a prerequisite understanding of key factors responsible for intracellular controlled release of these MSNs. The cellular uptake and subsequent bioactivity of nanoparticles is highly influenced by their size, in case of biological systems. The cellular uptake of liposome and different internalization fate in SK-BR-3 cells for various sizes of antibody coated gold and silver nanoparticles highlights size dependence. It has also been reported that nanoparticles effect drug loading and releasing profiles. Large particle size of polyethylene glycol (PEG) nanoparticles have shown better paclitaxel encapsulation efficiency in addition to slower drug-release rate.

MSNs act as an important vehicle for transportation of drug from an external surface of the cell into cytoplasm as well as control rate of release of drug into the cytoplasm. In the current scenario, the need of the hour is detailed and more comprehensive studies focused on the size effect of MSNs involved in delivery process at the intracellular level. Silica materials negatively charged and nonfunctionalized are absorbed in the cells through adsorptive endocytosis. Once absorbed, the major challenge after intracellular release is endosomal entrapment. Zhoa et al. have reported that MSNs with size >600 nm have caused membrane deformation of local cells, thus leading to cytotoxicity. This is the main reason why MSNs with size range 50–500 nm is synthesized and the effects of drug loading, cellular adsorption, release profile, and endosomal escape are studied in detail.

Targeted intracellular drug delivery application of MSNs is highly effective for a particle size range of 50–200 nm. Particles smaller than this range are not easy to synthesize due to inherent mesoporosity and for larger particles it becomes difficult to bypass physical membranes in the body. MSNs can be synthesized by spray drying and wet chemical synthesis approach. Size control through spray drying is not possible as it leads to wide particle size distribution, with considerable amounts of very small and larger particles. Wet chemical synthesis being the most preferred route utilizes tetraethoxysilane, TEOS as precursor for silica and cetyltrimethly ammonium bromide (CTAB) has been used under alkaline conditions as structure-directing agent (SDA). This route helps in synthesis of materials having mesopore dimensions in 3–4 nm range and most of the time cylindrical mesopores are arranged in hexagonal fashion in two dimensions). Table 19.1 mentions some important synthesis route and different methods for particle size control.

At typical concentration of 10 mol% of TEOS functional silanes can be used along with TEOS as precursor for silica and it also aids in attachment of different functional groups in situ onto the silica surface. Currently, major focus is on increasing the pore size of MSNs. Most macromolecular materials such as proteins (antibodies, enzymes) and nucleic acids (RNA, DNA) require larger pore size for their efficient encapsulation. Although mesopores are sufficient for small molecules, considering the macromolecules there is a need to increase the pore size of MSNs. Engineering of pore size is not a tedious