

Enhanced Osteogenesis by Molybdenum Disulfide Nanosheet Reinforced Hydroxyapatite Nanocomposite Scaffolds

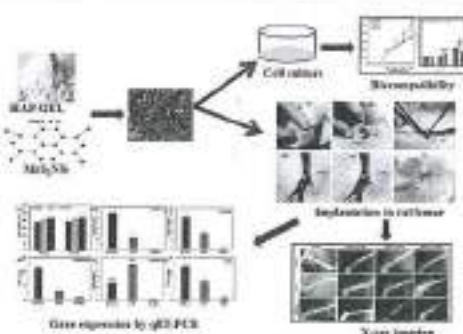
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Supporting Information

ABSTRACT: The advances in the arena of biomedical engineering enable us to fabricate novel biomaterials that provide a suitable platform for rapid bone regeneration. Herein, we have investigated the in vitro and in vivo osteogenic differentiation, proliferation, and bone regeneration capability of molybdenum disulfide nanosheets (MoS₂NSs) reinforced HAP nanocomposite scaffolds. The MG-63 cells were incubated with HAP and HAP/MoS₂NS nanocomposite and followed for various cellular activities. The cells incubated with HAP@2 shows higher cell adhesion, cell proliferation, and alkaline phosphatase activity (ALP) in contrast to HAP. The in vivo and in vitro results of the increased ALP level confirm that HAP@2 promotes osteogenic differentiation. This improved osteogenesis was validated with upregulation of osteogenic marker viz. transcription factor, RUNX-2 (~34 fold), collagen-1 (~15 fold), osteopontin (~11 fold), osteocalcin (~20 fold), and bone morphogenetic protein-2 (~12 fold) after 12 week postimplantation in comparison to drilled. The X-ray imaging demonstrates that HAP@2 implants promote rapid osteogenesis and bioresorbability than HAP and drilled. The outcomes of the present study provide a promising tool for the regeneration of bone deformities, without using any external growth factor.

KEYWORDS: tissue regeneration, scaffold, implantation, osteogenesis, nanosheets, bioresorbability



1. INTRODUCTION

In the past few years, bone disorders have become a significant problem for the modern medical world because of the increased burden on life style and trauma in our population. A central aim of regenerative medicine is to develop tactics that restore or replace organ and tissue functionality lost because of injury, infection, or age.¹ Autologous bone grafts keep on being the standard of consideration to fix bone deformities because of their osteoconductivity, osteogenicity, and osteoinductivity. Nonetheless, their utilization is constrained in light of donor-site morbidity from the follow-up surgery and short supply of host tissue for grafting.^{2,3} Other alternatives such as allografts and xenografts have the menace of disease transmission and immunological responses. Hence, different types of synthetic grafts have been developed and used as an alternative to auto- and allografts. Typical synthetic bone grafting materials come in a variety of physical forms such as granules, putties, liquids, powders, and porous rigid blocks to encourage taking care of, and conveyance to, the surgical site. In addition to these forms, synthetic bone grafts or substitutes emanate in a variety of assortments including bioactive ceramics, glasses, polymers, and polymer–ceramic composites.^{4,5} Generally, for reconstruction and repairing the bone lesions, synthetic grafts by means of metals, ceramics, and polymers are preferred.^{6,7} However, the available bioceramics- and biocompatible-metal-

based synthetic grafts fail to fulfill the anticipated results. It has been reported that the ceramics have lower fracture toughness as compared to human cortical bone, whereas metal fails to directly bond with living bone.⁸ Biomimetic implants are widely used in the field of tissue engineering and are intended to have physical, chemical, and biological properties like those of extracellular matrix (ECM), thereby providing a micro-environment for cell growth.^{9,10} Recently, Kikuchi et al. developed a hydroxyapatite/collagen (HAP/Col) nanocomposite to be used as a biodegradable artificial bone.¹¹ Among the various efforts made to enhance the osseointegration process, the bioactive material like hydroxyapatite [(Ca₁₀(PO₄)₆(OH)₂), HAP] has attracted more attention in orthopedic surgery as a bone-replacing material because of its bioactivity, biocompatibility, and excellent adaptation under in vivo conditions.¹²

In the last couple of years, molybdenum disulfide (MoS₂) has received much attention for application in tissue engineering,¹³ because of its distinct physicochemical and mechanical properties, as well as good biocompatibility.¹⁴ Molybdenum disulfide nanosheets (MoS₂NS) as transition

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