US005281627A

United States Patent [19]

Griffith

[11] Patent Number: 5,281,627

[45] Date of Patent: Jan. 25, 1994

[54] SUBSTITUTED ARGININES AND SUBSTITUTED HOMOARGININES AND USE THEREOF

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[21] Appl. No.: **889,345**

[22] Filed: **May 28, 1992**

[51] **Int. Cl.**[5] **A61K 31/195**

[52] **U.S. Cl.** **514/565**; 562/560

[58] **Field of Search** 562/560; 514/565

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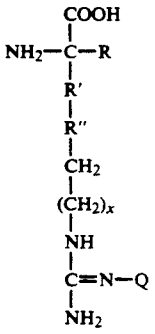
[57] **ABSTRACT**

Guanidino substituted arginines or homoarginines based on monoalkyl carbon-substituted ornithines or lysines, having the formula



wherein R is $(CH_2)_yCH_3$ or H, R′ is CH_2 or $C(H)(CH_2)_yCH_3$, and R″ is CH_2 or $C(H)(CH_2)_yCH_3$, with y ranging from 0 to 5, and x is 0 or 1 and Q is an alkyl group containing from 1 to 6 carbon atoms or NH_2 or NO_2, and only one of R, R′ and R″ providing an alkyl substituent on the ornithine or lysine moiety. Preferred compounds are α-methyl-N$^{\omega}$-methyl-DL-arginine, RS-β-methyl-N$^{\omega}$-methyl-DL-arginine, RS-γ-methyl-N$^{\omega}$-methyl-DL-arginine, α-methyl-N$^{\omega}$-amino-DL-arginine, RS-β-methyl-N$^{\omega}$-amino-DL-arginine, RS-γ-methyl-N$^{\omega}$-amino-DL-arginine, α-methyl-N$^{\omega}$-nitro-DL-arginine, RS-β-methyl-N$^{\omega}$-nitro-DL-arginine, and RS-γ-methyl-N$^{\omega}$-nitro-DL-arginine. A composition includes said compound together with a pharmaceutically acceptable carrier. Methods of use are directed to delivering said compound to inducible nitric oxide synthase to inhibit the ability of the enzyme to catalyze the conversion of arginine to nitric oxide, to administering said compound to inhibit pathological overproduction of nitric oxide from arginine and to administering said compound to a subject having systemic hypotension due to the pathological overproduction of nitric oxide and an α_1 adrenergic agonist to increase blood pressure in the subject to a clinically acceptable level.

4 Claims, 2 Drawing Sheets