

cise quantitation of their ability to inhibit arginine-dependent NO formation by the EMT6 enzyme system. Thus, from data such as that presented in FIG. 21 it can be calculated that L-NMA is a competitive inhibitor of arginine utilization with an apparent K_i or 5–10 μM . The ethyl-substituted compound is approximately 10-fold less active (FIG. 22).

It was concluded from these studies that nitric oxide synthesis from L-arginine is demonstrable in a wide variety of in vitro preparations, from an array of species. Nitric oxide is an important mediator of vasodilation in vivo and probably plays an important role in vascular homeostasis. Finally, N^G -substituted arginine analogs may be used as specific blockers of the enzymatic pathway for nitric oxide generation. Thus, this class of arginine antagonists may offer specific relief from hypotension resulting from conditions which cause excess nitric oxide generation, such as those indicated in Examples 1 and 2.

Changes may be made in the arginine antagonists and analogs or method steps of the invention without departing from the scope and spirit of the following claims.

What is claimed is:

1. A method for prophylaxis or treatment of an animal for systemic hypotension induced by gamma-interferon, tumor necrosis factor, interleukin-1 or interleukin-2 said method involving intravascularly administering a therapeutically effective amount of an N^G -substituted arginine or an N^G, N^G -disubstituted arginine to an animal possibly developing or having such induced systemic hypotension wherein the N^G -substituted or N^G, N^G -disubstituted arginine has a nitro, amino, lower alkyl, lower hydroxyalkyl or lower alkenyl substituent replacing a hydrogen of a guanidino amino group.
2. A method for prophylaxis or treatment of systemic hypotension in a patient induced by chemotherapeutic treatment with tumor necrosis factor or interleukin-2, said method involving intravascularly administering to said patient a therapeutically effective amount of N^G -substituted arginine or an N^G, N^G -disubstituted arginine to a patient wherein the N^G -substituted or N^G, N^G -disubstituted arginine has a nitro, amino, alkyl, hydroxyalkyl, or alkenyl substituent replacing a hydrogen of a guanidino amino group.
3. A method for treatment of an animal for systemic hypotension induced by exposure to endotoxin, said method involving intravascularly administering to said animal a therapeutically effective amount of N^G -substituted arginine or N^G, N^G -disubstituted arginine to an animal having such induced systemic hypotension, wherein the N^G -substituted or N^G, N^G -disubstituted arginine has a nitro, amino, lower alkyl, lower hydroxyalkyl, or lower alkenyl substituent replacing a hydrogen of a guanidino amino group.
4. The method of claim 1, 2, or 3 wherein the N^G -substituted arginine is a lower N^G -aminoarginine, N^G -nitroarginine, N^G -methylarginine, N^G -ethylarginine, or N^G -propylarginine.
5. The method of claim 1, 2 or 3 wherein the N^G -substituted arginine is N^G -alkyl arginine.
6. The method of claim 1, 2 or 3 wherein the N^G -substituted arginine is N^G -substituted L-arginine and the N^G, N^G -disubstituted arginine is N^G, N^G -disubstituted L-arginine.
7. The method of claim 1, 2 or 3 wherein said therapeutically effective amount of substituted or disubstituted arginine inhibits production in the animal or patient of nitric oxide from arginine.

tuted arginine inhibits production in the animal or patient of nitric oxide from arginine.

8. A method for prophylaxis or treatment of an animal for systemic hypotension caused by induced production of nitric oxide, said method involving administering a therapeutically effective amount of an arginine antagonist inhibiting production of said nitric oxide from arginine, to an animal possibly developing or having systemic hypotension.

9. A method for prophylaxis or treatment of an animal for systemic hypotension caused by nitric oxide production induced by gamma-interferon, tumor necrosis factor, interleukin-1, or interleukin-2, said method involving intravascularly administering a therapeutically effective amount of an arginine antagonist inhibiting production of nitric oxide from arginine, to an animal possibly developing or having such systemic hypotension.

10. A method for treatment of an animal for systemic hypotension caused by nitric oxide production induced by exposure to endotoxin, said method involving intravascularly administering a therapeutically effective amount of an arginine antagonist inhibiting production of said nitric oxide from arginine, to an animal having such systemic hypotension.

11. A method for prophylaxis or treatment of an animal for systemic hypotension induced by gamma-interferon, tumor necrosis factor, interleukin-1 or interleukin-2, said method involving intravascularly administering a therapeutically effective amount of lower N^G -alkylarginine lower N^G, N^G -dialkylarginine, N^G -aminoarginine or N^G -nitroarginine to an animal possibly developing or having such induced systemic hypotension.

12. The method of claim 11 wherein the N^G -alkylarginine or N^G, N^G -dialkylarginine has an alkyl substituent selected from the group consisting of methyl, ethyl, and propyl.

13. A method for prophylaxis or treatment of an animal for systemic hypotension induced by gamma-interferon, tumor necrosis factor, interleukin-1, or interleukin-2, said method involving intravascularly administering a therapeutically effective amount of N^G -substituted arginine or a N^G, N^G -disubstituted arginine wherein the N^G -substituted arginine or N^G, N^G -disubstituted arginine has a lower hydroxyalkyl, a lower carboxyalkyl or a lower aminoalkyl substituent replacing a hydrogen of a guanidino amino group.

14. A method for treatment of an animal for systemic hypotension induced by exposure to endotoxin, said method involving administering a therapeutically effective amount of lower N^G -alkylarginine lower N^G, N^G -dialkylarginine, N^G -aminoarginine or N^G -nitroarginine to an animal having such induced systemic hypotension.

15. A method for prophylaxis or treatment of systemic hypotension in a patient undergoing anticancer chemotherapy with tumor necrosis factor or interleukin-2, said method involving intravascularly administering a therapeutically effective amount of lower N^G -alkyl-arginine, N^G, N^G -dialkylarginine, lower N^G -aminoarginine or N^G -nitroarginine to said patient having or possible developing systemic hypotension induced by such chemotherapy.

16. A method for prophylaxis or treatment of a patient for systemic hypotension caused by induced production of nitric oxide, said method involving intravascularly administering a therapeutically effective amount of an arginine antagonist inhibiting production of said