Letter to the Editor

INSULIN, TOLBUTAMIDE, PHENFORMIN AND BLOOD SUGAR OF RANA TIGRINA*

Sir,

Adult frogs of either sex (250-500 *g*) were anaesthetized by injecting 50 *mg/kg* pentobarbitone sodium ip. They were kept moist during the experiment. Liver and heart were exposed without injuring abdominal veins. Left aorta was cleaned and ligated about 8 *mm* distal to its commencement. Polyethylene cannula (1 *mm* inner diameter) was tied into the left aorta, proximal to the ligature, with its tip directed towards the heart. Blood samples (0. 3 *ml*) were drawn through the cannula immediately before and 10 min after injecting the drugs and, subsequently, at hourly intervals for upto 5 hr. Blood sugar was estimated by the method of Nelson and Somogyi (3). All drugs including glucose solution were injected into the blood circulation through a liver lobe. By injecting Evans Blue solution it was ascertained, in separate experiments, that fluids injected into liver lobe immediately entered blood circulation. The work was conducted from August to November (room temperature controlled at about 24°C).

The preparation usually survived for upto 5 hr. In all 70 frogs were taken; for each dose or combination of drugs usually 5 animals were used. The initial blood sugar level in most of the frogs was between 20-50 *mg*/100 *ml* (range 15-81 *mg*/100 *ml*). In 12 control animals receiving 3-8 *ml/kg* of 0.6% NaCl solution, the blood sugar level of individual animals was found to be quite steady over the period of experiment. Ten min after injecting 300 *mg/kg* glucose (10% W/V solution) the blood sugar level in 8 frogs rose to 130-180 *mg*/100 *ml* and gradually returned to 50-80 *mg* after 5 hr. Insulin (40 U/*ml* and pH at 5.5; 5, 50 or 500 U/*kg*) brought down the blood sugar level only by 10-20% of the initial value. However, when injected with the latter 2 doses of insulin, glucose (300 *mg/kg*) produced hyperglycaemia which was about 50% less, in intensity and duration, than that induced by glucose alone. Tolbutamide (5% W/V solution and pH at 7.5; 30 and 200 *mg/kg*) did not significantly lower the initial blood sugar level nor the glucose-induced hyperglycaemia. Phenformin (0.5% W/V solution and pH at 5.0) was ineffective at 5 *mg/kg* dose but, at 50 *mg/kg* dose, it reduced, like higher doses of insulin, the glucose-induced hyperglycaemia by about 50%.

The results on insulin are consistent with the statement that frogs, other cold-blooded vertebrates and birds are comparatively resistant to it (1)

Houssay *et al* (2) observed that the initial blood sugar level (29-48 *mg*/100 *ml*) of male toads was lowered, in 6 experiments, by about 75% after injecting 200 *mg/kg* tolbutamide (2% W/V in 0.1 N NaOH solution); however, in the present work on *Rana tigrina*, it was found almost ineffective.

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In comparatively large doses insulin and phenformin could clearly reduce the glucose-induced hyperglycaemia in the frog (*Rana tigrina*).

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