Studies on the Detoxicating Hormone of the Liver (Yakriton).

Fifth Report.*

Prophylactic Effect of Yakriton against
Urea Intoxication.

By

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In the first report¹⁾ of these studies Yakriton was defined as the detoxicating hormone of the liver instead of the ammonia regulating hormone, because it had been presumed from other experiments, though these were very few in number, that Yakriton would represent other detoxicating principles as well. The present paper will offer one proof for that.

If Yakriton were only the ammonia regulating hormone,—the ammonia excreting principle, for instance, it would not be effectual for the detoxication of urea. If it were the urea forming hormone, not only will it not counteract the poisonous effects of an overdosage of urea, but it will also rather be harmful in cases of hypercarbamidemia. But if Yakriton should on the contrary represent the detoxicating liver hormone, then it will neutralize the injurious effects of hypercarbamidemia, as proven below.

As we²⁾ had already experienced that the detoxicating experiments should be done with animals of an equal detoxicating power, our first trial with urea was to classify rabbits according to their detoxicating activity. But it was not so simple in the case of urea as in that of ammonia. Animals that had developed severe convulsions (generally within one hour) could scarcely survive them, while those without them did not show any

* Read at the 32nd Annual Meeting of the Japanese Pediatric Society in Kyoto, April 3rd, 1927.

1) A. Sato, Tohoku J. Exp. Med., 1926, 8, 232.

2) A. Sato and H. Sakurada, Tohoku J. Exp. Med., 1926, 8, 347.

reliable symptoms according to which they could be classified. Not a few of them did indeed show some restlessness immediately after the intraperitoneal injection of the poison, while others at that time appeared quite unaffected. This discrepancy had, however, but little to do with the difference of the detoxicating activity of those animals, because those apparently quite unaffected immediately after the injection, might soon die with severe convulsions, while others very restless then might soon become calm and remain healthy. It is thus impossible to foretell the coming attacks of convulsions from the initial symptoms of the animals.

At present we have adopted such a method as to try an intraperitoneal injection of 10% solution of urea in an amount of 10 c.c. per kilogram of body weight and to repeat the trial several times within a short time (one week, for example, and the injection not more than once a day). At the final test of these injections the amount of the poison was doubled or trebled and then the majority of the animals used for the experimentation will have died of severe convul-

TABLE I.
Experiment of Prophylactic Effect of Yakriton against Urea Convulsions.

Date of experiments	10% urea solution intraperitoneally injected in amount of 20 c.c. per kilogram of body weight							Yakriton, 5 minutes previously used	Result of the final urea injection
	13. II.	14. II.	15. II.	16. II.	17. II.	18. II.	19. II.		
Control animals	No. 1535	(1040)* Injected	Not injected	(1000) Injected	(1020) Injected	(1050) Injected		Not used	Fatal convulsion after 30 minutes (1000)
	No. 1536	Not injected	(1230) Injected	Not injected	(1240) Injected	Not injected		Not used	Fatal convulsion after 80 minutes (1220)
Yakriton animals	No. 1528	(1050) Injected	Not injected	(940) Injected	Not injected	(980) Injected		Subcutaneously injected, 5 c.c. (ca 50 R.A.U.)§	No convulsion; remained in life (1000)
	No. 1534	(1300) Injected	Not injected	(1260) Injected	(1250) Injected	(1270) Injected		Subcutaneously injected, 12 c.c. (ca 120 R.A.U.)§	No convulsion; remained in life (1250)

* Figures in parenthesis = body weight in grams. § R.A.U. = Rabbit-ammonia-units.

sions. During the whole course those animals of an inferior detoxicating activity will have died, while those of an exceptionally active power of detoxication will have been excluded from the experiment, because the latter can be recognized by the fact that they remain utterly unaffected and show a good appetite even immediately after the injection of the poison.

Here will be given two series of experiments for the detoxicating effect of Yakriton against urea poisoning. The first result given in Table I shows our tentative experiment.

The following experiment (Table II) has been performed according to the method above described, in which the final amount of urea injected was doubled.

TABLE II.
*Experiment of Prophylactic Effect of Yakriton against
Urea Convulsions.*

		10% urea solution intraperitoneally injected in amount of 10 c.c. per kilogram of body weight				Yakriton, 5 minutes pre- viously used	Result of the final urea test*
Date of experiments		First injection 19. II.	Second injection 20. II.	Third injection 21. II.	Fourth injection 22. II.		Fifth injection 23. II.
Control animals	No. 1538	(1300)	(1300)	(1280)	(1280)	Not used	(1300) Fatal convulsion after 40 minutes
	No. 1543	(1530)	(1480)	(1480)	(1530)	Not used	(1530) Fatal convulsion after 40 minutes
Yakriton animals	No. 1544	(1030)	(1030)	(990)	(1000)	Subcutaneously injected, 2 c.c. (ca 100 R.A.U.)§	(1020) No convulsion; remained in life
	No. 1545	(1230)	(1240)	(1240)	(1250)	Subcutaneously injected, 2.4 c.c. (ca 120 R.A.U.)	(1270) No convulsion; remained in life

* In this final experiment the urea solution administered in double amounts.

§ R.A.U. = Rabbit-ammonia-units.

In these two experiments above tabulated it may be rather accidental that all of the control animals developed convulsions; such a result may not always be expected, unless some further study of the classification of urea-detoxicating activity be made.

But as the above results show, it is certain that Yakriton should contain or represent an active principle for detoxicating the urea poisoning, as

was predicted. As to the amounts of Yakriton we tried many more units than for the prevention of ammoniac convulsions³⁾; because we had taken into consideration the fact that animals scarcely outlive urea convulsions, while they can survive ammoniacal convulsions without serious damage to life provided that the amount of the ammonium salt is not too large. This use of larger amounts of Yakriton is, however, based only on our presumption; the least amount of Yakriton, sufficient for the detoxication of urea poisoning, will be published in the near future with chemical aspects of the work.

CONCLUSION.

Yakriton is not only the ammonia regulating principle, but also the urea regulating principle. It is thus made more probable that Yakriton should, as already predicted in the first report of these studies, represent the detoxicating hormone of the liver.

3) A. Sato, *Tohoku J. Exp. Med.*, 1927, 8, 354.