the urine, the fractional rate of iodoalbumin breakdown should increase. This would be so, since the radioactivity of the circulating albumin pools remains high, and thus the specific activity of the breakdown products would be, on the contrary, higher than in rats the iodoalbumin of which is rapidly depleted by proteinuria. Our results show the fraction broken down is greatly decreased.

The best explanation of our findings is provided by the assumption that in the nephrotic rats, kidneys are a major site of plasma albumin breakdown. Thus, the results strongly suggest that in amino-nucleoside nephrotic rats with extensive proteinuria, removal of kidneys markedly decreases plasma albumin breakdown, and that a major, and possibly predominant, part of plasma albumin breakdown in this type of acutely nephrotic animal occurs in the kidney.

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Inhibitory Properties of the Catecholamines

FOR some years considerable attention has been focused on the inhibitory action of γ-aminobutyric acid (GABA). One of the first systems used to demonstrate this property involved inhibition of the spontaneous discharge of the slowly adapting stretch receptor neurone of the crayfish[1,2]. This bio-assay procedure has been used to investigate the inhibitory characteristics of many other compounds[3-4], but none reported to date has proved more active than GABA. A number of aliphatic amino- and guanidino-acids have, however, shown activity approaching that of GABA, and pre-requisites for activity appear to be the presence in the molecule of an acidic and a suitably separated basic function. Such general characteristics are to be found among the catecholamines. The inhibitory characteristics of these substances were therefore investigated.

Pacifastacus leniusculus (Dana) was the crayfish used and the method was essentially that described by Florey[1] and by Elliott and Florey[5]. The commercially obtained compounds were made up in 'crayfish saline'[6] at *p*H 6·5–7 and the 'threshold blocking concentration' was determined; this was the concentration which would cause a transient (*c.* 20 sec.) block of the spontaneous discharge. The activity of any compound was expressed in arbitrary units, defined as the reciprocal of the concentration, in m.moles/litre, which produces a threshold block when applied to the stretch receptor neurone.

Results comparing the inhibitory activity of GABA and the catecholamines are given in Table 1. 3-Hydroxytyramine showed a much higher order of activity than GABA or the other catecholamines on every crayfish preparation used. Although there was great variability in the response of the different preparations to the substances tested, it was repeatedly shown that a given substance tested under two code numbers on a given preparation gave concordant results.

Table 1. INHIBITORY ACTIVITY OF GABA AND SOME CATECHOLAMINES ON THE CRAYFISH STRETCH RECEPTOR NEURONE

Substance	No. of preparations	Activity in units defined in text (mean)	Activity in units defined in text (range)
GABA	18	80	15–206
3-hydroxytyramine hydrogen chloride	15	6,250	566–41,580
L-noradrenaline bitartrate, water	7	110	5–468
L-adrenaline bitartrate	5	65	< 4·5–185

Our results on L-noradrenaline bitartrate and L-adrenaline bitartrate, indicating an activity comparable with that of GABA, are in conflict with those of Elliott and Florey[5], who reported that these compounds were inactive at a concentration of 1 mgm./ml. (less than 0·3 unit in each case). These workers used crayfish of the species *Orconectes virilis*, and did not specify the number of trials. The results we have obtained with many aliphatic amino- and guanidino-acids agree remarkably well with those of Edwards and Kuffler[3], who used both *O. virilis* and *Procambarus alleni*; it therefore seems unlikely that the difference in species of crayfish used can account for the difference in results between ourselves and Elliott and Florey.

The ability of various agents to block the inhibitory effects of 3-hydroxytyramine and of GABA was significantly different. Picrotoxin (10^{-3} *M*) blocked about 60 per cent of the activity of GABA, but was only slightly effective against 3-hydroxytyramine. Chlorpromazine ($1{\cdot}5 \times 10^{-4}$ *M*) and dibenzylene (8×10^{-4} *M*), on the other hand, were ineffective against GABA but blocked 3-hydroxytyramine almost completely. These results suggest that more than one receptor site on the stretch receptor neurone is involved.

The significance of these results remains to be assessed by work on other systems. The high activity of 3-hydroxytyramine lends support to the many investigators who have suggested that it may be an effector substance in its own right as well as a precursor of adrenaline and noradrenaline.

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