pharmacologically active[11] nucleotides. High levels of this enzyme were generally found in transplantable solid murine leukemias which were FU responsive.[10] The phosphoribosyltransferase level found in LPC-1 is higher than any value reported by Reyes and Hall.[10]

The LPC-1 cell line is not unique in its responsiveness to FU and resistance to FUdR; these characteristics are also shared by the lymphoma 4 neoplasm.[8,10] But the latter cell line demonstrated relatively high levels of both uridine phosphorylase[8] and the phosphoribosy transferase.[10] The LPC-1 neoplasm has provided us with a model for demonstrating the association between remarkable FU responsiveness and high levels of phosphoribosyltransferase in a cell line with very low levels of uridine phosphorylase. The finding that FUdR is not an effective drug in LPC-1 provides additional evidence that uridine phosphorylase levels are low *in vivo*, and that activity of the enzyme was not lost during preparation of cell extracts.

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Selective inhibition of monoamine oxidase in rat brain mitochondria

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MANY INHIBITORS of monoamine oxidase (MAO) have been found, and some have been reported to inhibit selectively the oxidation of particular substrates.[1–9] Previous studies have been done with only one substrate present at a time. We report here the effects of inhibitors on the simultaneous oxidation of two substrates, serotonin and tyramine, by MAO present in rat brain mitochondria.

Mitochondria were prepared from whole brain of male Wistar rats as described before.[5] The principle of the assay method was as used previously,[5] based upon the method of Wurtman and Axelrod.[10] Tyramine-H^3 (generally labeled, specific activity, 50 $\mu c/\mu$mole) and serotonin-2-^{14}C (specific activity, 2·8$\mu c/\mu$mole) were from New England Nuclear Corp. Each substrate was present at a 50 μM concentration in a total volume of 0·3 ml. Sodium phosphate buffer (final concentration was 0·25 M with respect to P) of pH 7·4 was used. After 20 min incubation at 37°, the reaction was stopped

by addition of 0·2 ml of 2 N HCl, and the deaminated metabolites were extracted into 6 ml ethyl acetate. Tritium and radiocarbon in the solvent extract were measured by liquid scintillation spectrometry. The reaction was linear with time, and the amount of enzyme was in the straight-line region of a graph of velocity versus enzyme concentration.

In the absence of inhibitor, 8·93 μmoles of serotonin and 2·86 μmoles of tyramine were oxidized per min of incubation. These velocities were 10 and 6 per cent lower for serotonin and for tyramine, respectively, than the rates when each substrate was present alone. The effects of four inhibitors are shown in Fig. 1. Lilly 51641, *N*-[2-(*o*-chlorophenoxy)-ethyl]-cyclopropylamine, preferentially blocked the oxidation of serotonin. For instance, 51641 at 10^{-7}M had no effect on tyramine oxidation but

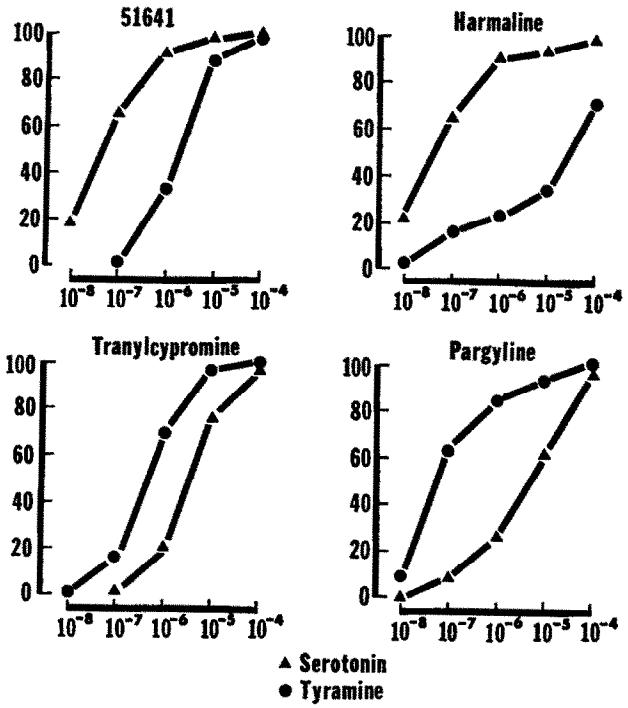

FIG. 1. Per cent inhibition (ordinates) of the simultaneous oxidation of two substrates by rat brain mitochondrial MAO. Molar concentrations of the inhibitors are shown on the abscissae. Each point is the result of triplicate determinations.

inhibited serotonin oxidation by 66 per cent. Harmaline also selectively inhibited serotonin oxidation. On the other hand, tranylcypromine and pargyline preferentially blocked the oxidation of tyramine. The results in Fig. 1 are not unexpected in the light of previous data[5] on inhibitor concentrations required to block the oxidation of each of these two substrates alone. The present data show that selective blockade of MAO action does occur when two substrates are present together. Earlier results[5] with pargyline had not shown such a high degree of selectively as that revealed in Fig. 1.

The most likely explanation for the data (although other explanations are possible) seems to be that separate enzymes are predominantly involved in the oxidation of serotonin and tyramine. Lilly 51641 and harmaline seem to have greater affinity for the enzyme that oxidizes serotonin, whereas tranylcypromine and pargyline inhibit the tyramine-oxidizing enzyme more readily.

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