Electronic supplementary materials *Mendeleev Commun.*, 2023, **33**, 556–558

Effect of hyaluronic acid encapsulation in a silica hydrogel matrix on drug penetration through the skin

Ekaterina S. Dolinina and Elena V. Parfenyuk

Ex vivo experimental measurements of HA penetration from hydrogels into the skin

HA penetration from pure HA hydrogels and HA–silica hybrid hydrogels was studied *ex vivo* using chicken breast skin as a model skin membrane. Subcutaneous fat was carefully removed. The skin samples were thoroughly washed with an aqueous solution of $NaHCO_3$, then with distilled water and dried with paper towels. The integrity of the skin was monitored visually. The skin sample was placed between the donor and receptor chambers of the vertical diffusion cell. Hydrogel samples (1 g) were carefully spread over the skin surface in donor chambers, which were then covered with aluminum foil to prevent the samples from drying out. The effective diffusion area of the skin was 7.065 cm^2. Acetate buffer solution (pH 5.5) (50 ml) was poured into the receptor chamber and continuously stirred with a magnetic stirrer at 100 rpm. The inner surface of the skin was in contact with the receptor medium. During the experiment, the temperature of the diffusion cells was maintained at 32 ± 2 °C. Samples (5 ml) of the receptor medium were withdrawn at specified time intervals for 12 h and the cell was refilled with an equivalent amount of fresh buffer solution. After centrifugation, the amount of HA in the samples was determined spectrophotometrically using Stains-all dye.[S1–S3] For this purpose, Stains-all (5 μg) was dissolved in a mixture of water (40 ml) + ethanol (10 ml). The dye solution was added to the withdrawn sample in a ratio of 1:2 (v/v). The amount of HA in the receptor medium was calculated from the absorbance at 640 nm (spectrophotometer SF-2000, St. Petersburg, Russia) using a calibration plot.

As an example, Figure S1 shows a typical spectrum of the receptor medium after HA penetration from HG2(1%)M prior to sample centrifugation. As can be seen from the figure, the spectrum exhibits intensive absorption in the region of 200–215 nm, which is related to light scattering by silica particles, and a small peak at 450 nm, associated with the dye aggregation state between dimers and J-aggregates.[S4] The band at 640 nm is the J-band, and its intensity is linearly dependent on the concentration of HA, which exists at pH 5.5 as a polyanion.[S1–S3]

Investigation of morphology by scanning electron microscopy (SEM)

To study the morphology of hydrogels, they were dried at a temperature of 150 °C for several days. Images of dried samples were taken on a Quattro S scanning microscope (Thermo Fisher Scientific, Czech).

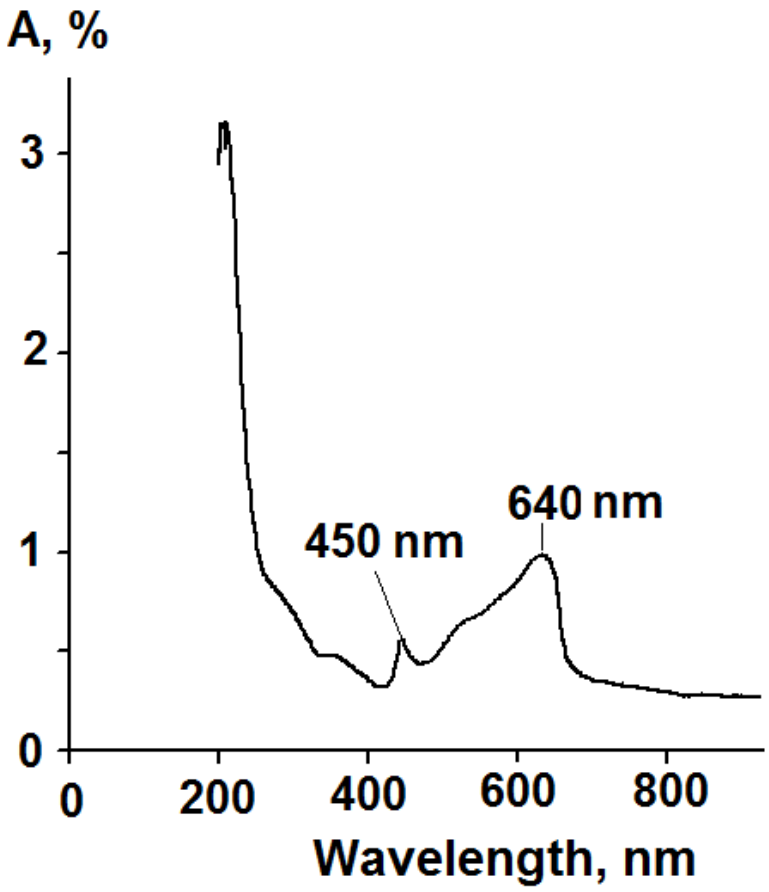

Figure S1 Absorption spectrum of the receptor medium after penetration of HA from HG2(1%)M (before centrifugation).

References

S1 R. D. Edstrom, *Anal. Biochem.*, 1969, **29**, 421.

S2 M. Fagnola, M. P. Pagani, S. Maffioletti, S. Tavazzi and A. Papagni, *Contact Lens and Anterior Eye*, 2009, **32,** 108.

S3 F. A. Maulvi, T. G. Soni and D. O. Shah, *J. Biomater. Sci., Polym. Ed.*, 2015, **26**, 1035.

S4 R. E. Kay, E. R. Walwick and C. K. Gifford, *J. Phys. Chem.*, 1964, **68**, 1896.