

Cross linking hyaluronic acid technic make the HA molecules result in a larger molecule. HA products can have different chemical structures wich may impact its ability to diffuse through a membrane.

An *in vitro* mesh bag test was conducted to observe how long each HA product remains in the mesh bag. In this study, both water and the HA product are free to move in and out of the Polyethylene terephthalate (PET) mesh bag (Figure 1).

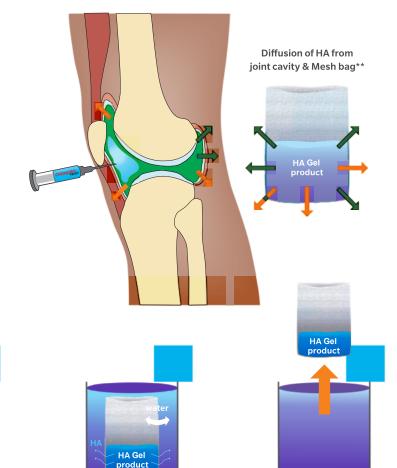






Figure 1: Methodology of PET mesh bag test: demonstrating HA dissolution

The HA samples were placed in the PET mesh bag, the mesh bag was immersed in a beaker containing a concentrated Blue Dextran dye mixed with phosphate buffered saline (PBS) and allowed to sit with gentle mixing. After immersion of the HA in the mesh bag, measurements of the absorption of the Blue Dextran solution remaining in the beaker were taken at 30 min, two hours, six hours and 24 hours. The amount of HA that flowed out of the bag, or the amount of PBS that flowed into the bag, was determined by measuring the absorption of the solution outside of the mesh bag.

Results

The Non Cross-Linked HA (NCL-HA) was observed to completely run out of the bag at two hours. This could possibly be due to the lack of cross-linking, which results in a smaller chemical structure and therefore it more easily flows out of the mesh bag. MMW diffused out of the bag completely by the six hour mark (Figure 2). After the six and 24 hour time mark, 38% and 75% respectively, of the total volume of HMW had diffused outside of the mesh bag (Figure 2). Upon visual inspection, most of the product left in the bag appeared to be the insoluble **NeoCross** (Figure 3).

NeoCross hyaluronate on the other hand did not flow outside of the mesh bag. The **NeoCross** structure is able to incorporate fluid from its surrounding environment, increasing the total fluid volume. Conversely, the less crosslinked formulations of HA along with their fluid carriers diffused out of the mesh bag (Figure 3). The **NeoCross** structure could be the reason for this resistance to diffuse outside of the mesh bag.

Residual volume ratio of HA products in PET mesh bag (Product + water absorbed into product)

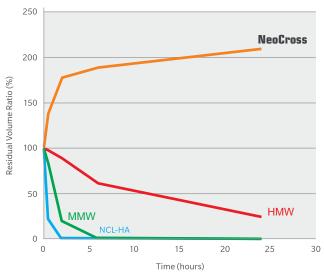


Figure 2: Results of mesh bag test.

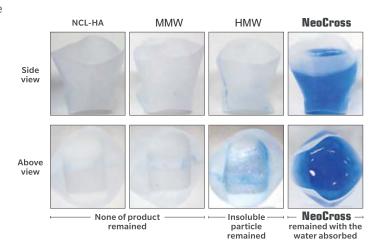


Figure 3: Mesh bags viewed from side and right above after 24 hours