Targeted Drug Delivery with Magnetic Nanoparticles

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Statement of Purpose: Anticancer drugs when given intravenously get distributed throughout the body as a function of the physicochemical properties of the molecule. A pharmacologically active concentration is reached at the required site i.e. in the tumor tissue only after an excessive concentration is reached at the rest of the body which causes severe toxicity hindering effective therapy. Cancer immunotherapy is currently being developed as an alternative to conventional chemotherapy where the carriers for anti-tumor agents would target the tumor cells and leave non-target tissues unaffected (1). This would realize a pharmacologically active concentration in the tumor cells while avoiding the toxicological problems. Magnetic nanoparticles are used in biomedicine for magnetic separation, therapeutic drug, gene and radionuclide delivery; catabolism of tumours; and as contrast enhancement agents for MRI applications. Magnetic nanoparticles can be manipulated to be localized in the desired region in the body by applying local magnetic field gradients, which helps in targeting the active ingredients tagged to these nanoparticles. An attempt has been made to load an antibiotic azithromycin (as a model drug) into magnetic nanoparticles and to coat these particles with poly lactic glycolic acid (PLGA). The drug release profile of these coated nanoparticles was studied in vitro.

Methods: Paramagnetic iron oxide nanoparticles were prepared similar to a reported procedure with slight modification (2). To the dried nanoparticles a solution of 100mg/ml of azithromycin was added and allowed to be get absorbed for 16 hours. This was freeze dried and was coated with PLGA as per the standard procedure. Some amount of the drug was also added into the PLGA solution before coating. After coating these particles were freeze dried and subjected to one more coating of PLGA. The particle size distributions of these coated and uncoated particles were evaluated using zetasizer nanoseries (Malvern Instruments). In vitro release studies of the drug loaded nanoparticles were done in phosphate buffered saline (PBS) at pH 7.4. 100 mg of the drug loaded particles were taken in 50 ml of PBS at 37°C. The samples are withdrawn at intervals of 1 hour and read in a UV spectrophotometer at 215 nm.

Results / Discussion: Particle size distributions of drug loaded PLGA coated and uncoated nanoparticles are shown in figure 1. For iron oxide nanoparticles the size ranged from 28.2 to 712nm with a Z-average of 177nm. However, after PLGA coating Z-average increased to a value of 446nm which ranged from 255 to 615nm for single coating and from 255 to 1110nm for double coating with a Z-average of 521nm.

The drug loading onto these coated particles were evaluated to be 11.2 ± 0.6 mg/100mg of nanoparticles. The in vitro drug release profile from the coated nanoparticles is shown in figure 2. A near zero order release kinetics was observed for both the coatings. The complete amount of the drug was released in about 48 hours in case of single coating, where as only 80% of the drug was released for double coating.

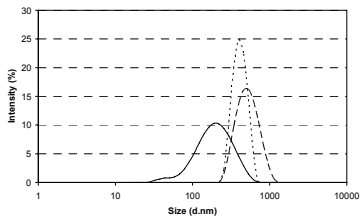

Figure 1: Particle size distribution of iron oxide nano-particles (——), with PLGA coating, single coating (-----), double coating (——)

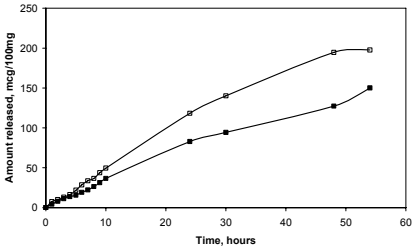

Figure 2: In vitro azithromycin release from PLGA coated drug loaded iron oxide magnetic nanoparticles; open square – single coating, closed square – double coating.

In magnetically targeted cancer therapy, the drug is attached to a biocompatible magnetic nanoparticle carrier. This carrier is injected into the patient intravenously. When the particles have entered the bloodstream, external, high-gradient magnetic fields are used to concentrate the complex at a specific target site within the body where the drug will be released and be taken up by the target tumor cells (3). This system has significant advantages compared to the traditional chemotherapy.

Conclusions: It has been demonstrated that the PLGA coated drug loaded nanoparticles can deliver the model antibiotic, azithromycin, in a sustained manner. Further, PLGA coating makes the particles more biocompatible and it seems to be suitable for the magnetically targeted delivery system for cytotoxic cancer drugs. This system seems to be also suitable for sustained release of antibiotics, e.g azithromycin itself. With its biological half life of over 50 hours this could be also used for single dose antibiotic therapy.

References:

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