

Inhibition of LPS-Induced Nitric Oxide Production by Styrylheterocycles.

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Styrylheterocycles were synthesized as a novel class of inhibitors on nitric oxide(NO) production. Their inhibitory activities were evaluated using lipopolysaccharide-stimulated RAW264.7 macrophage cells. This series of inhibitors are suggested as lead compounds for the development of potent and selective inhibitors

[PD1-18] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Synthesis of thiazolidinedione analogs

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Thiazolidinediones (TZDs) are a new class of compound that increase insulin sensitivity in type 2 diabetic patients. Thiazolidinediones (TZDs) act as ligands for a member of the nuclear hormone receptor superfamily, peroxisome proliferator-activated receptor- γ (PPAR- γ), which is highly expressed in fatty tissue and, moreover, has been shown to play an important role in fat cell differentiation. The strong interaction between the antidiabetic activity of TZDs and their ability to activate PPAR- γ suggests that PPAR- γ , through downstream-regulated genes, mediates the effects of TZDs. In this report, the synthesis of (5-[4-(2-biphenyl-4-yl)-5-methyl-oxazol-4-ylmethoxy]-benzyl]-thiazolidine-2,4-dione and its analogs are described.

[PD1-19] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Synthesis and properties of methylprednisolone-21sulfate sodium as a colon-specific prodrug of methylprednisolone

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Corticosteroids have been used most frequently for inflammatory bowel disease. To reduce side effects by the systemic absorption, colon-specific delivery is highly desirable. We expected that conversion of 21-hydroxyl glucocorticoids into a sulfate ester sodium will greatly increase the hydrophilicity, which consequently restrict the gastrointestinal absorption. Once delivered to the colon, sulfate ester will be hydrolyzed by the sulfatase originated from microbes and release the parent compound, glucocorticoids. In this study, we prepared methylprednisolone 21-sulfate sodium (MPS) and investigated its suitability as a colon-specific prodrug of methylprednisolone (MP). We compared the in vitro properties of MPS to that of prednisolone 21-sulfate sodium or dexamethasone 21-sulfate sodium. METHOD: MPS was obtained by reacting MP and sulfatrioxide triethylamine, and subsequently treating the product with NaCl solution. Stability in pH 1.2 and 6.8 buffer solutions and apparent partition coefficient in 1-octanol/pH 6.8 buffer were determined. Prodrug conversion was determined by incubating MPS with the contents of various segments of gastrointestinal tract of rats. RESULTS: MPS was stable and apparent partition coefficient of MP and MPS was 98.89 and 0.37, respectively. MPS was stable on incubation with the contents of the stomach or small intestine. With the cecal contents, MPS was decreased to 75% and 100% at 12 h and 24 h, respectively, producing MP 51% and 72% of the dose at 12 h and 24 h. The degree of A ring reduction and the effect of reduction inhibitors was greater for MP than PD. CONCLUSION: MPS was stable and expected to be non-absorbable in the GI tract and release MP in the cecum. It underwent reductive bioinactivation by the cecal contents to some degree, and yet it might serve as a promising colon-specific prodrug of glucocorticoids.

[PD1-20] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]