



<b>Title</b>	<b>Wy14643 and fenofibrate reduce contractions to hydrogen peroxide in aortae of spontaneously hypertensive rats</b>
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502

### Brain Oxidative Stress in Neural Mechanism of Programmed Hypertension to Maternal High Fructose Diet

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**Introduction.** Early life exposure to adverse environments can lead to a variety of adult diseases by a process referred to as developmental programming. Maternal high fructose diet (HFD) promotes programmed hypertension in adult offspring, although the underlying mechanism is not fully understood. Brain oxidative stress is pivotal in neural mechanism of hypertension.

**Aims.** We tested the hypothesis that brain oxidative stress contributes to programmed hypertension in adult offspring to maternal HFD.

**Methods.** Female normotensive Sprague-Dawley rats fed with HFD during gestation and lactation periods were used. Metabolic parameters were measured by biochemical assay in the offspring at the age of 3 months old. Blood pressure was monitored under conscious condition by the tail-cuff method. Tissue superoxide level was measured by electron spin resonance (ESR) spectroscopy. Test agents were given orally to mother during lactation or to the offspring at the age of 2-month-old.

**Results.** Maternal HFD during gestation and lactation led to insulin resistance, increase in sympathetic activity and hypertension in the 3-month-old young offspring. This was associated with augmented neurogenic sympathetic vasomotor tone and high tissue levels of superoxide at the brain stem. Maternal melatonin treatment or simvastatin treatment to the 2-month-old offspring significantly ameliorated oxidative stress in the brain stem, abrogated sympathetic overexcitation and prevented the development of programmed hypertension in the 3-month-old rats to maternal HFD.

**Discussion.** Maternal HFD induces an early onset of high blood pressure, which is associated with oxidative stress in the brain stem. Both maternal treatment with melatonin or simvastatin to the young offspring ameliorate brain oxidative stress and promote antihypertension. These results suggest that brain stem oxidative stress may contribute to programmed hypertension in the offspring to maternal HFD.

503

### Wy14643 and Fenofibrate Reduce Contractions to Hydrogen Peroxide in Aortae of Spontaneously Hypertensive Rats

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**Introduction.** Oxidative stress, with the production of hydrogen peroxide, contributes to the development of vascular dysfunction in hypertension (1). Hydrogen peroxide evokes contractions in many blood vessels, including rat aortae and renal arteries, and rabbit pulmonary arteries (1). Recent studies showed that Wy14643 and fenofibrate, agonists of peroxisome proliferator-activated receptor alpha, improve endothelial function in vascular diseases (2).

**Aim.** The present study was designed to examine whether or not Wy14643 and fenofibrate inhibit hydrogen peroxide-induced contractions in aortae of spontaneously hypertensive rats (SHR).

**Method.** Male SHR and their normotensive counterparts, Wistar Kyoto rats (WKY), of 40-44 weeks old were used. Thoracic aortic rings, with and without endothelium, were isolated and suspended in organ chambers for isometric tension recording.

**Results.** Hydrogen peroxide evoked endothelium-independent contractions in both SHR and WKY; the contraction was significantly greater in rings of SHR than in those of WKY, suggesting that hydrogen peroxide plays a role in vascular dysfunction in hypertension. Wy14643 and fenofibrate significantly reduced hydrogen peroxide-induced contractions in SHR rings with, but not in those without, endothelium, indicating that the inhibitory effect was endothelium-dependent.

**Discussion.** The smooth muscle of aortic rings of SHR has a higher sensitivity to hydrogen peroxide-induced contractions than WKY. Wy14643 and fenofibrate act on the endothelium to reduce hydrogen peroxide-induced contractions in hypertensive rat aortae.

(1) Csató V et al (2014) PLoS One 9: e103858

(2) Qu C et al (2012) Eur J Pharmacol 696: 101-110