

Appendix

HYA-JOINT Plus Cross-Linking

The cross-linker of HYA-JOINT Plus is 1,4-butanediol diglycidyl ether (BDDE). The epoxide groups in BDDE link to the primary hydroxyl groups in the hyaluronic acid through an ether bond or to hydrolyze into an alcohol (Fig. E-1).

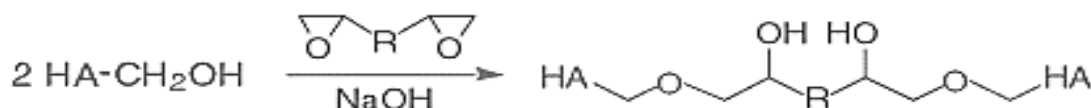


Fig. E-1

Cross-linking of hyaluronic acids with BDDE.

Synvisc-One Cross-Linking

Synvisc-One is composed of formaldehyde-modified hyaluronan (hylan A) and divinyl sulfone-modified hyaluronan (hylan B). Formaldehyde interacts directly with the hydroxyl radicals of hyaluronan (Fig. E-2), whereas the divinyl sulfone cross-linking process first deprotonates hydroxyl groups in alkaline medium to form alkoxy radicals, which then link with divinyl sulfone by the formation of sulfonyl-bis-ethyl cross links (Fig. E-3).

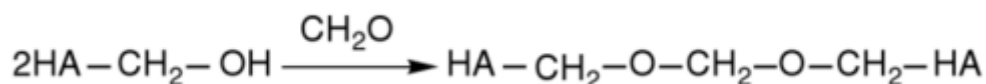


Fig. E-2

Cross-linking of hyaluronic acids with formaldehyde (hylan A).

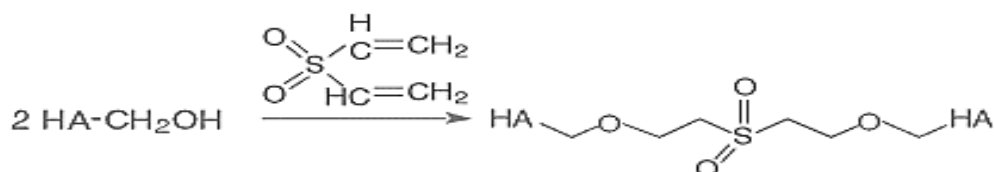


Fig. E-3

Cross-linking of hyaluronic acids with divinyl sulfone (hylan B).

Description of the Secondary Outcome Measures

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC, Likert scale) is a 24-item questionnaire with 3 subscales measuring pain,

stiffness, and physical function. The maximum total score is 96 points, with higher scores indicating worse outcomes.

The Lequesne index was used to assess the severity of knee symptoms during the previous week. It includes the measurement of pain, walking distance, and activities of daily living. The maximum score is 24 points, with higher scores representing worse function.

The timed “Up & Go” (TUG) test is a simple measurement of the time in seconds that it takes for a person to rise from an armchair, walk 3 m, turn around, walk back to the chair, and sit down.

The single-limb stance (SLS) test is done by raising one foot without touching it to the lower extremity (with the target knee) that is supporting the body weight and maintaining balance for as long as possible. Each participant performed 3 trials, and the best result of the 3 trials was recorded.

Patients were asked to rate their satisfaction with treatment, as compared with the pre-injection condition, using a 100-mm VAS (0 = completely dissatisfied and 100 = completely satisfied).