Vasorelaxant effects of \( N \)-oleylethanolamide in the rat isolated aorta and mesenteric arterial bed

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Oleylethanolamide (OEA) is a fatty acid amide with a similar structure to the endocannabinoid anandamide, yet OEA does not bind to 'classical' cannabinoid receptors. Nevertheless, in common with anandamide, OEA can activate vanilloid (TRPV1) receptors, which can be found on sensory nerves (Alexander et al., 2007). Although OEA is reported to regulate metabolism and feeding behaviour \textit{in vivo}, relatively little is known about its vascular effects. However, OEA does relax isolated small mesenteric arteries via capsaicin-sensitive and endothelium-dependent mechanisms (Ho et al., 2008). This study therefore aimed to investigate the vascular effects of OEA with particular interest in the involvement of sensory nerves in the whole mesenteric arterial bed and aorta.

Mesenteric arterial beds, taken from male Wistar rats (249-310g), were cannulated and then perfused with warmed (37°C), gassed (95% O\(_2\) / 5% CO\(_2\)) Krebs-Henseleit solution. After 20 min equilibration, the preparations were either continually perfused with normal Krebs-Henseleit solution (n=7), or in the presence of 10 \( \mu \)M capsaicin (n=7) for 1 h to deplete sensory nerves of neurotransmitters (Harris et al., 2002). Following this period the preparations were again perfused with Krebs-Henseleit solution, before the addition of methoxamine (~25\( \mu \)M) to increase vessel tone. A concentration-response curve to OEA was then constructed. Thoracic aortic rings from the same animals were used in parallel to the whole mesenteric bed experiments, and followed a similar protocol. Aortic rings were pre-tensioned to 9.8 mN and contracted with approximately 40\( \mu \)M methoxamine.

OEA caused a complete concentration-dependent vasorelaxation in perfused mesenteric arterial beds, the potency of which was unaffected by capsaicin pre-treatment (\( pEC_{50} \): control = 6.6 ± 0.5; capsaicin pre-treated = 7.3 ± 0.5 (mean ± s. e. mean)). However, the maximal relaxation to OEA was significantly (\( p < 0.05 \), Student's t-test) reduced in preparations following capsaicin pre-treatment (\( R_{\text{max}} \): control = 117 ± 21 %; capsaicin pre-treated = 62 ± 12 %). In aortic rings, OEA also caused a concentration-dependent vasorelaxation (\( pEC_{50} \): control = 7.7 ± 0.5 (n=8); capsaicin pre-treated = 8.4 ± 0.4 (n=9)). In this tissue, OEA failed to evoke a complete relaxation, and capsaicin pre-treatment again resulted in a significant reduction of the maximal response following capsaicin pre-treatment (\( R_{\text{max}} \): control = 55 ± 9 % (n=8); capsaicin pre-treated = 29 ± 4 % (n=9)).

The findings from this study indicate that OEA causes vasorelaxation in the whole mesentery and thoracic aorta, partially via a sensory nerve-mediated mechanism, and additional mechanisms of action remain to be determined.

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