A complementary calorimetric approach for drug release investigations.

B. Bellich[a], M. Borgogna[b], A. Cesàro[a,c]

[a] Dept. of Chemical and Pharmaceutical Sciences University of Trieste, Via Giorgieri 1, I-34127 Trieste, Italy
[b] Dept. of Life Sciences, University of Trieste, Via Giorgieri 1, I-34127 Trieste, Italy
[c] Elettra Sincrotrone Trieste, Area Science Park, I-34149 Trieste, Italy

Purpose. DSC study of water diffusion is proposed as a complementary approach to investigate the matrix properties of polysaccharide gels in the pre-formulation step.
Methods. Calcium-alginate beads were prepared by drop-wise addition of the alginate solution (2% w/v) into a calcium chloride 0.050 M solution. Lysozyme and human insulin were loaded as model proteins. Additional components, such as chitosan, were added to the alginate. Release tests were carried out in Tris buffer/HCl 0.005 M with NaCl 0.15 M. A colorimetric assay (BCA test) was used to determine the amount of protein loaded and released. Calorimetric investigations were carried out using a heat-flux calorimeter; one bead was placed in an open pan and analyzed under nitrogen flux at a scan rate of 5 K/min.
Results. The additional components to the alginate basic formulation (such as chitosan, HPMC, ethanol) modify the LSZ release profile. Chitosan is the most effective. Release curves were fitted using the general Weibull equation. The parameter n is used as an indicator of the diffusion rate. The linear form of Clausius–Clapeyron equation was used for quantitative comparison purpose. The change in the slope (B) reflects changes in the "evaporation rate".
A good correlation between release and calorimetric data, supporting the hypothesis of the obstruction model, was obtained for lysozyme, except in the case of 1% HPMC, where slope B suggests obstruction but the release of LSZ is rapid. The obstruction effect of chitosan is clear in unloaded beads, nevertheless the addition of chitosan produces different effects in case of loaded beads with lysozyme or human insulin. Indeed, chitosan decreases insulin release (high n) but the slope B changes less than in the case of LSZ.
Conclusions. A wide data set on other relevant systems will enforce the correlation between the release/effusion phenomena. The correlation would allow to understand whether the interaction between chitosan and insulin is predominant with respect to alginate and chitosan, thus compromising the obstruction effect, and whether the interaction of lysozyme with alginate is hampered by HPMC.

References

Heyd, R.; Rampino, A.; Bellich, B.; Elisei, E.; Cesàro, A., Saboungi, M. L. Isothermal dehydration of thin films of water and sugar solutions. J. Chem. Phys. 140 124701 (2014).
Bellich, B.; Borgogna, M; Cok, M.; Cesaro A. Water evaporation from gel beads. J. Thermal Anal. Calorim. 103 81-88 (2011).
Bellich, B.; Borgogna, M.; Cok, M.; Cesàro, A. Release properties of hydrogels: water evaporation from alginate gel beads, Food Biophys. 6, 259–266 (2011).