

## The Soluble Guanylyl Cyclase Activator Induces a Nitric Oxide Production and Decreases Reactive Oxygen Species in Endothelial Cells

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**Introduction:** Previously, we have verified that the relaxation to NO donor sodium nitroprusside is potentiated in the presence of endothelium. Thus, the aim of this study was verify if the activation of soluble guanylyl cyclase (sGC) by ataciguat in endothelial cells induces a NO production, as well as identify the mechanism of this action.

**Methods:** Male wistar rats were used (400–500 g). To vascular reactivity study, thoracic aortas were used. The relaxation was performed to Ataciguat in aortas with (E+) and without (E-) endothelium. The potency (pD<sub>2</sub>) was measured. In Human Umbilical Vein *Endothelial Cells* (HUVEC) in culture, we have measured intracellular NO (by DAF-2DA fluorescence intensity FI) and reactivity oxygen species (ROS) by DHE fluorescence. HUVECs were treated for 30 minutes with Ataciguat (0.1, 1.0 and 10µM) or 100µM Tempol (SOD mimetic), without and with non-selective NOS inhibitor (L-NAME), or sGC inhibitor (ODQ), or calcium channel blocker (Verapamil). The Ethical Committee of the UFSCar (n<sup>o</sup> 012/2013) approved all protocols with rats.

**Results:** The presence of endothelium potentiated the relaxation induced by Ataciguat (pD<sub>2</sub> E+: 4.22±0.23, n=4 > pD<sub>2</sub> E-: 2.99±0.18, n=5, p<0.05). In the presence of L-NAME the effect of endothelium was abolished (pD<sub>2</sub> E+ L-NAME: 3.34±0.31, n=5). In HUVECs, the Ataciguat induced the NO production. In the presence of L-NAME or ODQ the NO production induced by Ataciguat 0.1µM was abolished, with no difference in the presence of Verapamil. ROS was increased in HUVECs stimulated with angiotensin II and Ataciguat treatment decreased the ROS production induced by Angiotensin II, with similar results to Tempol.

**Conclusion:** Taken together our results indicate that the activation of sGC in endothelial cells can induces a NO production by a mechanism independent of calcium influx and is able to decreases the ROS.

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