fibres which do not require a propagated action potential for contraction.

These responses resemble those of mammalian extra-ocular muscles (Bach-y-Rita & Ito, 1966; Browne, 1976) and show some similarity to frog rectus and to avian muscle (Ginsborg, 1960) – all of which contain slow tonic skeletal muscle.

Preliminary histochemical studies of cholinesterase in cremaster muscle suggest that some fibres have innervation different from the typical 'en plaque' end-plates found in focally-innervated muscle.

Rigorous proof of the existence of a type of slow tonic muscle in the cremaster requires electro-physiological and electronmicroscopic studies. But the responses described above suggest fairly strongly that fibres of this type are present.

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Fitting a general sigmoid model to pharmacological response curves

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In order to evaluate potency and drug activity it is necessary to quantify the relationship between the response and the dose. However, in some sets of data problems arise in a log-dose transformation and some of the data may have to be omitted.

Many attempts have been made to derive models from pharmacological principals (Ariens, 1954; Clark, 1937; Paton, 1961; Stephenson, 1956) but the most successful involve a function that can only be determined empirically, i.e. the efficacy.

Parker & Waud (1971) used the logistic curve

$$Y = \frac{1}{1 + A \exp(-bX)},$$

showing that it could be rearranged to give:

$$R(X) = M\frac{X^B}{X^B + C^B} \qquad (1)$$

Equation (1) has some of the required characteristics

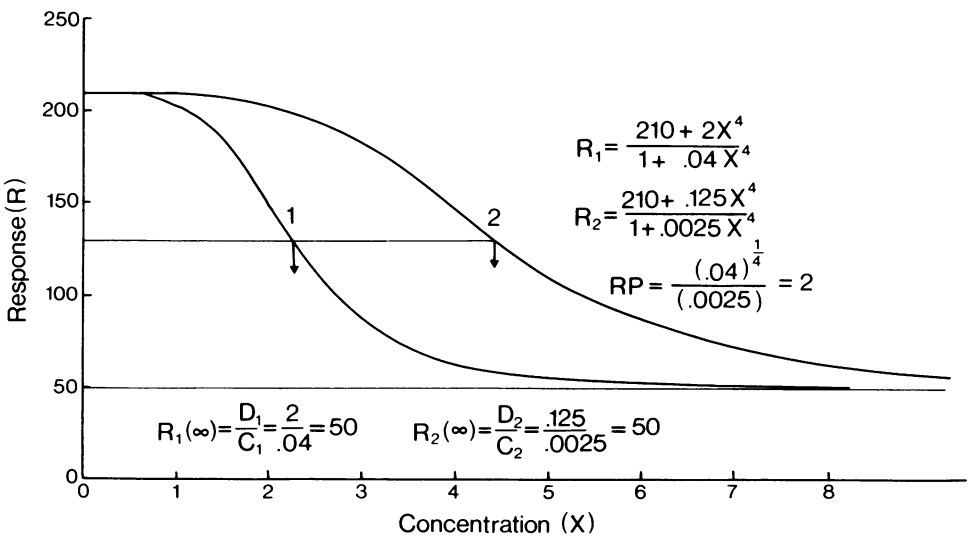

Figure 1 Parallel sigmoid curves.

and potentially a number of pharmacological parameters could be represented.

We have modified the logistic curve to a more general form in order to define the parameters in terms of a number of useful practical pharmacological entities:

$$R(X) = \frac{A + DX^B}{1 + CX^B} \qquad (2)$$

This curve has the right characteristics, namely sigmoid shape. Two theoretical dose-response curves are shown in Figure 1 for drugs working by a similar mechanism but of different potency.

For the two response curves to be parallel they must both have the same asymptotic value and the same value of B. The asymptotic value of R(X) indicates the maximum achievable response and is where

$$R(X) = R(\infty) = \frac{D}{C}.$$

The control response is where $R(X) = R(O) = A$.

$$\left(\frac{1}{C}\right)^{1/B}$$

is the ED_{50} and if B is the same value for the two curves the relative potency RB is

$$\left(\frac{C_1}{C_2}\right)^{1/B}.$$

Examples are shown for data having a Poisson distribution (from the acetylcholine writhing test), to data having a negative-exponential distribution (from the Roto-rod test), and for estimating potency of inhibitors of histamine release where the data was intractable by ordinary methods.

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A postsynaptic action of prostaglandin E_1 on sympathetic responses in guinea-pig ileum

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Prostaglandins inhibit the response of many tissues to sympathetic stimulation. It is now well established that one possible mechanism involved is a reduction of transmitter release (Hedqvist, 1969), but a postsynaptic action may sometimes also play a part (Clegg, 1966).

We have investigated the actions of prostaglandin E_1 on the responses of isolated guinea-pig ileum to stimulation of the perivascular nerves. The ileum was stimulated transmurally with just maximal stimuli at a frequency of 0.1 Hz. The perivascular nerve was stimulated with 8 s trains at a frequency of 1–32 Hz, immediately before each coaxial pulse (Watt, 1971). The frequency of perivascular stimulation required to produce a 50% inhibition of the coaxial twitch was increased by a factor of 1.5 ± 0.15 (mean ± s.e. mean $n = 10$ $P < 0.005$) in the presence of prostaglandin E_1 (57 nM). In similar experiments in which the coaxial twitch was inhibited by exogenous noradrenaline, prostaglandin E_1 (28 nM) increased the dose of noradrenaline necessary to produce a 50% inhibition by a factor of 2.3 ± 0.4; $n = 8$ ($P < 0.003$).

The effects of perivascular stimulation and of noradrenaline were also compared before and after treatment with indomethacin (7 μM). The frequency of perivascular stimulation then required to inhibit the coaxial twitch by 50% was 0.5 ± 0.2 of the frequency required to produce an equal inhibition of the untreated preparation. This effect of indomethacin was significant ($P < 0.015$).

Indomethacin also significantly reduced the concentration of noradrenaline necessary to inhibit the coaxial twitch by 50%; the concentration required being 0.3 ± 0.1 as great as that required in the untreated preparation ($P < 0.0002$). The results obtained with noradrenaline indicate that in the isolated guinea-pig ileum prostaglandin E_1, as well as any presynaptic action, has a postsynaptic action. The relatively greater effects both of prostaglandin E_1 and of indomethacin on the responses to noradrenaline than on the responses to perivascular stimulation, suggest an action of prostaglandin on adrenoreceptors