siderations may be plotted to reveal linear relationships similar to desensitization curves plotted from experimental data (Hicks, Okpako & Leach, 1968).

An equation giving better agreement with experimental data was

$$a_n = \frac{c}{K}\left(\frac{n}{(b-2nc)^2} - \frac{(n-1)}{[b-2c(n-1)]^2} + K\right)$$

REFERENCES

HERXHEIMER, H. (1952). Repeatable *microshocks* of constant strength in guinea pig anaphylaxis. *J. Physiol., Lond.*, **117**, 251–255.

HICKS, R., OKPAKO, D. T. & LEACH, G. D. H. (1968). Factors determining the development of anaphylactic hypersensitivity in the guinea pig, and their influence on mechanisms involved in desensitization. *Int. Archs Allergy.*, **33**, 29–44.

KING, C. A. & FRANCIS, G. E. (1966). A study on the absorption of antibody by chopped guinea-pig lung and subsequent fixation of antigen. *Immunochemistry*, **3**, 347–358.

Cellulose sulphate, a tool in the evaluation of the plasma kininogen level in the rat

J. T. MCCORMICK* and JUDITH SENIOR

Department of Pharmacology, Brighton Polytechnic, and School of Studies in Pharmacology, University of Bradford

The plasma kininogen concentration rises with advancing gestation in the pregnant rat; by day 22 of pregnancy the level is approximately twice that found in a normal non-pregnant female (McCormick & Senior, unpublished work). Wiegerhausen, Klausch, Hennighausen & Sosat (1968) found that during parturition in the rat there appeared to be some cleavage of the plasma kininogen. The present study failed to demonstrate a significant fall in plasma kininogen level during parturition; this may be due to a rapid repletion of the kininogen stores. In order to investigate this possibility and in an attempt to elucidate the sudden rise in plasma kininogen concentration during the last few days of gestation, the kininogen depleting agent cellulose sulphate was administered to female rats and the time course of plasma kininogen regeneration was monitored.

Cellulose sulphate was prepared using the method of Astrup, Galsmer & Volkert (1944); a dose of 1 mg/kg dissolved in physiological saline was injected into the femoral vein of ether anaesthetized female rats of the C.S.E. strain. Using the micromethod of Diniz & Carvalho (1963) the plasma kininogen concentration was determined in blood samples taken at various time intervals following the injection of the sulphopolysaccharide.

Three groups of animals were used, non-pregnant rats in oestrus and dioestrus and 22 day pregnant rats. Twenty min after the injection of cellulose sulphate there was a significant fall in the plasma kininogen content in all three groups. This low level was maintained for 40 min and was followed by a gradual repletion of the plasma kininogen stores. Full repletion was obtained within 10 h following drug administration.

About 3 h after the injection of cellulose sulphate there appeared to be an interruption in the repletion of the plasma kininogen stores followed by a partial depletion. In dioestrus and 22 day pregnant rats this secondary depletion was

statistically significant ($P<0.05$). The physiological significance of this observation is obscure.

From the results it can be calculated that the repletion of the plasma kininogen stores proceeded about three times faster in the pregnant group than in either of the non-pregnant groups. This increase in the rate of regeneration of plasma kininogen in 22 day pregnant rats may help to account for the rapid increase in the plasma kininogen towards the end of gestation.

REFERENCES

ASTRUP, T., GALSMAR, B. & VOLKERT, M. (1944). Polysaccharide sulfuric acids as anticoagulants. *Acta Physiol. scand.*, **7**, 215.

DINIZ, C. R. & CARVALHO, I. F. (1963). A micromethod for the determination of bradykininogen under several conditions. *Ann. N.Y. Acad. Sci.*, **104**, 77.

WIEGERHAUSEN, B., KLAUSCH, G., HENNIGHAUSEN, G. & SOSAT, R. (1968). Der kininogenspiegel von ratten und kaninchen wahrend der gestation. *Experientia*, **24**, 1128.

The effect of indomethacin on the tracheal smooth muscle of the guinea-pig

J. B. FARMER, D. G. FARRAR* and J. WILSON

Department of Pharmacology and Biochemistry, Research and Development Laboratories, Fisons Ltd., Pharmaceutical Division, Loughborough, Leics.

Farmer & Coleman (1970) described a preparation of the isolated intact guinea-pig trachea in which alterations in muscle tone were recorded as changes in intraluminal pressure. A high resting intraluminal pressure can be obtained in this preparation (Coleman & Farmer, 1971) and this may be due either to the intrinsic tone of the smooth muscle or to mediators released as a result of the experimental technique.

In the present study, indomethacin (0·05 to 0·8 μg/ml) was found to produce a dose-related relaxation of the tracheal preparation. As indomethacin has been shown to inhibit the synthesis of prostaglandins (Vane, 1971) the possibility was considered that prostaglandins may be involved in the maintenance of the tone of the preparation. However, Northover (1967) showed that indomethacin could inhibit smooth muscle in a non-specific manner, and experiments were carried out to determine whether the observed relaxation of the trachea could be explained in this way. The effects of indomethacin on responses of the trachea to methacholine were therefore compared with its effects on intrinsic tone. The responses to methacholine were inhibited by indomethacin, but only in concentrations approximately 270 times higher than those which inhibited tone (Table 1). In

TABLE 1. *ED_{50} values of the inhibitory effects of isoprenaline, papaverine and indomethacin on (A) the intrinsic tone and (B) methacholine-induced contractions of the guinea-pig tracheal tube preparation*

	(A) Intrinsic tone			(B) Methacholine-induced contractions			Ratio of ED_{50}'s
Drug	No. of tissues	ED_{50} (μg/ml)	95% Confidence limits	No. of tissues	ED_{50} (μg/ml)	95% Confidence limits	B / A
Isoprenaline	7	0·0016	0·0013 – 0·0018	6	0·031	0·022 – 0·042	19·4
Papaverine	8	0·29	0·26 – 0·34	16	3·7	3·1 – 4·4	12·8
Indomethacin	17	0·45	0·33 – 0·63	22	121	106 – 137	269