end-plate region (Creese & Maclagan, 1967) and remains for long periods (Taylor, Dixon, Creese & Case, 1967).

Rat diaphragms were soaked in solutions which contained varying concentrations of decamethonium-(^{3}H-methyl) chloride, and after 1 h the muscles were washed for 10 min in physiological saline, frozen, sliced into strips 1 mm wide and counted by scintillation methods (Taylor, Creese, Nedergaard & Case, 1965). At concentrations of 10–100 μM there was a peak uptake in the strip which contained the band of end-plates, and the radioactivity in the tissue increased linearly with time. The uptake at the end of the fibres was much smaller.

At lower concentrations of decamethonium the peak uptake was progressively reduced, and at a concentration of 0·01 μM the uptake at the end-plate region was no different from that at the end of the fibres. Saturation could be demonstrated by plotting the uptake as a clearance (ml/g) against concentration of decamethonium, and half-saturation occurred at 2·5 μM. Similar curves have been obtained with denervated guinea-pig muscle, and also with rat diaphragms which were depolarized in solution containing potassium methyl sulphate (for example, England, 1969).

At high concentrations the peak uptake (when expressed as ml/g) was again reduced and the kinetics resembled those of a carrier-like system. If the results in rat muscle are interpreted in terms of receptors then at least two sites are necessary, a high-affinity site with half-saturation at 2·5 μM plus a low-affinity transport system with half-saturation at approximately 2 mM.

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Apparent correlations between pA_2 and pD_2' values in a group of drugs with antihistaminic and anticholinergic properties

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A group of seventy-five substances was tested on the guinea-pig isolated ileum for antihistaminic activity and on the rat isolated intestine for anticholinergic activity. The majority of the substances were newly synthetised antihistaminic substances, belonging to various chemical classes; a few were classical antihistaminic or anticholinergic drugs. For sixty-six substances both pA_2 and pD_2' values could be calculated with respect to the histaminergic system and for sixty-nine substances with respect to the cholinergic system. The pA_2 and pD_2' values are measures of the affinity of the drug to the specific and to the non-competitive receptors, respectively (van den Brink; 1969).

The pA_2 values were plotted against the corresponding pD_2' values, and the resulting scatter-graphs demonstrated that the two types of measures are correlated. It can be argued, however, that the correlation found in the data on the histaminergic system is probably spurious; it can be explained by certain unavoidable limitations in the experimental method. However, these limitations can explain only partially the correlation found in the data on the cholinergic system, and they play no role whatever in the correlation of the data obtained with a series of sixteen antihistamines of closely related structure. In these cases the correlation can be explained by the supposition that the structural differences are " non-specific "—that is, that they do not play a role in specific " receptor-complementarity ". Instead they may influence the relation between dose and biophase concentration or change the affinity by changes in less specific binding forces, such as hydrophobic forces acting on additional receptor areas. Thus " non-specific " modifications in the molecular structures of drugs may influence different classes of affinity values in analogous ways without implying that the different receptors themselves are structurally related.

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Mechanism of the antagonism of the hypotensive action of guanethidine by propranolol (T)

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The effect of the chronic administration of clonidine (St 155) on vascular smooth muscle (T)

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Extraction and assay of urogastrone (T)

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Parkinsonism treated with L-dopa: interactions with other diseases and other drugs (T)

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Mode of anti-depressant action of imipramine in man (T)

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