



US005413777A

# United States Patent [19]

[11] Patent Number: **5,413,777**

Sheth et al.

[45] Date of Patent: **May 9, 1995**

[54] **PULSATILE ONCE-A-DAY DELIVERY SYSTEMS FOR MINOCYCLINE**

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0327295 8/1989 European Pat. Off. .  
0418565 3/1991 European Pat. Off. .

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### [57] ABSTRACT

[21] Appl. No.: **91,322**

Pharmaceutical delivery systems containing 7-dimethyl-6-deoxy-6-demethyltetracycline or a non-toxic acid addition salt thereof comprising mixtures or separate administration units of pH sensitive polymer coated spherical granules adapted to release the minocycline in a medium having a pH of in the range of from about 4.0 to about 7.5 and coated or uncoated quick release granules adapted to release minocycline in a medium having a pH of less than about 3.9 or minocycline powder, pH adapted multi-coated compositions and oral dosage unit form liquids, capsules or tablets containing the above are provided. These systems and formulations provide at least minimum therapeutic blood levels of minocycline for at least about 24 hours when administered to a subject only once-a-day. Methods for the preparation of the systems and formulations are provided as well.

[22] Filed: **Jul. 14, 1993**

### Related U.S. Application Data

[60] Division of Ser. No. 892,383, May 27, 1992, Pat. No. 5,300,304, which is a continuation of Ser. No. 410,708, Sep. 21, 1989, abandoned.

[51] Int. Cl.<sup>6</sup> ..... **A61K 9/14; A61K 9/16; A61K 9/54; A61K 9/56**

[52] U.S. Cl. .... **424/490; 424/458; 424/459; 424/461; 424/462; 424/468; 424/470; 424/489; 424/494; 424/497; 514/937**

[58] Field of Search ..... **424/489, 490, 497, 458, 424/461, 462, 494**

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**10 Claims, 14 Drawing Sheets**

