

of damage due to high shear forces generated during mixing and injection of proteins or cells mixed with an ALG solution into the body [24]. The 1% *w/v* aqueous solution of sodium ALG has a dynamic viscosity of 20–400 mPa·s at 20°C. The solubility of ALGs is dependent on the solvent pH (a decrease in pH below pK_a 3.38–3.65 may result in polymer precipitation), ionic strength, and the gelling ions used [2]. It also depends on the polymer structure, like ALG with more MG blocks (heterogeneous structure) is soluble at low pH as compared to poly-M or poly-G ALG molecules, which tend to precipitate under such conditions [18]. According to the Mark–Houwink relationship ($[\eta] = K M^a$), the parameters for sodium ALG in 0.1 M NaCl solution at 25°C are $K = 2 \times 10^{-3}$ and $a = 0.97$, where $[\eta]$ is the intrinsic viscosity (mL/g) and M is the viscosity-average molecular weight (g/mol). With decrease in pH, the viscosity of ALG solutions increases and reaches around pH 3–3.5, which is due to the protonation of carboxylate groups in the ALG backbone and formation of hydrogen bonds [23]. Therefore, manipulation of the molecular weight and its distribution can independently control the viscosity of the solution before gel formation and gelling stiffness after gel formation. By changing the combination of high and low molecular weight ALG polymers, the elasticity of gels can be increased significantly with the least increase in viscosity of the solution [24].

1.4.4 Ionic Cross-Linking

Alginate forms hydrogels by chelating divalent cations. Ionic cross-linking agents like divalent cations are combined with the aqueous solution of ALGs in order to make hydrogels [21]. The cations are taken in high concentration in a solution, and ALG microdroplets are dropped into the cationic solution to form heterogenous microcapsules structured in the shape of an egg box. This results in formation of a gel by cross-linking of ALG to divalent cations (Figure 1.4).

1.4.5 Chemical Properties

Polysaccharides get cleaved hydrolytically under acidic conditions. The mechanism of acid hydrolysis of the glycosidic bond involves three steps: (1) formation of conjugate acid due to protonation of the glycosidic oxygen, (2) formation of a nonreducing end group and a carbonium–oxonium ion due to the heterolysis of the conjugate acid, and (3) formation of a reducing end group due to the rapid addition of water to the carbonium–oxonium ion. Sodium ALG can be stored as a dry