Purpose
Current colon-specific drug delivery approaches utilize one of two main physiological characteristics: the pH change or microflora along the gastrointestinal tract. However, single-triggered systems are less reliable due to the variation of above parameters in individuals and in disease conditions like ulcerative colitis. In this study, we developed a novel pH- and enzyme-sensitive nanoparticles using a polymeric mixture of pH-sensitive Eudragit S100 (ES) and enzyme-sensitive azo-polyurethane (Azo-pu) to overcome any restriction associated with single-triggered approach and deliver drug specifically and sufficiently to the inflamed colon. Budesonide (BDS) was loaded in the nanoparticles as an anti-inflammatory drug.

Methods
Nanoparticles were prepared by an oil-in-water (O/W) emulsion solvent evaporation method and characterized for size, encapsulation efficiency, and in-vitro release at different pH and in the presence of rat cecal contents. The therapeutic potential of the prepared nanoparticles was evaluated using the trinitrobenzensulfonic acid (TNBS) colitis rat model, in comparison with only ES nanoparticles and to an aqueous solution of BDS.

Results
The scanning electron microscopy (SEM), dynamic light scattering (DLS) and qNano data showed the successful formation of nanoparticles with a size of less than 200 nm and 65% to 70% drug encapsulation efficiency. The prepared nanoparticles refrained from the premature drug release at acidic conditions and released the drug at over pH 7.0 in a sustained manner. In addition, the enzyme-triggered release was observed in the presence of rat cecal contents at pH 5.5 which mimic the colonic pH environment in the ulcerative colitis patient. Furthermore, it was found that delivery by polymeric mixture nanoparticles alleviated the TNBS-induced colitis in rats significantly better than by only ES nanoparticles or BDS solution with the same dose.

Conclusion
The pH- and enzyme-sensitive nanoparticles presented in this study, have the ability to deliver the drug to the inflamed colon due to the dual mechanisms and could be a promising strategy in the therapy of inflammatory bowel disease.