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Lithium ions selectively enhances contractions of porcine isolated splenic artery to high concentrations of phenylephrine and L-erythromethoxamine

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Introduction: Dehpour and colleagues (1993) reported that 1-5mM lithium ions enhanced the sensitivity of the rat isolated anococcygeus muscle to the selective α_1-adrenoceptor agonist methoxamine. In the present study, we have used the porcine isolated splenic artery, a preparation that mainly possesses alpha$_1$-adrenoceptors (Barbieri *et al,* 1998), to examine the effect of lithium ions on contractile responses elicited by α_1-adrenoceptor agonists

Methods: The porcine isolated splenic artery (PSA) was dissected from spleens obtained from a local abattoir, stored overnight at 4^{o}C, and 5mm ring segments prepared for isometric tension recording in Krebs-Henseleit solution gassed with 95%O_2/5%CO_2 and maintained at 37^{o}C. After responses to 60mM KCl were established (used to standardise all responses), the effect of either a single application (30µM), or cumulative addition, to noradrenaline (NA), phenylephrine (PE), L-erythromethoxamine (LEM) or cirazoline (Ciraz) was determined in the presence and absence of 1-2mM lithium ions (Li).

Results: Table 1 shows that contractions to 30µM NA, 30µM PE and 30µM LEM were not sustained over 60 min, while response to 30µM cirazoline were stable. The presence of 1mM lithium (which had on effect on basal tone) prevented the decline in responses to PE and LEM, but not responses to either NA or cirazoline. When the agonists were added cumulatively, neither the potency nor maximum response of NA or cirazoline were affected by the presence of lithium ions. In contrast, the potency of LEM and PE were significantly reduced 2-fold, but the maximum contraction was increased by greater than 50%.

Table 1: Response of the PSA to either a maximally-effective concentration

or cumulative addition of various selective α_1-adrenoceptor agonists.

	Response to 30µM (% of 60mM KCl)		**Cumulative Response Curve**	
	3 min	**60 min**	**Max (% 60mM KCl)**	**pD_2**
NA	161.1 ± 14.1	16.7 ± 8.8#	228.1 ± 19.0	5.62±0.09
NA & 1mM Li	169.2 ± 24	17.2 ± 6.5#	243.3 ± 17.6	5.65±0.12
LEM	135.3 ± 14.0	23.5 ± 5.8#	99.4 ± 16.0	6.29±0.07
LEM & 1mM Li	150.3 ± 17.6	178.4 ± 26.8**	275.2 ± 38.0*	5.97±0.08*
PE	125.3 ± 26.8	35.3 ± 12.5#	116.9 ± 11.6	6.07±0.04

PE & 1mM LI	100.2 ± 32.4	143.5 ± 41.7****	190.7 ± 10.7****	5.63±0.08****
Cirazoline	103.6 ± 27.2	132.3 ± 27.2	155.0 ±12.7	7.17±0.07
Ciraz & 1mM Li	105.3 ± 36.3	144.6 ± 28.1	183.7 ± 3.5	7.10±0.08

Responses shown are the mean (± SEM) of 4-8 observations in paired segments.

- Statistically significant decline in response single application of an agonist (3 min vs 60 min, $p < 0.01$ paired Student's t-test). Statistically significant difference from paired segment - ***** $p<0.05$ and ** $p<0.005$.

Conclusion: Lithium ions did not increase the potency of α_1-adrenoceptors agonists in the PSA, but selectively enhanced the maximum response to PE and LEM, in a synergistic manner, and reduce the waning of contractions following prolonged exposure to maximally-effective concentrations.

References:

Barbieri A *et al.* (1998). *Naunyn Schmideberg's Arch Pharmacol* **357**, 654-661

Dephour AR *et al.* (1993). *Gen Pharmacol* **24**, 841-845