

### Effect and comparison of cross-linking reagents on collagen scaffold

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In this study Genipin (GP) and Grape Seed Extract (GSE), a significantly less cytotoxic cross-linking agent compared to EDC-NHS, was used to cross-link collagen-CS scaffold for jurkat cell. In other words, we evaluated the effects of cross-linking reagents on the cell growth and cytokine production in three-dimensional culture. These reports showed that cell growth in the EDC-NHS was significantly higher than that of the other groups. Cross-linking of collagen using the reactive hydroxy-, amino- and carboxy- groups on the collagen molecule has been described previously. Recently, non-toxic cross-linking agent has been described based on water-soluble carbodiimide and N-hydroxysuccimide (EDC-NHS). Scanning electron microscopy (SEM) revealed the porous surface of each scaffolds maintained their spherical morphology. In addition, cytokine amount through IFN- $\gamma$ , TNF- $\alpha$ , IL-2, and IL-6 assay, that GP and GSE revealed higher than EDC-NHS. GP showed high cross-linking ability, along with toxicity and immune response, respectively. GSE compared with the GP or the EDC-NHS more toxic to the cell itself, given the three-dimensional scaffolds for the culture of cross-linking agent was inappropriate at this time.