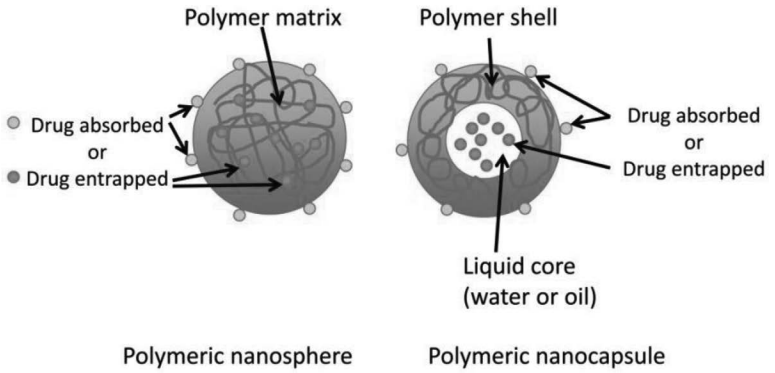

FIGURE 64.2 Schematic representation of polymer-based nanoparticles. Polymeric nanosphere and polymeric nanocapsule. (Modified from Dragicevic and Maibach, 2018).

i.e. at the uppermost SC layer (Lademann et al., 1999; Zhang et al., 2008). Only few nanoparticles permeated the skin passively through the hair follicles (Toll et al., 2004; Lademann et al., 2007; Rancan et al., 2009). Lademann et al. (2007) found a preferential deposition of poly(D,L-lactic-co-glycolic acid) (PLGA) nanoparticles of 320 nm diameter in hair follicles *in vitro* in porcine skin. Rancan et al. (2009) reported deposition of polylactic nanoparticles of 228 and 365 nm diameter in 50% of the available vellus hair follicles. Wang et al. (2008) demonstrated a deposition of PLGA nanoparticles around hair follicles and sebaceous glands *in vitro* in human skin. Further, compared to free drugs (free rhodamine B [Rh B] and fluorescein isothiocyanate [FITC]) showing a negligible skin penetration and localization in hair follicles, the drug-loaded nanoparticles were preferentially deposited in hair follicles (Alvarez-Roman et al., 2004b; Küchler et al., 2009). In conclusion, the consensus is that nanoparticles cannot penetrate the intact skin; however, they can penetrate the follicular pathway, which is insufficient for an effective treatment of skin diseases. In addition, the skin penetration ability of nanoparticles depends on their composition, size, shape and other physicochemical factors.

Hence, to enable sufficient penetration of nanoparticles into the skin, i.e. to overcome the SC barrier, an effective additional penetration enhancement method is needed together with nanoparticles.

64.1.2 Combined Use of Nanoparticles and Microneedles

Microneedle (MN) technology has been used frequently as it facilitates intra/transdermal delivery of drugs in a minimally invasive fashion (Katikaneni, 2015; Arya et al., 2017; Baek et al., 2017; Dul et al., 2017; Kim et al., 2017; Ripolin et al., 2017; Permana et al., 2019; Vora et al., 2020; Courtenay et al., 2020). In brief, the mechanism of action of MNs is based on creating transient microconduits which penetrate through the SC, extend into the viable epidermis and hence facilitate drug permeation, as well as the penetration of drug carriers. It is a powerful enhancement method when used alone, e.g. for intradermal vaccination and gene delivery (Chabri et al., 2004; Prausnitz, 2004; Coulman et al., 2006a, 2006b; Frerichs et al., 2008; Hirschberg et al., 2008; Ali et al., 2016; Puri et al., 2016; Dul et al., 2017; Ita, 2017; Pamornpathomkul et al., 2017b), intradermal lymph targeting of drugs (Permana et al., 2020), intradermal delivery of cosmetic actives (Puri et al., 2016), transdermal delivery of large and small biomolecules(e.g. insulin and other drugs; Martanto et al., 2004; Cormier et al., 2004; Kearney et al., 2016; Modepalli et al., 2016; Kim et al. 2017; Courtenay et al., 2020; Kurnia Anjani et al., 2020), as well as when combined with other physical methods, such as with iontophoresis for the transdermal delivery of methotrexate (Vermulapalli et al., 2008), daniplestim (Katikaneni et al., 2010), and others. It has also been combined with electroporation for the delivery of FITC-dextrans (Yan et al., 2010) or with sonophoresis for the transdermal delivery