Pharmacological Properties of a Glycoalkaloidal Fraction Obtained from *Solanum auriculatum* Ait.

In the course of screening various chemical substances occurring in Solanaceae, pharmacological activity was found in a glycoalkaloidal fraction (called M-11 by us for the present) obtained from the berries of *Solanum auriculatum* Ait.

Berries of *Solanum auriculatum* Ait. were air-dried and extracted with 90% ethanol. The ethanol-free extract was repeatedly shaken with ether. The ether-insoluble fraction was dissolved in ethanol and decolorized with charcoal. It was filtered, dried in partial vacuum, and the residue was dissolved in water. The aqueous solution was strongly basified with ammonia and re-extracted with *n*-butanol. The dry glycoalkaloidal fraction was obtained by distilling off the *n*-butanol in partial vacuum (yield 67 mg/g air-dried berries). A 2% solution, dissolved in a 2:1 propylene glycol/water solvent was made up to the desired volume with normal saline and injected intraperitoneally unless otherwise mentioned. Control experiments were performed to exclude the effects of the solvent.

With M-11 1.5 mg/kg i.v., blood pressure was lowered inconsistently in intact cats, but not in spinal cats. The hypotensive response could not be blocked by atropine or mepyramine. Respiration was transiently depressed. At a concentration of $4 \cdot 10^{-5}$, M-11 contracts moderately isolated guinea-pig ileum and rat uterus in the presence of atropine (10^{-6}) and mepyramine maleate (10^{-6}, in ileum only). No neuromuscular relaxation was seen in cat sciatic nerve-gastrocnemius preparation with M-11 7.5 mg/kg given intraarterially.

Behavioural changes were observed when mice and rats were injected with 1, 5, 10 and 20 mg/kg of M-11. After administration of the M-11 (but not solvent) mice and rats did not fall asleep, but became quiet within 15 min. Spontaneous motility, interest in each other and response to auditory and tactile stimuli were noticeably reduced. These changes were maximal after 30–60 min, and all but disappeared within 2 h.

M-11 prolongs pentobarbitone sleeping time. Groups of 10 mice were injected with M-11, followed 30 min later by sodium pentobarbitone 50 mg/kg. Sleeping times were: control (solvent) 59.2 ± S.E. 6.4 min; with M-11 1 mg/kg, 75.4 ± 7.1 min; with 5 mg/kg, 85.6 ± 8.2 min; with 10 mg/kg, 91.2 ± 8.0 min; and with 20 mg/kg, 103.6 ± 10.3 min. In this connection, the effect of altering the interval of administration between M-11 10 mg/kg and sodium pentobarbitone 50 mg/kg was studied. Sleeping time was found to be: control, 59.2 ± S.E. 6.4 min; interval 15 min, 115 ± 15.5 min; interval 30 min, 112 ± 9.3 min; interval 45 min, 86 ± 8.2 min; interval 60 min, 63 ± 11.6 min. Optimal prolongation of sleeping time apparently occurs when M-11 precedes pentobarbitone by 15–30 min.

M-11 reduced rectal temperature in mice by 0.5–1.7 °C, generally within 15 min after administration (Table); the hypothermic effect gradually disappeared within 2–2½ h.

In rats and mice, no protection was obtained against metrazole-induced seizure (80 mg/kg) with M-11 (20 mg/kg) administered 30 min prior to metrazole.

Pre-treatment with M-11 (20 mg/kg, given 30 min before amphetamine) gave some protection against amphetamine toxicity in congregated mice[1] (24 h mortality: treated 4 out of 10, untreated control 9 out of 10).

Lymphocytopenia in response to cold stress (2–4 °C for 1 h) was reduced by pre-treating rats (M-11 20 mg/kg) 30 min prior to exposure. Taking pre-stress lymphocyte count as 100%, post-stress count decreased by 46.3, 63.3, 53.2 and 49.0% respectively (mean 52.9%) in control animals; in pre-treated rats, the reduction was 19.9, 24.0, 59.4 and 34.8% (mean 34.5%).

The above findings of behavioural changes, hypothermia, pentobarbitone sleeping time prolongation, protection against amphetamine toxicity and reduction of stress lymphocytopenia suggest that M-11 possesses a fair degree of central depressant action, possibly in the nature of a tranquilizer[2].

Lowering of rectal temperature in °C (mean ± S.E., groups of 5 mice) after intraperitoneal injection of M-11

M-11 i.p. mg/kg	Time in min Control	15	45	75	105	135
Nil (solvent)	37.71 ± 0.21	37.49 ± 0.18	37.38 ± 0.31	37.64 ± 0.12	37.8 ± 0.21	37.67 ± 0.42
1	37.76 ± 0.63	37.21 ± 0.5	37.38 ± 0.51	37.71 ± 0.28	37.5 ± 0.16	37.6 ± 0.22
5	37.62 ± 0.44	36.58 ± 0.14	37.03 ± 0.13	37.34 ± 0.5	37.7 ± 0.16	37.4 ± 0.41
10	37.44 ± 0.14	35.77 ± 0.26	36.39 ± 0.32	37.0 ± 0.22	37.0 ± 0.18	37.66 ± 0.26
20	37.17 ± 0.29	35.44 ± 0.36	36.02 ± 0.36	36.15 ± 0.38	36.43 ± 0.47	37.13 ± 0.34

Zusammenfassung. Ein glykoalkaloider Teil von *Solanum auriculatum* Ait. beruhigt Ratten und Mäuse und verlängert die Pentobarbitone Schlafperiode. Die Körpertemperatur fällt und die Amphetamin-Toxizität wird verringert; auch die Lymphocytopenia nach Stress ist schwächer. Diese Wirkungen, welche mit Dosen von 1–20 mg/kg erreicht wurden, weisen auf ZNS-hemmende Potenzen hin.

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[1] J. H. BURN and RONEEN HOBBS, Arch. int. Pharmacodyn. *113*, 290 (1958).

[2] We wish to thank the Principal, Medical College, Calcutta, for permission to publish these findings; Prof. S. SENGUPTA, Head of the Department of Pharmacology for much help and encouragement; and Smith, Kline & French (India) for their gift of *d*-amphetamine.