above the therapeutic level for seven days [46]. Furthermore, administration via IM produced comparable plasma results, thus indicating that MNs could potentially be used for the sustained release of antiretrovirals in humans [46].

With reference to hydrogel-forming MNs, as the MN itself is drug-free (Figure 39.2E), its key function is to act as a rate-controlling membrane, permitting sustained drug delivery from an attached drug-containing reservoir [47]. By adjusting the polymeric cross-linked density, which controls the rate of swelling, drug delivery across the skin is controlled by the formulator, rather than the stratum corneum. This was first demonstrated by Donnelly et al., in which MNs composed of poly(methyl vinyl ether/maleic acid) (PMVE/MA), cross-linked with poly(ethylene glycol) (PEG) delivered sustained doses of FITC-BSA, metronidazole, and insulin over 24 hours. To further exemplify the potential of this technology, Hardy et al. developed a stimulus responsive hydrogel-forming MN composed of 2-hydroxethly methacrylate and ethylene glycol dimethacrylate that enabled the delivery of ibuprofen upon application of light. *In vitro*, this light-responsive MN system delivered three doses of ibuprofen (50 mg) over a period of 160 hours [48]. Evidently, despite their infancy, hydrogel-forming MNs have the potential to further enhance the field of drug delivery; however, questions have been asked as to what applications this MN may have. Although in the early stages of development, hydrogel-forming MNs have successfully delivered clinically relevant drugs *in vivo*, including metformin, donepezil, and bevacizumab, in a sustained manner [49–51]. Therefore, with continued development, this minimally invasive form of administration offers a range of potential benefits for patients and health care providers alike.

39.3.2 Immediate Transdermal Drug Delivery Using Microneedles

Given the difficulties associated with controlling drug delivery through traditional transdermal delivery systems, it is understandable why the controlled release of drugs using MNs has been explored extensively. Instant or rapid drug release from MNs has often been overlooked in MN-based controlled drug delivery, because it was considered a negative result when the aim was to develop long-term, controlled-release strategies. However, in some cases, instant or rapid delivery of a drug is desirable, for example, for analgesia and gene delivery for tissue repair [35].

Factors that affect drug release from MN formulations include polymer–drug interactions, polymer surface properties, and the porosity of the dry materials [52]. Drug release from dissolving MN formulations in particular therefore have been manipulated by the polymers used in fabrication. Often, water-soluble polysaccharides and similar compounds, e.g., sodium chondroitin sulfate (SCS), PVP, hyaluronic acid (HA), dextran, hydroxypropyl methylcellulose (HPMC), HPC, CMC, and amylopectin, are used in instant-release MN formulations [14, 53–55].

Thus, instant drug release from MNs may be considered beneficial for the treatment of various diseases, where the general advantages of MN treatment over other transdermal or intradermal devices will be of benefit. To overcome limitations of current dihydroergotamine mesylate (for acute migraine) formulations, such as pain, adverse side effects, and poor bioavailability, a dissolving MN system was utilized. The patches dissolved in two minutes within porcine skin and gave 97% bioavailability. Ito et al. developed a two-layered (dextran MN and hyaluronate MN) dissolving MN system for the delivery of sumatriptan in rats. The bioavailabilities of sumatriptan from the dissolving MNs were calculated as $100.7 \pm 18.8\%$ for hyaluronate MNs and $93.6 \pm 10.2\%$ for dextran MNs, with a release time of 30 minutes. Successful delivery of ibuprofen incorporated into dissolving MNs was demonstrated by McCrudden et al. [56]. C_{max} was achieved after four hours (339 μg/mL), approximately 26 times greater than the human therapeutic plasma level. Chen et al. formulated dissolving MNs for the delivery of meloxicam *in vitro*. Drug was rapidly released from the MNs (91.72% within 30 minutes) and gave a bioavailability of 122.3%.

Pain relief and reduced inflammation are not the only targets of instant-release MNs. For example, bleomycin, a potent wart treatment, is mostly delivered through intralesional injection. Lee et al. fabricated PVA MNs to make the treatment more patient friendly and found that >80% of the