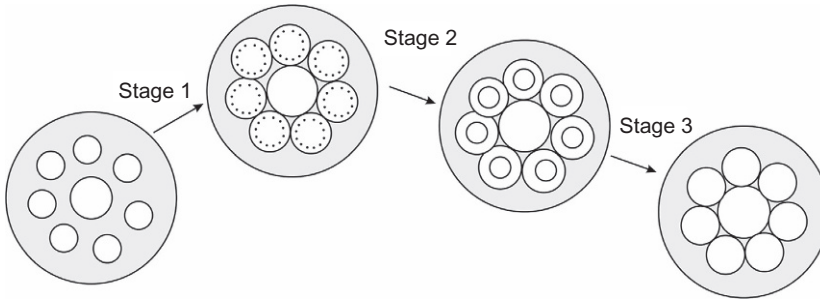

FIG. 19.10 Three-stage degradation mechanism of MSN.

19.7 TOXICITY AND SAFETY CONSIDERATION OF MSNs

19.7.1 Particle Toxicity

The limit for safe concentration can get compromised due to particle toxicity if careful selection of solvents and suspending media is not done. The synthesis mechanism strictly depends on solvents and suspending media, which further affect the shelf life of drug carrier. MSNs carrier can undergo changes in the silica matrix if we choose aqueous solution and ethanol as suspending media, which have a tendency to react with silica hence limiting their shelf life. Dimethyl sulfoxide (DMSO), which acts as carrier for drugs with limited water solubility can also act as preferred suspension medium. Although ethanol and DMSO are used up to certain concentrations that cells can withstand, still an increased apoptosis has been seen in the presence of DMSO even at concentration below cellular threshold limit. During storage of MSN in the suspension media, it is necessary for the MSN to retain the loaded drug, hence this whole process is an interplay of several factors, which need to be carefully monitored. Some researchers have suggested dissolution and testing of particles in medium having serum proteins so as to simulate physiological conditions.

19.7.2 Porosity and Toxicity

It has been reported that porous silica materials compared to their nonporous amorphous silica counterparts are more effective in limiting toxicity. Nonporous silica has shown more hemolytic activity of blood cells. Further studies have revealed that effective surface charge on MSNs and amorphous silica has no role to play in their hemolytic activity. In fact, it was concluded that strong electrostatic interactions between trimethylammonium head groups of membrane lipids and silanols could be the reason for hemolysis. However, for the acid modifications where sulfonic acid has higher affinity for head groups of membrane lipids this phenomenon was absent. It becomes quite clear from these studies that hemolysis effect is highly specific for silanols. MSNs have high surface porosity, and this in turn reduces silanol density on their surface