4.2.1.1 Ionic Cross-Linking

The most common method for preparing alginate hydrogel is to combine a solution of alginate with a solution of conic cross-linking agents, such as divalent cation, e.g., Ca^{2+}. Alginate chains are believed to caution guluronate blocks, which can easily bind with divalent cations. The guluronate block of one alginate then combines with that of the other alginate chain and form a function, what is termed as cross-linking and resulting in gel structure [4]. Calcium chloride, calcium sulfate, and calcium carbonate can be used as cross-linking agents [5]. Gelation control, uniformity, strength structure and mechanical integrity of gels, and gelation temperature strongly affect the mechanical properties of gels [6]. At lower temperature, the reactivity of cross-linkers is reduced and cross-linking becomes slower. One of the important drawbacks of conically cross-linked alginate gel is the limited long-term stability in physiological conditions, because the divalent gel is released to the surrounding media due to some exchange reactions, and this makes the gel soluble; sometimes this feature may be beneficial and sometimes it may be negative.

4.2.1.2 Covalent Cross-Linking

Covalent cross-linking is studied to a great extent, and it finds application in tissue engineering. Covalent cross-linking in alginate can lead to elastic deformation of cells without much stress [7]. But covalent linking agents are generally toxic so the unreacted chemicals need to be removed from the gel. The covalently cross-linked alginate carrying polyethylene glycol (PEG) was first investigated. By the use of PEG, the loss of the hydrophilic character of hydrogel is compensated [8]. Later, alginate hydrogels containing poly(aldehyde guluronate) (PAG), multifunctional cross-linker such as adipic acid dihydrazide (AAD), etc. are introduced [9].

Latest cross-linking agents are photocross-linking agents that carry methacrylate. Alginate modified with α-phenoxy cinnamylideneace tyl chloride, etc. are important among them [10].

4.2.1.3 Thermal Gelation

Thermosensitive hydrogels are widely studied because of their applications in the field of drug delivery. Due to their adjustable swelling properties, there is modulation in drug release from gels [11]. One important example are poly(N-isopropylacrylamide) hydrogels. The transition temperature can be varied by copolymerization with hydrophilic monomers