where log K_H is known as the conditional stability constant. Fortunately, α_L can be calculated from the known dissociation constants of EDTA, and its value can be calculated from:

$$\alpha_L = \left\{1 + \frac{[H+]}{K_4} + \frac{[H+]}{K_4 K_3} + \cdots\right\} = 1 + 10^{(pK_4 - pH)} + 10^{(pK_4 + pK_3\, pH)} + \cdots \tag{7.17}$$

Thus at pH = 4, the conditional stability constants of some metal–EDTA complexes are calculated as follows:

$$\log K_H \text{ EDTA } Ba^{2+} = 0.6 \tag{7.18}$$

$$\log K_H \text{ EDTA } Mg^{2+} = 1.5 \tag{7.19}$$

$$\log K_H \text{ EDTA } Ca^{2+} = 3.4 \tag{7.20}$$

$$\log K_H \text{ EDTA } Zn^{2+} = 9.5 \tag{7.21}$$

$$\log K_H \text{ EDTA } Fe^{2+} = 17.9 \tag{7.22}$$

Thus, at pH = 4, the zinc and ferric complexes will exist; however, calcium, magnesium, and barium will be only weakly complexed, if at all.

The inclusion of EDTA is occasionally not advantageous, as there are a number of reports of EDTA catalyzing the decomposition of drugs. Citric acid, tartaric acid, glycerin, and sorbitol can also be considered complexing agents; however, these are often ineffective. Interestingly, some Japanese formulators often resort to amino acids or tryptophan, because of a ban on EDTA in a particular country.

7.4.4 Photostability

For drug substances, photostability testing should consist of two parts: forced degradation testing and confirmatory testing. The purpose of forced degradation testing studies is to evaluate the overall photosensitivity of the material for method development purposes and/or degradation pathway elucidation. This testing may involve the drug substance alone and/or in simple solutions or suspensions to validate the analytical procedures. In these studies, the samples should be in chemically inert and transparent containers. In these forced degradation studies, a variety of exposure conditions may be used, depending on the photosensitivity of the drug substance involved and the intensity of the light sources used. For development and validation purposes, it is appropriate to limit the exposure and end the studies if extensive decomposition occurs. Under forced conditions, decomposition products that are unlikely to be formed under the conditions used for confirmatory studies may be observed. This information may be useful in developing and validating suitable analytical methods. If in practice it is demonstrated that they are not formed in the confirmatory studies, these degradation products need not be examined further. The forced degradation studies should be designed to provide suitable information to develop and validate test methods for the confirmatory studies. These test methods should be capable of resolving and detecting photolytic degradants that appear during the confirmatory studies.