daily food intake and to assessing accurately the "3,6-anhydrogalactose" figure for the control faeces blank (0·37% as $C_6H_8O_4$).

The above results show that, when native and partially degraded iota-carrageenans were fed to young rats, at a concentration of 5% in the diet, there were no significant differences in the faecal excretion of the two polymers and the weight gained by the animals.

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Correlation of urinary histamine excretion and 24 h urine volumes in rats and man

Urinary output of free histamine has frequently been used as an indicator of the level of whole body histamine metabolism (Johnston & Kahlson, 1967). The reliability of this measurement has been discussed in relation to the origin of urinary histamine and the very small fraction it represents of the total histamine metabolites (Lindell & Westling, 1966).

We report here a correlation of urinary histamine excretion and the 24 h urine volume in rats and man. This correlation has been the subject of frequent fruitless speculation, being considered unlikely by Anrep (1944) and Duner & Pernow (1956).

Female albino rats, either Wistar (SNR strain) or Sprague Dawley (Charles River strain), 150–250 g, were allowed free access to food and water, the diet being made by mixing Dixon's 41B meal with egg white, casting into sticks and baking. The rats were housed in glass metabolism cages ('Metabowl', Jencon's), and the 24 h urine output collected into 1 ml of 3N hydrochloric acid. Histamine was estimated by the fluorometric method of Oates, Marsh & Sjoerdsma (1962). Successive daily collections of 24 h urines were made. Rats No. 8–11 had 0·1N ammonium chloride solution instead of drinking water, and in addition, on days 4–6 of the experiment, rats 8–11 received 200 mg/kg of histidine hydrochloride subcutaneously.

In 9 of 11 rats there was a good correlation of histamine content and 24 h urine volume (Table 1).

Treatment with ammonium chloride gave a urine of low pH, which would be expected to facilitate the excretion of histamine, but the correlation of histamine excretion and urine volume was not disturbed. Treatment with L-histidine also did not affect the correlation.

Table 1. *Correlation of free histamine output and 24 h urine volumes in rats*

Rat No.	Strain and treatment	No. of samples analysed	Correlation coefficient †	Slope	Intercept	*P* value
1	Wistar	15	0·2	0·323	16·6922	n.s.
2	no treatment	15	0·87	1·6837	−2·8439	<0·001
3		16	0·31	0·3116	14·8033	n.s.
4	Sprague Dawley	9	0·97	2·0271	−7·2074	<0·001
5		7	0·91	1·5978	−3·4863	<0·01
6	no treatment	7	0·71	0·7953	5·8839	<0·1
7		8	0·72	1·0156	0·3683	<0·05
8	Sprague Dawley	6	0·93	1·7846	−2·767	<0·01
9	Ammonium chloride plus histidine HCl*	6	0·72	0·6819	11·0849	<0·1
10		6	0·73	2·5705	−26·1378	<0·1
11		6	0·88	1·4127	4·9158	<0·05

† Bravais-Pearson coefficient of linear correlation (γ).
* 0·1N NH_4Cl substituted for drinking water during experiment.
On days 4–6 inclusive these animals received histidine hydrochloride 200 mg/kg, s.c. daily.

In addition we found a good correlation of histamine content and 24 h urine volume (correlation coefficient = 0·70 P = 0·05) in a female patient hospitalized with suspected mastocytosis (see Fig. 1).

There are large differences in the slopes for individual histamine content versus urine volume relations (Table 1) and for this reason it would be hard to detect the relation by pooling data from individuals.

If the data we have obtained in rats prove to be similar in man when more subjects have been examined, then similar reasoning would explain the lack of correlation when data from individuals are pooled.

Speculation upon the mode of excretion of histamine in rats and man may be premature using such circumstantial evidence, but filtration and passive tubular reabsorption fit the data fairly well. Some support for this suggestion may be obtained

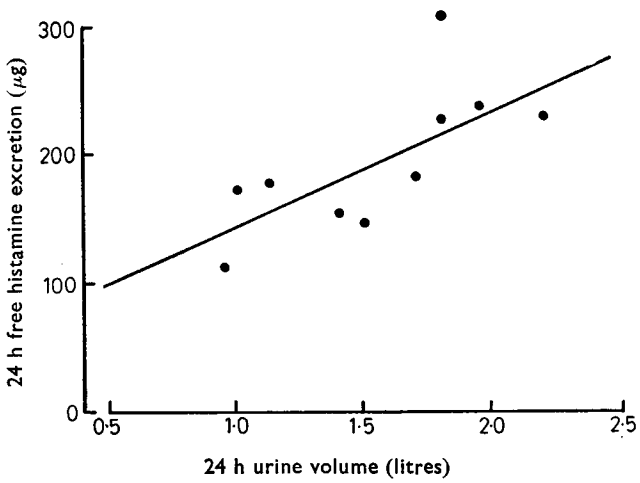

FIG. 1. Excretion of free histamine by a female patient. The points represent free histamine excreted in successive 24 h samples of urine.

from Duner & Pernow (1958), who showed a correlation of blood level of histamine and 24 h urine volume in man given a continuous infusion of histamine. These results cast doubt on the utility of urinary histamine output as a measure of histamine turnover.

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Macrocationic enzyme inhibition: pepsin and two polylysines

The strongly acid nature of pepsin is explained by its relatively high content of acidic amino-acids (Taylor, 1968). This property forms the principal basis of association between pepsin and its highly basic natural inhibitor which, together with miscellaneous peptides, constitute the enzymatically inactive pepsinogen (Herriott, 1962). A similar basis has been adduced for the interaction between pepsin and certain basic polyamino-acids, notably poly-L-lysine; and for one polylysine (degree of polymerization, n = 36) inhibition of peptic activity at pH 1·7 and 6 was claimed, digestion of haemoglobin and the clotting of milk being used at the two pH values respectively, to measure the activity of the pepsin (Katchalski, Berger & Neumann, 1954). These authors found that the inhibitory action of polylysine appeared to be instantaneous because pre-incubation of pepsin and polylysine for 5–30 min yielded a constant level of inhibition. It was shown later (Dellert & Stahmann, 1955) that the amount of inhibition of pepsin by a polylysine of mol. wt. 2580 rose to completion when a certain polylysine concentration range was entered, but disappeared as the macrocation concentration was increased to excess. In addition, insoluble complex formation between the polylysine and pepsin did not occur at high macrocation concentrations where inhibition was absent. This appears to be in accord both with knowledge of macroion interaction and the notion that the resulting pepsin inhibition is due to insoluble complex formation involving pepsin and the macrocation. This report deals with the inhibition of pepsin by two polylysines of different molecular weights.

The poly-L-lysines (LY102, LY115) had stated molecular weights of 12 300 and 43 870 (degree of polymerization 59 and 210 respectively), were derived from parent poly ε-carbobenzoxy-L-lysines and were purchased from Miles-Yeda Ltd., Rehovoth, Israel. They were used in solution in acetate buffer, pH 5, I = 0·05 (Long, 1961).

Twice crystallized pig pepsin (Sigma) was used at a concentration of 200 μg/ml in buffer. Gayelord-Hauser dried skim milk was reconstituted by triturating 20 g with water, adding 10 ml buffer, 5 ml 0·2M $CaCl_2$ and diluting to 100 ml with water. Solutions were mixed at 35·5° and milk clotting was carried out at this temperature.

Polylysine solution (or buffer) was mixed in equal volume with pepsin solution and at intervals of time after mixing 0·5 ml of the mixture was added to 5 ml reconstituted