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[54] METHOD OF INHIBITING NITRIC OXIDE FORMATION

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Related U.S. Application Data

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[51] **Int. Cl.**[5] **A61K 31/155**

[52] **U.S. Cl.** **514/632**; 514/634

[58] **Field of Search** 514/634, 632

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,544,670	10/1985	Studt et al.	514/617
4,758,583	7/1988	Cerami et al.	514/399
4,870,210	9/1989	Musser	564/228
4,983,604	1/1991	Ulrich et al.	514/238.5
5,128,360	7/1992	Cerami et al.	514/400
5,246,970	9/1993	Williamson et al.	514/632

FOREIGN PATENT DOCUMENTS

450598 10/1991 European Pat. Off. .

OTHER PUBLICATIONS

Bredt et al., Nature 351, 714–718 (1991).
Moncada et al., Pharmacol. Rev. 43, 109–142 (1991).
Brownlee et al., Science 232, 1629–1632 (1986).
Bucala et al., J. Clin. Invest. 87, 432–438 (1991).
Tilton et al., Invest. Ophthalmol. Vis. Sci. 31, 342 (1990).
Williamson et al., Diabetes & Metabolisme 16, 369–370 (1990).
Chang et al., Diabetes 40 (Supp. 1) 210A (1991).
Corbett et al., J. Biol. Chem. 266, 21351–21354 (1991).
Chem. Absts. 115: 248104, of Griffith WO 91 04,023 (1989).

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[57] **ABSTRACT**

A method is disclosed for inhibiting nitric oxide formation in a warm blooded mammal afflicted with an acute or chronic inflammatory disease which comprises administering to said mammal an effective nitric oxide inhibitory amount of methyl-, or 1,1-dimethyl-, or amino-substituted guanidines.

10 Claims, 4 Drawing Sheets