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(54) **METHOD FOR TREATING MEIBOMIAN GLAND DISEASE**

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(58) **Field of Search** ..... 514/528, 912

(56) **References Cited**

**U.S. PATENT DOCUMENTS**

5,523,297 A \* 6/1996 Pruzanski et al. .... 514/152

**OTHER PUBLICATIONS**

Caton, J., Evaluation of Periostat for Patient Management, Compendium, 1999, vol. 20, No. 5, pp. 451-462.

Mikino et al., "A Case of Rosacea Keratitis With Infectious Keratitis", Folia Ophthalmologica Japonica, vol. 48, (1997), pp. 1387-1391.

Ng et al., "Case Report—Ocular Rosacea", Singapore Medical Journal, vol. 37, No. 1 (1996) pp. 111-112.

Browning et al., "Ocular Rosacea", Survey of Ophthalmology, vol. 31, No. 3 (1986), pp. 145-158.

Salamon, Samuel M., "Tetracyclines in Ophthalmology", Survey of Ophthalmology, vol. 29, No. 4 (1985), pp. 265-275.

Quarterman et al., "Ocular Rosacea—Signs, Symptoms, and Tear Studies . . .", Arch Dermatol, vol. 133, No. 1 (1997), pp. 49-54.

Zengin et al., "Meibomian Gland Dysfunction and Tear Film Abnormalities in Rosacea", Cornea, Vol. 14, No. 2 (1995), pp. 144-146.

Massey et al., "Effect of Drug Vehicle on Human Ocular Retention of Topically Applied Tetracycline", American Journal of Ophthalmology, vol. 81, No. 2 (1976), pp. 151-156.

Eady et al., "Modulation of Comedonal Levels of Interleukin-1 in Acne Patients Treated With Tetracyclines", Journal of Investigative Dermatology, vol. 101, No. 1 (1993), pp. 86-91.

Ballinger et al., "Tetracycline Inhibits Pro-inflammatory Cytokine Release From Mononuclear Cells", Gastroenterology, vol. 112, No. 4 (1997), p. A926, XP-002081054.

Medline Abstract 94254381, Heiligenhaus et al., 1994.\*

\* cited by examiner

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(57) **ABSTRACT**

A method for treating a patient having meibomian gland disease, ocular irritation associated with delayed tear clearance, or recurrent corneal epithelial erosion, is disclosed. Preferably, the method concerns treatment of a patient with topical tetracycline, a derivative or analogue of tetracycline, or a chemically modified tetracycline (CMT). Oral administration of a CMT is also disclosed as part of the method for treating meibomian gland disease, ocular irritation associated with delayed tear clearance, or recurrent corneal epithelial erosion.

**24 Claims, 8 Drawing Sheets**