addition of either one or two methyl groups on the terminal nitrogen of the side chain slightly reduced the potency, the potency ratio for alpha-methyl-5-HT, N-methyl-5-HT and bufotenine being 3 (range 2–5), 6·5 (range 4–9) and 10 (range 2–26) respectively compared with 5-HT.

It is concluded that 5-HT acts directly on a specific 5-HT receptor on the Retzius cell membrane to increase chloride conductance.

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Some characteristics of the uptake process in the isolated blood perfused cat spleen resistant to desmethylimipramine and 17-β-oestradiol

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It has recently been shown that a process exists in the isolated blood perfused cat spleen which, after complete inhibition of $Uptake_1$ and $Uptake_2$ by desmethylimipramine (DMI) ($3{\cdot}3\times10^{-5}$M) and 17-β-oestradiol (17βO) ($1{\cdot}8\times10^{-4}$M), takes up (−)-noradrenaline (NA) (Blakeley, Powis & Summers, 1972).

Uptake by this process from 1 μg pulses of ^{3}H-NA has been measured during perfusion of spleens with different media. Two pulses were given while the spleen was perfused with blood. The uptake inhibitors DMI and 17βO were given between the pulses. Under these conditions uptake of the second pulse was $90{\cdot}62\%\pm1{\cdot}53$ (S.E. of mean) of the first. The red cells were removed by gentle centrifugation and the spleen perfused with plasma. Uptake of the next pulse was reduced to $54{\cdot}36\pm5{\cdot}52\%$ ($n=5$, $P<0{\cdot}001$). The red cells were then resuspended in Krebs–Henseleit solution containing DMI ($3{\cdot}3\times10^{-5}$M) and 17βO ($1{\cdot}8\times10^{-5}$M—an almost saturated solution). This medium restored uptake to $86{\cdot}84\pm6{\cdot}88\%$ ($n=5$, $P>0{\cdot}2$), not significantly different from that observed during blood perfusion. Subsequent perfusion with plain Krebs–Henseleit solution was followed by a drop in uptake to $49{\cdot}29\pm6{\cdot}65\%$ ($n=5$, $P<0{\cdot}001$).

After the injection of a pulse in the presence of DMI and 17βO about 75% of the NA appeared unchanged in the venous blood during the subsequent 3 min, together with a small quantity (<1%) of normetanephrine. Smaller amounts (about 6%) of NA and normetanephrine (<0·5%) came over in the next 12 minutes. Only trace amounts (<0·1%) of MAO metabolites were found in blood. Fifteen minutes after the pulse the spleen was homogenized and examined for retained NA and metabolites. About half the pulse retained was present as unchanged NA and the rest consisted of equal parts of MAO and MAO/COMT metabolites. No normetanephrine was found in the spleen.

Unlike $Uptake_1$ (Kirpekar & Puig, 1971), uptake of pulses was inhibited by nerve stimulation. ^{3}H-NA pulses were accompanied by a volume marker, ^{14}C-polyethylene glycol. Stimulation of the splenic nerves at 3 Hz produced only small vascular and capsular responses of the spleen and produced no effect on flow judged from the pattern of overflow of the volume marker, yet uptake was reduced to $66{\cdot}46\pm1{\cdot}89\%$ of controls ($n=3$, $P<0{\cdot}05$).

These results suggest that the uptake process operated most efficiently in the presence of blood and was inhibited by low frequency nerve stimulation. About half the NA taken up was retained unchanged and half was metabolized.

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Monoamines in the guinea-pig intestine

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Noradrenaline (NA) and 5-hydroxytryptamine (5-HT) are present in the mammalian small intestine (Erspamer, 1954 ; Shore, 1959). NA-containing axons, originating from prevertebral ganglia, occur in the myenteric and submucous plexuses and around blood vessels (Norberg, 1964).

TABLE 1. *Distribution of noradrenaline (NA) and 5-hydroxytryptamine (5-HT) in the guinea-pig intestine and the changes produced by extrinsic denervation (applying a probe cooled with liquid nitrogen on a nerve-vascular mesenteric bundle) and drug treatments. Values are in μg/g ± S.E. of mean of fresh tissue and are corrected for recovery. Number of experiments in parentheses.* ****P < 0·001, ***P < 0·005, **P < 0·01 *and* *P < 0·025

	Longitudinal muscle-myenteric plexus	Circular muscle-submucous plexus-submucosa-mucosa	
	NA μg/g	NA μg/g	5-HT μg/g
Duodenum	0·75 ± 0·18 (3)	0·52 ± 0·09 (3)	30·1 ± 6·9 (3)
Ileum	0·56 ± 0·06 (8)	0·54 ± 0·08 (8)	6·35 ± 0·86 (7)
Colon	1·33 ± 0·08 (8)	0·56 ± 0·07 (8)	2·35 ± 0·34 (8)
Taenia coli	0·82 ± 0·14 (6)	—	—
Rectum	0·91 ± 0·19 (5)	0·72 ± 0·08 (5)	1·51 ± 0·37 (4)
	Extrinsic denervation (5 days before)		
Ileum (control†)	0·56 ± 0·18 (4)	0·56 ± 0·07 (4)	8·90 ± 0·60 (4)
Ileum denervated)	0·03 ± 0·01 (4)****	0·06 ± 0·01 (4)****	10·0 ± 1·8 (4)
	6-Hydroxydopamine (35 mg/kg, I.V.‡)		
Ileum	0·22 ± 0·03 (4)***	0·11 ± 0·02 (4)**	6·46 ± 0·42 (4)
Colon	0·43 ± 0·17 (4)****	0·08 ± 0·03 (4)****	3·88 ± 1·10 (4)
	Reserpine (0·05 mg/kg, S.C., 3 days before)		
Ileum	0·08 ± 0·03 (3)***	0·09 ± 0·01 (3)*	3·44 ± 0·26 (3)
Colon	0·21 ± 0·07 (3)****	0·12 ± 0·02 (3)***	2·23 ± 0·35 (3)

† Taken from a non-denervated, neighbouring ileum loop.
‡ The drug was given in divided doses on the first and third day, and animals were killed on the sixth day.

Segments of small and large intestine from duodenum to rectum were studied. Amines were estimated fluorimetrically (Juorio, 1971). The intestinal wall was dissected, separating longitudinal muscle and myenteric plexus (10–20% of total weight of the wall for the ileum) on one side and circular muscle, submucous plexus, submucosa and mucosa on the other. NA and 5-HT were found as shown in Table 1. The longitudinal muscle-myenteric plexus of the colon had the highest NA concentration, which is probably accounted for by the occurrence of intramural adrenergic neurones in this part of the gut (Costa, Furness & Gabella, 1971). The ileum had the lowest concentration of NA, approximately in the same amount in both parts of the wall. Since a large portion of the circular muscle-submucosa-mucosa is made of epithelial cells, the NA concentration in the part of this preparation where axons are, is higher than in the