

## Changes in ionic fluxes in uterine smooth muscle induced by carbachol

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We studied the action of carbachol (CCh) on  $^{24}\text{Na}$ ,  $^{42}\text{K}$  and  $^{36}\text{Cl}$  fluxes. Uteri were obtained from virgin rats stimulated with a 0.5 mg/kg diethylstilboestrol injection 24 h before the experiment. Strips of longitudinal smooth muscle were mounted isometrically and equilibrated with a normal Ringer solution at 37°C. For efflux studies they were equilibrated for at least 90 min to  $^{24}\text{Na}$ , 120 min to  $^{42}\text{K}$  and 90 min to  $^{36}\text{Cl}$ . In polarized muscles CCh increased  $^{42}\text{K}$  and  $^{36}\text{Cl}$  effluxes, the increase being dose-dependent. Dose  $^{42}\text{K}$  efflux curves and dose-muscle contraction curves are superimposable.  $^{24}\text{Na}$  efflux was not affected. Influxes were determined by extrapolating to zero time the tissue radioactivity curve of the effluxes performed after 5 min exposure to  $^{24}\text{Na}$  or  $^{36}\text{Cl}$ , and 10 min to  $^{42}\text{K}$  (Casteels, 1969). Na influx was increased by CCh  $1.6 \times 10^{-4}$  M (control  $7.76 \pm 0.52$  mM kg $^{-1}$  5 min $^{-1}$ ,  $n = 24$  and CCh  $9.57 \pm 0.51$ ,  $n = 6$ ,  $P < 0.05$ ) as well as K $^{+}$  influx (control  $9.66 \pm 0.64$  mM kg $^{-1}$  10 min $^{-1}$ ,  $n = 24$ , CCh  $12.42 \pm 1.42$ ,  $n = 6$ ,  $P < 0.05$ ), but Cl $^{-}$  influx was not affected (control  $4.18 \pm 0.41$  mM kg $^{-1}$  5 min $^{-1}$ ,  $n = 6$ , CCh  $3.45 \pm 0.57$ ,  $n = 5$ , NS). Another series of strips was depolarized with a high K $^{+}$  (101 mM) solution. Under these conditions CCh still increased  $^{42}\text{K}$  and  $^{36}\text{Cl}$  effluxes but its effect was greatly reduced by depolarization. On the other hand  $^{24}\text{Na}$  efflux appeared increased by CCh under these conditions. Na influx was still increased (control  $1.59 \pm 0.026$  mM kg $^{-1}$  5 min $^{-1}$ ,  $n = 7$ , CCh  $1.78 \pm 0.068$ ,  $n = 8$ ,  $P < 0.05$ ), but K $^{+}$  influx measured by the extrapolation technique was not modified by CCh (control  $19.93 \pm 1.79$  mM kg $^{-1}$  10 min $^{-1}$ ,  $n = 12$ , CCh  $18.13 \pm 1.35$ ,  $n = 6$ , NS) and

Cl $^{-}$  influx (control  $10.82 \pm 1.00$  mM kg $^{-1}$  5 min $^{-1}$ ,  $n = 6$ , CCh  $11.70 \pm 1.33$ ,  $n = 6$ , NS) was not affected. CCh seems to depolarize the rat uterine smooth muscle through an increase in Na permeability, since this drug always increases Na $^{+}$  influx and Na $^{+}$  efflux of depolarized muscles. CCh seems to increase also the membrane permeability to K $^{+}$  since it enhances both the K $^{+}$  uptake and efflux of polarized tissues as well as K $^{+}$  efflux of depolarized tissues. Nonetheless, since K $^{+}$  efflux is greatly reduced, but not suppressed by depolarization it has to be admitted that a great part of the increased K $^{+}$  efflux of polarized tissues has to be secondary to the depolarization and spike discharges produced by the drug. The residual increase in Cl $^{-}$  efflux in high K $^{+}$  solutions suggests a possible primary increase in Cl $^{-}$  permeability.

These results confirm partially the studies performed in guinea-pig taenia coli where CCh increases Na $^{+}$ , K $^{+}$  and Cl $^{-}$  efflux of depolarized muscles (Durbin & Jenkinson, 1961), but on the other hand in rat uterine smooth muscle dose  $^{42}\text{K}$  efflux and dose-contraction curves are superimposable as opposed to guinea-pig ileum where Burgen & Spero (1968) found that dose  $^{86}\text{Rb}$  efflux curves are displaced to the right of dose-contraction curves.

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### References

- CASTEELS, R. (1969). Calculation of the membrane potential in smooth muscle cells of the guinea pig's taenia coli, by Goldman equation. *J. Physiol.*, **205**, 193-208.
- BURGEN, A.S.V. & SPERO, L. (1968). The action of acetylcholine and other drugs on the efflux of potassium and rubidium from smooth muscle of the guinea pig intestine. *Brit. J. Pharmac.*, **34**, 99-115.
- DURBIN, R.P. & JENKINSON, D.H. (1961). The effect of carbachol on the permeability of depolarized smooth muscle to inorganic ions. *J. Physiol.*, **157**, 74-99.