The PPARβ/δ agonist GW0742 prevents LPS-induced nitrite production in rat parenchyma but not in aorta or pulmonary arteries.

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Peroxisome proliferator activated receptors (PPARs) are therapeutic targets in the treatment of inflammatory lung disease. The PPARβ/δ agonist GW0742 has potent anti-inflammatory effects in the vasculature (1) which has been linked to a decrease in the production of iNOS in the heart (1) and activation of Akt-eNOS in arteries (2). Here in this study we measured changes in LPS induced NO production in rat arteries and lung parenchyma.

Male Wistar (300-350g) rats were killed by CO₂ followed by cervical dislocation, and the aorta, conductance and resistance pulmonary arteries and lung parenchyma were dissected under sterile conditions, and placed into 24 well plates. Following incubation with 1µg/ml LPS with/without 10⁻⁷ M GW0742 tissues were incubated for 24 hours, and Griess assay performed to measure nitrite production (a measure of NO release) (3).

Our results show that LPS induces a significant increase in NO production from arteries and parenchyma (Figure 1). Incubation with GW0742 alone has no effect on basal nitrite levels and does not have an effect on LPS-induced NO production in all types of arteries. In comparison, GW0742 significantly reduces LPS induced NO release in lung parenchyma comparable to inhibition by 10⁻⁴M L-NAME and 10⁻⁵M 1400W.

![Figure 1.](image-url)

2mm rings of aorta, conductance pulmonary artery (CPS), resistance pulmonary artery (RPA) and 1mm² lung parenchyma strips (lung) were incubated with 1ug/ml LPS ± 10⁻⁷ M GW0742 in DMEM for 24 hours. Supernatant was removed and Griess assay performed to measure nitrite. Data are expressed as mean ± SEM; * and f denote p<0.05 by one way ANOVA and Tukey’s post-hoc test, respectively.
In summary, incubation for 24 hours with $10^{-7}$M GW0742 significantly reduced LPS induced nitrite production in lung parenchyma but not in aorta or pulmonary arteries (conductance and resistance). These data suggest that the effects of PPARβ/δ agonists are tissue specific and might support their use as anti-inflammatory agents in lung disease.


(2) Quintela et al. (2014) Br J Pharmacol 171: 3089–3102.