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[54] MICROGEL DRUG DELIVERY SYSTEM

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[58] Field of Search **428/402; 424/486, 78, 424/79, 487; 524/522; 523/105**

[56] References Cited

U.S. PATENT DOCUMENTS

4,138,383	2/1979	Rembaum et al.	260/29.7
4,329,332	5/1982	Couvreur et al.	424/497
4,424,311	1/1984	Nagaoka et al.	525/303
4,622,367	11/1986	Horák et al.	428/402
4,891,324	1/1990	Pease et al.	428/402

FOREIGN PATENT DOCUMENTS

240424 3/1987 European Pat. Off. .

OTHER PUBLICATIONS

Poste et al., *Biotechnology* (Dec. 1983), pp. 869-877.
 Couvreur et al., *Polymeric Nanoparticles and Microspheres*, CRC Press, Boca Raton, Fla., pp. 27-93.
 Andrade et al., *Adv. Poly. Sci.* 79:1-63 (1986).

Nagaoka et al., *Polymers as Biomaterials* Plenum Press, pp. 361-374 (1984).

Journal of Pharmaceutical Sciences, vol. 78, No. 6, Jun. 1989, "Blood Clearance and Organ Distribution of Intravenously Administered Polymethacrylic Nanoparticles in Mice".

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[57] ABSTRACT

A copolymer microparticle is presented which is derived from at least about 5 weight percent of free carboxylic acid group-containing vinyl monomers, monomers which have a poly(alkylene oxide) appended thereto, oleophilic monomers and other nonionic hydrophilic monomers. Microgels containing these copolymers having a median water swollen diameter of about 0.01 to about 1.0 micrometer are disclosed. Pharmaceutical and diagnostic compositions are disclosed comprising a therapeutic or diagnostic agent and microgels comprising a copolymer derived from at least about 5 weight percent of non-esterified carboxylic acid group-containing vinyl monomers, oleophilic monomers and other nonionic hydrophilic monomers, with the proviso that when the median water swollen diameter of the microgels is 0.1 micrometer or greater, at least 5 weight percent of the monomers have a poly(alkylene oxide) appended thereto. Diagnostic and therapeutic methods are also disclosed wherein the microgels are substantially protein non-adsorbent and substantially refractory to phagocytosis.

7 Claims, 8 Drawing Sheets

