



- [54] **COVALENT MICROPARTICLE-DRUG CONJUGATES FOR BIOLOGICAL TARGETING**
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Related U.S. Application Data

- [63] Continuation of Ser. No. 441,770, May 16, 1995, Pat. No. 5,543,391, and Ser. No. 246,941, May 19, 1994, Pat. No. 5,543,390, which is a continuation-in-part of Ser. No. 142,771, Oct. 26, 1993, Pat. No. 5,543,389, which is a continuation-in-part of Ser. No. 911,209, Jul. 9, 1992, Pat. No. 5,256,641, which is a continuation-in-part of Ser. No. 607,982, Nov. 1, 1990, Pat. No. 5,149,794.
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- [58] **Field of Search** **514/2, 78; 424/450; 536/21, 51; 530/300, 331, 329**

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[57] **ABSTRACT**

This invention provides novel methods and reagents for specifically delivering biologically active compounds to phagocytic mammalian cells. The invention also relates to specific uptake of such biologically active compounds by phagocytic cells and delivery of such compounds to specific sites intracellularly. The invention specifically relates to methods of facilitating the entry of antiviral and antimicrobial drugs and other agents into phagocytic cells and for targeting such compounds to specific organelles within the cell. The invention specifically provides compositions of matter and pharmaceutical embodiments of such compositions comprising conjugates of such antimicrobial drugs and agents covalently linked to particulate carriers generally termed microparticles. In particular embodiments, the antimicrobial drug is covalently linked to a microparticle via an organic linker molecule which is the target of a microorganism-specific protein having enzymatic activity. Thus, the invention provides cell targeting of drugs wherein the targeted drug is only released in cells infected with a particular microorganism. Alternative embodiments of such specific drug delivery compositions also contain polar lipid carrier molecules effective in achieving intracellular organelle targeting in infected phagocytic mammalian cells. Particular embodiments of such conjugates comprise antimicrobial drugs or agents covalently linked both to a microparticle via an organic linker molecule and to a polar lipid compound, to facilitate targeting of such drugs or agents to particular subcellular organelles within the cell. Also provided are porous microparticles impregnated with antiviral and antimicrobial drugs and agents wherein the surface or outside extent of the microparticle is covered with a degradable coating that is specifically degraded within an infected phagocytic mammalian cell. Also provided are nonporous microparticles coated with an antiviral or antimicrobial drug and further coated wherein the surface or outside extent of the microparticle is covered with a degradable coating that is specifically degraded within an infected phagocytic mammalian cell. Methods of inhibiting, attenuating, arresting, combating and overcoming microbial infection of phagocytic mammalian cells in vivo and in vitro are also provided.