14. On the Hypoglycemic Action of Oxalic Acid. (2nd Report.)

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(Comm. by T. KUMAGAI, M.S.A., June 12, 1948.)

In the previous report¹⁾ we have reasoned out a conclusion that there must be two kinds of oxalic acid, physiologically active and inactive. The reason why: (1) water extract of "Renriso", *Lathyrus palustris* L. var *macranthus* (White) has a remarkable therapeutic effect for diabetes mellitus. (2) An effectual substance, which has the same chemical and physical properties as oxalic acid was presented from "Renriso". (3) We ascertained that 1-2 mg of this oxalic acid-like substance would kill 1-1.5 kg weight rabbits within 45 hrs. with hypoglycemic convulsion. (4) On the other hand oxalic acids for sale and more than 100 mg of this acid kills rabbits of 1-1.5 kg weight.

Rabbits die under hypoglycemic convulsion by the injection of this active oxalic acid as in the case of Insulin injection. According to many author's experiments a toxicosis of oxalic acid is thought to be caused by the removal of calcium from the tissues and from the blood. Therefore we have measured calcium content in blood of poisoned rabbits. For the determination of calcium the method of Clark-Collip (J. Biol. Chem., 63, 1925) was adopted. It was observed that the amount of calcium in blood serum of five normal healthy rabbits is within from 9 to 15 mg. per 100 cc. By subcutaneous administration of about 200 mg. of oxalic acid Merk, calcium content of blood serum is in the minimum normal value, but 500 mg. of this acid reduces calcium content to 2.8 mg per 100 cc. Compared with the control, decrease of calcium content is not remarkable when 1 g of the sample has been given to a rabbit of 3.7 kg weight. Soon after the hypoglycemic convulsion, caused by injection of 1 to 5 mg oxalic acid, which was prepared from "Renriso" and *Rumex japonicus* Meisn. The amount of calcium of blood serum was measured

1) Vol. 21, No. 9 of the Proc.

Table I. Variation of Calcium Content in blood of Oxalic Acid injected Rabbits.

Materials	Rabbits		Amount of admin- istration (mg)	Blood sugar and calcium content after injection (mg%)										Remarks	
				before injection	0-6		6-12		12-24		24-48		48-72(hrs.)		
	blood sugar	Ca			blood sugar	Ca	blood sugar	Ca	blood sugar	Ca	blood sugar	Ca			
	Weight (g)	Number		Weight (g)											
Oxalic acid (Mirk)	A. 10	969	200	113		134			146		125		43	8.3	Death 54 hrs. after in- jection, heart puncture
do	A. 13	1070	500	131		181	2.8								Death 40 minutes after injection, heart puncture
do	A. 12	3750	1000	120	14.4	129	10.1		145	9.1	117	10.2	77	9.04	Vigorous enough 70 hrs. after injection
Oxalic acid ("Renriso")	A. 71	1300	1	63		64			75		75		32	15.9	Convulsion 54 hrs. after injection, heart puncture
Oxalic acid (Rumex Japonicus Meisn.)	A. 68	1300	5	83		74		66	48		16	12.7			Convulsion 47 hrs. after injection heart puncture

and we have known the calcium content within normal value (Table I). There is no doubt on the ground that convulsed rabbits have recovered from poisoning by injection of grape sugar.

Oxalic acid is distributed universally over the vegetable world. But its physiological meaning is not clear. According to many authors oxalic acid is perhaps an excreta of metabolism. Some authors think that it may be an intermediate product of metabolism. It is known that in the human being and animals oxalic acid is excreted in their urine. To examine the action of oxalic acid in urine we have separated this acid in urine by the following process: 100 litre urine has been gathered, making a weak alkaline solution by adding ammonia and calcium chloride. The precipitate has been filtered and washed with water several times and by adding acetic acid the soluble salts were dissolved and the solution has been extracted with ether in Soxhlet apparatus for 48 hrs; after evaporation of ether oxalic acid has been separated from other mixed substances. 1 mg of this purified substance kills similarly rabbits under hypoglycemic convulsion as with oxalic acid from "Renriso". (Table II.)

Furthermore we prepared oxalic acid from tea-leaves, woodsorrel, sorrel-dock, *Rumex japonicus* Meisn. *Polygonum Reynoutria* Makino and several moulds. And we ascertained that their pharmacological action and toxic symptoms are the same as oxalic acid from "Renriso". In the way we have known that there is in nature many oxalic acid of same physiological action as the one from "Renriso".

Table II. Hypoglycemic Action of Oxalic Acid, separated from several Vegetables.

Materials	Rabbit		Amount of administ- ration (mg)	Variation of blood sugar after injection (mg %)										Time laps- ed to con- vulsion	Blood sugar in convul- sion
	Number	Weight (g)		Before injection	0-3	3-6	6-12	12-24	24-30	30-48	48-54	54-72 (hrs)			
Green tea- leaves	548 550	1030 1230	1 5	75 73	75 61		39 21	30 21				26 26	30 21		
black tea- leaves	539 540	1300 1500	1 5	77 79	86	79 83	66 68	81 54	70 59	64 36	18 14	72 55	26 14		
Rumex japonicus Meisn.	549 A. 27 551	1030 1250 1300	1 2 5	71 80 82	78 89 73	87	30 74 43	21 66 74	90 41	70 47	60 36	26 60 54	21 36 36		
Polygonum Reynoutria Makino	A. 28 545	1165 1320	2 5	80 81	85 68	75	75 54	24 17	17	43		24 52	24 43		
Woodsorrel	546 A. 24	1220 1060	1 2	81 86	63 86	98	40 84	38 58	70	28		28 48	8 28		
Sorrel dock	536 A. 25	1250 1070	1 1	83 90	54 80	85	49 78	44 76	36	56		45 58	36 24		
“Renriso”	A. 4 A. 5 A. 37	1000 1200 1350	1 1 1 (peroral)	78 94 99	80 87 88	76 76 98	43 50 96	38 48 95	101	50	17	25 28 62	38 48 7		
Urine	A. 3 532	1115 1400	1 1	108 70	98	78	56 70	50	27			29 46	50 27		
Mould (1)	A. 1	1300	1	75	97	88	83	48	32	27	24	60	24		
Mould (2)	A. 2	1300	1	84	106	81	56	59	25	24		48	24		