39.2.6 Polymers

Polymers are commonly used for the manufacture of dissolving, biodegradable, or hydrogel-forming MNs, but solid, hollow, or coated polymeric MNs have also been reported. A wide range of synthetic polymers, proteins, and polysaccharides has been studied due to their excellent biocompatibility, degradability, and low cost [33]. Even though MNs prepared from polymers are not as strong as silicon, metal, ceramic, or glass MNs, they are able to penetrate the skin and show higher toughness than ceramic or glass MNs [9]. Dissolving MNs are mostly prepared from polysaccharides such as carboxymethyl cellulose (CMC), amylopectin, dextrin, hydroxypropyl cellulose (HPC), alginate, and hyaluronic acid or synthetic polymers such as poly(vinyl pyrrolidone) (PVP), poly(vinyl alcohol) (PVA), or poly(methyl vinyl ether/maleic anhydride (Gantrez AN-139). MNs manufactured from poly(lactic-co-glycolic acid) (PLGA), poly-L-lactic acid (PLLA), poly(glycolic acid) (PGA), and chitosan are biodegradable. Both types of polymeric MNs, dissolving and biodegradable, carry their payload inside the MNs and release it upon dissolution or biodegradation. In contrast, hydrogel-forming MNs consist of cross-linked polymers that absorb ISF upon skin insertion and form aqueous conduits through which the therapeutic agent, located in a separate reservoir, can permeate into the body (Figure 39.2E). The first hydrogel-forming MNs were made from poly (methyl vinyl ether/maleic anhydride) (Gantrez AN-139) or poly (methyl vinyl ether/maleic acid) (Gantrez S-97), crosslinked with polyethylene glycol. Sodium hydrogen carbonate was used as a pore-forming agent to modify the swelling properties. Other hydrogel-forming MNs were made from PVA in combination with either a mixture of polysaccharides or dextran and CMC or gelatin [24]. Most of these polymers have been previously used for other medical applications and are considered biocompatible. While some of them are biodegradable, others can be, if absorbed, eliminated in the kidney by glomerular filtration if their MW is below the glomerular threshold [34]. Most polymeric MNs are prepared by micromolding, with polydimethylsiloxane being the most commonly used mold material next to metals. Other techniques include hot embossing, droplet-borne air blowing, electro-drawing, injection molding, laser micromachining, drawing lithography, photolithography, investment molding, continuous liquid-phase interface production, dipping, solvent casting, and x-ray methods [35]. The long-term impact of repeated administration of polymers within the skin from repeated MN application is yet to be fully understood. The importance of the long-term safety of MNs, particularly when used for the treatment of chronic conditions, is discussed further in Section 39.7.2.

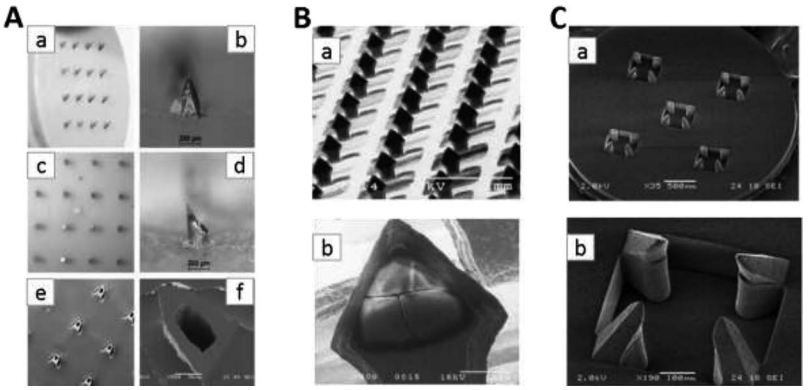

FIGURE 39.4 (A) Different types of stainless-steel MNs: (a) hollow stainless-steel 4 × 4 MN array, (b) higher magnification of a single hollow stainless-steel needle; (c) solid stainless-steel 4 × 4 MN array, (d) higher magnification of a single solid stainless-steel needle; (e) hollow silicon 4 × 4 MN array, (f) higher magnification of a single hollow silicon needle. (B) Scanning electron micrographs of titanium MNs coated with 80 µg of desmopressin per array: (a) general view, 1 mm scale, (b) front view of a single MN, 50 µm scale. (C) Scanning electron micrographs of ceramic MNs: (a) general view, 500 µm scale, (b) detailed view of a single MN, 100 µm scale. All images reproduced with permission [26, 36, 37].