Physicochemical Characterization and *In Vitro* Evaluation of Bismuth-Doped Mesoporous Bioactive Glass Nanoparticles for Bone Void-Filling Applications

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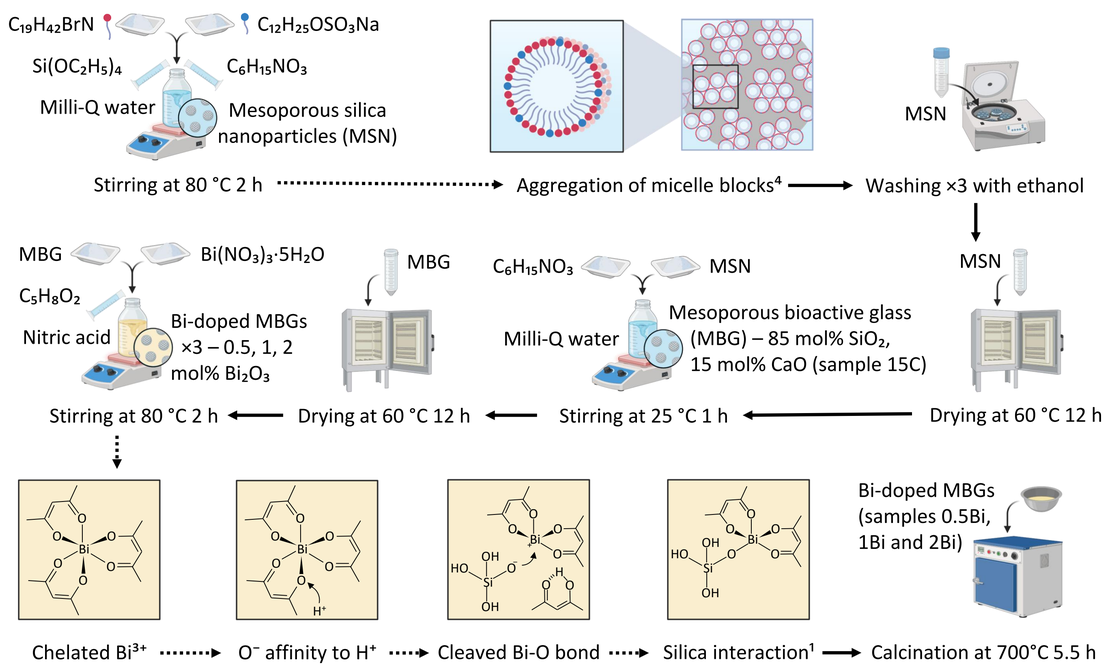
Introduction

The incorporation of bismuth is intended to enhance the performance of the silica–calcium bioactive glass system by introducing additional properties such as radiopacity[1], photothermal conversion[2], and possible therapeutic benefits[3], while preserving the mesoporous structure advantageous for drug or biomolecule delivery. The materials were synthesized via a sol-gel route to produce mesoporous silica nanoparticles, followed by sequential impregnation with calcium and varying concentrations of bismuth (0, 0.5, 1, and 2 mol% Bi_2O_3), and final calcination. Comprehensive characterization was carried out to assess the cell viability, bioactivity, ion release, antibacterial activity and radiopacity, supporting the potential of bismuth doped mesoporous bioactive glass nanoparticles in bone regeneration applications.

Method



Structure and Composition

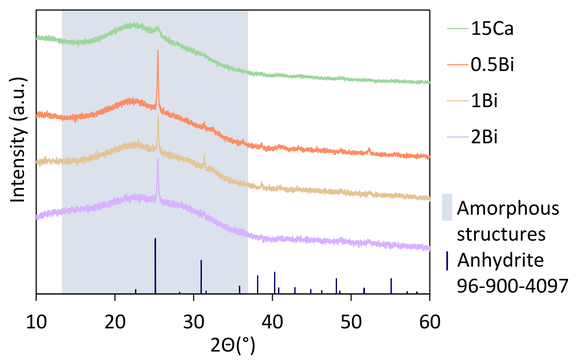


Fig. 1 XRD patterns of as-prepared samples.

Sample	Bi_2O_3	CaO	SO_3	SiO_2
15C	0.00 ± 0.00	13.41 ± 0.43	1.12 ± 0.08	85.45 ± 2.98
0.5Bi	0.43 ± 0.01	12.22 ± 0.62	0.88 ± 0.07	86.47 ± 2.65
1Bi	0.94 ± 0.04	13.20 ± 0.22	0.96 ± 0.08	84.89 ± 2.55
2Bi	1.85 ± 0.01	13.26 ± 0.12	1.09 ± 0.25	83.83 ± 1.12

Fig. 3 Actual oxide composition in mol% of as-prepared samples measured by ICP-OES.

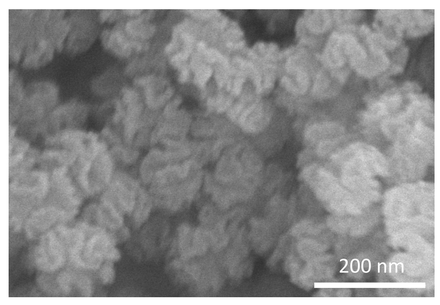


Fig. 2 Representative SEM image of the samples.

All the samples presented a dendritic morphology
For the MSN sample:
Surface area 297.02 m^2/g
Total pore volume 2.51 cm^3/g
Pore size distributions 17 & 31 nm
Average particle size ~120 nm

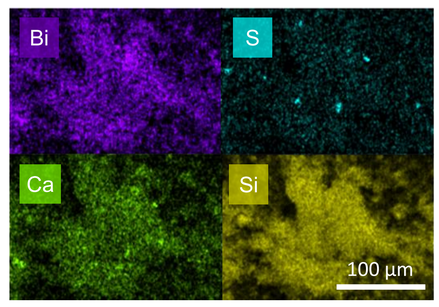


Fig. 4 Elemental distribution in sample 2Bi via EDX. (scale bar is the same for all images)

Cell Viability

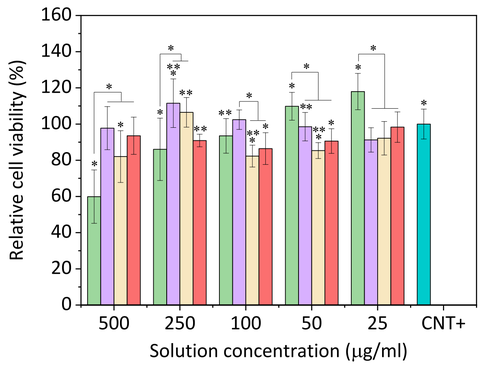


Fig. 5 Direct cell viability test of MG-63 exposed to samples immersed in DMEM (*p < 0.05; ns > 0.05; n = 3; CNT+ indicates regular culture medium.)

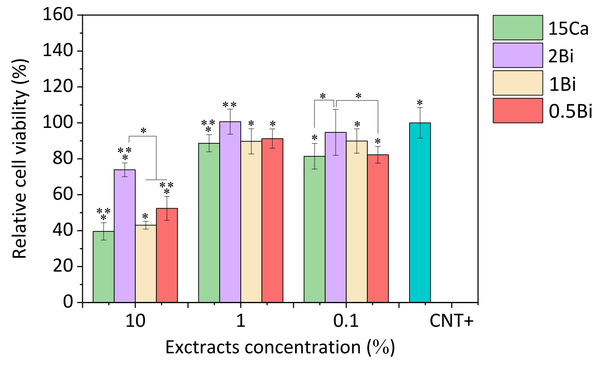


Fig. 6 Indirect viability test of MG-63 cell exposed to filtered dissolution products of the samples at 10, 1, and 0.1% (w/v). (*p < 0.05; ns > 0.05; n = 3; CNT+ indicates regular culture medium.)

Bioactivity

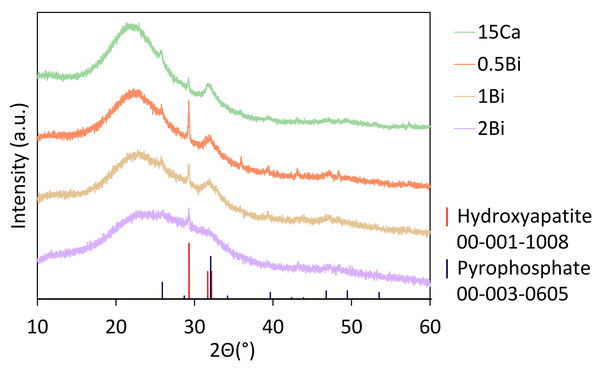


Fig. 7 XRD patterns of samples after 7 days of immersion in SBF.

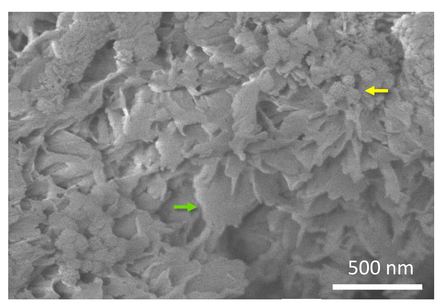


Fig. 8 Representative SEM image of the samples after 7 days in SBF.

SEM image showing dendritic Bi-doped MBGs surrounded by plate-like calcium phosphate deposits. (image from sample 1B)

Antibacterial Activity

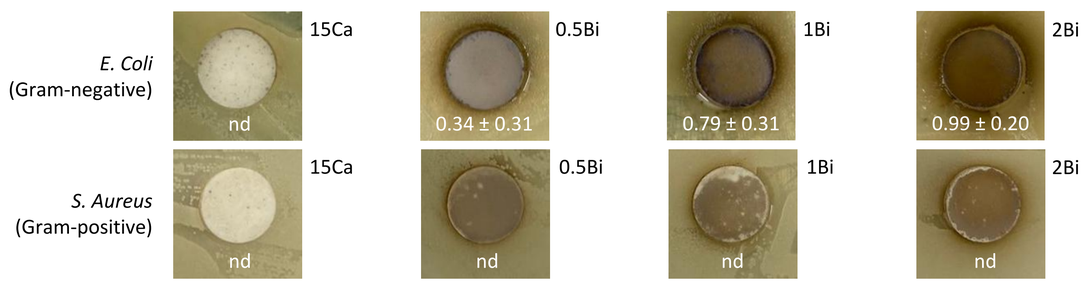


Fig. 9 Measurement in mm of inhibition zones of pressed samples pellets against *E. coli* and *S. aureus*. (nd: not detected)

Ion Release

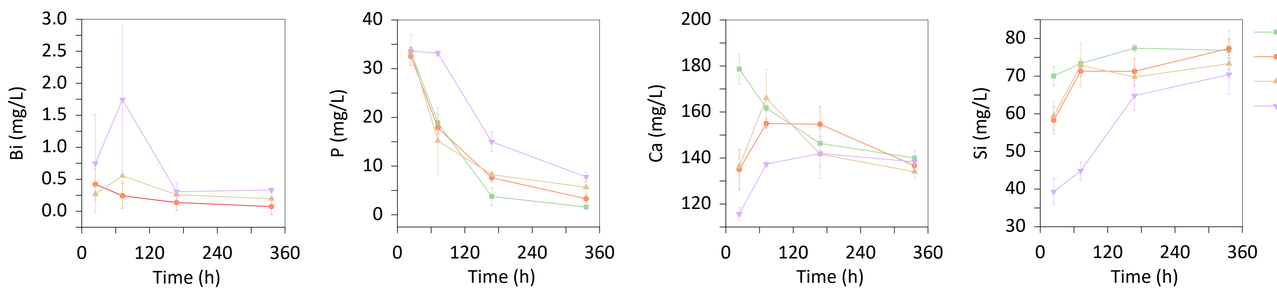


Fig. 10 Ion dissolution profiles of the samples in SBF.

Radiopacity

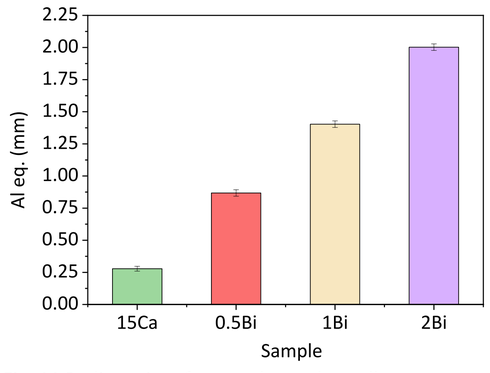


Fig. 11 Radiopacity of pressed samples pellets expressed as aluminum equivalent following the ISO 13116:2014 standard.

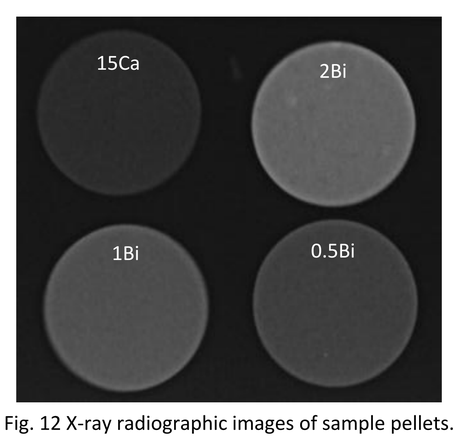


Fig. 12 X-ray radiographic images of sample pellets.

Conclusions

- The nanoparticles maintained dendritic mesoporous structure after synthesis and calcination.
- Minor sulfur-containing crystals were detected, no crystalline bismuth phases formed, confirming successful Bi doping.
- All samples showed bioactivity, evidenced by calcium phosphate formation after SBF immersion.
- Cell viability was confirmed in both direct and indirect assays, with no significant toxicity observed.
- Bismuth was rapidly released within the first 7 days, suggesting potential for early therapeutic effects. Higher Bi content slightly delayed P, Ca and Si ion release but did not reduce their final concentrations.
- No effect against *S. Aureus* and minimal response in *E. Coli* is insufficient to support antibacterial properties.
- Radiopacity increased with Bi content, resulting in notably enhanced visibility.

References:

[1] Saha, R. et al. Ceram. Int. 2024, 50, DOI: 10.1016/j.ceramint.2024.09.036.
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