GMP FACILITIES FOR BIOREACTOR-BASED TISSUE ENGINEERING

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GMP facilities have been traditionally conceived for standard sterile pharmaceutical production, based on chemical compounds concepts.

Production for cell-based active ingredients need a significant reinvention, that bioreactors for Biocomet project realized improving stability of products together with high potential compliance to current pharma products standards.

FROM HYDROGELS TO REINFORCED COMPOSITE STRUCTURES AS A POTENTIAL BONE SUBSTITUENTS

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There have been numerous investigations based on the synthesis of new biodegradable scaffolds for bone tissue replacement. To achieve required features of potential biomaterial substituent, wide range of synthetic and natural polymers along with calcium phosphate phases were used. The main goal is to produce a material that can mimic extracellular matrix of natural bone. Chitosan has shown to be a good candidate for tissue engineering materials due to its chemical similarity to biological molecules and short-time biodegradability in vivo through specific enzymatic reactions. Likewise, chitosan can be processed by different techniques for scaffold production (lyophilization, electrospinning, thermally induced phase separation, particulate leaching, microsphere sintering, etc). Scaffold's topography (surface roughness), charge and wettability, microstructure and interconnected porosity

are the main factors influencing the cell adhesion and activity, neovascularization and angiogenesis. Besides surface properties, the alteration of scaffold's composition during neotissue formation affects further cell proliferation and growth. Calcium phosphate salts have shown good resorption ability in physiological conditions, and depending on its composition, higher solubility. Even though chitosan/hydroxyapatite scaffolds show favourable properties for bone tissue engineering, biomechanical properties of those systems can not meet applications in vivo. To overcome the mechanical drawback, additional synthetic polymers have been used.

Up till now, we have demonstrated the importance of scaffold's composition and microstructure in cell proliferation and differentiation on chitosan/hydroxyapatite three-dimensional structures. In vitro cell cultures in static and dynamical conditions with different cell lines have indicated suitable amount of in situ formed HA within chitosan porous matrix. Since chitosan/hydroxyapatite porous structures form hydrogels in physiological conditions, their mechanical properties do not meet the conditions as bone implants. To overcome those limitations, 3D-printed PLA structure have been applied as a supporting construct for porous chitosan/hydroxyapatite porous hydrogel. Osteogenic evaluation with mesenchymal stem cells after 21 day of culture confirmed good osteogenic properties of three-component porous structure and subsequently indicated its potential application as bone substituent.