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Bioglass promotes wound healing by affecting gap junction connexin 43 mediated endothelial cell behavior

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Abstract

It is well known that gap junctions play an important role in wound healing, and bioactive glass (BG) has been shown to help healing when applied as a wound dressing. However, the effects of BG on gap junctional communication between cells involved in wound healing is not well understood. We hypothesized that BG may be able to affect gap junction mediated cell behavior to enhance wound healing. Therefore, we set out to investigate the effects of BG on gap junction related behavior of endothelial cells in order to elucidate the mechanisms through which BG is operating. In *in vitro* studies, BG ion extracts prevented death of human umbilical vein endothelial cells (HUVEC) following hypoxia in a dose dependent manner, possibly through connexin hemichannel modulation. In addition, BG showed stimulatory effects on gap junction communication between HUVECs and upregulated connexin43 (Cx43) expression. Furthermore, BG prompted expression of vascular endothelial growth factor and basic fibroblast growth factor as well as their receptors, and vascular endothelial cadherin in HUVECs, all of which are beneficial for vascularization. *In vivo* wound healing results showed that the wound closure of full-thickness excisional wounds of rats was accelerated by BG with reduced inflammation during initial stages of healing and stimulated angiogenesis during the proliferation stage. Therefore, BG can stimulate wound healing through affecting gap junctions and gap junction related endothelial