The Pro-erectile facilitator effect of LIB-01 in anesthetized Wistar rats is likely mediated mainly via an NO/cGMP-independent pathway

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Objectives To evaluate whether the pro-erectile facilitator effect of LIB-01 could be mediated via the NO/cGMP pathway by studying the endothelium dependent, -independent and nitrergic relaxations of cavernosal strips from Wistar rats in presence of SAE5, the active substance of LIB-01 which is a semi-synthetic molecule, originating from ethnopharmacological use for the treatment of sexual disability.

Methods Corpus cavernosum (CC) strips (2 strips per rat) were obtained from Wistar rats (n=10) and placed immediately in organ chambers (5 ml) for isometric tension studies. The CC were incubated with either SAE5 at 10^{-6}M or 10^{-5}M or DMSO (vehicle of SAE5) and pre-contracted by phenylephrine $3x10^{-5}$M. Concentration response curves or frequency response curves were then performed on pre-contracted strips in 3 steps: (i) cumulative addition of increasing acetylcholine (Ach) concentrations (10^{-9} M to 10^{-4} M, in semi-log increments, (ii) stimulation by increasing frequencies of electrical field stimulation (EFS) (1 ms - 10 s - 300 mA, 1 to 32 Hz), and (iii), cumulative addition of increasing sodium nitroprusside (SNP) concentrations (10^{-9} M to 10^{-5} M, in log increments).

Results We previously reported a prolonged pro-erectile effect of LIB-01 at 15mg/kg in anesthetized Wistar rats. SAE5 at 10^{-5} M but not at 10^{-6}M slightly increased the endothelium dependent relaxations induced by Ach compared to vehicle (E max=-19.8 ± 2.7% vs. -17.6 ± 1.5%, respectively $p<0.05$, student's t-test). However, SAE5 did not exert any effect neither on nitrergic relaxation-induced by EFS nor on endothelium independent relaxations induced by SNP.

Conclusions In contrast to current pro-erectile drugs, and despite the slight endothelium-dependent relaxation observed at relatively high concentrations of SAE5, the observed pro-erectile effect of LIB-01 in anesthetized rats is likely not mediated by the functional upregulation of the NO/cGMP pathway. These results postulate that the mechanism of LIB-01 differentiates from current pro-erectile drugs.