obtained increased grain yields. The increased growth of rice seedlings observed in the present study may be due to the cumulative effects of both N-fixation and the synthesis of growth-promoting substances[12] and this area of investigation is receiving our attention. It may therefore be generalised that the *Azotobacter* isolates from the C_4 plant species are not only more efficient, but also exhibit more growth-promoting effect than the isolates from the C_3 plants.

Tamil Nadu Agricultural University,
Coimbatore 641 003,
July 29, 1976.

D. PURUSHOTHAMAN.
C. KASIRAJAN.
G. RANGASWAMI.

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INHIBITION OF INDUCTION OF STREPTOZOTOCIN DIABETES BY MANNOHEPTULOSE

STREPTOZOTOCIN (SZN), derived from *Streptomyces achromogenes,* induces diabetes by destruction of the beta cells of pancreatic islets[12]. Chemically, it is 2-deoxy, -2- (3-methyl-nitrosoureido) -D- glucopyranose[9]. Its diabetogenic action is prevented by 2-deoxyglucose (2DG)[6] which is an inhibitor of insulin release[10] and of glucose metabolism[13]. This, and some other observations[2,5], suggest that the betacytotoxic action of SZN is related to insulin release or glucose metabolism. Against this possibility is an observation[6] that SZN diabetes was not prevented by mannoheptulose (MH), a more potent inhibitor of insulin release[3] and glucose metabolism[4]. In view of the theoretical importance of this negative finding, we have investigated again the interaction between MH and SZN.

The diabetogenic action of a single injection of SZN (gift from Upjohn Co.) at different time intervals after a dose of MH (from Sigma Chemicals Co.) was determined, comparing the glucose tolerance of the treated male albino mice (20 to 25 g) with that of untreated controls and of mice receiving the same dose of SZN alone. Glucose tolerance was estimated as the area (GTA) under the glucose tolerance curve, after a glucose load of 3 g/kg after 16 hours of fasting. Blood samples collected from the orbital sinus at 0, 60 and 120 min after glucose injection were analysed for reducing sugar[1]. The mean control GTA was 228 mg hr/100 ml. ($\pm$ 19, S.D., in 24 mice). The increase (*i.e.*, Δ GTA) over this value, on the fifth day after treatment was a measure of the resultant diabetes and was calculated as percentage (% Δ GTA) of the mean control GTA. SZN (in citrate buffer at 5° C, pH 4·5), MH (in isotonic saline at 5° C) and glucose (in water) were given intraperitoneally in volumes of 0·01 ml./g body weight.

Mice which received SZN alone (Group A, Table I) or along with MH (Group B) became equally diabetic. But when MH preceded SZN with increasing time intervals (Group C, D, E), there was progressive reduction in the effect of SZN. With an interval of 60 min (Group E), diabetes was completely prevented. At 75 min (Group F), MH became altogether ineffective. Thus the protective action of MH against SZN was very much time dependent and the optimal time for MH administration was 60 min before SZN. A slightly lower dose of MH (125 mg/kg, Group G) was ineffective against the same dose of SZN (125 mg/kg). Thus the minimal dose of MH effective against 125 mg/kg SZN was 150 mg/kg. This dose was equally effective against a more severely diabetogenic dose of SZN (175 mg/kg, Groups H and I).

The present study establishes that MH can prevent the diabetogenic action of SZN. The preferential uptake of SZN by mouse beta cells is related to the glucose moiety in this nitrosourea[11]. The entry of MH into mouse beta cells is also by a glucose sensitive transport mechanism[8]. But the protective action of MH against SZN is not by competition for a common transport mechanism, because the protection is offered not when the circulating MH : SZN ratio would have been the highest (Group B), but 60 min later (Group I), by which time the

TABLE I

Effect of MH on the Diabetogenic action of SZN

Group* No.	Dose of SZN mg/kg	Mannoheptulose		GTA ± SD mg hr/ 100 ml.	% Δ GTA
		Dose, mg/kg	Time before SZN, min		
A	125	0	..	640 ± 17	+180
B	125	150	0	642 ± 16	+181
C	125	150	30	587 ± 22	+157
D	125	150	45	492 ± 19	+115
E	125	150	60	229 ± 21	0
F	125	150	75	619 ± 17	+171
G	125	125	60	649 ± 10	+184
H	175	0	..	930 ± 9	+407
I	175	150	60	230 ± 20	0

*All groups consisted of 6 mice each. For abbreviations and experimental details, *see* text.

blood concentration of MH would have fallen by half[3]. 60 min after intravenous administration of MH, maximal hyperglycaemia developed in rabbits[3], as also almost complete disappearance of circulating insulin in rats[7]. These considerations suggest a non-competitive mechanism for the action of MH. The similarity between MH and 2DG in preventing SZN diabetes, strengthens the possibility that the mechanism of action of SZN might be related to either glucose metabolism or insulin release. The failure of MH to protect rats against SZN in a previous study[6] is best explained by the very short time interval (15 min) by which the sugar had preceded SZN. The apparent constancy of the minimal effective dose of MH against varying doses of SZN is also interesting and is being investigated.

Department of Physiology,
Christian Medical College,
Vellore 632 002,

L. N RAMANI.
P. ZACHARIAH.

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