

mycin D as indicated. The supernatant was removed and PGE₂ and nitrite formation were determined. These results further demonstrate that aminoguanidine attenuates IL-1-induced PGE₂ production, and completely prevents IL-1-induced nitrite formation by β -cells. The transcriptional inhibitor actinomycin D completely prevents PGE₂ and nitrite formation by β -cells, indicated the requirement for mRNA transcription. These findings indicate that IL-1 induces COX-2 and iNOS expression and that nitric oxide directly activates COX-2.

As further corroboration of the activity and interaction of nitric oxide in COX and PGE₂ production, rat islets were pretreated with 5 units/ml IL-1 or IL-1 and actinomycin D (1 μ M) for 18 h. The islets were washed and then cultured for 2 h with 30 μ M arachidonic acid (COX substrate) in the presence or absence of SIN-1 (1mM; nitric oxide donor compound) and hemoglobin (Hb; scavenger of nitric oxide) as indicated. The results are presented in FIG. 7 and demonstrate that nitric oxide, released spontaneously by SIN-1, stimulates the activity of both constitutive COX (COX-1; control and IL-1+Act D treatment) and inducible COX (COX-2; IL-1 treated group). Hemoglobin attenuates SIN-1 stimulated PGE₂ formation indicating that the effects of SIN-1 on COX activity is mediated by nitric oxide.

The inhibitors of nitric oxide formation described herein can be used for administration to warm blooded mammals by conventional means, preferably in formulations with pharmaceutically acceptable diluents and carriers. The amount of the active inhibitor to be administered must be an effective amount, that is, an amount which is medically beneficial but does not present toxic effects which outweigh the advantages which accompany its use. It would be expected that the adult human daily dosage would normally range upward from about one milligram per kilo of body weight of the drug. Suitable routes of administration include, where appropriate, topical delivery via salves, ointments and solutions; or locally through suppositories, pessaries, and the like; orally in the forms of capsules, tablets, syrups, elixirs and the like; and parenteral administration, e.g. intravenously, intraperitoneally or subcutaneously. Intravenous administration of the drug in aqueous solution such as physiologic saline is illustrative. Appropriate formulations of the drug in pharmaceutically acceptable diluents and carriers in therapeutic dosage form can be prepared by reference to general texts in the field such as, for example, *Remington's Pharmaceutical Sciences*, Ed. Arthur Osol.

16th ed., 1980, Mack Publishing Co., Easton, Penn. Various other examples will be apparent to the person skilled in the art after reading the present disclosure without departing from the spirit and scope of the invention. It is intended that all such examples be included within the scope of the appended claims.

What is claimed is:

1. A method of inhibiting nitric oxide production in a warm blooded mammal afflicted with the physiological conditions manifested by an acute or chronic inflammatory disease or condition said method comprising administering topically to said mammal a nitric oxide inhibitory effective amount of aminoguanidine wherein the inflammatory disease or condition is a member selected from the group consisting of acute and chronic vaginitis; insect bites; thermal burns; chemical burns; electrical burns; sunburn; acute and delayed hypersensitivity; acute or chronic psoriasis; eczema; contact dermatitis; poison ivy; poison oak; and poison sumac.

2. A method of inhibiting nitric oxide production in a warm blooded mammal afflicted with the physiological conditions manifested by an acute or chronic inflammatory disease or condition said method comprising administering orally to said mammal a nitric oxide inhibitory effective amount of aminoguanidine wherein the inflammatory disease or condition is a member selected from the group consisting of acute and chronic gastroenteritis and colitis; acute and chronic cystitis and urethritis; and inflammatory bowel/Crohn's disease.

3. A method of inhibiting nitric oxide production in a warm blooded mammal afflicted with the physiological conditions manifested by an acute or chronic inflammatory disease or condition said method comprising administering parenterally to said mammal a nitric oxide inhibitory effective amount of aminoguanidine wherein the inflammatory disease or condition is a member selected from the group consisting of acute and chronic fungal infections; acute and chronic pericarditis; acute and chronic peritonitis; acute and chronic synovitis; acute and chronic pleuritis; acute and chronic tendinitis; uremic pericarditis; acute and chronic cholecystitis; meningitis; encephalitis; graft vs. host disease; pernicious anemia; multiple sclerosis; transplant rejection; inflammation due to toxic shock or trauma; adult respiratory distress syndrome; and reperfusion injury.

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