# THE ANTAGONIST 14, 15 EPOXYEICOSA-5(Z)-ENOIC ACID HAS VASODILATOR PROPERTIES IN MESENTERIC VESSELS

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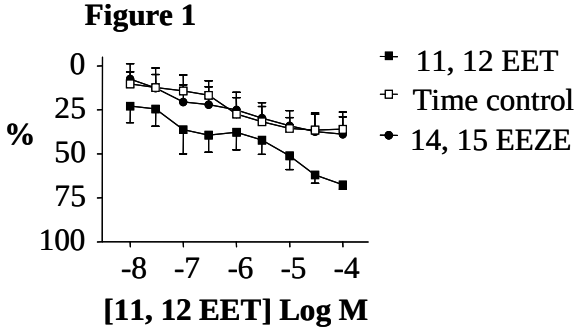
There is now overwhelming evidence for Epoxyeicosatrienoic acids (EETs) as endothelial derived hyperpolarising factor (EDHF). Most recently, a number of pharmacological tools have been developed for the study of EETs in relation to EDHF responses. EETs have been shown to cause relaxation by activating smooth muscle large conductance $Ca^{2+}$ sensitive $K^+$ ($BK_{Ca}$) (Archer *et al*, 2003). This dilatory response has been shown to be specifically inhibited by its analogue 14, 15-epoxyeicosa-5 (Z) enoic acid (14, 15 EEZE) in both human internal mammary artery and bovine coronary artery (Archer *et al*, 2003). Here we have investigated the antagonist effects of 14, 15 EEZE in murine arteries.

Male Black 6 mice (12-18 weeks) were killed by lethal exposure to $CO_2$. First order arteries were isolated and mounted in wire myographs immersed in physiological salt solution (PSS). Arteries were equilibrated (30 mins) and tensions normalised as described previously (Mulvany and Halpern, 1977). Arteries incubated for 30 minutes with or without 3µg/ml 14, 15 EEZE. A concentration response curve to 11, 12 EET was performed cumulatively on arteries pre-contracted with $EC_{80}$ U46619. In some experiments, arteries were pre-contracted with EC80 U46619, and concentration response to 14, 15 EEZE performed cumulatively.



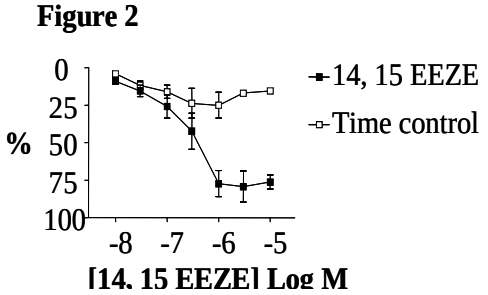




Figure 1: Vasodilatory effects of 11, 12 EET is inhibited by pre-incubation with 14, 15 EEZE. Figure 2: Vasodilatory effects of 14, 15 EEZE in U46619 pre-contracted arteries. Data is shown as % of U46619 induced tone.

11, 12 EET is an effective vasodilator of murine mesenteric arteries (figure 1), which can be inhibited by the CYP epoxygenase antagonist 14, 15 EEZE. However, 14, 15 EEZE is an effective vasodilator (figure 2) in U46619 pre-contracted arteries.

We have not identified the mechanism by which 14, 15 EEZE induced vasodilation. However, the possibility exists that it is a partial agonist for the EET/EDHF receptor. These results illustrate an important pharmacological property of these antagonists, which is being increasingly used to study the nature of EDHF.

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Archer SL *et al* (2003). Circulation 107:769-776.

Mulvany MJ and Halpern W (1977) Circ.Res. 41:19-26.