

## THE EFFECT OF NITRITE IONS ON COLONIC MUCOSA OF THE RAT

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The colonic mucosal cells of several species including man, rat, rabbit, and sheep resemble those of the rumen in that their major source of metabolic energy is the short chain fatty acids, especially butyric acid. These are derived from the bacterial fermentation (Cummings 1981). It has been shown in the colonic mucosa of patients with ulcerative colitis that the oxidation of  $^{14}\text{C}$ -labelled butyrate is deranged, and that nitrite ions stimulate butyrate oxidation in isolated colonocytes by about 50% (unpublished observations). These experiments were undertaken to extend the observations in colonocytes to the in situ rat colon.

Porton rats (200-250g) were anaesthetised. The renal pedicles were tied; the colon was transected at the caecum and rectum, washed, and filled with an iso-osmotic solution of 80mM NaCl, 40mM sodium butyrate, and 60mM mannitol. One ml of the instillate was removed for determinations of initial concentrations, and 2.5ml left in the colon for 40 minutes. At zero-time, 10  $\mu\text{mol}$  of  $\text{NaNO}_2$  or NaCl was injected into the inferior vena cava. Absorption of sodium and chloride ions, bicarbonate production, and concentration of nitrate and nitrite ions in the blood and colon were measured.  $^{51}\text{Cr}$ -EDTA was used as a non-absorbable marker to allow correction for volume changes. Sodium was measured by flame photometry, chloride on a chloride meter, and bicarbonate on a blood gas analyser. Nitrite was estimated colorimetrically (Radcliffe and Nicholas 1968), and nitrate by enzymic reduction to nitrite.

Blood nitrate and nitrite concentrations at 40 minutes were  $63.1 \pm 8.9\text{mM}$  and  $7.1 \pm 4.4\text{mM}$ , respectively. Recovery of nitrite as nitrite plus nitrate distributed in total body water pool was  $99\% \pm 11$ . The table shows net changes in the colon.

	Net colonic ion flux*				
	(nmol/min/cm <sup>2</sup> )				
	Na <sup>+</sup>	Cl <sup>-</sup>	HCO <sub>3</sub> <sup>-</sup>	NO <sub>3</sub> <sup>-</sup>	NO <sub>2</sub> <sup>-</sup>
NaCl	-103±17(7)	-63±14(6)	+100±4(7)	0(7)	0(7)
NaNO <sub>2</sub>	-121±9(8)	-134±13(8)	+122±6(7)	+0.11±0.01(7)	0.11±0.01(7)
P**	NS	0.01	0.02	0.01	0.01

\* Mean + s.e.m.(N); - indicates net absorption and + net secretion  
\*\*Significance by Mann-Whitney U-test.

Bicarbonate secretion and chloride absorption were stimulated in nitrite-treated rats suggesting that butyrate oxidation is stimulated by nitrite in vivo as well as in vitro. The effect of nitrite ions on energy metabolism of the colonic mucosa requires further investigation in both health and disease.

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