



[54] PULSATILE DRUG DELIVERY SYSTEM

[75] Inventors: Gordon L. Amidon; Glen D. Leesman, both of Ann Arbor, Mich.

[73] Assignee: University of Michigan, Ann Arbor, Mich.

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Related U.S. Application Data

[63] Continuation of Ser. No. 475,644, Feb. 5, 1990, abandoned.

[51] Int. Cl.<sup>5</sup> ..... A61K 9/48

[52] U.S. Cl. .... 424/451; 424/464; 424/473; 424/480

[58] Field of Search ..... 424/473, 451, 464

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Primary Examiner—Thurman K. Page  
Assistant Examiner—D. Gabrielle Phelan  
Attorney, Agent, or Firm—Rohm & Monsanto

[57] ABSTRACT

A drug delivery system for administering a drug in controlled pulse doses to an aqueous environment in the body of a living being has one or more, and preferably less than ten, individual drug-containing subunits in a unitary drug depot, such as a tablet or capsule. The individual subunits are designed to dissolve at different sites and/or times in the gastrointestinal tract to release pulse doses of drug into the portal system in an analogous manner to the rate of release from an immediate release dosage form administered according to an appropriate dosing schedule. The dissolution time of the individual subunits can be controlled by several methods including the provision of pH-sensitive enteric coatings and permeability-controlled coatings. The drug delivery system has significant advantages for the oral administration of first-pass metabolized drugs which exhibit a non-linear relationship between input rate of the drug into the portal system and bioavailability.

18 Claims, 5 Drawing Sheets

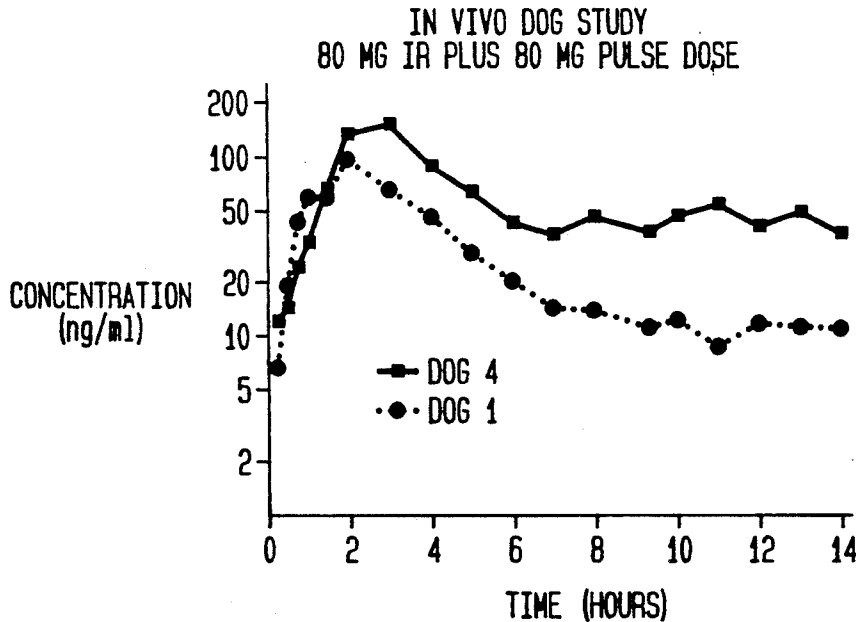


FIG. 1

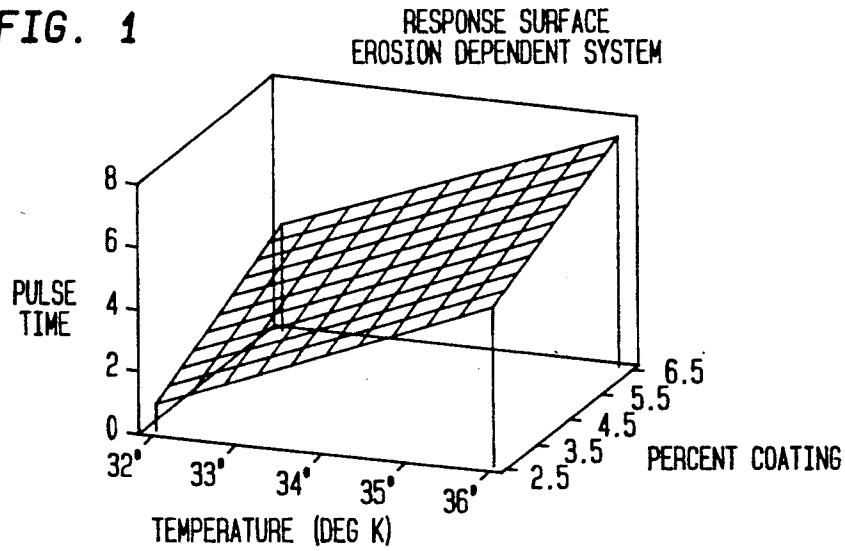


FIG. 2

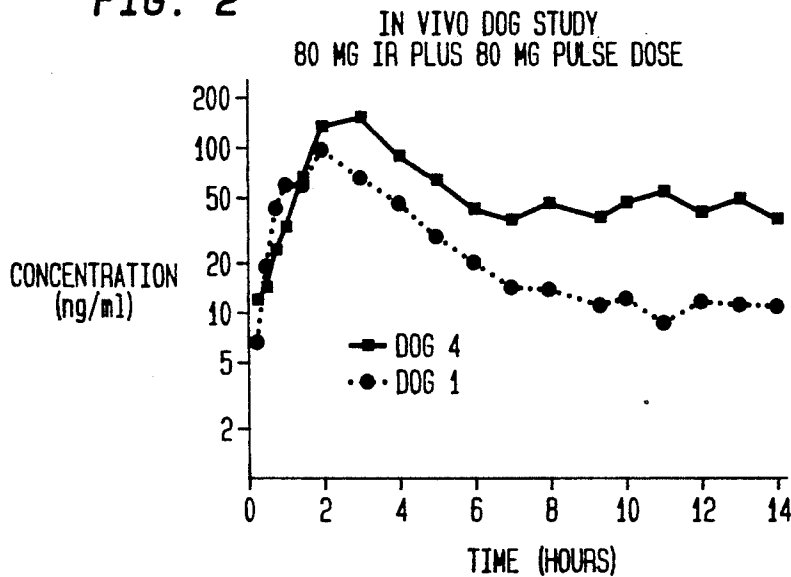


FIG. 3

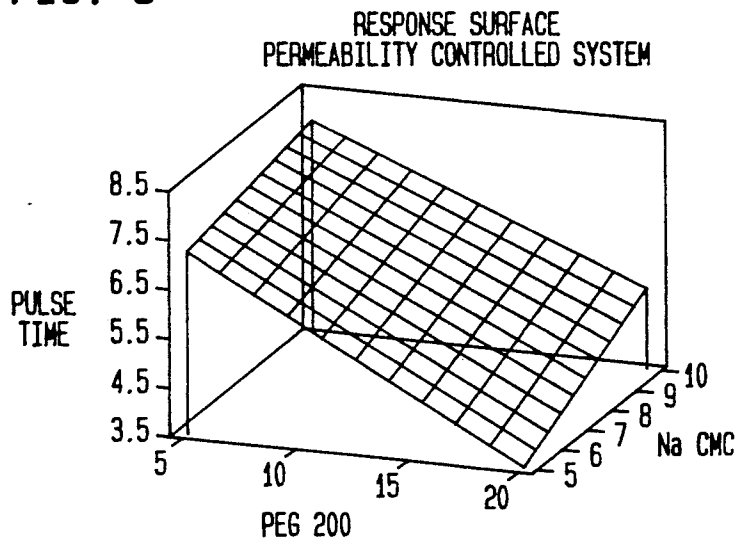


FIG. 4

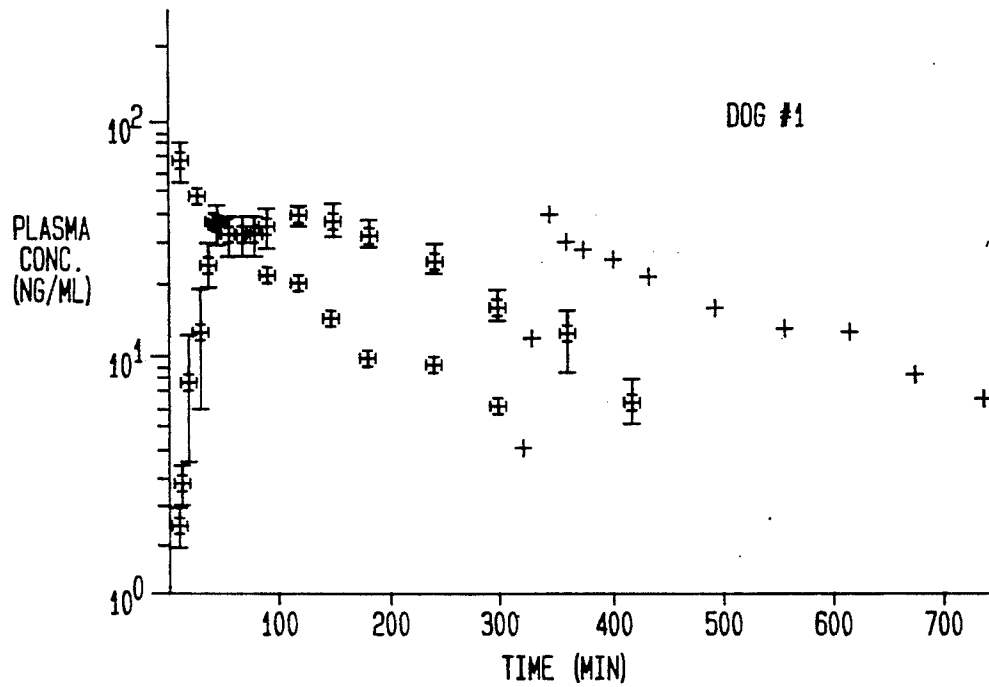


FIG. 8

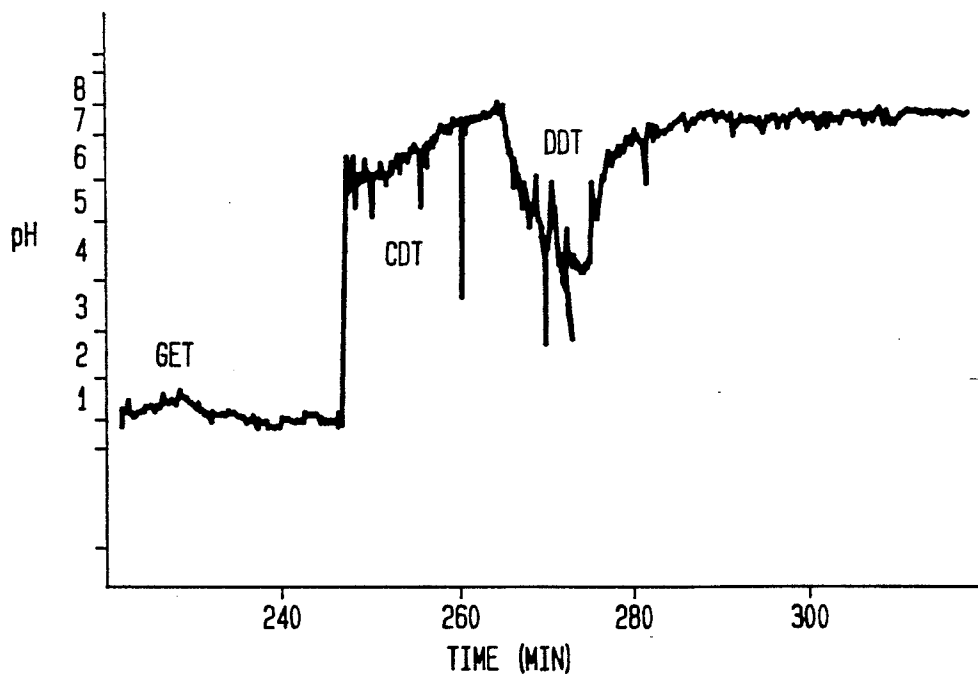


FIG. 5

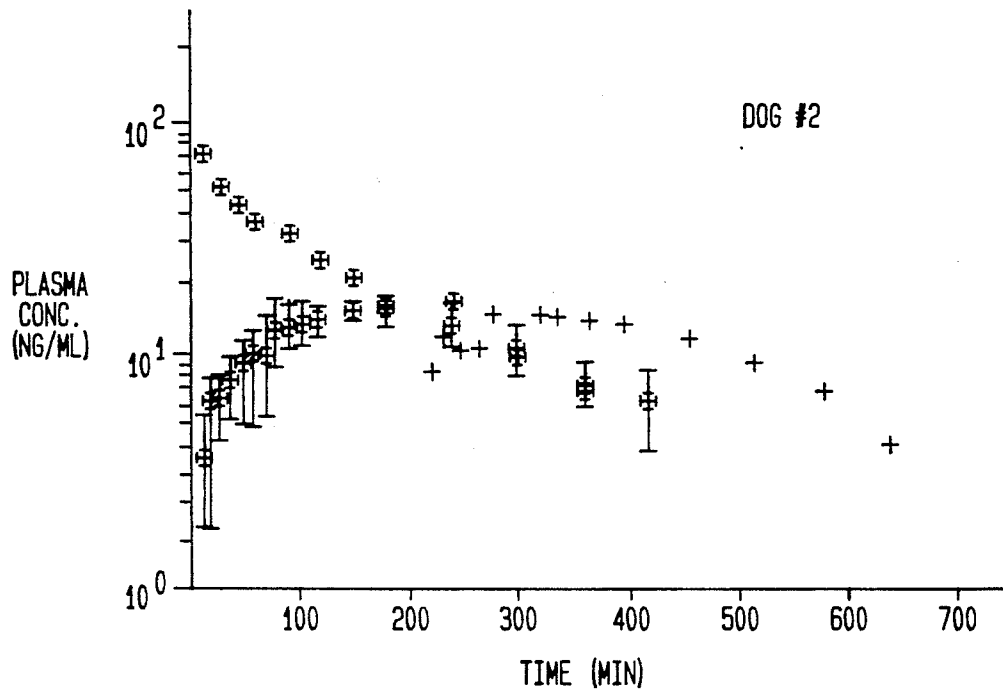


FIG. 9

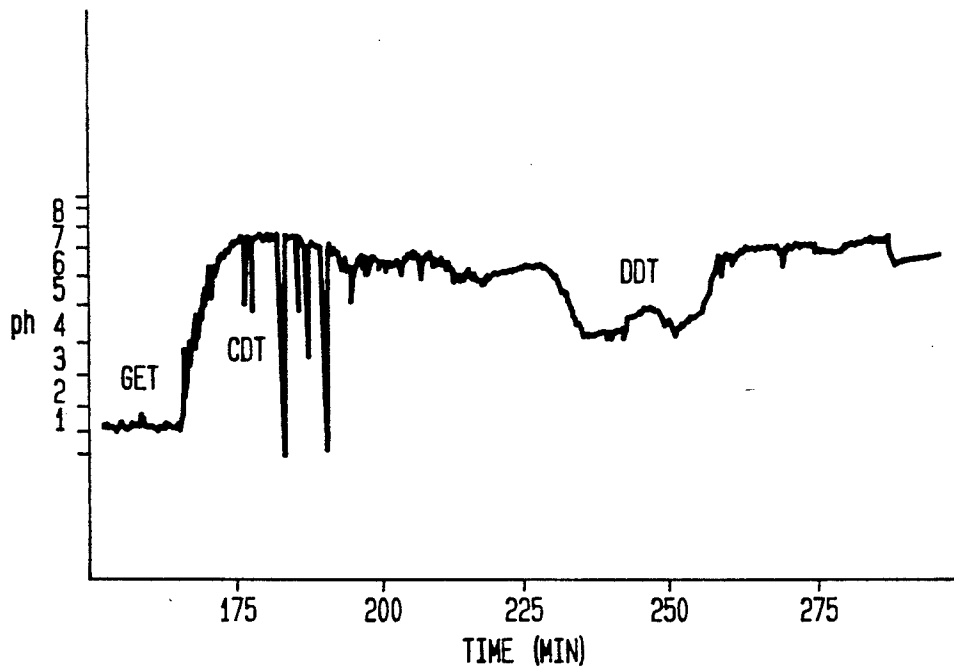


FIG. 6

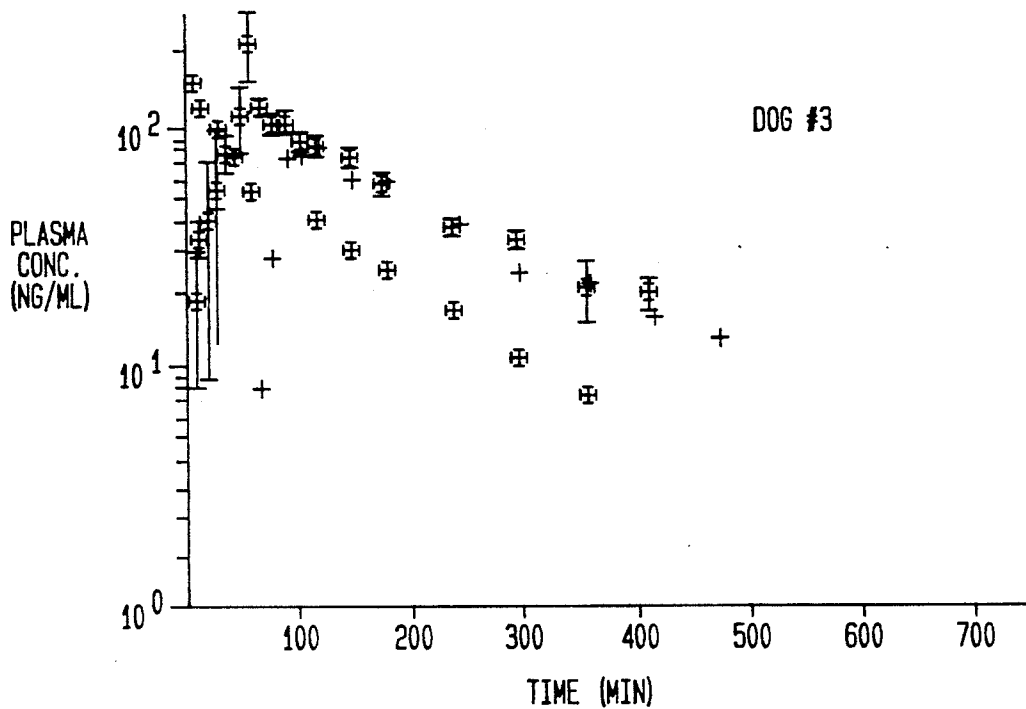
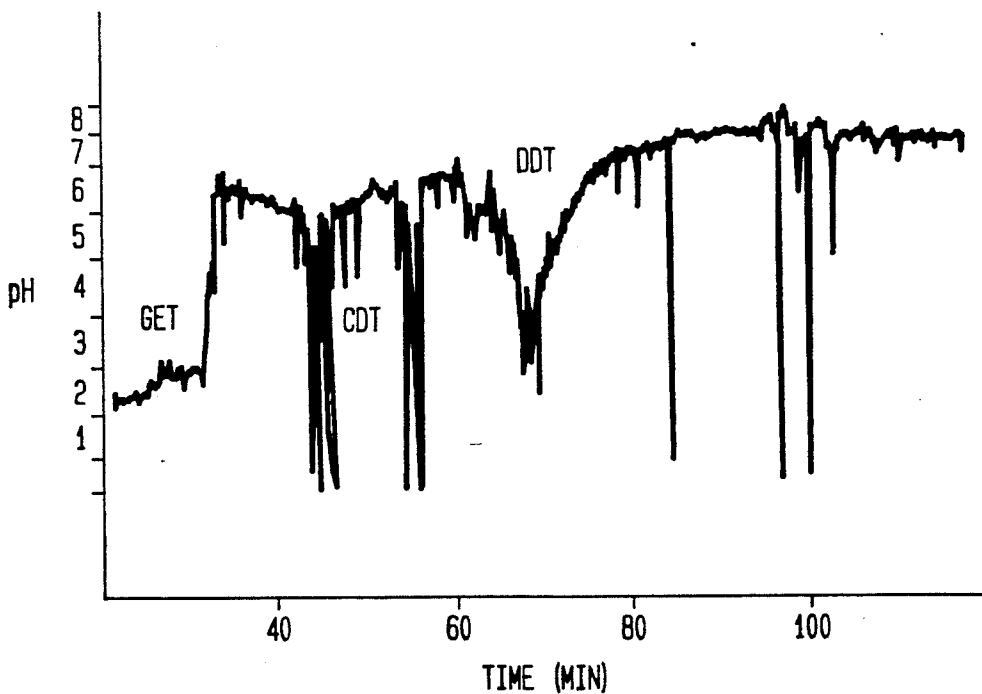


FIG. 10



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