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Cationic albumin modified magnetite nanoparticles for localized delivery of sodium methotrexate

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We aimed to develop methotrexate-loaded cationic albumin-conjugated magnetite nanoparticles (MNP) with proper physicochemical characteristics. Citric acid-stabilized Fe3O4 nanoparticles, averagely sized about 10 nm, were prepared by co-precipitation of FeCl2.4H2O and FeCl3.6H2O (1:2 molar ratio). Magnetite nanoparticles were capped with citrate ions (MNP-CA) by incubating at 90ºC. Bovine serum albumin became cationic by substituting anionic side chain carboxyl groups with primary amine groups using ethylenediamine (EDA) and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) at pH of 4.75 in ice bath while stirring. The reaction was quenched with acetic acid, and dialyzed extensively against distilled water. We have used carbodiimide amidation chemistry for binding of different amounts of cationic albumin onto the MNP-CA (10 mg) in 2 ml of phosphate buffered solution (pH=8) by addition of 10 mg EDC and 6 mg N-hydroxysuccinimide. The detailed structural analyses by XRD, FT-IR, TEM, SEM, SDS-PAGE, Bradford assay and VSM proved stepwise modification of Fe3O4 nanoparticles with citric acid and cationic albumin. These nanoparticles exhibited good colloidal stability upon mixing with phosphate buffered saline and serum containing medium and proper magnetization. To load MTX, the nanoparticles were incubated with different amounts of MTX overnight at pH = 7.5 while stirring. Then, unreacted MTX was removed using magnetic decantation or Amicon ultrafiltration centrifugal microdevice (cut-off = 10kDa). The filtrates were analyzed by a validated HPLC-UV method to calculate loading parameters. An inverse correlation was found between loading efficiency and total drug concentration. The capacity for drug loading was increased significantly by cationization reaction. MTX release was studied at 37 C by dialysis method (Spectra/por, cut-off = 8–10 kDa) exhibited a prolonged and pH-dependent pattern. Conclusively, regarding biocompatibility, biodegradability and special targeting characteristics of cationic albumin in addition to unique features of magnetite nanoparticles could be served as a localized and prolonged release system for chemotherapeutic agents (e.g. methotrexate).

Keywords: Cationic albumin; Magnetite nanoparticles; Methotrexate