

increasing the acidic or alkalinity of the local cellular environment and scientists have been keen to exploit differences in healthy and diseased pH characteristics to enable localized drug delivery. For example, certain cancers are associated with a decrease in local tumour environment pH serving as a target for the delivery of chemotherapeutic payloads, selectively reducing damage to healthy cells (Kato et al. 2013). Urinary catheter associated infections are commonly accompanied with an increase in alkalinity due to the conversion of urea in the urine to highly basic ammonia by the enzyme urease, produced by pathogenic bacteria such as *Proteus mirabilis* (Stickler et al. 2006). Healthy human body systems and tissues also demonstrate localized diversity in pH (Table 1). In the gastrointestinal tract the pH of the stomach is attributed to be between pH 1.0–3.0, whilst the upper small intestine has an increased pH of 4.8–8.2, with the colon averaging pH 7.0 (Schmaljohann 2006). Oral dosage formulations make use of this variation to control the site of drug release, and optimize absorbance (Philip and Philip 2010). For example enteric-coating utilized in active ingredients such as aspirin and omeprazole are insoluble in acid media (stomach) but soluble in neutral/alkaline media (intestine). The active ingredients are protected from release in the stomach where conditions may cause stability issues (omeprazole) or side effects (aspirin) (Becker et al. 2004).

Hydrogels respond to the pH of their surrounding environments by either swelling or deswelling. This process is dependent on the presence of ionisable functional groups within the polymeric backbone and their respective logarithmic acid dissociation constant ( $pK_a$ ), resulting in an overall charge density (Ninawe and Parulekar 2011). The pH and ionic composition of the solution in direct contact with the hydrogel is also an important consideration in determining the charge density and overall swelling/deswelling effect. Swelling results from absorption of water into the hydrogel whilst expulsion causes deswelling guided by electrostatic interactions with the aqueous environment. Anionic hydrogels possess functional groups that are ionized in solutions with a pH greater than their respective  $pK_a$ . Anionic hydrogels therefore become ionized and swell, due to electrostatic repulsions, in solutions where pH is greater than  $pK_a$  (Kim et al. 2003). The opposite is true of cationic moieties which become ionized and swollen at pH lower than pH. Acrylic acid and methacrylic acid are the most commonly utilized synthetic anionic monomers governed primarily by the presence of a carboxylic functional group. Acrylamide, diethylaminoethyl methacrylate

**Table 1.** pH of various human systems, tissue and cellular compartments. Adapted from Schmaljohann 2006.

Tissue/cellular compartment	pH
Blood	7.34–7.45
Stomach	1.0–3.0
Upper small intestine	4.8–8.2
Colon	7.0–7.5
Tumour, extracellular	7.2–6.5
Early endosome	6.0–6.5
Late endosome	4.5–5.0
Vagina	3.8–4.5
Inflamed tissue/wound	5.4–7.4