Oligomers as Rheological Modulators in Structured Biopolymer Systems

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ABSTRACT

Both in foods as well as in pharmaceutical products it is often required to optimize rheological properties with respect to e.g. mechanical response, and setting and melting properties. Such optimizations are usually performed by changing polymer concentration or combining different polymers. A far simpler way to tailor the rheological properties would be to manipulate the systems applying oligomers. So contrary to rendering the overall polymer concentration, the use of oligomers would make it possible to de-couple viscosity and mechanical properties.

INTRODUCTION

In their own right, oligomers have traditionally not been looked upon as having long range structural capabilities. This is of course due to their limited structuring potential when present alone. It is a well-known and established fact that a reduced molecular weight of a gelling polymer leads to an increase in the degree of non-ideality within the network formed[1]. This is due to a fractional increase in the loose-end and sol fraction, the net result being less elastically active segments per unit volume gel formed.

In combination with high molecular weight biopolymers, on the other hand, several reports on oligomers acting as modification agents exist[2,3]. The forthcoming examples will show how oligomers can impose structural modifications in such ordered biopolymer systems pointing towards the possibility to tailor new product properties (alginate and gelatin) or to modify physiological viscoelastic materials (mucins/mucus).

LMW GELATINS

The presence of low molecular weight gelatin fragments (sub-α) results in reduced mechanical properties of gelatin gels. It has been discussed if this may be due to a direct influence on the percolation of the gelatin network[4] or if these fragments have no effect at all suggesting that the observed reduction in gel rigidity in the presence of such fragments is a mere reduced content of high-MW chains[5]. Some recent papers[6,7] support the view that low-MW gelatin fragments do have a direct influence on network percolation. This can be looked upon as a displacement effect where LMW fragments enter into ordered gelatin junction zones (triple helical structures) without providing any functionality since they are too short to connect to other ordered junctions. The net effect thus seems to be that the presence of low-MW fragments competitively inhibits high-MW gelatin chains to enter into ordered junction sites and hence perturbs the connectivity of the final gelatin network.

Banner Pharmacaps has patented and apply gelatin hydrolysates in order to obtain a soft inner matrix of their chewable capsule compositions[8].

ALGINATE OLIGOGULURONATES

Since the two monomers of the alginate molecule (guluronic (G) and mannuronic (M) acids) do not occur randomly but rather in a block-wise fashion, combined with the fact that the different glycosidic linkages have different susceptibility towards acid hydrolysis, it is relatively easy to isolate the oligo-guluronates (G-blocks with typically more than 90% G with an average Dp in the 10-20 range). It is the same structures that are responsible for the binding of e.g. Ca^{2+} ions and hence the gel forming properties of alginates.

When these oligomers are mixed with a high MW gelling alginate, the net result with respect to the mechanical properties of the final gel strongly depends on the level of calcium ions present. As shown in Figure 1, there is a net weakening of the gel at low to medium Ca^{2+}, whereas at higher calcium ion concentrations a net strengthening is observed.

A decreased Young's modulus at low to medium Ca^{2+} concentrations can easily be attributed to the ability of these free G-blocks to bind Ca-ions without participating in the network structure. At high Ca-concentrations, however, Youngs modulus increases with G-block concentration. Considering the small addition of G-blocks to the gelling system (still approximately 98% water) the observed effect can not be that of an e.g. inert crystalline-like G-block filler. An explanation model that opens up for interactions between free G-block oligomers and the high Mw gelling alginate must therefore be considered.

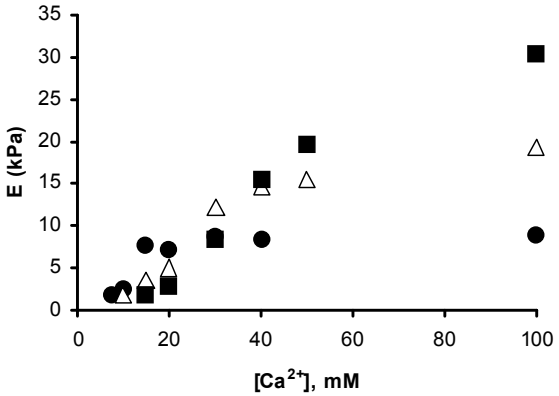

Figure 1. Young's modulus as function of added G-blocks and calcium concentration at a constant cp=10 mg/ml of a high-G gelling alginate. (•) without G-blocks, (Δ) with 5mg/ml G-blocks and (■) with 10mg/ml G-blocks.

There is no straight forward explanation for the observed effects at high $[Ca^{2+}]$ within the framework of the original egg-box model of alginate junction zones[9], which suggests a dimerization of alginate chains. If, however, a further lateral association of alginate chains beyond dimerization is opened up, it would be possible to imagine G-block oligomers to act between topologically restricted G-blocks within molecules of the gelling alginate and hence shortening the elastic segments of the resulting gel. Such a multimodal molecular model has been suggested following a small-angle X-ray scattering (SAXS) study of alginate gels[10]. At high $[Ca^{2+}]$ and high content of G-residues, which matches exactly the present situation, cross-sectional dimensions of the junction zones indicate lateral association far beyond that of a dimerization.

Since these oligomeric G-blocks will contribute only minimally to viscosity, this method represents a way for preparing alginate gels where an increased mechanical response is de-coupled from an increase in viscosity of the gelling solution.

Oligoguluronates do not only exhibit modulating properties in systems with their mother molecule (alginate) but also in considerable more complex systems. Figure 2 shows the mechanical spectra of a pure model mucin gel (Pig Gastric Mucin, PGM, having similar structural build-up as human respiratory mucin) and the effect on that system upon introducing high Mw alginate as well as oligoguluronates to the mixed PGM/Alginate system. As expected and as reported earlier[11], an introduction of HMW alginate to PGM increases the mechanical response to a greater extent than just by adding the response of the two biopolymers alone. Furthermore, upon addition of G-blocks to this mixed system, the mechanical response is reduced to such an extent that it is even lower than that of the pure PGM. This result clearly shows that G-blocks are able to displace alginate/PGM interactions and perhaps even PGM/PGM interactions. The latter finding has resulted in a broad approach where the potential of applying G-blocks for increased mucosal bioavailability of macromolecular pharmaceuticals are being studied.

The potential of G-blocks to prevent PGM/alginate interactions, referred to as electrostatic competitive inhibition, implies a substantial potential with respect to symptom relief for patients suffering from cystic fibrosis. This medical indication usually implies an infection with *Pseudomonas aeruginosa,* a bacterium producing mannuronate-rich high-Mw alginate *in vivo*, or an infection with *Burkholderia* species producing other anionic polysaccharides. Reduced mechanical properties following introduction of G-blocks to *ex vivo* sputum from patients diagnosed positive for *P. aeruginosa* have also been proven[12]. As a result of these findings, human clinical testing of G-blocks as a pseudo-mycolytic in patients suffering from cystic fibrosis has now commenced.

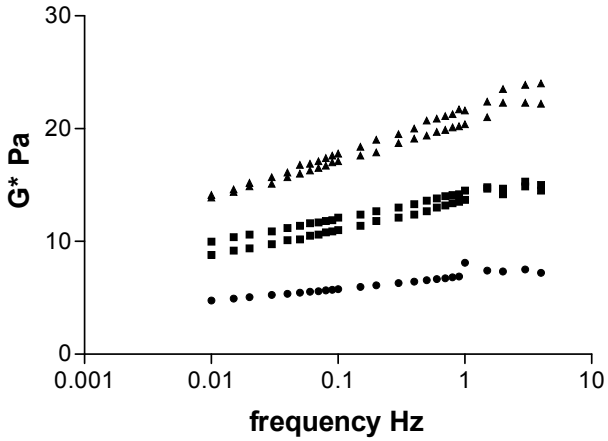

Figure 2. Mechanical spectra of purified pig gastric mucus (■) equilibrated with 30 mg/ml HMW alginate (▲) and finally equilibrated with 30 mg/ml oligoguluronate (G-block; ●) DP_n 19.

CONCLUSIONS

A few examples on the functionality and potential applications of hydrocolloid oligomers have been presented. Such oligomers seem to conceal considerably more than what is presently acknowledged about their structure-function and application potential in ordered biopolymer systems.

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