LETTERS TO THE EDITOR

Bitter Principles of Cucurbitaceæ

SIR,—Through the courtesy of Dr. D. A. Sutton of the National Chemical Research Laboratory, Pretoria, we have had an opportunity of examining several pure crystalline compounds recently isolated from species of Cucumis by Dr. Enslin[1] of that laboratory. To assist others who may be interested in this field we desire to report on the toxicities and certain pharmacological properties of the substances examined.

Cucurbitacin A, derived from *Cucumis myriocarpus* and *C. leptodermis*, was administered intraperitoneally to groups of five male albino mice at three dose levels (0·62, 1·25 and 2·5 mg./kg.), and groups of two female albino rats at three dose levels (1·0, 2·0 and 4·0 mg./kg.). The estimates of the LD50 according to Kärber's formula[2], were found to be 1·2 mg./kg. and 2 mg./kg. for mice and rats respectively. Respiratory distress was observed at lethal or near lethal doses and at autopsy some rats showed evidence of acute pulmonary œdema. This phenomenon was also observed in a rabbit anæsthetised with 1·8 g./kg. of urethane intravenously. A total of 6 mg./kg. given intravenously in divided doses over a three-hour period caused respiratory distress followed by death. Approximately 5 ml. of blood stained fluid was drained post-mortem from the bronchial tree. In a cat anæsthetised with chloralose, 60 mg./kg. intravenously, the compound had no appreciable immediate effects on the blood pressure and respiration, when given intravenously in amounts which varied from 0·04 to 0·32 mg./kg. This cat was also given Cucurbitacin B which also had no apparent immediate effect. The animal, however, died with acute pulmonary œdema after a total of 0·7 mg./kg. of Cucurbitacin A and 0·3 mg./kg. of Cucurbitacin B. A quantity of about 10 ml. of fluid was collected from the bronchial tree after death by postural drainage and compression of the chest wall. Macroscopically, the lungs were congested and a cut section exuded a pinkish fluid on pressure; the lungs did not sink in water. Histological examination revealed engorgement of the blood vessels.

Cucurbitacin B, obtained chiefly from *Cucumis africanus* and *Lagenria leucantha* was administered intraperitoneally to groups of five male albino mice at three dose levels (0·62, 1·25 and 2·5 mg./kg.). Lethal doses again caused pulmonary œdema and the LD50 according to Kärber's formula[2] was 1 mg./kg.

Cucurbitacin C, obtained from *Cucumis sativus* had an intraperitoneal LD50, according to Kärber's formula[2], of 0·8 mg./kg. in male albino mice. Five animals were used at each dose of 0·62, 1·25 and 2·5 mg./kg. Respiratory distress was again observed with lethal and near lethal doses. Groups of two female albino rats received amounts up to 4 mg./kg. without causing death but at this dose respiratory distress was present.

The dihydro derivative of Cucurbitacin A was also examined and found to be considerably less toxic. Amounts up to 80 mg./kg. intraperitoneally had no apparent effect in male albino mice. Intravenous administration of doses up to 5 mg./kg. in a rabbit, anæsthetised with urethane, 1·5 g./kg. intravenously, did not apparently increase the respiratory tract secretion. A total of approximately 12 mg./kg. was given over a four and a half hour period.

Due to the small quantities of the materials available and to their low solubilities, the investigations were necessarily limited. The results, however, indicate quite clearly that Cucurbitacin A, B and C are comparatively toxic compounds, lethal amounts causing acute pulmonary œdema. The dihydro

derivative of Cucurbitacin A is considerably less toxic and at the dose levels employed no apparent effect on respiratory tract secretion was observed.

We wish to thank the Directors of the British Drug Houses Limited for permission to publish these results.

A. DAVID,
D. K. VALLANCE.

Biological Laboratories,
The British Drug Houses Ltd.,
Godalming, Surrey.

February 22, 1955.

REFERENCES

1. Enslin, *J. Sci. Food Agric.*, 1954, **5**, 410.
2. Kärber, *Arch. exp. Path. Pharmak.*, 1931, **162**, 480.

Nicotine Monomethiodide

SIR,—Because of regrettable oversight, for which we apologise, the following errors and omissions have occurred in our paper on nicotine monomethiodide, which appeared in the January number of this journal.

On page 28, Fig. 1: The scale of values of logϵ (molar) should start at 1·5 (not 2·0) and run up to 4·5 (not 5·0).

On page 31, line 27: log ϵ should be 4·11 (not 4, 11).

On page 31, line 7 from the bottom: An analysis has been omitted:—Found: Pt, 33·6; Calculated for $C_{11}H_{18}Cl_6N_2Pt$: Pt, 33·3 per cent.

On page 31, line 6 from the bottom: logϵ should be 3·69 (not 3·39).

On page 32, the last two lines of the section on crystallisation: the ion estimated was, of course, I^- (not I^+).

Department of Pharmacology,
Yale University School of Medicine,
New Haven, Connecticut. — R. B. BARLOW.

Department of Chemistry,
Queen's University, Belfast. — N. A. DOBSON.

February 1, 1955.

(ABSTRACTS *continued from page 293.*)

Streptomycin, Rectal Absorption in Rabbits. L. S. Carvalho and M. L. P. da Silva. (*Rev. Portuguesa Farm.*, 1954, **4**, 121.) A 50 mg. dose of streptomycin sulphate was administered in one suppository with either a water-soluble base [polyethyleneglycol 6000 (75 per cent.) and polyethyleneglycol 1500 (15 per cent.)] or a cocoa butter base. Blood levels of the antibiotic were measured by taking samples from the marginal vein of the rabbit ear 1/4, 1/2, 1, 3, 5, 7, 9 and 11 hours after the administration of the suppository and submitting them to the FDA method for the determination of streptomycin in serum. With both bases the antibiotic appeared in the blood after 15 minutes, but the concentration during the first 5 hours was found to be markedly higher in the animals administered the water-soluble suppository than in those given the cocoa butter base suppository. J. R. F.