it has been suggested that they may be of immunological importance[6]. They are probably normally broken down by some lytic mechanism in the circulating blood, although large numbers may reach the lungs. The phenomenon of trophoblast deportation to the lungs during normal pregnancy has also been reported for the chinchilla[7] (also personal observation).

These results show that extra-uterine transplantation, particularly to the testis, may be a profitable technique to investigate further the remarkable migratory behaviour of hamster trophoblast cells.

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## Effect of Degraded Carrageenin on Gastric Secretion Stimulated by Histamine and 'Histalog'

THERE is some evidence that in the guinea-pig, the oral administration of degraded carrageenin, a sulphated polysaccharide, causes a slight temporary reduction of gastric acidity in response to histamine[1]. We have had occasion to study the effect on gastric secretion when degraded carrageenin is administered subcutaneously. The results indicate that carrageenin parenterally has a pronounced inhibitory action on the acid secretory response to histamine but, somewhat paradoxically, not on the secretory response to 'Histalog' (betazole hydrochloride), a structural isomer of histamine.

Gastric juices were obtained from fasted unanaesthetized adult male guinea-pigs by intubation 1 h after the intramuscular injection of an aqueous solution of histamine acid phosphate (1 mg/kg) or 'Histalog' (100 mg/kg). Degraded carrageenin (5 per cent aqueous solution) had been injected subcutaneously 9 h previously in a dose of 400 mg/kg body weight. The results are shown in Table 1.

Table 1. EFFECT ON STIMULATED GASTRIC SECRETION OF DEGRADED CARRAGEENIN ADMINISTERED SUBCUTANEOUSLY

(Means ±1 *S.D.*)

| Treatment and No. of animals | Gastric secretion: Volume (ml.) | | Gastric secretion: Total acid conc. (m.equiv/l.) | |
|---|---|---|---|---|
| Histamine only (10) | 8·9 ± 2·2 | $P < 0.01$ | 128·6 ± 8·2 | $P < 0.001$ |
| Carrageenin + histamine (10) | 3·7 ± 3·3 | | 106·1 ± 13·1 | |
| 'Histalog' only (8) | 16·2 ± 2·5 | $P > 0.10$ | 132·5 ± 10·3 | $P > 0.60$ |
| Carrageenin + 'Histalog' (10) | 14·0 ± 3·5 | | 134·6 ± 8·0 | |

Carrageenin markedly reduces the volume and total acid concentration of the gastric juice secreted in response to histamine. How it produces this effect is not known. It may be that it renders histamine inactive by forming a complex with histamine as in the case of heparin[2], which is also a sulphated polysaccharide. By the use of 'Histalog' it has, however, been possible to establish that carrageenin does not directly interfere with the acid secretory mechanism. These results are of interest in relation to the role of histamine in gastric secretion.

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# HAEMATOLOGY

## Enhancement of the Activity of Optimum Concentrations of Urokinase by the Venom of *Echis carinata*

THE venom of *Echis carinata* (saw-scaled or carpet viper) is known to have powerful haemotoxic actions, promoting coagulation in whole blood or plasma and digesting fibrin[1]. We have recently investigated the action of this venom on the fibrinolytic enzyme system using the caseinolytic assay system of Remmert and Cohen[2] as modified by Alkjaersig[3]. Urokinase (2,000 U/ml.) was substituted for streptokinase, and 0·1 molar phosphate buffer for acid and alkali. Results are expressed in casein units/ml. Where *Echis* venom was used, 0·5 ml. of a 1 mg/ml. solution of a desiccator-dried preparation reconstituted in 0·9 per cent saline was incorporated in the system in place of 0·5 ml. of the phosphate buffer used in the assay. Similarly, buffer was substituted for urokinase and plasminogen in the experiments in which these reagents were omitted.

Table 1. CASEINOLYTIC ASSAYS

| Urokinase | Venom | Plasminogen | Casein units/ml. |
|---|---|---|---|
| + | − | + | 1·7 ± 0·3 |
| + | + | + | 5·1 ± 0·4 |
| − | + | + | 2·9 ± 0·2 |
| − | − | + | 0·5 ± 0·1 |
| − | + | − | 2·0 ± 0·1 |

The results are shown in Table 1, which presents the mean values and standard deviations for seven assays performed in duplicate. It will be seen that the venom of *Echis carinata* has direct caseinolytic activity (2·0 ± 0·1 units of activity); it also has the ability to produce partial activation of plasminogen, the increase in proteolytic activity of a venom-plasminogen mixture compared with venom alone being 0·4 ± 0·2 units ($t = 6.28$, $P < 0.001$). This compares with an activation of 1·7 ± 0·3 units produced by urokinase, due allowance being made in all cases for the spontaneous activity of plasminogen (0·5 ± 0·1 units). Of more importance, however, the results also show that the venom can augment the activity of an optimum concentration (2,000 U/ml.) of urokinase as a plasminogen activator, the activity produced by incubation together of urokinase, venom and plasminogen being 5·1 ± 0·4 U/ml., this being 1·4 ± 0·3 U more than that to be anticipated from the separate incubation of venom and plasminogen/urokinase with casein ($t = 11.96$, $P < 0.001$).

It has also been shown that the venom does not augment the activity of spontaneously activated plasmin and it would therefore appear that the augmentation of caseinolytic activity results from an action of the venom on plasminogen or on urokinase; but as incubation of venom and urokinase results in striking loss of urokinase activity it would seem probable that the venom acts directly on plasminogen. It may be that the action of the venom on the plasminogen molecule is to produce an alteration in its tertiary structure so that more arginine and lysine bonds are made available to attack by urokinase.

The inhibitor of plasminogen activation (ε-aminocaproic acid) has been added to the system but has no effect on the ability of the venom to augment plasminogen activation by urokinase. However, addition of a specific antivenom (Behringwerke A.G.) to the test system results in inhibition of proteolytic activity, plasminogen activation and also augmentation of the action of urokinase.

If the fraction of the venom which produces this unique effect can be isolated from the coagulant fraction it may have an important place in thrombolytic therapy as an adjuvant to urokinase and streptokinase, producing