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Endothelium-dependent and - independent relaxation of the isolated aorta of the rat by Quercetin

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The dietary metabolite quercetin has been reported to possess vascular protective effects and induce vasodilatation however the mechanisms by which this flavonoid induces such actions are not entirely clear. We aimed to characterise the effects of quercetin in the isolated aorta of the rat.

Concentration-response curves to quercetin (10^{-6}–$6x10^{-4}$M) were generated in endothelium-containing (+EC) and –denuded (-EC) rings of thoracic aorta from female Sprague Dawley rats (200-250g). The influence of NOS and guanylate cyclase in vascular reactivity were determined following use of the inhibitors L-NAME (10^{-4}M) and ODQ (10^{-5}M) respectively. In separate experiments the time-dependent influence of quercetin (30 min incubation at $6x10^{-4}$M followed by washout) on repeated contractions to PE (10^{-5}M) were determined. Data are expressed as mean± s.e. mean, n=3-6; statistical comparisons were determined by ANOVA followed by a post-hoc multiple comparisons Bonferroni test.

The maximal relaxation produced by quercetin in +EC rings (106±2%) was not different from that generated in –EC rings (109±3%), in +EC rings treated with L-NAME (100±2%) or ODQ (98.2±1) suggesting that quercetin produces a powerful EC- and NO-independent relaxation. However the pEC_{50} produced for quercetin in –EC (3.83±0.02, $P<0.01$) or in +EC rings treated with L-NAME (3.64±0.05, $P<0.05$) or ODQ (3.62±0.07, $P<0.001$) was significantly higher than that generated in +EC rings (4.52±0.14) suggesting that quercetin enhances vascular relaxation through stimulation of EC and activation of the NO pathway. The contractile response produced by a repeated single addition of PE to +EC rings remained consistent over a 230 min time period. In contrast following a 30 min exposure to quercetin contractions to PE were significantly depressed in +EC and –EC rings however those of the +EC rings recovered at a slower rate. This suggests that the depression of PE-induced contraction induced by quercetin appears to be augmented by an EC-dependent mechanism.

These results demonstrate that in the isolated aorta of the rat quercetin induces both EC-dependent and -independent relaxation. The EC component relies on NOS and guanylate cyclase activity and quercetin appears to sustain activation of these pathways for up to 3 hrs following a short exposure and subsequent washout. However a significant EC -independent depression of muscle contraction exists also.