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Characterization of the visco-elastic properties of hyaluronic acid

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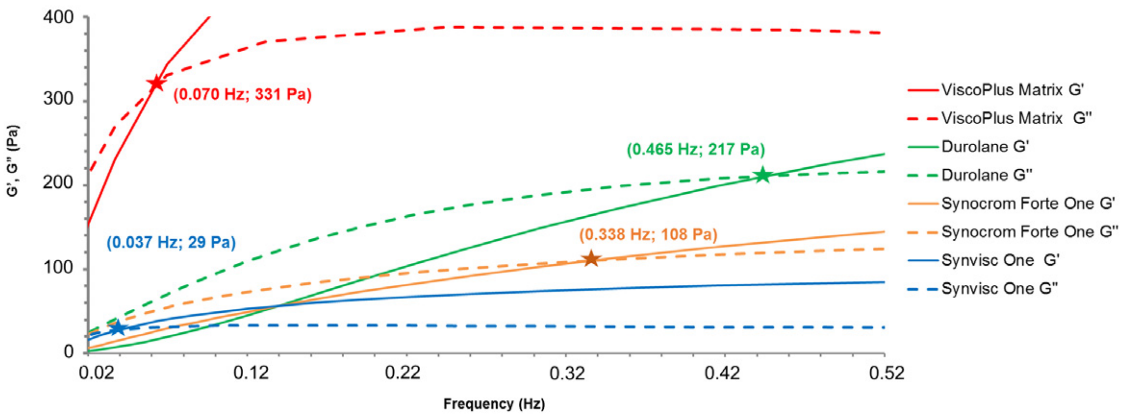

Fig. 1. Viscoelasticity shown by four cross-linked HA preparations. The variations in elastic modulus G' and the viscous modulus G'' with frequency are shown. The continuous lines stand for the elastic modulus and the discontinuous lines for the viscous modulus. The cross-over point values are highlighted ($\star$). The HA hydrogels analyzed were: Viscoplus Matrix (VPM), Durolane (D), Synocrom Forte One (SCF) and Synvisc One (SVO).

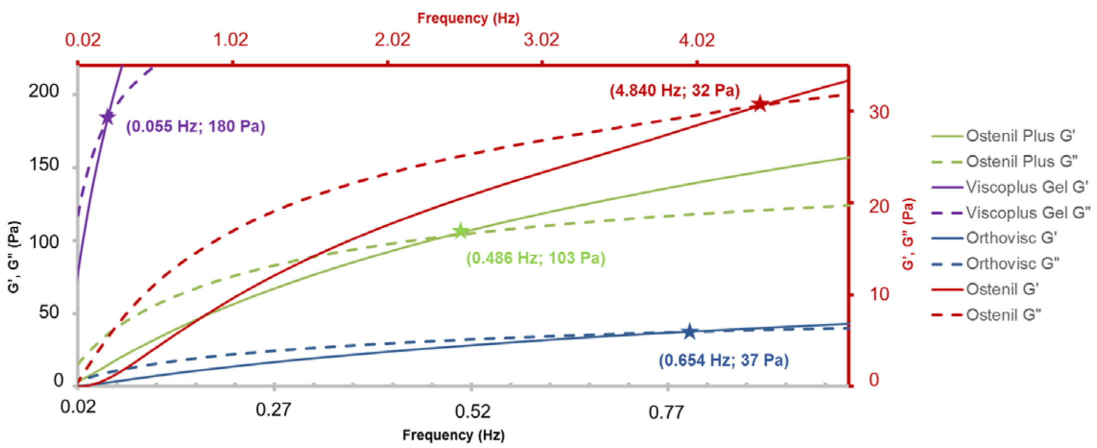

Fig. 2. Viscoelasticity shown by four linear-HA preparations. The variations in elastic modulus G' and the viscous modulus G'' with frequency are shown. The continuous lines stand for the elastic modulus and the discontinuous lines for the viscous modulus. The cross-over point values are highlighted ($\star$). The HA solutions studied were: Ostenil Plus (OP), Viscoplus Gel (VPG), Orthovisc (Ort) and Ostenil (Ost). The red x- and y-axes apply only to data for Ostensil G.

2. Results

With respect to the 4 HA hydrogels studied, comparison of crossover frequencies (Hz, see Fig. 1) allowed their division into two main groups: the CL-HA of the first one presented crossover frequencies in the order of magnitude of 10^{-2} Hz (SVO and VPM), while the other HA preparations showed crossover frequencies in the order of 10^{-1} Hz (SFO and D). In contrast, only one of the 4 studied linear HA reached the transition point to become a mainly elastic fluid at very low frequency (in the order of magnitude of 10^{-2} Hz, VPG, see Fig. 2), whereas two others exhibited crossover frequencies in the order of 10^{-1} Hz (OP and Ort) and the other one (Ost) remained as a predominantly viscous fluid at frequencies as high as 4.8 Hz.

The lowest values of $G' = G''$ obtained at the crossover point corresponded to the CL-HA SVO and the linear HA solutions Ost and Ort (~30–40 Pa). The CL-HA SFO, and linear HA VPG and OP, gave rise to values more than 3 times higher (~100 Pa), D 7 times higher (~200 Pa) and VPM 11 times higher (~300).

The rheological parameters at frequencies of 0.5 Hz and 2.5 Hz are displayed in Table 1. They reveal that the HA hydrogels were more elastic ($\tan \delta < 1$) than viscous ($\tan \delta > 1$) at both frequencies [i.e. the elastic component (G') prevailed over the viscous component (G'')] except for D at 0.5 Hz. In contrast, although the linear HA solutions Ort and OP at 2.5 Hz as well as VPG at both studied frequencies showed a similar behavior ($\tan \delta < 1$), a predominantly viscous behavior was shown in Ort and OP at 0.5 Hz and Ost at both frequencies.

Statistically significant differences were determined for every comparison between the 4 HA hydrogels except two: the $\tan \delta$ of SVO vs. this parameter of VPG at 2.5 Hz and the $\tan \delta$ of SFO vs. this parameter of D at 2.5 Hz.

3. Discussion

Previous reports have described comparisons of the rheological properties among different commercial HA preparations and human synovial fluid, and reviewed the in vivo performance of injected HA in osteoarthritis. Here we compared the rheological properties of 8 different HA preparations in vitro, to support their employment for different biomedical applications.

The frequency and $G' = G''$ value at the crossover point of an HA preparation define its viscoelasticity. In this way, our rheological studied showed visco-elastic behavior in the 8 solutions analyzed. One product, CL-HA VPM showed a remarkably higher $G' = G''$ value at this point with a very low crossover frequency.

According to Balazs, 0.5 Hz and 2.5 Hz are the transition points from a quiet state to the beginning of a walking movement and running movement. At these frequencies, the G' values presented by the CL-HA VPM were particularly higher than the values observed in the other HA products. This difference was also detected in the G'' values at both frequencies.

The quality of HA preparations for diverse biomedical applications has widely been related to these rheological parameters, so that the suitability of the fluid in this context increased with them. For instance, Edsman et al. state that the resistance to deformation or gel strength increases with the G^* value (where $G^* = ((G')^2 + (G'')^2)^{1/2}$, the vector sum of G' and G'' or the modulus of the vector $G' + iG''$). In this way, the visco-elastic properties (i.e. the rheological relevance) of the HA preparations can be ordered according to the values of G^* at both transition points (0.5 Hz and 2.5 Hz) as follows: ViscoPlus Matrix > ViscoPlus Gel > Durolane > Synocrome Forte One > Ostenil Plus > Synvisc One > Orthovisc > Ostenil.