INTRODUCTION:
According to the American College of Rheumatology (2000), intra-articular treatment with Hyaluronic Acid (HA) and hylans is becoming more accepted as an osteoarthritis therapy. HA is responsible for the viscoelastic properties of synovial fluid, which is greatly diminished in osteoarthritic joints in both concentration and molecular weight. For this reason, the main objective of intra-articular treatment with HA is to restore the viscoelastic properties of the synovial fluid. HA is an uniform, linear and un-branched molecule consisting of multiple identical disaccharide units. The only difference between unmodified HA is the length of individual molecules. Two commercial products (Durolane and Synvisc) have modified the HA to increase the residence time in the joint. Synvisc is composed of two components, soluble Hylan A formed through the reaction of protein to extend the HA chain and Hylan B which is Hylan A reacted with divinyl sulfone to form a cross linked gel. Durolane is a stabilized HA based gel for intra-articular treatment of OA, using patented NASHA technology. In this study we investigated if a daily use intraarticular drugs as HA used to treat osteoarthritis could be degraded by the concomitant use with Bupivacaine (local anaesthetic). Bupivacaine is usually administrate as anaesthesia for arthroscopy surgery, postoperative intraarticular pain management and also use concomitantly with HA to decrease injection pain and post-injection discomfort that often appear with HA administration. Often this patients will be susceptible for an HA treatment at the same time or at the immediately postoperative period.

METHODS:
Six commercial HA have been used for this in vitro study (Synvisc™, Coxarthrum™, Go-on™, Hyalgan™, Synocrom™ and Durolane™) with Bupivacaine at three different concentrations (0.25%, 0.50% and 0.75%) without or with adrenaline (1/200,000). All products were used before their expire dates. Samples were diluted to reach a similar concentration (0.5mg/ml) and incubated 24 hours at 37°C. Molecular Exclusion HPLC have been used for determination of molecular weight and degradation percentage of HA from the retention times obtained by HPLC. Anova-Manova, (Newman-Keuls test) correlation have been used to determine statistical significance.

RESULTS:
Coxarthrum®, Hylgan®, Synocrom® and Go-on® have shown more degradation than Synvisc® and Durolane® (p<0.05) with bupivacaine. Figure 1A shows the HA percentages of degradation without adrenaline. Higher concentration of Bupivacaine increased the degradation of HA in all cases (p<0.05) and the concomitant use of adrenaline increased the degradation (in different significance degree) of all the HA as shown in Figure 1B.

DISCUSSION:
Bupivacaine concomitant intraarticular administration with HA must be valued before use and probably avoid, because this local anesthetic increased HA degradation of all the HA studied. Daily clinical practice is often based in not correct scientific models and after a habit practice we can found a not correct practice as the extended custom of use local anesthetic with HA. This degradation seems to affect more over low molecular weight HA and not stabilized products. Durolane® suffered less degradation than the others HA. In this study we have found that the HA in Durolane® is not only bound into the particles, but there is also a soluble fraction which can be separated from the HA gel particles and that this soluble fraction is more resistant to free radical and bupivacaine breakdown than the soluble components of other hyaluronan based products. In conclusion it has been shown that Bupivacaine increased degradation of HA. Stabilized product (NASHA™ technology) as Durolane® suffered less degradation than the others not stabilized HA.

REFERENCES: