



**Fig. 4.** Scanning electron micrographs of 15% PMVE/MA hydrogels cross-linked with PEG molecular weight 10,000 Daltons in 2:1 ratio (Thakur et al. 2009).

acid form of PMVE/MA and PEG was found to increase the swelling capacity of the resulting material (Donnelly et al. 2014a). For example, after 1 hour, the percentage swelling of what is termed ‘super swelling hydrogels’ (20% w/w acid form of PMVE/MA, 7.5% w/w PEG 10,000 and 3% w/w  $\text{Na}_2\text{CO}_3$ ) was 1119%, compared to only 250% for the original formulation (15% w/w PMVE/MA, 7.5% w/w PEG 10,000). Infrared spectrometry indicated that this action was due to sodium salt formation on free acid groups on the copolymer, thus reducing ester-based cross-linking. The extremely porous structure formed was also evidenced by the average molecular weight between crosslinks,  $M_c$ , determined to be 6,793,627 g/mol, highlighting the potential for diffusion of macromolecules through this network.

The glass transition temperature of the PMVE/MA and PEG hydrogel first described for microneedle manufacture ( $55.82 \pm 0.97^\circ\text{C}$ ) is well above typical room temperatures, thus, at ambient temperature, the polymer chains within the network are not sufficiently mobile and the material is relatively hard (Donnelly et al. 2012). The mechanical properties of these materials, therefore, allow skin insertion and mechanical resistance to fracture when dry, making this type of hydrogel a good candidate for microneedle manufacture. Insertion forces as low as 0.03 N per needle resulted in 100% needle penetration *in vitro* and regardless of the force applied, none of the needles on the array broke or shattered upon application into the skin. Upon mechanical testing, a force of 23.55 N was required to break the hydrogel microneedle base-plate, with an angle of approximately  $79.28^\circ$  at break point, demonstrating both the strength of the material and, also, its conformability, important for application to the uneven skin surface. The hydrogel-forming microneedle arrays were also demonstrated to retain their mechanical integrity when swollen, being sufficiently robust in this state to ensure the microneedles were removed intact from the skin.

In a different polymeric approach, Hardy et al. (2016) described formation of hydrogel-forming microneedles using 2-hydroxyethyl methacrylate (pHEMA) cross-linked with ethylene glycol dimethacrylate (EGDMA). Prepared using the same micromoulding technique as described by Donnelly et al. (2012), polymerization and cross-linking occurred simultaneously when the monomer gel mixture was placed in