(VR40). Variable ratio schedules typically produce very high baseline rates of responding (Ferster & Skinner, 1957). In the present study, since the pellet is delivered into a tray below the panel, the rat keeps its head and eyes, but not necessarily its attention, directed towards the panel, with a minimum of irrelevant movements apart from those involved in eating the occasional pellet. Therefore photic stimuli for evoking visual responses are in this demonstration produced by a flash unit (1 J/flash) delivered to the rat through the translucent panel. Ratio schedules have another property: once established they are relatively insensitive to treatments which do not produce motor impairment (Dews, 1956). This is an advantage because the rate of responding is not intended to reflect treatment-induced changes in behaviour, but to yield a constant behavioural output against which electrophysiological effects of treatments can be assessed. Without this control, drug effects might be indistinguishable from the changes observed in the untreated animal when similar gross behaviour changes occur naturally (Herz, Fraling, Nieder & Farber, 1967).

We have implanted the rats with various kinds of electrodes in cortical and subcortical areas. The electrode leads are soldered to an 8-pin miniature socket (TO5 transistor base) which is secured to the skull with stainless steel screws and dental acrylic cement. A multi-channel mercury swivel commutator prevents twisting of the cable which leads from the animal to the amplifiers and recording apparatus. Potentials time-locked to the stimulus are electronically stored and summated using an averaging computer (Biomac 1000). This procedure in effect increases the signal to noise ratio of the evoked potentials, which are comparatively small relative to the background electrical activity of the conscious brain.

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Evidence for interaction between chlorpromazine and aldolase

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Chlorpromazine is known to inhibit rabbit muscle aldolase (Chowdhury, Rogers, Skinner, Spector & Watts, 1969) and these authors suggest that inhibition may be due to a conformational change of the enzyme. Chlorpromazine acts as a fluorescent probe: in aqueous solution a small fluorescence spectrum is produced which is greatly enhanced in the presence of aldolase. Also, shifts in the fluorescence spectrum of aldolase–chlorpromazine mixtures are consistent with a conformational change

of the protein. Polyacrylamide gel filtration has further demonstrated the presence of a tightly coupled aldolase–chlorpromazine complex.

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Human pharmacology of taloximine

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Taloximine is a phthalazine derivative [1-hydroxyimino-4-(2-dimethylamino-ethoxy-1-2-dihydrophthalazine monochloride monohydrate)] with respiratory stimulant and bronchodilator properties in animals (Daly, Lightowler & Pickering, 1969). Its respiratory stimulant action is mediated through chemoreceptors in the carotid and aortic bodies (Pearson & Griffin, 1969). This demonstration presents results of studies of taloximine in man.

Human tissue studies

The activity of taloximine was compared with that of aminophylline on human smooth muscle prepared by the method described by Coupar & Turner (1969). The compounds were approximately equipotent in causing direct relaxation of stomach, ileum, colon, rectum and bronchus. Taloximine did not affect the rate of spontaneous contractions of stomach, colon (longitudinal muscle), rectum or uterus, but caused a marked increase in rate of contraction of circular muscle of the colon. It was approximately equipotent with aminophylline in reducing the height of spontaneous contractions of ileum, colon (longitudinal muscle) and rectum, but was less effective than aminophylline on the stomach and failed to reduce amplitude in circular muscle of colon in concentrations of up to 1 mg/ml.

Metabolic fate

Oral route. Fall in plasma concentration of taloximine with time was biphasic after oral administration of 2·0 g. The half times of the two exponentials were 4·8 and 17·1 h respectively.

The following were found in the urine in 24 h after 2·0 g of taloximine; unchanged taloximine, a phthalazinone, demethylated taloximine and a ring hydroxylated form. Taloximine and its metabolites were present in free, glucuronated and sulphated forms, each of which was measured quantitatively. The total phthalazines recovered from the urine accounted for 23·2% of the total dose.

Intravenous route. After intravenous administration of 200 mg taloximine to one subject there was a biphasic fall in plasma taloximine concentration, the half times being 0·6 h and 2·7 h respectively.

Bile was collected from an indwelling T-tube inserted during operation into the common bile-duct of a patient undergoing cholecystectomy in whom common