dividual drugs. The mean percentage of free tryptophan in serum (28.1% ± 1.7) was not changed with diazepam (27.6% ± 1.1).

It is evident that the effect of diazepam and its metabolites on the interaction between L-tryptophan and albumen is competitive, and involves a single binding site. However, serum concentrations of diazepam and its metabolites in man are too low to produce an increase in free tryptophan by displacement from albumen.

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The binding properties of [^{3}H]-mepyramine in the brain of the guinea-pig and the rat

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[^{3}H]-Mepyramine binds selectively to histamine H_1 receptors in homogenates of longitudinal muscle from guinea-pig ileum (Hill, Young & Marrian, 1977) and has been used to demonstrate the presence of H_1 receptors in the brain of the guinea-pig (Hill & Young, 1978) and the rat (Chang, Tran & Snyder, 1978). However, the regional distribution of H_1 receptors in guinea-pig brain (Hill, Emson & Young, 1978) differs from that in the rat (Chang *et al.*, 1978), the most striking contrast being in the large amount of receptor material in guinea-pig cerebellum. Our own unpublished measurements on the rat have confirmed this difference, but also appeared to suggest that in certain respects the properties of [^{3}H]-mepyramine binding in rat brain did not correspond well with those in guinea-pig brain.

The binding of [^{3}H]-mepyramine to H_1 receptors in a membrane fraction from guinea-pig brain, measured in Na-K phosphate buffer (50 mM pH 7.5), and defined as the binding sensitive to 2×10^{-6}M promethazine, appears to saturate with a K_d near 1.7 nM, in reasonable accord with the value expected from measurements on the inhibition by mepyramine of the contractile response to histamine of guinea-pig ileum. In contrast, the binding to an analogous fraction from rat brain did not obviously saturate below 32 nM and in each of 4 experiments analysis of the curve, using the method of Wilkinson (1961), indicated an apparent K_d for [^{3}H]-mepyramine in the region of 10 nM. The discrepancy was still apparent when the affinity of mepyramine for H_1 receptors in rat brain was determined from the inhibition of the binding of [^{3}H]-mepyramine (1 nM) by non-radioactive mepyramine, where the IC_{50} was 1.2×10^{-8}M (cf IC_{50} 1.8×10^{-9}M in guinea-pig brain under the same conditions. There was a marked difference in the potency of the isomers of chlorpheniramine, in agreement with Chang *et al.* (1978), but the potency of the (+)-isomer was again much greater in the guinea-pig (IC_{50} 1.8×10^{-9}M) than the rat (1.0×10^{-8}M). However, not all ligands showed differences of this magnitude. Promethazine appeared to be at least as potent, if not more so, in the rat as in the guinea-pig and the difference in the IC_{50} values for chlorpromazine was also small. Histamine was practically equipotent in the two species. It must be noted, however, that the accuracy of these measurements in the rat is limited by the relatively large proportion of non-specific binding (*c.* 70% with 1 nM [^{3}H]-mepyramine).

The differences between the species might reflect either an actual difference between the H_1 receptors or the presence of a relatively large proportion of secondary binding sites in the rat. Some support is given to the latter possibility by the presence of low-affinity promethazine-sensitive binding of [^{3}H]-mepyramine in rat intestinal smooth muscle, a tissue notably insensitive to histamine.

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