Controlled-release Drug Delivery Through Precision Particle Fabrication

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Technology description

This patent-pending technology can produce uniformly sized microparticles (5 to 500m) made from biocompatible, biodegradable polymers. These particles release the drugs they contain with an unprecedented level of control, enabling custom-designed drug release profiles and effectively managing the burst effect. Precision Particle Fabrication (PPF) uses acoustic excitation and/or flow-limited field-injection electrostatic spraying technologies to fabricate either uniformly sized micro- or nanoparticles of predefined, complex size distributions. The sphere-shaped particles can be formed from a variety of materials, including FDA-approved, biodegradable polymers such as poly(lactic-co-glycolic acid) and polyanhydrides. This capability makes PPF ideal for drug delivery applications. The PPF technology has been tested in in vitro experiments, which demonstrated zero-order, constant rate drug release from uniform microspheres. Studies are being conducted to demonstrate similar performance in vivo.

DESCRIPTION/DETAILS

How it Works

Solutions of poly(D,L-lactide-co-glycolide) (PLG) containing a specific drug (rhodamine B and piroxicam were used in experiments) are pumped through a small glass nozzle at a specific flow rate while an ultrasonic transducer controlled by a frequency generator disrupts the stream into uniform droplets. A carrier stream flows around the emerging PLG stream, and these streams flow into a poly(vinyl alcohol) solution. The particles are stirred, filtered, rinsed with distilled water, and then lyophilized. This process yields microspheres that are very uniform, typically having >90% of the particles within 2-?_m of the average diameter (see Figure 2). The particles exhibit a smooth, slightly porous surface and dense polymer interior similar to microspheres produced using conventional emulsion techniques.

In Vitro Testing

Drug release depends upon the size of the microspheres. The smallest microspheres (10-?_m diameter) exhibited a rapid initial rate of release, with 40% to 60% of encapsulated drug released within the first 48 hours (see Figure 3 attached). Initial release rates decreased with increasing microsphere diameter. In addition, the initial release rate decreased with increasing drug loading. The PPF technology can be used to create mixtures of microparticles of varying sizes. Varying the particle size enables the user to generate custom-designed release profiles. As shown in Figure 4, the mixture can be designed to have zero-order release.

Application area

Injections: Microspheres made with this technology allow vaccines to be administered in a single shot rather than multiple boosters. Local delivery of the therapeutic agent also can be achieved, maximizing efficacy while minimizing side effects.
Chemotherapy: The microspheres can deliver cancer chemotherapeutics through controlled release, minimizing the need for multiple treatments. These microspheres also may deliver cytotoxic anti-cancer agents via capillary embolization, which is used to block the flow of blood to a tumor.
Intravenous Drug Delivery: Due to their minute size, these particles can be used intravenously to deliver water-soluble and -insoluble drugs (e.g., NSAID-piroxicam).
Inhaled Drug Delivery: Drugs such as insulin could be delivered in a time-release form using this technology, decreasing frequency of administration.

Advantages

Predefined kinetics and control of burst effect: Microparticles can be of a uniform size or a defined size distribution for a specific drug-release profile. Profiles can allow for long-duration drug release and can minimize the burst often seen with other drug delivery methods. Release kinetics can be controlled by the size of the microspheres. Mixtures can provide zero-order release of drugs.
Particle uniformity: Particles as small as 5 to 500?_m in diameter can be fabricated with greater than 95% of them within ?2-3% of the average size. (Figure 1)
Scalable: The PPF process is readily scaled-up. Production rates of tens of grams/minute have been achieved at the bench scale, and rates of hundreds of grams/minute are achievable.

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