of all, the product would be present one half as positive ion (RH^+), one half as uncharged species (R). If the buffer is denoted HB, then, in concentrating a solution of this there would be two solubility products:

$$S_{RHCl} = [RH^+][Cl^-] \tag{7.16}$$

$$S_{RHB} = [RH^+][B^-] \tag{7.17}$$

aside from the solubilities S_{HB} and S_R. As the solution, hence, starts precipitating substances other than ice at the eutectic point, the species with the lowest S value or solubility product will at first precipitate out. This. for instance, could be RHB. As this precipitates out, both $[RH^+]$ and $[B^-]$ will decrease. At a given point R will start precipitating out. This will prevent further precipitation of RHB, because $[B^-]$ is now sufficiently low to be at the limit, had $[RH^+]$ not been affected. At a given point, because the amount of liquid water decreases as the process continues (freezing out of ice), the solubility limit of either HB or RHCl will be exceeded, and either species will then precipitate out until the remainder is left to freeze out as the last amount of water is solidified at the eutectic point.

The point is that the cake will contain four species: R, RHCl, HB, and RHB. And the question then is, under the present labelling policies, how does one properly label such a mixture?

11. OXIDATION

Oxidations are moisture mediated, as are hydrolyses. Often products that are oxidation sensitive are stored in glass rather than polymer bottles because, however good, these latter still allow permeation of oxygen.

In a glass bottle, if it is considered hermetic, and it often is, the oxygen in the head space will be consumed, and the amount of "initial" decomposition of the produce will tie in with the amount of oxygen available in the head space. It is a common phenomenon that solid dosage forms show an initial loss corresponding to the ratio between the amount of head space divided by the number of tablets in the bottle.

Often the oxygen is used up, and treatment of the data should be such that regression should be carried out on the data points after the *intial* drop.

Example 10.1.

A bottle contains 100 tablets and a head space of 25 mL of air. Each tablet contains 100 mg of drug substance of molecular weight 500. If the nonoxidative decomposition of the drug is 0.1% per month, how much would be expected, on the average, to remain after 3 years? Assume that one O_2 decomposes two drug molecules (i.e., $A + 1/2O_2 \rightarrow AO$).

Answer.

25 mL of air space at 25°C is $25/22.4 = 1.11$ moles of air, containing 22% of oxygen, so that the amount of available oxygen in the headspace is 0.22 millimoles.