## The effect of surface ion-doping on the bioactive glass cytocompatibility and antibacterial performance

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In the realm of orthopaedic infection treatments, biofilm prevention while fostering bone growth remains a critical challenge. Moreover, the pressing global threat of rapidly advancing antimicrobial resistance calls for alternatives to traditional antibiotics. Bioactive glasses doped with silver (Ag) or copper (Cu) ions emerge as promising candidates for addressing these challenges. However, concerns regarding the potential toxicity of these dopants must be carefully addressed, as their presence could pose cytotoxic risks.

This study investigates the cytocompatibility and antibacterial performance of two bioactive glasses, either doped with Ag- (Ag-SBA2) or Cu-ions (Cu-SBA3) via an ion exchange process in an aqueous solution. Human adipose stem cells (hASCs) were subjected to various culture conditions, including direct culture on glass discs with and without preincubation, as well as culture in a medium containing glass dissolution byproduct. In addition, the effect of protein adsorption on the cell response was studied by adsorbing fibronectin on the glass discs before direct culture with hASCs. The glasses' antibacterial properties against multidrug-resistant and Gram-positive bacteria, *Staphylococcus aureus*, were evaluated by following two different protocols: i) the International standard ISO 22196, and ii) the protocol published by authors from UPO university [1].

Ag-SBA2 and Cu-SBA3 initially inhibited the hASC viability in direct cell culture. However, viable cells with healthy morphology were maintained when cultured directly on pre-treated discs or indirectly with glass dissolution byproducts. This suggests that the cytotoxicity effect seems to arise from the contact toxicity between the cells and the material surface. Fibronectin adsorption significantly enhanced the cytocompatibility of Ag-SBA2, while Cu-SBA3 requires further optimization. Regarding antibacterial activity, Cu-SBA3 demonstrated a statistically significant reduction in metabolic activity and viable numbers of bacterial colonies adhered to the surface of Cu-SBA3 in comparison with the non-doped one after 24 hours, indicating its potential as a bioactive and antibacterial surface.

In conclusion, Ag-SBA2, through its contact toxicity, has the potential to treat early infection, without compromising long-term cytocompatibility and bioactivity. However, further optimization of the Cu-SBA3 glass is necessary due to its cytotoxicity towards hASCs.

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