animals that received the monoamine oxidase inhibitor and the α-methyltyrosine-containing diet, motor activity and brain amine levels were lower than corresponding control values. However, values for the spontaneous locomotor activity and the brain content of noradrenaline were significantly higher in the pheniprazine-α-methyltyrosine group than in saline-α-methyltyrosine group. Although pheniprazine partially blocked the behavioural depression and noradrenaline depletion it did not alter plasma levels of α-methyltyrosine. Thus the behavioural depression after a 24 hr diet containing α-methytyrosine appears to be related to the brain levels of catecholamines.

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The tensile strength of lactose tablets

SIR,—As part of an examination of the compaction properties of spray-dried and crystalline lactose, we have compared the tensile strengths of tablets prepared from the two forms of lactose, by means of the diametral compression test. This procedure was devised by Carneiro & Barcellos (1953) to assess the tensile strength of concrete and it has since been applied to coal (Berenbaum & Brodie, 1959); ceramics (Rudnick, Hunter & Holden, 1963); dental amalgam (Eden & Waterstrat, 1965) and dental gypsum plasters and stones (Earnshaw & Smith, 1966). Three size fractions and unfractionated samples of crystalline (B.D.H. Laboratory reagent grade) and spray-dried (McKesson Robbins) lactose, were used to prepare tablets, in the form of cylinders, 1·27 cm. in diameter, and approximately 0·3 cm thick. These tablets were compressed diametrically at a rate of 0·1 cm/min between the platens of an Instron Physical Testing Instrument using conditions that induced a uniform tensile stress across the diametral plane joining the two lines of contact of the specimen and platen, normal to that plane. The magnitude of the stress is given by the equation (Timoshenko, 1934; Froch, 1948).

$$\sigma x = \frac{2P}{\pi Dt}$$

where σx is the tensile stress, P the applied load and D and t the diameter and thickness of the specimen. The tensile strength can be calculated from the breaking load, by application of the above equation, provided failure occurs in tension. All the specimens tested met the requirements for tensile failure

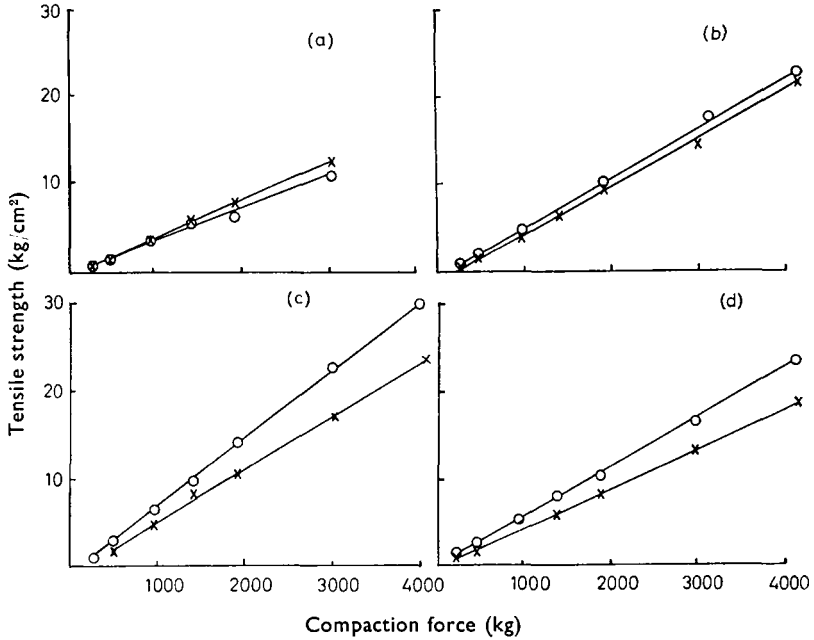

FIG. 1. The tensile strength of lactose tablets prepared at different compaction forces. —○— tablets of spray dried lactose. ——×—— tablets of crystalline lactose. (a) Size fraction 150–210 μ. (b) Size fraction 75–104 μ. (c) Size fraction <32 μ. (d) Unfractionated sample.

specified by Rudnick & others (1963). The use of the diametral compression test and its analysis of strength, allows the dimensions of the tablet to be taken into account, and by choice of parameters ensures that failure occurs by only one mechanism. This is in contrast to the use of crushing strength which is often used to evaluate tablet strength but which is only a measure of the force at which the tablet breaks.

The results shown in Fig. 1 are the mean of five determinations. They illustrate a linear relation between tensile strength and compaction force for all powder samples under the conditions of the test. The tensile strength of the compacts increases with a decrease in particle size. The rate of increase in tensile strength with compaction force also increases with decrease in particle size. The rate of increase is greater for the two smaller size fractions, and the unfractionated spray-dried lactose than for the crystalline lactose, but the reverse is true for the largest size fraction which gave compacts of crystalline lactose having higher tensile strength than the corresponding spray-dried material. These results illustrate differences in the tensile strength of compacted crystalline and spray-dried lactose which could be related to the different tabletting characteristics of the two forms of lactose which was reported by Gunsel & Lachman (1963).

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Determination of methylimidazoleacetic acids in human urine by gas chromatography

SIR,—In man, about one half of injected labelled histamine is excreted in urine as 1-methylimidazole-4-acetic acid (1,4-MeImAA) (Schayer, 1959). Tham (1965, 1966) described a gas-liquid chromatographic method for the assay of this acid and its isomer 1-methylimidazole-5-acetic acid (1,5-MeImAA), in human urine. The MeImAAs are separated from urine by ion-exchange chromatography, converted to the methyl esters, extracted into chloroform from alkaline buffer and then analysed by gas-liquid chromatography. A method for estimating the excretion of these compounds by thin-layer chromatography has also been published (Granerus & Magnusson, 1965).

This department has used Tham's method for some time with columns of nominally the same chemical specification, but removal of neutral esters from the urine extracts, by chloroform extraction from acid buffer, was needed to eliminate interfering peaks (Fig. 1A) without substantially affecting the basic MeImAA methyl esters (Fig. 1B), and as an internal standard 1-benzylimidazole proved more convenient. In view of the current interest in histamine and its metabolism, the modified technique may interest others.

Urine samples (24 hr) collected in polythene bottles containing 10 ml 12 N hydrochloric acid are stored at 1° until analysis in batches of ten. Aliquots (50–100 ml) are adjusted to pH 8·8 with 10 N sodium hydroxide and filtered. Aliquots (40–80 ml) of the filtrates are run on 40 × 1·7 cm columns of Dowex

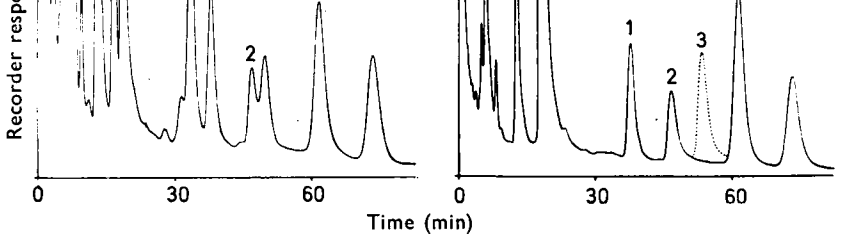

FIG. 1. A. Gas chromatogram of a urine sample purified on Dowex 1, esterified, and then extracted into chloroform from pH 8·0 buffer. Peak 1 corresponds to 1,4-methylimidazoleacetic acid, methyl ester and peak 2 corresponds to 1,5-methylimidazoleacetic acid, methyl ester.

B. Gas chromatogram of the same urine sample, prepared as for (A) above, but further purified by chloroform extraction at pH 4·0 before extraction at pH 8·0. Peaks 1 and 2 are as above; the dotted peak 3 shows the position of 1-benzylimidazole when added as internal standard.