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Sildenafil increases the force of right atrial contractions *in vitro via* the NO-guanylyl cyclase pathway involving β-adrenoceptor linked mechanisms

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Abstract:
Sildenafil, a drug used in the treatment of erectile dysfunction, is a phosphodiesterase 5A inhibitor that increases cyclic guanosine monophosphate (cGMP) levels. In addition to its vascular actions, sildenafil is also known to alter cardiac functions. This study was undertaken to elucidate the effect of sildenafil on cardiac contractility and the underlying mechanisms. The experiments were conducted on spontaneously-beating right atria isolated from adult rats. The effect of sildenafil on the isometric contractions *in vitro* was examined in the absence or presence of antagonists. Sildenafil (0.001–10 μM) produced a concentration-dependent increase in the atrial force of contraction without altering the atrial rate, even up to 10 μM. A concentration as low as 0.001 μM produced a significant increase (16%) in force and the increase was about 50% at 10 μM. Pretreatment with methylene blue (a guanylyl cyclase inhibitor) or N-ω-nitro-L-arginine methyl ester (L-NAME, a nitric oxide synthase inhibitor) blocked the force changes induced by sildenafil. Sildenafil-induced increase in force of contraction was also blocked by propranolol (a β-adrenoceptor antagonist) and diltiazem (an L-type Ca^{2+} channel antagonist). The present results demonstrate that sildenafil increases the atrial force of contraction involving cGMP-β-adrenoceptor-Ca^{2+} channel-dependent mechanisms.

Key words:
phosphodiesterase 5A inhibitor, cGMP, L-NAME, methylene blue, propranolol, Ca^{2+} channels, diltiazem