amine which inhibited the uptake of 5-HT by nerve ending particles also showed inhibitory effect on isolated synaptic vesicles. These results imply that if reserpine and desipramine are able to be transported through neuronal membrane they are capable of blocking the intracellular 5-HT concentrating mechanism located at synaptic vesicles level. On the other hand cocaine showed no significant effect on 5-HT uptake by synaptic vesicles even when the concentration of 5-HT in the medium was decreased to 1 μg/ml. This result together with the previous observation that cocaine caused an inhibition of the uptake of 5-HT by nerve ending particles (Segawa & Kuruma, 1968) indicates that cocaine selectively blocks the neuronal membrane pump in the same way as it does with catecholamine uptake. Imipramine was reported to be capable of blocking the 5-HT concentrating mechanism located at the level of cell membrane (Fuxe & Ungerstedt, 1968). Our result showed that imipramine significantly blocked 5-HT uptake by synaptic vesicles under the experimental condition described above.

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References

Carlsson, A. & Waldeck, B. (1965). *Acta pharmac. tox.*, **22**, 293–300.
DeRobertis, E., Rodriguez de Lores Arnaiz, G. & Pellegrino de Iraldi, A. (1962). *Nature, Lond.*, **194**, 794–795.
DeRobertis, E., Rodriguez de Lores Arnaiz, G., Salganicoff, L., Pellegrino de Iraldi, A. & Zieher, L. M. (1963). *J. Neurochem.*, **10**, 225–235.
Fuxe, K. & Ungerstedt, U. (1968). *J. Pharm. Pharmac.*, **20**, 150–151.
Hillarp, N.-A. & Malmfors, T. (1964). *Life Sci.*, **3**, 703–708.
Malmfors, T. (1965). *Acta physiol. scand.*, **64**, *Suppl.* 248.
Maynert, E. W., Levi, R. & DeLorenzo, A. J. D. (1964). *J. Pharmac. exp. Ther.*, **144**, 385–392.
Segawa, T. & Kuruma, I. (1968). *J. Pharm. Pharmac.*, **20**, 320–322.
Snyder, S. H., Axelrod, J. & Zweig, M. (1965). *Biochem. Pharmac.*, **14**, 831–835.

Development of antihistamine and anti-allergic activity after prolonged administration of a plant saponin from *Clerodendron serratum*

SIR,—It was of interest that both the alcoholic extract and the saponin isolated from the root bark of an indigenous plant, *Clerodendron serratum*, which has been used for the treatment of bronchial asthma, caused release of histamine from lung tissue (Gupta & Gupta, 1967). Prolonged administration of the saponin in 20 mg/kg doses caused significant depletion of the amine from the lungs of rats treated with the drug (Gupta, Mahesh Rai & Gupta, 1967). The saponin fraction like other histamine releasers was not found to manifest any antihistamine activity or to give protection against anaphylactic shock in sensitized guinea-pigs exposed to egg albumin (antigen) micro-aerosols (Mongar & Schild, 1952). However, the continued daily administration of the drug, 20 mg/kg (1/15 of the LD50 dose 307·7 mg/kg), intramuscularly for 20 days to sensitized guinea-pigs was found to gradually develop protection against anaphylaxis. This became evident from the significant ($P < 0{\cdot}05$) delay in onset of dyspnoea in treated animals exposed to 1·0% egg albumin micro-aerosol as compared to the controls. At the end of 20 days, the treated animals on continued exposure to the micro-aerosol for 10 min, did not manifest air hunger or asphyxial convulsion as was observed in untreated controls before collapse. The results are summarized in Table 1.

TABLE 1. SHOWING THE EFFECT OF PROLONGED ADMINISTRATION OF CLERODENDRON SAPONIN AGAINST ANAPHYLACTIC MICRO-AEROSOLS IN GUINEA-PIGS

	Average time (sec) for onset of dyspnoea			Collapse (preconvulsive time, sec)	Protection %
	Before treatment	1 hr after treatment	10 days after treatment	20 days after treatment	
Control (3)	130 ±28	106 ±22	168 ±5	230 ±36	Nil
Saponin—*C. serratum* (3)	133 ±25	117 ±21	366 ±73	>600	100

The lungs from animals killed were extracted with concentrated hydrochloric acid for 2 hr (Francis, Melville & Douglas, 1963). The filtrate, after extraction successively with light petroleum, ethyl acetate, carbon tetrachloride or ethyl ether, gave an oily substance which on dissolving in equal parts of saline and propylene glycol was tested for antihistamine and anti-allergic activity on isolated strips of guinea-pig ileum.

The constrictor responses to the standard doses of histamine of the isolated strip of ileum suspended in a 10 ml Tyrode bath were found to remain inhibited to below 50% for an average period of 16·0 ± 8·1 min after addition of 2 mg of the lung extract obtained from treated animals, while this inhibition was of much shorter duration (6·3 ± 2·6 min) after addition of the equivalent doses of the extracts from control animals. The lung extracts from treated animals were significantly more effective compared with controls in inhibiting the constrictor responses of slow reacting substance obtained from perfusion of the sensitized lung with egg albumin. Development of the antihistamine and anti-allergic activity observed in the treated animals may be as a result of adaptation to chemical stress induced by release of histamine by the drug, in view of the fact that development of a "Resistin" like substance has been reported by Karady, Kovacs & others (1957). These observations seem to throw some light on explaining the beneficial effects of the plant saponin in bronchial asthma and might also suggest the use of non-toxic histamine releasers in the treatment of allergies, the possibility of which was indicated earlier by Gaddum (1948).

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References

Frances, L. E., Melville, K. I. & Douglas, D. E. (1963). *Can. J. Biochem. Physiol.*, **41**, 1961–1969.

Gaddum, J. H. (1948). *Pharmacology*, p. 237, 3rd edn, London: Oxford University Press.

Gupta, S. S. & Gupta, N. K. (1967). *Indian J. med. Sci.*, **21**, 795–799.

Gupta, S. S., Mahesh Rai & Gupta, N. K. (1967). *Curr. Sci.*, **36**, 41–43.

Karady, S., Kovacs, B. A., Kovacs, J., Szerdahelyi, M. & Vajda, P. (1951). *Archs int. Pharmacodyn. Thér.*, **88**, 253.

Mongar, J. L. & Schild, H. O. (1952). *J. Physiol., Lond.*, **118**, 461–478.