

NO-donating oximes relax corpora cavernosa through mechanisms other than those involved in arterial relaxation.

INTRODUCTION: Erectile dysfunction (ED) as well as many cardiovascular diseases are associated with impaired NO-bioavailability. Recently, oxime derivatives have emerged as vasodilators due to their NO-donating capacities. However, whether these oximes offer therapeutic perspectives as alternative NO-delivery strategy for the treatment of ED is unexplored.

AIMS: This study aims to analyze the influence of formaldoxime (FAL), formamidoxime (FAM) and cinnamaldoxime (CAOx) on corporal tension and to elucidate the underlying molecular mechanisms.

METHODS: Organ bath studies were carried out measuring isometric tension on isolated mice corpora cavernosa (CC), thoracic aorta and femoral artery. After contraction with norepinephrine (NOR), cumulative concentration-response curves of FAL, FAM and CAOx (100 nmol/L–1 mmol/L) were performed.

MAIN OUTCOME MEASURES: FAL-/FAM-induced relaxations were evaluated in the absence/presence of various inhibitors of different molecular pathways.

RESULTS: FAL, FAM and CAOx relax isolated CC as well as aorta and femoral artery from mice. ODQ (sGC-inhibitor), DPI (non-selective flavoprotein inhibitor) and 7-ER (inhibitor of CYP450 1A1 and NADPH-dependent reductases) substantially blocked the FAL-/FAM-induced relaxation in the arteries, but not in CC. Only a small inhibition of the FAM response was observed with ODQ.

CONCLUSIONS: This study shows for the first time that NO-donating oximes relax mice CC. Therefore oximes are a new group of molecules with potential for the treatment of ED. However, the underlying mechanism(s) of the FAL-/FAM-induced corporal relaxation clearly differ(s) from the one(s) involved in arterial vasorelaxation.