

BQ-788, ETB Receptor Antagonist

Overview

Ishikawa et al¹ reported that BQ-788 [N-cis-2, 6- dimethylpiperidinocarbonyl - L-gamma- methylleucyl-D-l-methoxycarbonyltryptophanyl- D-norleucine] to be a potent and competitive inhibitor of 125I-ET-1 binding to ETB receptors on human Girardi heart cells (IC₅₀, 1.2 nM) but only a poor inhibitor of the ET-1 binding to ETA receptors on human neuroblastoma cell line SK-N-MC cells (IC₅₀, 1300 nM). On the basis of a recent study using BQ-123 (ETA receptor antagonist) and BQ-788 (ETB receptor antagonist) to investigate which of the ET receptor subtypes (ETA or ErB) participate in the rapid clearance of endothelin from circulation, Fukuroda et al² have concluded that ETB receptors play an important role in the clearance of ET-1. Fukuroda et al report that in the rabbit isolated pulmonary artery only a combination of BQ-123 and BQ-788 completely inhibited the contractions induced by 1 nM ET-1, but the two receptor antagonists individually did not inhibit the contractile action of ET-1. The authors concluded that the activation of either ETA or ETB receptors is sufficient to elicit ET-1 induced contraction, and blockade of both receptor subtypes would be necessary for the inhibition of some ETA/ETB composite types of responses. Doleansjuste has used BQ-123 and BQ-788 to characterize the receptors responsible for ET-I induced release of thromboxane A (2) from the guinea pig lung and endothelium-derived nitric oxide from the rabbit perf used kidney. The effects of BQ-788 on isolated blood vessel and small intestine were studied using rat aorta, rabbit saphenous vein, and guinea pig ileum. Thus, being a potent and selective ETB receptor antagonist, BQ-788 may be considered as a powerful tool for investigating the role of endothelins in physiological and pathological processes.

References

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