



**HYDROGEN SULFIDE (H<sub>2</sub>S) RELAXES HUMAN AND RABBIT CORPUS  
CAVERNOSUM IN VITRO**

Romina Nassini<sup>1</sup>, Patacchini R.<sup>2</sup>, Materazzi S.<sup>1</sup>, Mondaini N.<sup>1</sup>, Natali A.<sup>1</sup>, Geppetti P.<sup>1</sup> and Harrison S.<sup>1</sup>.

<sup>1</sup>Department of Critical Care Medicine & Surgery, University of Florence, Florence, Italy; and

<sup>2</sup>Department of Pharmacology, Chiesi Pharmaceuticals, Parma, Italy; Florence, Italy.

Nitric oxide has been since a long time recognized as an important mediator, that among many other biological functions largely contributes to sinusoidal smooth muscle cells relaxation and penile erection. As nitric oxide, hydrogen sulphide ( $H_2S$ ) is an endogenous gas produced in the body from cysteine by at least two enzymatic pathways, cystathionine  $\beta$ -synthase and cystathionine  $\gamma$ -lyase (1).  $H_2S$  exerts a wide variety of biological effects at both central and peripheral levels including the vascular system (1). In this study, we have investigated the function of  $H_2S$ , by using sodium hydrosulphide (NaHS) as a donor of  $H_2S$ , in preparations of human and rabbit isolated corpus cavernosum in comparison to known relaxants of the corporal muscle. In noradrenaline (NA) pre-contracted corpus cavernosum strips, NaHS induced a concentration-dependent ( $EC_{50} \sim 4$  mM) relaxation. For comparison sodium nitroprusside relaxed this preparation with a  $EC_{50}$  of approximately 30  $\mu$ M. The relaxant response to NaHS was not influenced by the presence of L-NAME (nitric oxide synthase inhibitor), ODQ (guanylate cyclase inhibitor) or the removal of endothelium. The relaxation to 30 mM NaHS ( $72 \pm 9\%$  of NA;  $P < 0.05$ ,  $n = 6$ ) in human corpus cavernosum was significantly reduced by pretreatment with H-89 (protein kinase inhibitor A:  $10 \pm 8\%$  of NA) or 2',5'-dideoxyadenosine 3'-triphosphate (adenylyl cyclase inhibitor:  $34 \pm 9\%$  of NA) ( $n=6$  each). Conversely, the relaxant response to NaHS was unaffected by pre-treatment with potassium (ATP- or  $Ca^{2+}$ -activated) channel blockers, prostaglandin ( $EP_{1/2}$  and  $EP_4$ ) and VIP receptor antagonists, or inhibition of cyclooxygenases. Comparable results to those obtained in the human preparation were also obtained in the rabbit corpus cavernosum. Present results indicate that the  $H_2S$ -induced relaxation is not mediated by stimulating endothelial nitric oxide synthase but, rather, by the activation of adenylyl cyclase activity, and may represent a novel mechanism which contributes to the relaxation of the corpus cavernosum. The intriguing hypothesis that this novel pathway may contribute to the physiology and pathophysiology of the erectile function must be, however, verified by further studies.

1. Li L, Bhatia M, Moore PK. Hydrogen sulphide - a novel mediator of inflammation? *Curr Opin Pharmacol.* 2006 6:125-9.