

A Safe-by-Design Approach for the Synthesis of a Novel Cross-linked Hyaluronic Acid with Improved Biological and Physical Properties

Sabrina Sciabica ^{1,†}, Riccardo Barbari ^{1,†}, Riccardo Fontana ², Giovanni Tafuro ³, Alessandra Semenzato ⁴, Daniela Traini ^{5,6}, Dina M. Silva ⁶, Larissa Gomes Dos Reis ⁶, Luisa Canilli ⁷, Massimo Terno ⁷, Peggy Marconi ², Anna Baldisserotto ^{1,*}, Silvia Vertuani ^{1,*} and Stefano Manfredini ¹

¹ Department of Life Sciences and Biotechnology, University of Ferrara, via L. Borsari 46, 44121 Ferrara, Italy

² Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, via Fossato di Mortara 64/B, 44121 Ferrara, Italy

³ Unired Srl, via Niccolò Tommaseo 69, 35131 Padova, Italy

⁴ Department of Pharmaceutical and Pharmacological Sciences, University of Padova, via Marzolo 5, 35131 Padova, Italy

⁵ Macquarie Medical School, Faculty of Medicine, Health & Human Sciences, Macquarie University, Campus Macquarie Park, Sydney 2109, Australia

⁶ Woolcock Institute of Medical Research, 431 Glebe Point Road, Glebe, Sydney 2037, Australia

⁷ Istituto Ganassini S.p.a., Via Carlo Boncompagni, 63, 20139 Milano, Italy

* Correspondence: bldnna@unife.it (A.B.); vrs@unife.it (S.V.); Tel.: +39-0532-455258 (A.B.); +39-0532-455294 (S.V.)

† These authors contributed equally to this work.

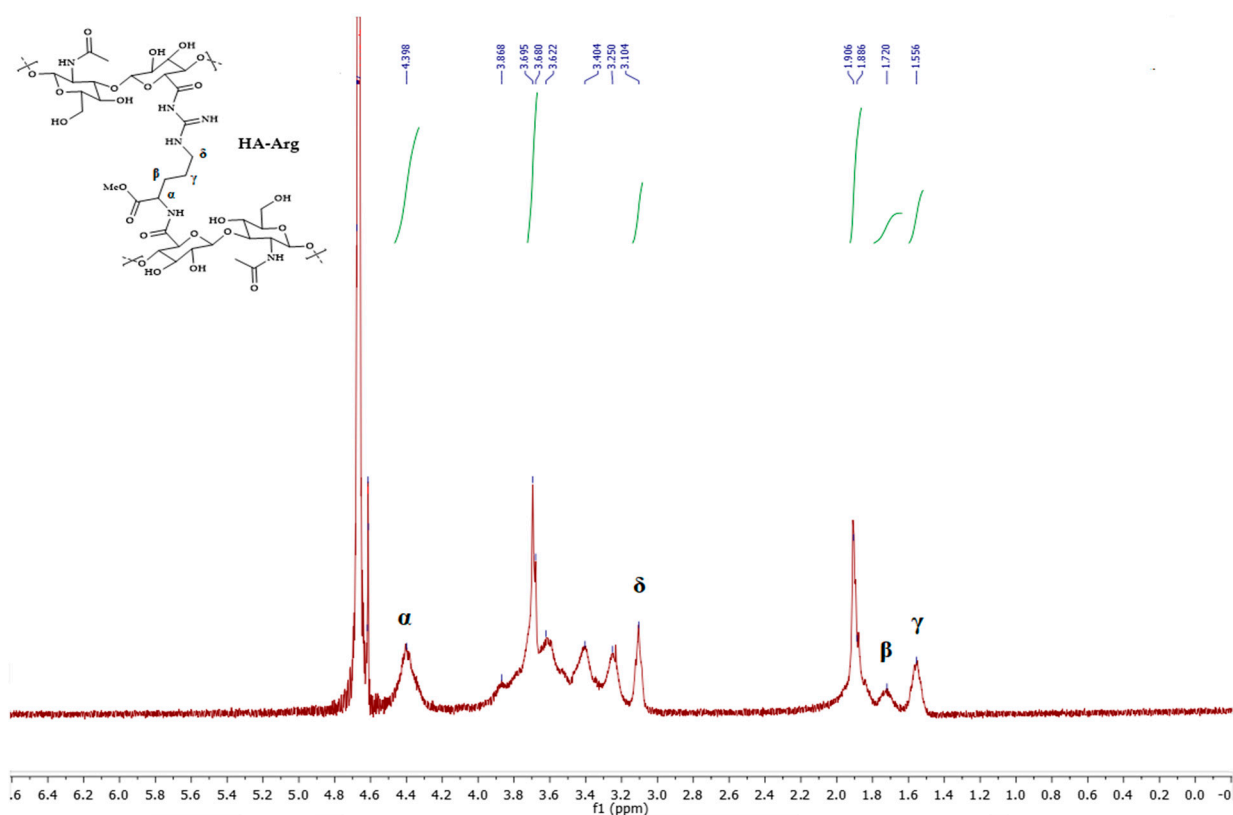


Figure S1. ¹H NMR spectra of cross-linked product HA-Arg.

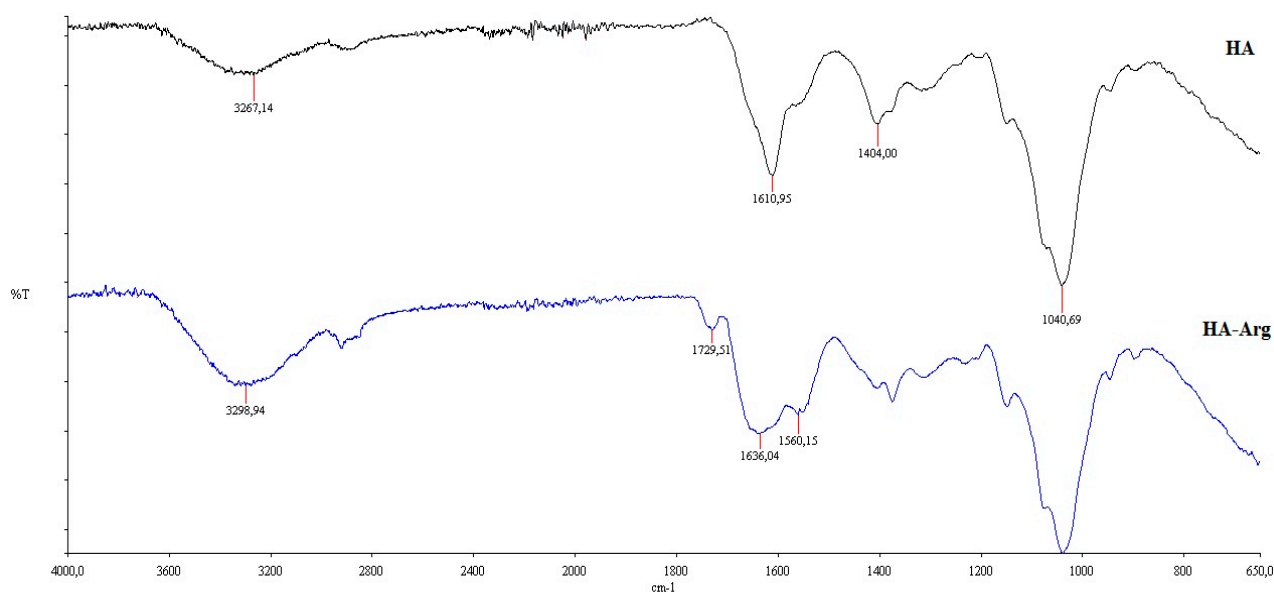


Figure S2. IR spectra of native HA and HA-Arg.

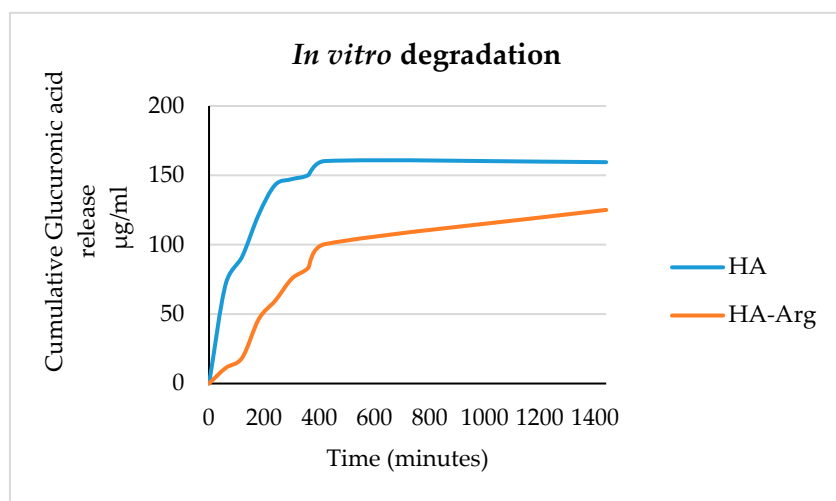


Figure S3. Glucuronic acid released from in vitro degradation of HA, and HA-Arg in PBS, pH 7.4 at 37 °C, with 50U/ml of hyaluronidase.