Pharmacology of trace amine-induced vasodilatation: roles of endothelium and intracellular sites

Alex Voisey[1], Kenneth Broadley[1], and William Ford[1]

[1]Cardiff University

August 1, 2022

Abstract

Abstract Background and Purposes: Although trace amines, including β-phenylethylamine (β-PEA), cause vasoconstriction, they also induce endothelial nitric oxide release via an unknown mechanism. This study evaluates the cellular site of action and receptors mediating β-PEA-induced vasodilation. Experimental Approach: In vitro vasodilator responses to β-PEA were assessed using aortic rings and third-order mesenteric arteries of male Sprague-Dawley rats. Key Results: β-PEA-induced concentration-dependent vasodilation of pre-constricted aortic rings and third-order mesenteric arteries were partially sensitive and insensitive to endothelium removal, respectively. In aortic rings vasodilator responses to β-PEA were unaffected by EPPTB, a selective antagonist of murine trace amine associated receptor 1 (TAAR1), or antagonists of β2-adrenoceptors and muscarinic acetylcholine M3 receptors. The inhibitor of uptake-2 transport, decynium-22, abolished β-PEA-induced vasodilation revealing a vasoconstrictor response. Conclusion and Implications: Vasodilator responses to β-PEA do not involve cell surface receptors. We propose that β-PEA utilises uptake-2 transporters to gain access to an intracellular site. Although the identify of the intracellular site is unknown, the mechanism is similar to that previously reported where intracellular TAAR1 medated responses in HEK293 cells. Vasodilatation is the dominant response to trace amines of mesenteric vessels whereas in the aorta, it opposes vasoconstriction.

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