Title:	Customized polymeric nanoparticles for targeting inflammatory disorders
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Abstract:	Inflammation, as a hallmark, is an underlying mechanism implicated in various pathological disorders including cancer, ulcerative colitis (UC), rheumatoid arthritis (RA) etc. Existing conventional approaches in UC and RA treatment include nonsteroidal anti-inflammatory drugs (NSAIDs), disease-modifying antirheumatic drugs (DMARDs), corticosteroids, biological drugs and natural agents. However these conventional drugs have several inherent limitations like poor aqueous solubility, low oral absorption, high first pass metabolism, rapid clearance, low bioavailability, off target systemic side effects etc., which limit their employability in clinical settings. Nanotechnological advancements have significantly contributed to amelioration of inflammation and associated disease severity. In this thesis, formulation and characterization of customized polymeric nanoparticles is described for delivery of pharmacological agents, targeting inflammation involved in acute experimental colitis as well as experimental arthritis. Nanoparticles were formulated by ionic gelation, nanoprecipitation and solvent evaporation method and characterized for their various physicochemical characteristics like particle size, zeta potential, and polydispersity index with dynamic light scattering. Particle shape and surface morphological features were studied with transmission electron microscopy, scanning electron microscopy and atomic force microscopy. Drug loading capacity and drug entrapment efficiency was analyzed with UV-vis spectroscopy. These nanoparticles were further evaluated in-vitro for their biocompatibility against normal human foreskin fibroblasts (BJ) and othercell lines. Furthermore, safety and pharmacological efficacy of these nanoparticles was assessed in-vivo in collagen-induced arthritis in Wistar rats and dextran sodium sulphate-induced colitis in Swiss Albino mice models. Eudragit-coated 5-ASA loaded gelatin NPs (chapter 5) were used for oral administration while dual drugs loaded NPs (chapter 4 & 6) were used via i.v. route. Results of these studies indicated that nanoparticle possessed favorable physicochemical characteristics in terms of particle size, zeta, polydispersity, shape, surface morphology etc. and delivery of anti-inflammatory agents mediated by these, largely ameliorated the severity of inflammation in the pre-clinical models of diseases. Most of the physical observations in animals, biochemical parameters, and immunohistochemical markers exhibited a significantly greater degree of restoration by treatment of drug loaded nanoparticles as compared to naïve drugs alone.
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