APPLIED BIOCHEMISTRY AND BIOTECHNOLOGY 7, 63–65 (1982)

Magnetic Microspheres for Targeting of Drugs

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Accepted February 18, 1981

Abstract

Magnetic microspheres were prepared from starch. The microspheres could be crosslinked with various agents, and drugs could be entrapped adsorbed, or covalently coupled to the microspheres.

Index Entries: Magnetic microspheres, for drug targeting; microspheres, magnetic, for drug targeting; drug targeting, with magnetic microspheres; targeting, of drugs, with magnetic microspheres; starch, magnetic microspheres from;

Introduction

Specific delivery of drugs to desired target sites with a minimum of side effects constitutes one of the most exciting challenges in medicine. Several methods for targeting of drugs are described in the literature; however, none of these methods are general and because of this are usable only in special cases.

One way of achieving such targeting of drugs is by the use of magnetic microspheres in combination with an external magnetic field. In general, when using magnetic particles in drug delivery, the following requirements should ideally be met:

1. The particles should be small enough to remain in circulation after injection (i.e., $\phi = 0.5$ μm).
2. The magnetic material should be nontoxic.
3. The polymer should be biocompatible, i.e., nontoxic and non-immunogenic.

0273–2289/82/0912–0063$02.00

4. The polymer should allow binding of drugs by covalent attachment, adsorption, or entrapment.

We have chosen starch as support since it appears to fulfill the above criteria regarding the polymer, and since the body has an enzyme (α-amylase) that is capable of degrading starch and thereby releasing the drug at the target site.

Preparation of Magnetic Microspheres

Various methods can be applied to dissolve the starch polymer. However, the most satisfactory one seems to be the following: 20–40 g of partially hydrolyzed starch (mw, 40,000) is dissolved in 100 mL of dimethyl sulfoxide (DMSO) under gentle

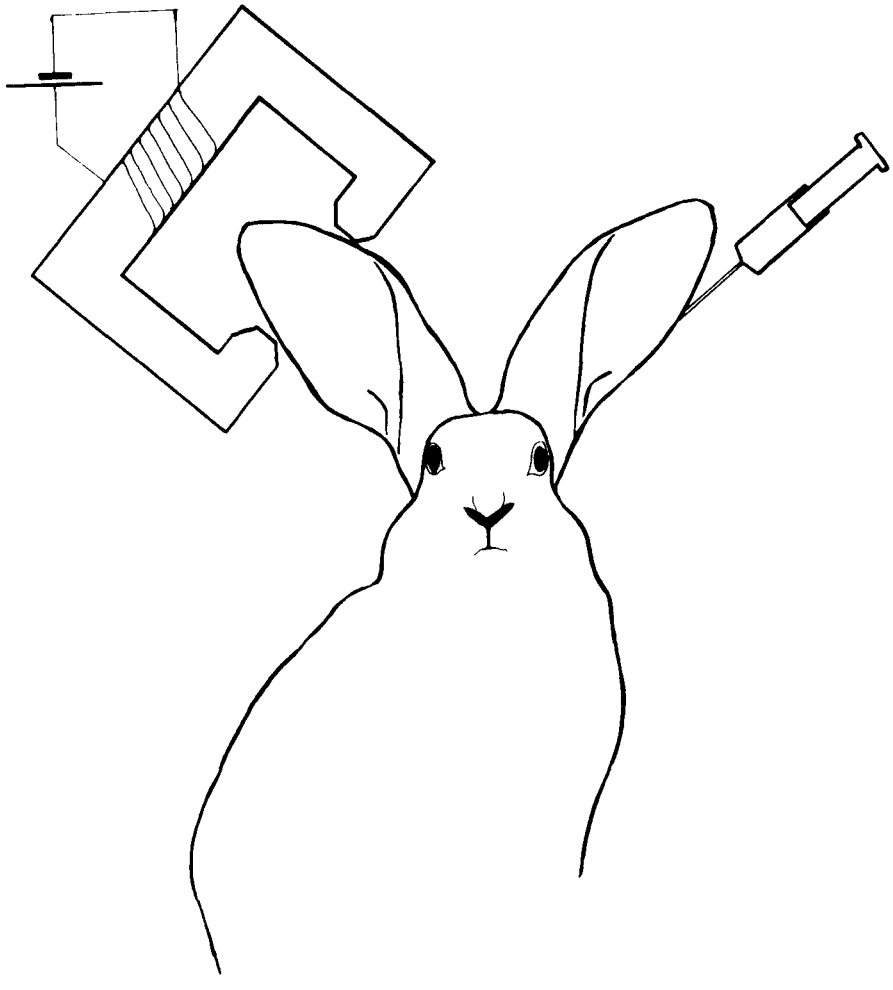

Fig. 1. In a typical rabbit experiment ^{125}I-labeled magnetic microspheres were injected in one ear while the other ear was placed in the gap of the electromagnet (0.7 Tesla). After 10 min the rabbit was killed, the distal parts of the ears were cut off, and the radioactivity was measured in a gamma counter.

heating. The starch solution is mixed with magnetite particles (ϕ, 10–20 nm; Renaissance Technologies Corp. 85 Factory Street, Nashua, New Hampshire 03060, USA) rendering a solution that behaves like a magnetic fluid. One volume of this solution is then mixed with 10 volumes of corn oil, or any other vegetable oil, and microspheres with a diameter below 1 μm are formed by sonication or high-pressure homogenization. The microsphere–oil suspension is slowly poured into 20 volumes of acetone while stirring at high speed. The microspheres precipitate and are washed four times with acetone and then transferred to water. The magnetic microspheres can then be stabilized by various covalent crosslinking procedures that allow subsequent covalent coupling of drugs to the support. Alternatively, the drugs can be adsorbed to or entrapped in the starch polymer.

Animal Experiments

In rabbits ^{125}I-labeled magnetic microspheres were used according to Fig. 1 and in all experiments an enrichment factor of 4 to 8 was obtained (*1*). Likewise, enrichment of magnetic material could be found in the capillaries of the superior parts of the brain in rats following injection of magnetic material and applying an outer magnetic field over the skulls (*2*).

References

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