Abstract

The increasing demand for safe and human-relevant testing methods in cosmetic and biomedical research has driven the development of *in-vitro* skin models as alternatives to the conventional approaches. A critical factor in the development of these models is the selection of biomaterials that effectively support keratinocyte growth and function. This study evaluated the cell-material compatibility and physicomechanical characteristics of ionically crosslinked gelatin/sodium alginate (SA) hydrogels as two-dimensional (2D) coatings for HaCaT keratinocytes, serving as a preliminary step toward the development of a three-dimensional (3D) *in-vitro* skin model. A preliminary 4 × 4 factorial screening of gelatin and SA concentrations was performed to identify formulations with suitable handling and mechanical characteristics, after which nine formulations were selected for further evaluation. The hydrogels were ionically crosslinked using calcium chloride ($CaCl_2$), and cell viability was assessed using the MTS assay. Physicomechanical characterization was conducted through swelling and biodegradation analyses. The MTS assay demonstrated that all selected formulations supported HaCaT metabolic activity, with no significant differences in cell viability among formulations ($p > 0.05$). In contrast, significant differences were observed in both swelling behavior and biodegradation profile ($p < 0.05$), with SA concentration identified as the primary factor influencing physicomechanical performance. Among the tested formulations, 6% gelatin + 2.5% SA (B3) exhibited the highest mean cell viability while maintaining favorable structural stability, making it the most promising formulation for further development. Overall, these findings demonstrate the potential of ionically crosslinked gelatin/SA hydrogels as biomaterial coatings for keratinocyte culture and provide a foundation for future fabrication of 3D *in-vitro* skin models.

Keywords: HaCaT cells, 2D coating, gelatin, sodium alginate, keratinocytes, *in-vitro* skin model, MTS, swelling, biodegradation