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Genotoxicity of selected hydrogels loaded with iron oxide nanoparticles for potential application in regenerative medicine

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Current advanced methods in regenerative medicine are trying to develop suitable materials that can restore and reproduce the favorable and natural environment needed for skin regeneration. The development of advanced multifunctional materials for wound treatment with the ability to provide multiple functions at once is crucial for clinical application. The utilization of nanohydrogels in regenerative medicine provides an innovative way to treat skin injuries.

As it is important to evaluate the biosafety of nanohydrogels as a degradable biomaterial for use in the biomedical field, the aim of this study was to determine the genotoxic effects of newly prepared nanocomposites. The model system represents different types of skin cells, keratinocytes (HaCaT), and fibroblasts (HFF-1). The experiments were focused on determining the genotoxic effect of nanocomposites and their individual components in *in vitro* conditions. Three hydrogels (Alginate, Pluronic F127, and GelMA) with different chemical compositions and iron oxide nanoparticles were used for nanohydrogel build-up. For genotoxicity determination, we used three different methods: comet assay, fpg-modified comet assay, and micronucleus test to determine aneugenic, clastogenic, and DNA damage.

Initial results after 24 h nanohydrogel exposure, measured by comet assay showed a significant increase in DNA damage in the case of GelMA nanohydrogel. We did not observe any DNA damage in the two other nanohydrogels. Subsequently, we used an fpg-modified comet assay to determine if this DNA damage is caused by base oxidation. However, we did not observe any differences between samples with and without fpg enzyme treatment. We assume that DNA damage is a result of single or double-strand breaks incurred as the attempted repair of UV radiation-induced base damage in DNA. From the results of the micronucleus test, we noticed a higher amount of apoptotic and necrotic cells after GelMA exposure, also the presence of micronuclei was significantly higher.

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