Mucosal drug delivery is a technique for administration of drugs through mucous membranes lining the gastrointestinal tract, respiratory tract, urogenital tract and ocular surface. It has several advantages including increased residence time at the site of absorption/action, decreased administration frequency and thus better patient compliance. However, with conventional mucosal drug delivery these could only be achieved to a certain degree. Thus, in this study, two strategies have been used to improve the efficiency of mucosal drug delivery through the preparation of mucoadhesive and mucus-penetrating nanoparticles. Thiolated silica nanoparticles have been synthesised using 3-mercaptopropyltrimethoxysilane and functionalised with either polyethylene glycol (PEG) or poly (2-ethyl-2-oxazoline) (POZ). The sizes of thiolated, PEGylated and POZylated silica nanoparticles were 53±1, 68±1 and 59±1 nm, respectively. The particle size of both thiolated and POZylated nanoparticles significantly increased at pH≤2, whereas no particle size change was observed at pH 2.5-9 for both these two types of nanoparticles. On the other hand, the size of PEGylated nanoparticles did not change over the studied pH range (1.5-9). Thiolated nanoparticles were more mucoadhesive in the rat small intestine than both PEGylated and POZylated nanoparticles. This may indirectly indicate the mucus-penetrative properties of both PEGylated and POZylated nanoparticles. Each of these nanoparticles has potential applications in mucosal drug delivery.