Product Information Bulletin

NOVAMATRIX™
Ultrapure Polymer Systems

Stability and shelf life of PRONOVA UP sodium alginates

Alginate is a linear polysaccharide consisting of (1→4)-linked β-D-mannuronate (M) and its C-5 epimer α-L-guluronate (G) (Figure 1). The monomers can appear in homopolymeric blocks of consecutive G-residues (G-blocks) or consecutive M-residues (M-blocks), alternating M- and G-residues (MG-blocks), or randomly organized blocks.

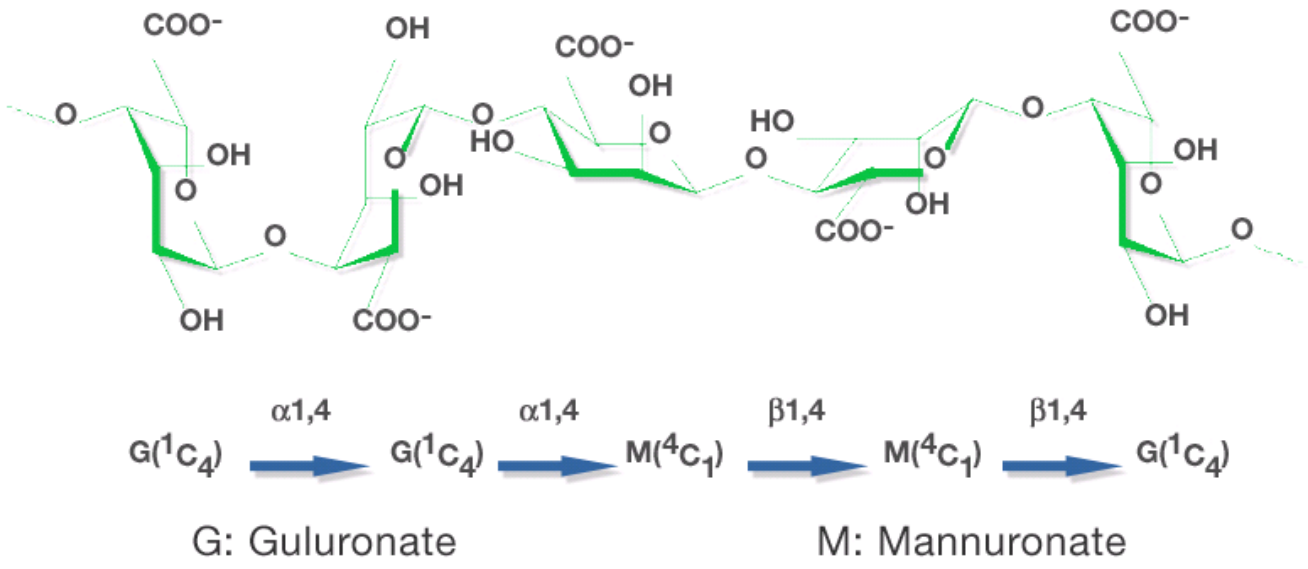

Figure 1: Representative structure of alginate, showing monomer identities, and linkage types.

For most applications of alginates, the molar mass (molecular weight) is an important parameter determining the functionality of the alginate for that specific application. Aqueous solutions of alginates are viscous, the observed solution viscosity being dependent on molar mass, concentration of alginate, temperature, and potentially also presence of salts and other compounds in the formulation. Viscosity measurements are often used as a simple measurable parameter of changes in the molar mass of a polymer, and thereby can be used as a stability indicating parameter.

Depolymerization of alginates will occur in solution and in the solid state due to a variety of mechanisms. Smidsrød et al (1963) observed that the presence of oxygen affected the stability of non-purified alginates in solution due to the presence of phenolic reducing substances that gave rise to oxidative-reductive free radical depolymerization (ORD). On the other hand, Holme et al. (2003; 2008) have shown that purified alginates in the solid state and in solution are depolymerized primarily by acid catalyzed hydrolysis and alkaline catalyzed mechanisms. The highest stability was observed in a pH interval of 5 to 8. Increased temperature will increase the rate of depolymerization for all mechanisms mentioned above (Holme et al. 2003; 2008). In vivo data on the kinetics and mechanism of depolymerization of alginates are scarce. There are no mammalian enzymes that are active towards alginates, however, even in mammals, one must expect random depolymerization mechanisms like the ones described above to occur. This document reports on the stability, shelf-life and storage conditions for PRONOVA UP sodium alginate powders.

NovaMatrix conducts stability studies according to ICH guidelines for all our product ranges. For sodium alginates, the parameters monitored are appearance of powder, dry matter content, intrinsic viscosity, apparent viscosity, pH, molar mass, chemical composition, ash content, endotoxins, and microbial purity.

Apparent viscosity, intrinsic viscosity, and molar mass, which are all indicative measurements of depolymerization, have been observed to change significantly upon time under certain storage conditions. Figure 2 shows example data for the apparent viscosity (measured in 1% (w/w) sodium alginate solution at 20°C using Brookfield viscosimeter at 20 rpm) from a stability study conducted on PRONOVA UP LVG (low viscosity, high-G sodium alginate). No significant change in apparent viscosity is apparent after 5 years of storage at 2-8°C/ambient relative humidity (RH), or at -18°C. For storage at 25°C/60% RH, apparent viscosity displayed approximately 20% decrease after 5 years, while at 40°C/75% RH, apparent viscosity was reduced by approx. 40% after 12 months.

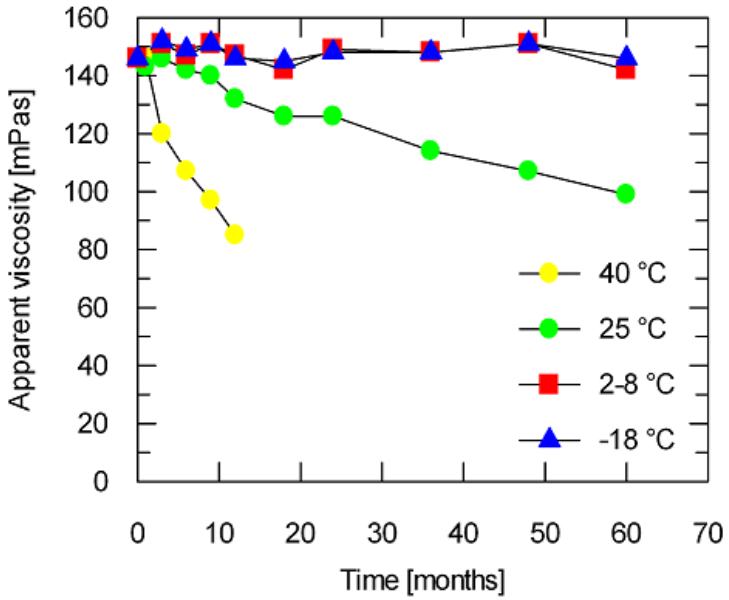

Figure 2: Apparent viscosity values observed during 60 months of storage of PRONOVA UP LVG.

Based upon stability studies, NovaMatrix recommends refrigerated storage (2-8°C) of all PRONOVA UP sodium alginates. We label PRONOVA UP LVG/LVM/MVG/MVM with a shelf life of 3 years under refrigerated storage. PRONOVA UP VLVG and VLVM are new products currently not labeled with a shelf life, as stability studies are pending. We expect these very low viscosity products to be at least as stable as PRONOVA UP LVG/LVM/MVG/MVM. All PRONOVA UP sodium alginates are delivered in a closed polyethylene container. During storage, the lid of the container should be kept closed.

Our stability programs show that PRONOVA UP sodium alginates can be stored at room temperature (25°C/ 60% RH) for 6-9 months without significant reduction of apparent viscosity. Therefore, we do not consider cool/cold shipment of products to customers a necessity, as transportation and transit times are normally a matter of a few days.

PRONOVA UP specifications with respect to apparent viscosity are intended to be broad and suitable for a range of applications. We can offer customer-dedicated specifications if required.

References:

Smidsrød, O., Haug, A., and Larsen, B. "Degradation of alginates in the presence of reducing compounds", Acta. Chem. Scand. **17** (1963), p2628-2637.
Holme, H.K., Lindmo, K., Kristiansen, A., and Smidsrød, O. "Thermal depolymerization of alginate in the solid state", Carbohydr. Polym. **54** (2003), p431-438.
Holme, H.K., Davidsen, L., Kristiansen, A. and Smidsrød, O. "Kinetics and mechanisms of depolymerization of alginate and chitosan in aqueous solution", Carbohydr. Polym., Manuscript in press (2008).

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Technical Service

The information contained in this bulletin is intended to be general in nature. Techniques and data pertaining to specific uses for NovaMatrix/FMC products and new developments will be published periodically in the form of supplemental application bulletins. Our technical staff is ready to offer assistance in the use of NovaMatrix/FMC products.

Regulatory Status

PRONOVA™ sodium alginate meets the standards set forth in the current editions of the United States Pharmacopeia/National Formulary and European Pharmacopoeia. PRONOVA™ sodium alginate satisfies ASTM F 2064 for use in tissue engineered medical products (TEMPs). PRONOVA™ sodium alginate is manufactured in compliance with cGMP and described in a DMF submitted to the US FDA.

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