Table1 Scaffolds loaded with BMP-2 by physical methods for spatial and temporal control

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| Control release  methods | Materials | Manufacture process | Spatial control | Temporal control | Mechanical properties | Results | Reference |
| Physical adsorption | Calcium phosphate;  Mesoporous silica; | Extruded-based bioprinting | Grid-like Cube:  Height:15 mm  Length:4mm  Wideth:3 mm  Pore size:250 μm  Mesoporous size:6 nm | 1 day: 65%  5 days: 80% | Not reported | The complex scaffolds stimulated the osteogenesis of human bone marrow stromal cells in vitro, bone regeneration in vivo, and ingrowth of vascular tissue as shown in a rabbit femur defect repair model. | [[26](#_ENREF_26)] |
| Physical adsorption | Laponite;  Alginate(alg);  Methylcellulose (MC) | Extruded-based bioprinting | Core-shell strands:  Shell: alg-MC bioinks  Core: BMP-2-Laponite-alg-MC bioinks | Cumulative release:  1 day:30%  7 days: 35%  14days:37%  21days:39% | Not reported | The shell bioinks and core depot inks have been demonstrated to be valuable functional materials for BMP-2 delivery and promote osteogenesis. | [[29](#_ENREF_29)] |
| Physical adsorption | Silk;  HAP; | Extruded-based bioprinting | Cylinder:  Porosity: 30%  Height:12 mm  Diameter: 6 mm  Layer height:450 μm | 7 days: 2.5-3.5% | Compressivestrength:4.71 ± 1.01 MPa | It showed that BMP-2 could be loaded into the construct and retain bioactivity, as evidenced by the improved osteogenic differentiation of MSCs. | [[31](#_ENREF_31)] |
| Physical adsorption | Tonic acid;  PCL | rapid prototyping method | Cylinder:  Height:4mm  Diameter:8 mm  Pore size: over 150 μm | One day: 37.51%  Seven days: 47.62%  28 days: 66.19  % | Not reported | 3D scaffolds increased the osteogenic differentiation of the cells | [[37](#_ENREF_37)] |
| Single capping layer | PLGA;  Poly dopamine | Extruded-based printing | Cylinder:  Pore size:468.9-491.3 μm  Coating thickness: 3.66-5.18 μm | First 72 hours; 9.38%  The efficiency of immobilization improved 9.70 times. | Compressive strength: 16.74 ± 1.62 MPa | The complex scaffolds promoted improved adhesion, proliferation, and osteogenesis differentiation of MC3T3-E1 cells in vitro. Polydopamine didn’t impact mechanical strength. | [[39](#_ENREF_39)] |
| Multiple capping layers | MBG;  PEGS | Foam templating process | Cylinder:  Diameter:7 mm  Height:16 mm  Macroporous size: 200-400 μm  Mesoporous size: 7.8 nm  Coating thickness: 6-8 μm | Seven days: 25% | Not reported | The complex scaffold facilitated a rapid healing initiation and advanced regeneration throughout the repair of large bone defects in ectopic bone formation models of rats and radius bone defects in rabbits. | [[49](#_ENREF_49)] |
| Bioink encapsulation | HAP;  Chitosan;  sodium hyaluronate | Extruded-based bioprinting | Cylinder:  Diameter:15 mm  Height:2.5 mm  Pore size: 500-600 μm  Porosity:80-90% | First day: 40%  14 days: 80% | Compressive strength: 6.02 ± 0.19 MPa | The cover improved the mechanical strength of scaffolds. The modified scaffolds showed an additive effect of enhancing osteogenic differentiation of MC3T3-E1 cells and promoted the new bone formation in the calvarial bone defect model of rabbits. | [[53](#_ENREF_53)] |
| Bioink encapsulation | PLGA;  Laponite | Phase-inversion synthesis | Circle membradiameter:8 mm | First day; about 10%  Continual release for 30 days | Not reported | compared with the 2-day release of BMP-2, sustained release of BMP-2 over 30 days induced 3.7 times higher bone volume and 7.4 times higher bone mineral density in the calvarial defect model of rat | [[54](#_ENREF_54)] |
| Bioink encapsulation | Titanium;  Chitosan- Hyaluronic acid hydrogel | Selective laser melting | Cylinder:  Diameter: 2.5 mm  Length:3mm  Pore size: 300 μm  Porosity:’ 55% | First day; 18%  14 days: 95% | Not reported | The composite scaffold improved the bone regeneration and the percentage of bone volume per total volume in the femur defect model of rat | [[57](#_ENREF_57)] |
| Nanoparticles encapsulation | CPC;  PLGA fibers | Self-set in mold | Disc:  Radius: 4 mm  Pore size:1-200 µm  Porosity; 40% | First day: 26%  Three days: 36.2 %  14 days: 43.7% | Not reported | Composite scaffolds enhanced BMP-2 release and were sufficient to promote bone defect healing in the bone defect model of sheep. | [[58](#_ENREF_58)] |
| Nanoparticles encapsulation | TCP;  PLGA | Extruded-based printing | Grid-like cube:  Dimension; 10 × 10 × 10 mm  Pore size: 200 µm | First day: 35%  42 days: 79% | Compressive strength: 2.5 MPa  Elastic modulus; 14.1 MPa | Scaffolds improved not only the osteogenic differentiation of BMSCs in vitro but also new bone formation in cranial defects of rats. | [[59](#_ENREF_59)] |
| Nanoparticles encapsulation | HAP;  PLGA;  PCL | 3D printing technique | square-shaped cube  dimension: 10 × 10 × 10 mm  porosity: 64.96 ± 0.87%  encapsulation particle size: 544.3  ± 39.4 nm | Three days: 17%  30 days: 66%  Encapsulation efficiency; 68.1% | compressive strength: 5.10 ± 0.49 MPa | The composite specimen showed optimal cellular cytocompatibility, no cytotoxicity, and improved bone regeneration in a rabbit calvarial defect mode | [[64](#_ENREF_64)] |
| Nanoparticles encapsulation | PLGA;  Chitosan;  HAP | Extruded-based bioprinting | Cube:  Dimension: 13 × 6 × 4 mm  Pore size: 431.31 ± 18.40 μm  Porosity: 73.64 ± 1.82 %  Nanosphere size: 200-500 nm | Two days; 9.54 ± 0.86 %.  30 days: 61.38 ± 2.39 % | Not reported | The complex effectively controlled the early burst release of rhBMP-2 and successfully repaired the critical bone defect area of the rabbit mandible. | [[63](#_ENREF_63)] |
| Nanoparticles encapsulation | PLLA;  calcium  phosphate | Fused deposition modeling | Grid-like cube;  Thickness:3.0 mm  Width: 3.5 mm  Pore size: 1.0 mm | Not reported | compressive  strength: 0.9 ± 0.04 MPa  elastic modulus: 9.8 ± 0.23 MPa | The scaffold exhibited superior performance in directing the behaviors of human bone marrow-derived mesenchymal stem cells. | [48] |