Research Article

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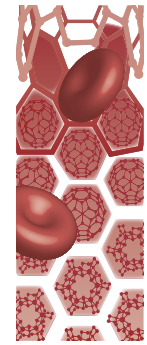

Effective uptake of folate-functionalized ethionamide-loaded hybrid system: targeting alveolar macrophages

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Aim: To assess the targeting ability of hybrid nanosystems functionalized with folate. It also aimed to reduce stomach intolerance by substituting the oral route for parenteral delivery. **Method:** The nanosystems, prepared by nanoprecipitation technique, utilized a one-step method to prepare nanoparticles followed by surface functionalization through adsorption. The prepared nanosystems underwent physical characterization, *in vitro* and *in vivo* evaluations. **Result:** The nanosystems were effective in targeting the alveolar macrophages. Ethionamide was released from the formulation over 5 days. Fourier-transform infrared results proved the structural characteristics, and the positive charge further improved the targeting efficacy on the functionalized system. **Conclusion:** The hybrid formulation improved the release characteristics. Reduction in dosing frequency due to prolonged release improves compliance with the dosage regimen.

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Keywords: chitosan–folate conjugate • fluorescence-activated cell sorter • hybrid nanoparticles • macrophage targeting • nanoparticle tracking analysis

Hybrid nanosystems have gained immense importance in recent times. They incorporate the various properties of a lipid in conjunction with a polymeric material. The use of lipids in the hybrid system provides a hydrophobic lipid moiety loaded with a hydrophobic drug. Hydrophobic drugs suffer from poor loading and drug leakage from the delivery systems [1–4]. To overcome these shortcomings, polymers can be suitably added to the lipidic systems. The addition of a polymer imparts structural integrity, better loading characters and control over release patterns. The hybrid systems are nowadays considered for their improved surface characteristics, providing more options for surface modifications due to free functional groups. The selection of lipid and polymer is essential while designing a hybrid nanosystem [1,5–7]. The choice of materials also holds importance in surface modifications, depending on the free functional groups present after formulation. Surface modifications can either be chemical depending upon functional groups or based on charges on the surface. Functionalization can be easily achieved by coating the prepared material with oppositely charged modifiers [8,9].

Macrophages express different receptors on the surface in response to the infection they encounter. The macrophages overproduce mannose and folate receptors in active tubercular infections, cancer, leishmaniasis, salmonella, listeria and other intracellular microorganisms affecting them [10]. Alveolar macrophages (AMs) present in the lungs also show similar characteristic features of macrophages. AMs act as first-line defence systems for all types of inhaled pathogens/microparticles [11,12]. During the internalizing and rapid intracellular engulfment, AMs become the site of microbe multiplication in tuberculosis, leishmania, streptococcus infection and influenza. Targeting to AM can be achieved passively and actively based on the size, shape, surface charge and receptor