Table2 Scaffolds loaded with BMP-2 by chemical methods for spatial and temporal control

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| Control release  methods s | Materials | Manufacture process | Spatial control | Temporal control (Cumulative release) | Mechanical properties | Results | Reference |
| Chemical adsorption | Titanium | Electron beam melting;  Plasma treatment | Mesh:  pore size: 600 μm and 1-3 μm  thickness: 500 μm Porosity:76.07% | One day: 18.7%  14 days:34.2% | Density: 1.06 g/cc  Elastic modulus: 6.4 GPa | The scaffold was rendered osteoconductive and osteoinductive, which facilitated bone tissue integration in vitro | [[70](#_ENREF_70)] |
| Chemical adsorption | Titanium | Selective laser melting;  plasma treatment | Gyroid sheet:  pore size: >300 μm  diameter: 10 mm  height: 4 mm Porosity: 73% | Continual release even after 40 days | The quasi-elastic gradient: 1713 ± 198 MPa  Compressive strength: 69.4 ± 2.8 MPa | Grafts significantly enhanced their bone-inductive performance in the dorsum of Fisher rats. | [[71](#_ENREF_71)] |
| Chemical adsorption | Titanium;  Calcium ion;  phosphorus ion | Selective laser melting;  Micro-arc oxidation;  Electrodeposition | Grid-like plate:  10 × 10 × 2  mm3  Pore size:600μm | Continual release up to 35 days. | Not reported | The improved bone formation was identified at 12 weeks post-implantation of the composite scaffold in the calvarial critical size defect model of rats. | [[69](#_ENREF_69)] |
| Chemical adsorption | HAP;  TCP | Digital light processing | Block-shape cube:  Height:9 mm  Width:9 mm  Height:10 mm  Pore size:1.2 mm | Not reported | Not reported | The 3D-printed custom graft with rhBMP-2 showed bone regeneration effects similar to that of deproteinized bovine bone minerals with rhBMP-2 in dogs’ lower jaw defect model. | [[74](#_ENREF_74)] |
| Chemical adsorption | Nanohydroxyapatite;  polyamide 66 | Prefabrication | Cylinder:  Diameter: 4.5 mm  Height: 2.5 mm  Pore size:205 μm  Porosity:54.7 %  Wall thickness:178 μm | Three days: 52.31%  15 days: 81.07% | Compressive strength: 14.88 MPa | The multi-functionalized scaffolds improved BMSC adhesion, proliferation, and osteogenic differentiation in vitro and promoted osteogenesis bone formation in a rat atrophic nonunion model in vivo. | [[100](#_ENREF_100)] |
| Chemical adsorption | PLGA;  Multi-walled carbon nanotubes | Lyophilized method | Grid-like disc:  Pore size:  100-300  Height:2 mm  Diameter:10 mm | Continual release over 21 days | Not reported | The different covalent bonding modes had various impacts on osteogenesis. | [[80](#_ENREF_80)] |
| Chemical adsorption | Poly (ethylene glycol);  Photo-resin; | Digital light processing | Pillars bound-like cube:  Porosity: 75%-94%  Diameter:5.8 mm  Diameter:2.6 mm | Not reported | Effective modules: 0.5-4.0 MPa | These systems supported cell viability and direct differentiation. | [[83](#_ENREF_83)] |
| Chemical adsorption | PLC;  Poly (oligo (ethylene glycol) methacrylate) | Additive manufacturing | Cylinder:  Squared-shaped pores  Height:4 mm  Diameter:4 mm | The constant stimulus for ten days | Not reported | The platform enhanced cell differentiation. | [[76](#_ENREF_76)] |
| Chemical adsorption | TCP;  polydopamine | 3D printing technique | Cylinder:  Pore size: 600 nm- 1.5 μm  Height:8mm  Diameter:8 mm | Culture for seven days. | Not reported | The modified scaffold can vigorously promote the osteogenic differentiation of MC-3T3-E1 cells in vitro. | [[93](#_ENREF_93)] |
| Chemical adsorption | HAP;  Oligonucleotide | Extrude-based bioprinting | Grid-like cube:  Diameter:5 mm  Thickness:3 mm  Height:  Macro pore size: 226 μm  Micropore size: 203 nm  Porosity: 58.02% | Continual impact for 21 days | Compressive strength: 9.34 MPa | The scaffold could effectively mediate cell adhesion, proliferation, osteogenesis, and bone regeneration in ectopic osteogenesis and the bone defect model of Sprague Dawley (SD) rats. | [[82](#_ENREF_82)] |