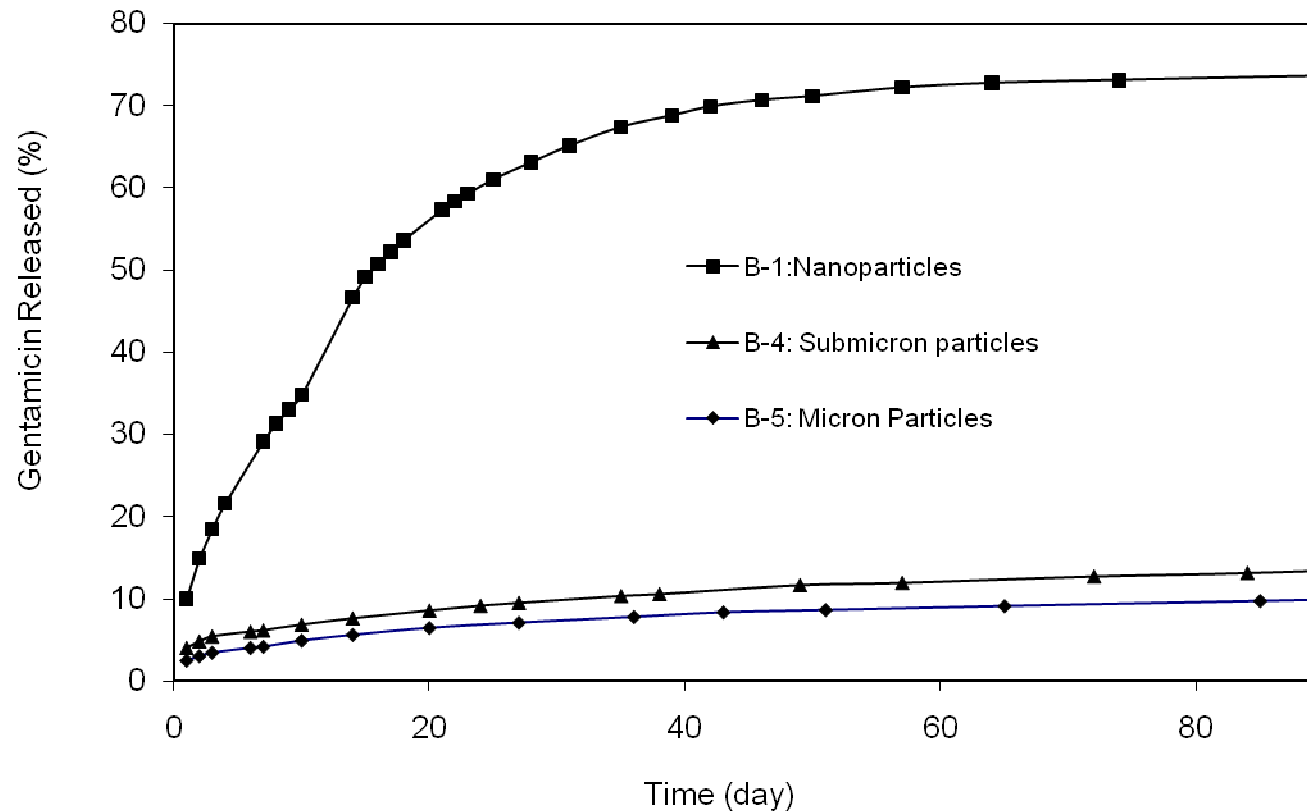
GTMC-Bone  
Cement

Low Silica  
Concentration  
( $<6\%$ )

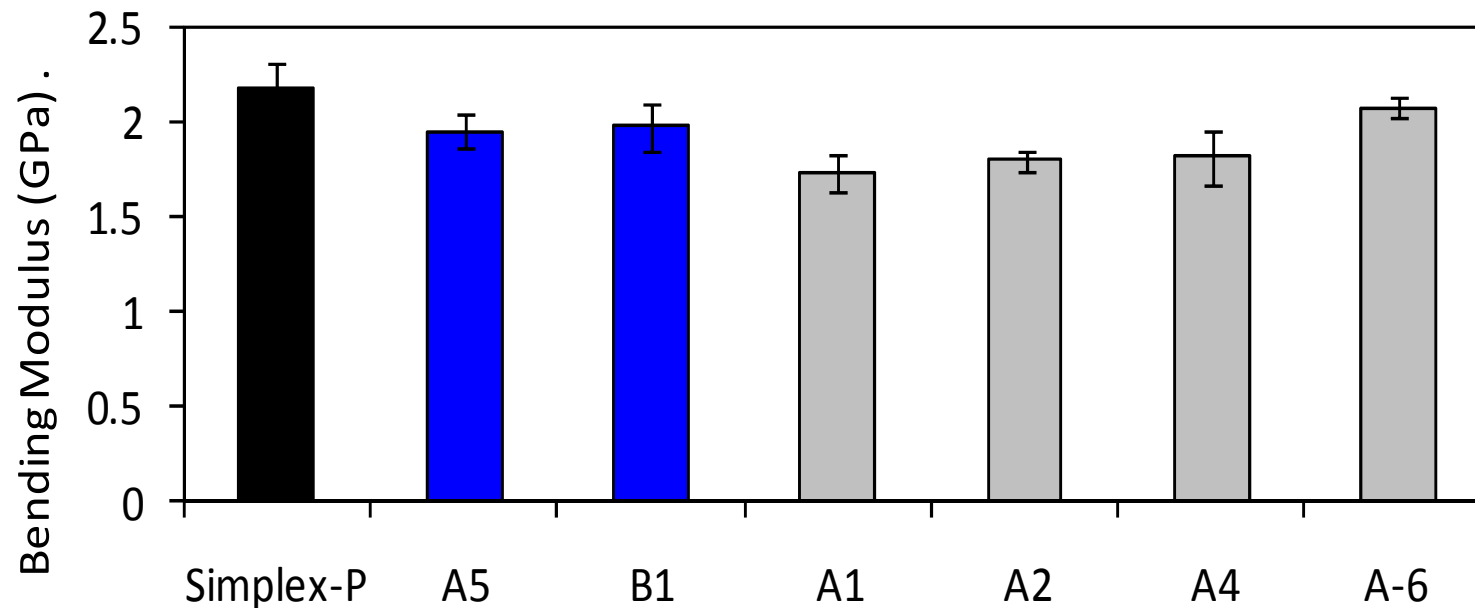
High Silica  
Concentration  
( $>6\%$ )

\* Particle-particle contact of MSN built effective diffusion network for drug molecules release from bone cement matrix

# Effect of Particle Size of Mesoporous silica



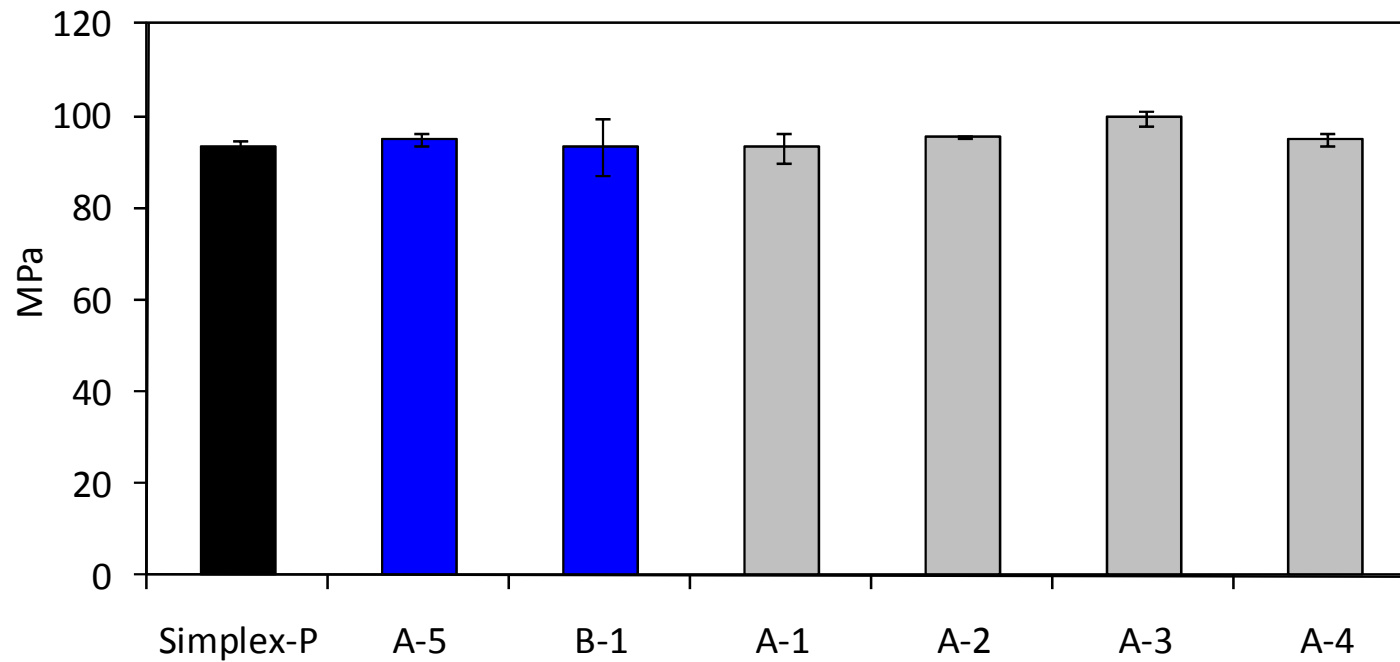
# Mechanical Properties: Bending



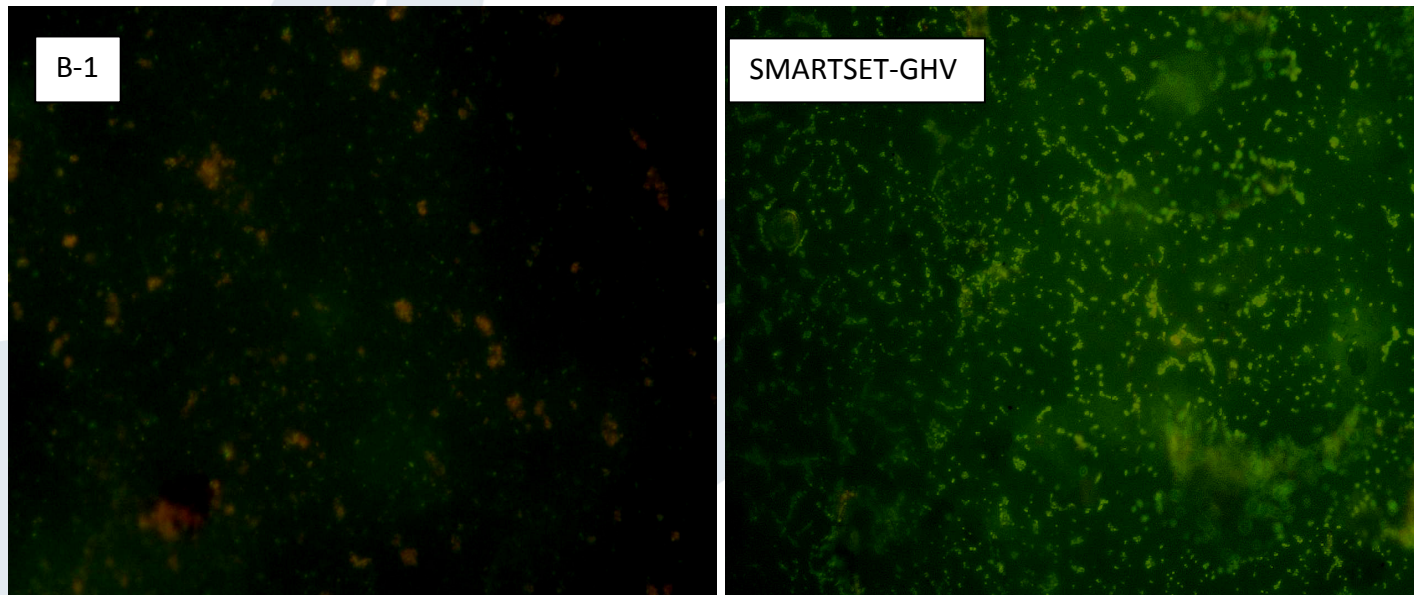
\* Simplex-P is commercial bone cement.

1 GPa : 1000MPa

# Mechanical Properties: Compression Strength



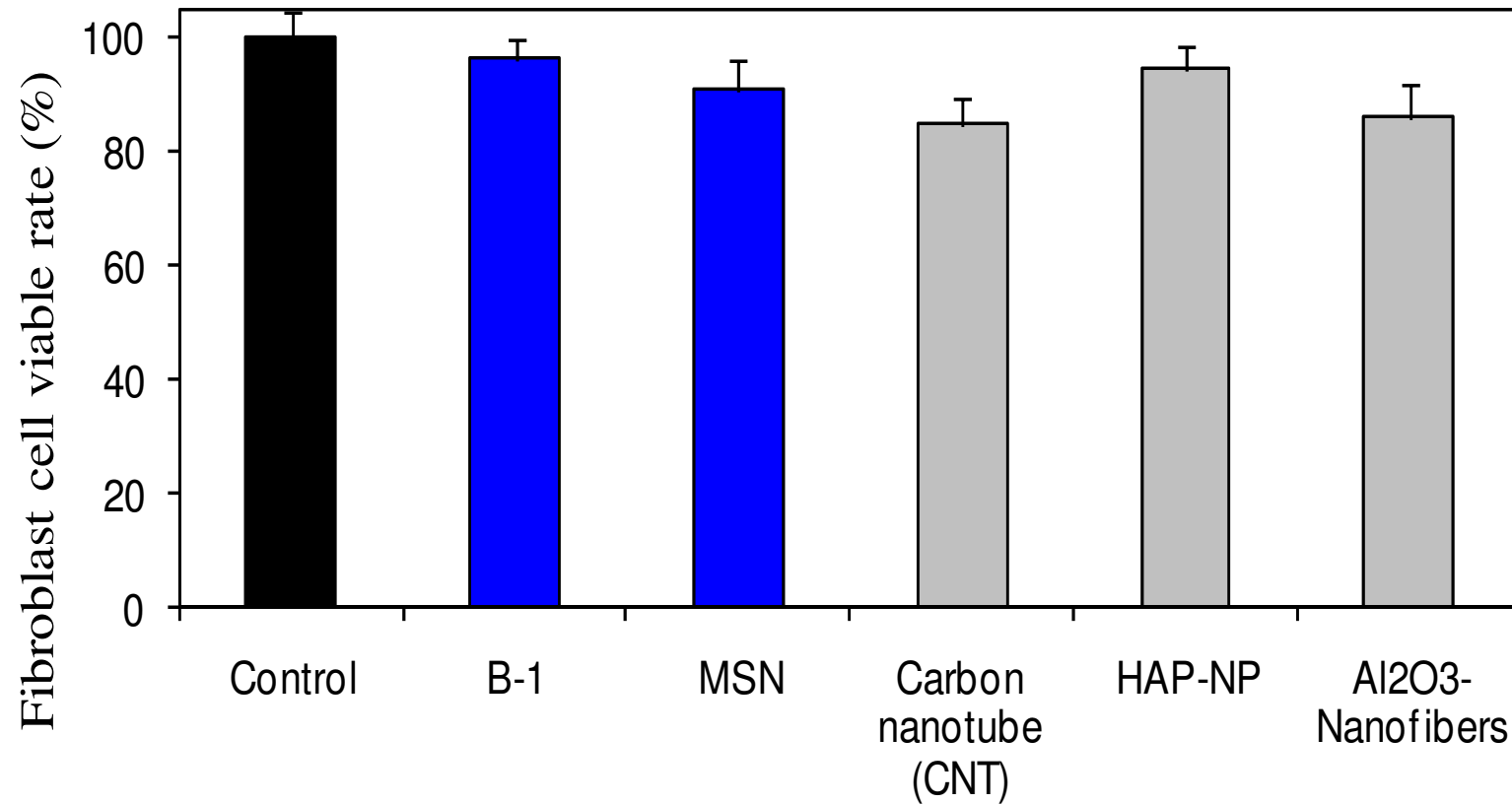
# Antibacteria Test



Viable cell: Green

Nonviable: Red

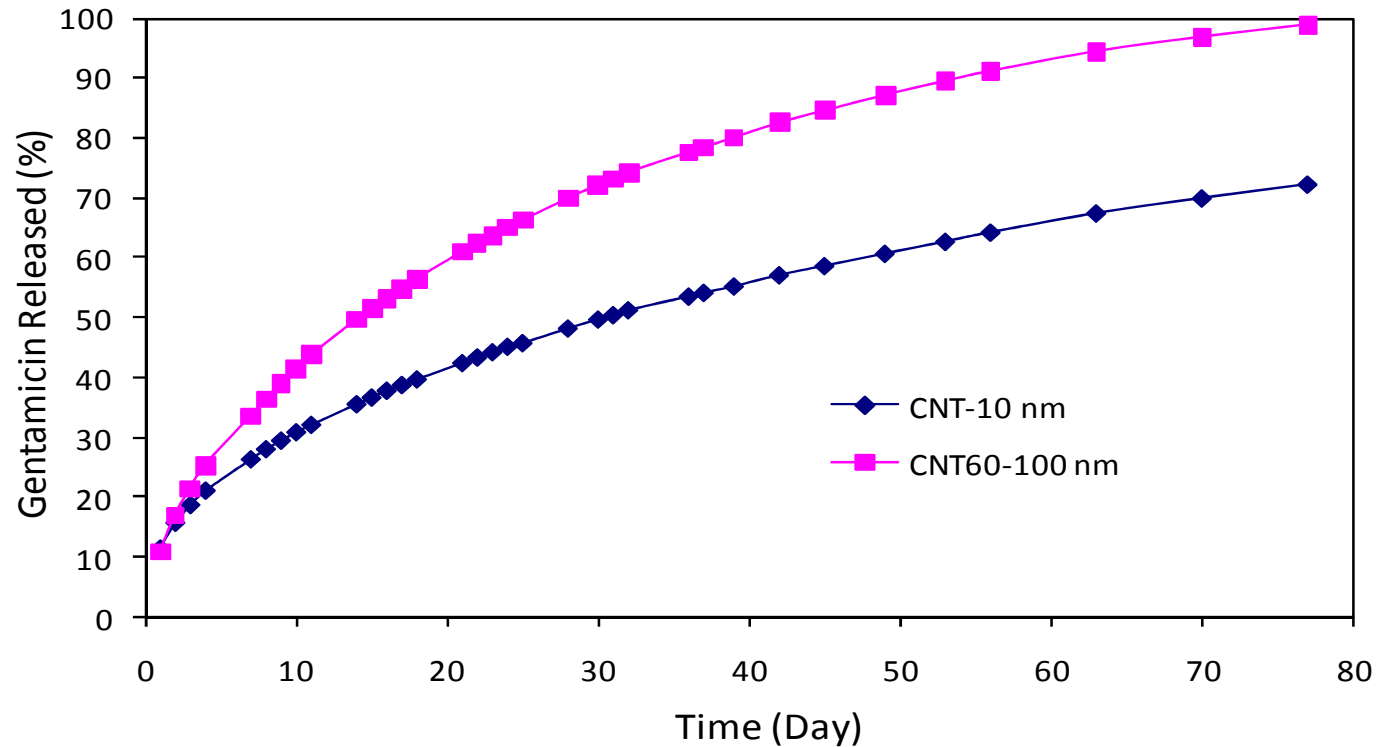
# Cytotoxicity Measurements



# Other Fillers

- Carbon Nanotubes (CNT)
- Hydroxyapatite (HAP) nanorods/nanoparticles
- Al<sub>2</sub>O<sub>3</sub> nanofibres

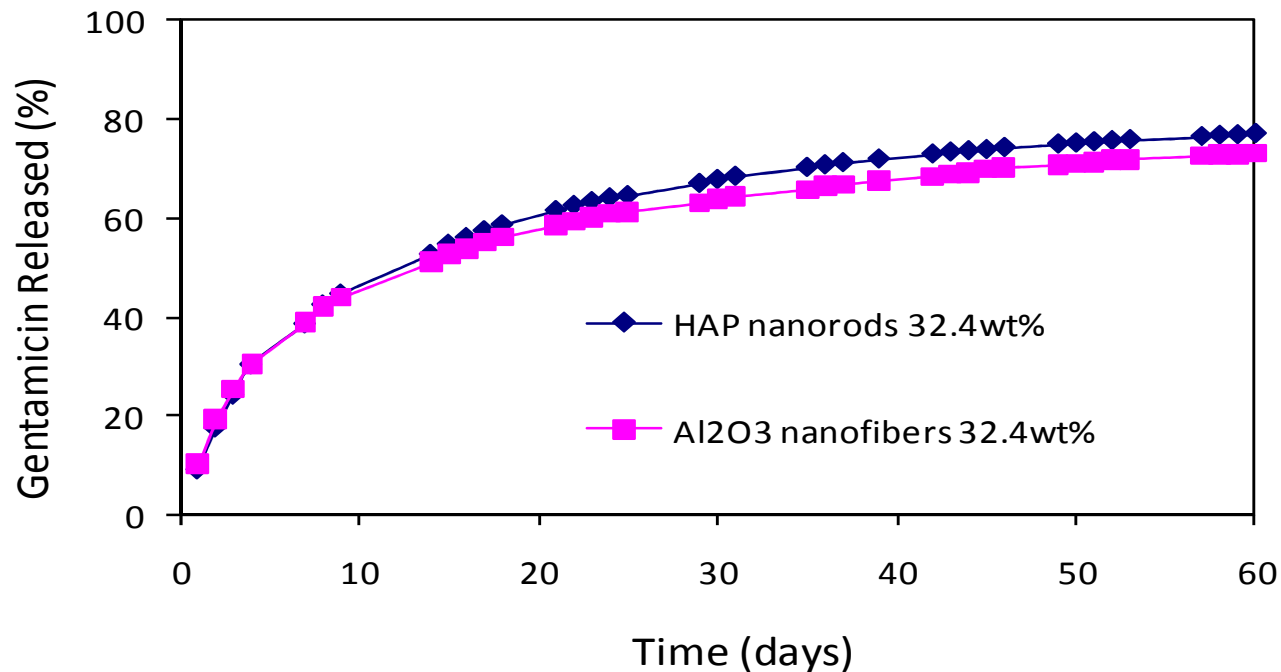
# Drug Release from CNT formulated Bone Cement (SmartSet-HV)



sample	PMMA	MMA	CNT	GTMC
CNT10 nm	2.0 g	1 ml	5.35%	3.21%
CNT60-100	2.0 g	1 ml	5.35%	3.21%

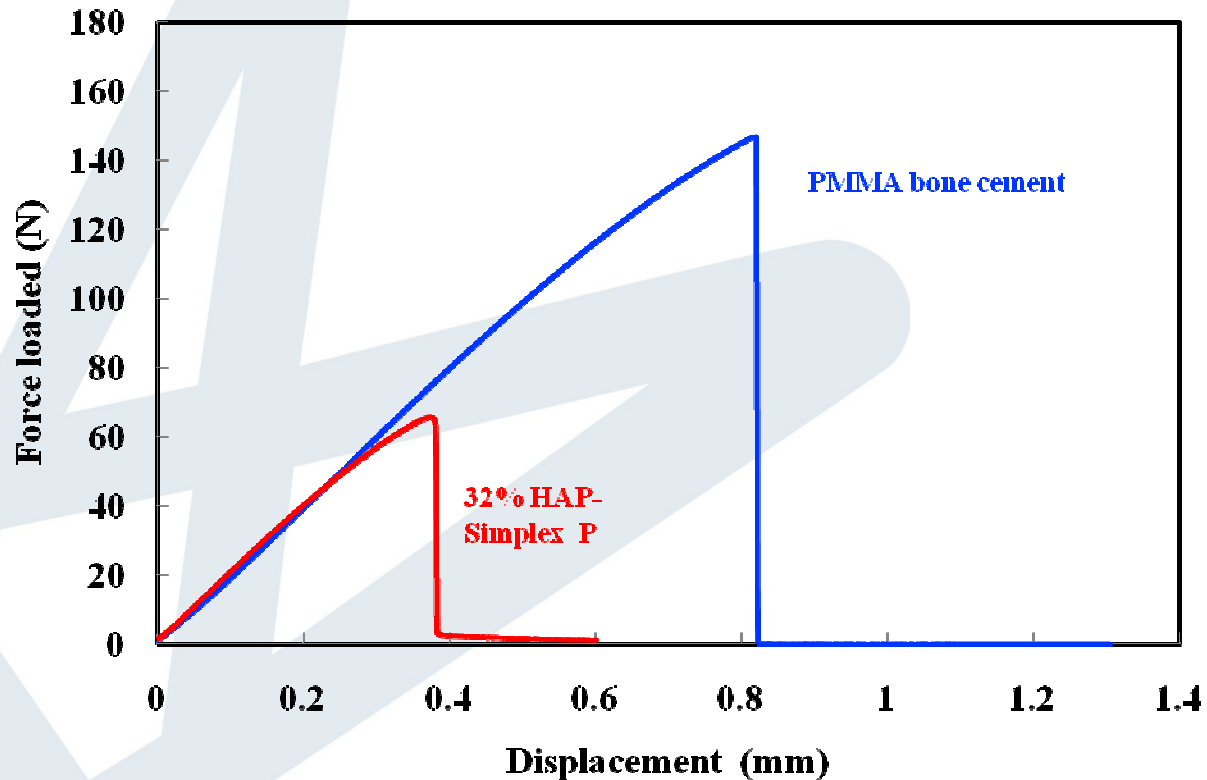


# Drug Release from Composite Bone Cement formulated with HAP Nanorods and Al<sub>2</sub>O<sub>3</sub> nanofibers



Gentamicin: 4.85 wt%

# Bending Test of HAP - PMMA Bone Cement



HAP formulated PMMA bone cement have much weaker mechanical property

# Summary

- Our work incorporates mesoporous silica nanoparticles into bone cements as drug carriers to enable controlled release of antibiotics
- Compared to commercial antibiotics-loaded bone cement, our work achieves a breakthrough in terms of:
  - High drug release efficiency (70% vs 5%)
  - Sustained drug release (80 days vs 1 day)
- MSN formulated bone cement exhibited good antibacterial properties and retained the original mechanical strength of the bone cement: high application potential

# Acknowledgements

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Singapore)