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[54] **PREVENTING CONVERSION OF CITRULLINE TO ARGININOSUCCINATE TO LIMIT PATHOLOGICAL NITRIC OXIDE OVERPRODUCTION**

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[58] **Field of Search** 514/33, 561, 564

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[57] **ABSTRACT**

Administration of argininosuccinate synthetase activity reducing agents, e.g., argininosuccinate synthetase induction blocking agents (e.g., antibiotics that bind to DNA sequences present in the upstream regulatory region of the argininosuccinate synthetase gene, such as mithramycin) and argininosuccinate synthetase inhibitors (e.g., L-citrulline antagonists such as methyl citrulline and L-aspartate antagonists such as D-aspartate) is useful to prevent or treat sepsis or cytokine-induced systemic hypotension, is useful in the treatment of sepsis or cytokine-induced systemic hypotension to restore vascular sensitivity to the effects of α_1-adrenergic agonists, and is useful to suppress an immune response, e.g., in treating inflammation. In one embodiment, certain argininosuccinate synthetase activity reducing agents are used together with arginine antagonists to treat sepsis or cytokine induced hypotension.

13 Claims, 5 Drawing Sheets