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Fabrication of magnetic ZIF-8 hybrid nanostructures: A pH-responsive delivery vehicle for berberine

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Zeolitic imidazolium framework (ZIF-8) materials are crystalline tri-dimensional networks consisting of metal ions or metal clusters bridged tetrahedrally *via* the imidazole linker, exhibiting high microporosity, large surface area, thermal and chemical stabilities with characteristics of both MOFs (*e.g.* easily tunable pores and cavities) and zeolites (*e.g.* high aqueous stability), which render them as excellent platforms for drug delivery studies. Herein, a facile methodology is developed to fabricate magnetic, microporous and pH-responsive drug delivery vehicles based on iron oxide and zeolitic imidazolium framework (Fe_3O_4 and ZIF-8) structures to form hybrid magnetic ZIF-8 nanoparticles (Fe_3O_4 @ZIF-8 NPs) to entrap the anti-cancer drug “berberine (Bn)”, a naturally occurring plant alkaloid which is isolated from *Mahonia leschenaultii* roots. The synthesized Fe_3O_4 @ZIF-8 NPs are extensively characterized by powder XRD, SEM and HR-TEM analyses. This Bn-encapsulated Fe_3O_4 @ZIF-8 NPs display high drug loading capacity (4.8 mg /10 mg), pH sensitive release profile and magnetic response. Controlled berberine release experiments are carried out at pH values of 7.4, 6.2 and 5.0, and release at pH 5.0 is 2.5 times as fast as that at pH 7.4 and 1.5 times fast as that of pH 6.2. MTT assay and confocal microscopic images are used to evaluate the cytotoxicity of Bn and Bn loaded Fe_3O_4 @ZIF-8 NPs in MCF-7 cell lines, which indicate lower cytotoxicity towards MCF-7 cells. In addition, results of other controlled drug delivery studies from our group, *i.e.*, silica nano-assembled capsules for delivering doxorubicin and microporous carbon for delivering berberine will also be presented.

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Fabrication and characterization of FP metered dose inhaler for pulmonary drug delivery

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The purpose of present research work was to fabricate FP metered dose inhaler and study the effect of spray drying parameter on production yield and particle size. Spray-dried powders can be used to deliver particles to the lungs via a MDI. Nanoparticles were generated using polymer chitosan, mannitol along with L-leucine. The effects of various experimental parameters were optimized by means of experimental box-behnken design. Production yield, encapsulation efficiency and dissolution study along with characterization by scanning electron microscopy, X-ray diffraction, DSC, IR. Particle size and zeta potential were evaluated by using zetatracc particle size analyzer, cascade impactor using investigated aerodynamic properties. Histopathology of lung were also examined for the normal group, cigarette smoke exposed group, treatment group and was compared with marketed group investigated the characteristic of developed MDI. Experimental design it was evaluated that inlet temperature and polymer concentration influence on the production yield. Feed flow rate impact on particle size. Results showed that spray drying technique yield 985 to 4060nm indicate nano-size range. Entrapment efficiency was found between 89.35% and 98.36%. Zeta potential shows good stability index of nanoparticle formulation. Prepared nanoparticles emit 36 to 45% investigated by cascade impactor indicate deep targeting of FP to alveoli. Diffusion kinetic was found to be predominant as mechanism follow Higuchi. Histopathology revealed that MDI protects the lungs against the chronic inflammation and airspace enlargement reducing. By Developed MDI shows good spray pattern of MDI shows uniform and spherical spot with better uniformity 95.64±0.12% in term of content per puff and also found non inflammable. Spray drying technique yield optimum size for deposition beyond the narrow airway into the alveoli. That is suitable for respiratory deposition. This delivery platform opens up a wide range of treatment applications of pulmonary and systemic diseases using targeted delivery strategies via nano-particle

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