Structure-Activity Studies for Potassium-Channel Opening in Pinacidil-Type Cyanoguanidines and Nitroethenediamines

Paul W. Manley* and Ulrich Quast

Pinacidil (rac-1; N-cyano-N’-(4-pyridinyl)-N”-(1,2,3-trimethylpropyl)guanidine) is a vasorelaxant drug [1] which acts primarily as a K-channel opener in vascular smooth-muscle cells [2]. As part of a structure-activity study aimed to

Received: December 11, 1990


12. Activated by 1% HCl (5 min r.t.) then washed with EtOH, Et2O and dried at 20°/0.1 Torr.

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© Schweizer. Chemiker-Verband; ISSN 0009-4293

Herbstversammlung Bern
19. Oktober 1990
Sektion für Medizinische Chemie

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Swiss Chemical Society
Structure-Activity Studies for Potassium-Channel Opening in Pinacidil-Type Cyanoguanidines and Nitroethenediamines

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Pinacidil (rac-I; N-cyano-N'(4-piryldinyl)-N''-(1,2-trimethylpropyl)guanidine) is a vasorelaxing drug [1] which acts primarily through the opening of membrane K channels in vascular smooth-muscle cells [2]. As part of a structure-activity study aimed to-
The Search for Peptidoleukotriene Antagonists


The peptidoleukotrienes LTC₄, LTD₄, and LTE₄ are thought to play a major role in allergic asthma, due to their potent bronchoconstrictor and inflammatory properties. The first leukotriene (LT) antagonist, FPL55712, was discovered in 1973 six years before the structures of the LT's were defined by Samuelsson and Corey. Initial chemical approaches to the discovery of new LT antagonists were based mainly on the structure of FPL55712 and, after 1980, on the structure of LTD₄, LY171883, L-648051, Ro23-3544, CGP35949D, and YM-16638 are examples of FPL55712 analogs that are or were in clinical development. However, the clinical data reported so far are not encouraging. These compounds, as well as the first LT analogs, can be considered to be 'first generation' antagonists showing antagonist potency in the range of FPL55712. Recently 'second generation' antagonists with greatly enhanced potency have been developed.

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