US008206740B2

(12) **United States Patent**
Chang et al.

(10) **Patent No.: US 8,206,740 B2**
(45) **Date of Patent: *Jun. 26, 2012**

(54) **ONCE DAILY FORMULATIONS OF TETRACYCLINES**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 626 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **12/155,676**

(22) Filed: **Jun. 6, 2008**

(65) **Prior Publication Data**

US 2009/0011006 A1 Jan. 8, 2009

Related U.S. Application Data

(63) Continuation of application No. 10/819,620, filed on Apr. 7, 2004, now Pat. No. 7,749,532.

(60) Provisional application No. 60/460,963, filed on Apr. 7, 2003, provisional application No. 60/547,964, filed on Feb. 26, 2004.

(51) **Int. Cl.**
A61K 9/54 (2006.01)

(52) **U.S. Cl.** **424/458**

(58) **Field of Classification Search** ..... None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,293,539 A 10/1981 Ludwig et al.
4,666,897 A 5/1987 Golub et al.
4,704,383 A 11/1987 McNamara et al.
4,837,030 A 6/1989 Valorose, Jr. et al.
4,935,411 A 6/1990 McNamara et al.
4,935,412 A 6/1990 McNamara et al.
5,045,538 A 9/1991 Schneider et al.
5,122,519 A 6/1992 Ritter
5,167,964 A 12/1992 Muhammad et al.
5,188,836 A 2/1993 Muhammad et al.
5,223,248 A 6/1993 McNamara et al.
5,238,686 A 8/1993 Eichel et al.
5,258,371 A 11/1993 Golub et al.
5,260,292 A 11/1993 Robinson et al.
5,277,916 A 1/1994 Dwyer et al.
5,283,065 A 2/1994 Doyon et al.
5,286,497 A 2/1994 Hendrickson et al.

(Continued)

FOREIGN PATENT DOCUMENTS

EP 0 410 099 A1 1/1991

(Continued)

OTHER PUBLICATIONS

Notice of Allowance mailed on Apr. 29, 2010, in prior U.S. Appl. No. 10/819,620, 7 pages.

(Continued)

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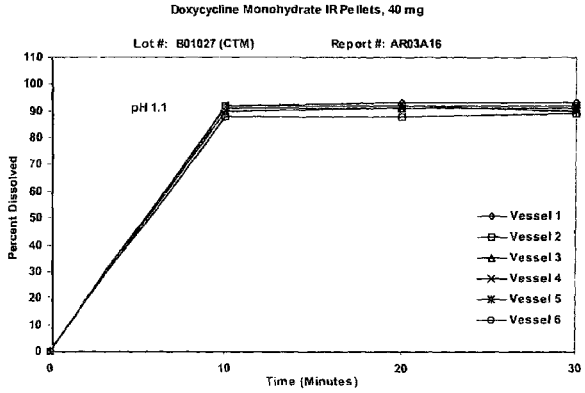
(57) **ABSTRACT**

Disclosed are once-daily formulations containing tetracyclines, especially doxycycline. Such formulations are useful, for instance, for the treatment of collagenase destructive enzyme-dependent diseases, such as periodontal disease and acne, and acute and chronic inflammatory disease states, such as rosacea and arthritis.

29 Claims, 6 Drawing Sheets



Dissolution profile for doxycycline monohydrate IR beads