

# Piezoelectric biodegradable 3D polyhydroxybutyrate-based scaffolds for bone tissue engineering

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Recently, the development of biodegradable piezoelectric scaffolds has obtained a great attention in the field of tissue engineering and regenerative medicine (TERM) due to possibility to provide electrical stimulation of cells and avoid second surgery. In this regard, natural polyhydroxybutyrate (PHB) polymer is considered as the most promising material, which is a non-toxic, biodegradable and piezoelectric in nature. However, its crystalline structure and piezoelectric properties are scarcely studied. Hence, in the present study, the first investigation of the piezoelectric response of biodegradable electrospun scaffolds based on PHB and their application for bone tissue regeneration in dynamic mechanical conditions is reported. In addition to the well-known shear piezoelectric response of PHB, piezoelectric force microscopy at the nanoscale revealed the out-of-plane response in PHB microfibers. XRD analysis showed the presence of  $\alpha$ - and  $\beta$ -phases in PHB scaffolds, which have shear and normal piezoelectric coefficients, respectively. *In vitro* assays resulted in the influence of the piezoelectric response of PHB scaffolds on the biomimetic mineralization in dynamic mechanical conditions. PHB scaffolds demonstrated ~2 times increase in a relative amount of CaCO<sub>3</sub> formed on the surface of fibers as well as ~4 times increase in an effective piezoelectric charge coefficient ( $d_{33}$ ) compared to that for PHB-3-hydroxyvalerate (PHBV) scaffolds. No toxic effect of PHB scaffolds on the osteoblastic cells is observed. In turn, a CaCO<sub>3</sub> layer on the surface of PHB scaffolds allows changing the wettability from hydrophobic to hydrophilic, thereby resulting in significantly improved cell adhesion and proliferation. Thus, hybrid biodegradable piezo-active PHB scaffolds are a promising platform for bone regeneration.

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