

Saluretic Action of Ethacrynic Acid in the Mouse

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The new saluretic-diuretic agent, ethacrynic acid, has been reported to be inactive in the rat. It was examined for activity in another rodent, the mouse, an animal frequently used for the initial screening of biological activity of new agents. This agent was found to produce a dose-related increase in the excretion of sodium and chloride ions. These data indicate that the saluretic-diuretic activity of ethacrynic acid would have been detectable in an initial evaluation of this agent in the mouse.

BEYER AND associates (1) recently described the pharmacology of a new saluretic-diuretic agent, ethacrynic acid. An interesting feature of this compound was the variation in activity observed in different species of laboratory animals. In the dog, ethacrynic acid was found to produce a response equal in magnitude to that of the organomercurials. In the monkey, rabbit, and guinea pig ethacrynic acid was less active, and in the rat the compound was devoid of activity. The action of ethacrynic acid in the mouse, another rodent, was not reported. When the drug was administered to mice in the authors' laboratory, it appeared to produce a diuresis. Since the mouse is used frequently in the initial evaluation of a compound, it was of interest to determine if this gross observation could be substantiated.

under each beaker to collect the urine. At the end of the 3-hr. collection period, the animals were exposed to an atmosphere of ether in order to stimulate emptying of the bladders. The urine was then diluted and analyzed for sodium and potassium (Coleman flame photometer) and chloride (Buchler-Cotlove chloridometer).

The data obtained were analyzed statistically using the Student *t* test, group comparison (2).

RESULTS AND DISCUSSION

Ethacrynic acid was found to possess significant ($p < 0.05$) saluretic activity in the mouse (Table I). Sodium excretion was significantly elevated at 6.25 mg./Kg. and at all doses employed greater than this. A significant increase in chloride excretion was observed with all dosages studied. Since ethacrynic

TABLE I.—EFFECT OF ETHACRYNIC ACID ON ELECTROLYTE EXCRETION BY THE MOUSE^a

Excretion of	Dose of Ethacrynic Acid, mg./Kg.						
	0.00 (24) ^b	3.125 (10) ^b	6.25 (11) ^b	12.5 (12) ^b	25 (12) ^b	50 (12) ^b	100 (12) ^b
Sodium	40.4	39.4	59.0	78.2	84.1	110.5	87.0
(% of load)	(3.9)	(3.7)	(1.5)	(4.4)	(4.7)	(7.9)	(4.3)
Chloride	41.9	70.3	103.8	107.0	119.6	159.4	146.0
(% of load)	(5.9)	(6.7)	(3.1)	(7.4)	(6.1)	(9.2)	(7.4)
Potassium	1.4	1.9	2.5	1.6	1.9	2.2	2.6
(meq./Kg.)	(0.2)	(0.2)	(0.2)	(0.2)	(0.3)	(0.2)	(0.3)

^a Mean \pm standard error. ^b Number of mice in each group.

METHODS

Male albino mice (Sutter strain), weighing 20–28 Gm., were used. The animals were fasted overnight but allowed free access to water until the time of the experiment. All animals were hydrated orally with 0.9% NaCl, 50 ml./Kg. Ethacrynic acid (3.125–100 mg./Kg.) was dissolved in the oral load. Urine was collected from individual animals by caging them under 600-ml. beakers which were inverted over fine mesh screen. Petri dishes were placed

acid has only a minimal inhibitory effect on carbonic anhydrase (1), the greater increase in chloride excretion relative to sodium excretion was not unexpected. The increased excretion of sodium and chloride appeared to be maximal at 50 mg./Kg. Potassium excretion was significantly elevated at 6.25, 50, and 100 mg./Kg.

These data demonstrate that the mouse more closely resembles the guinea pig, rabbit, and dog than the rat with respect to responsiveness to the saluretic action of ethacrynic acid. It would appear that the saluretic-diuretic activity of this agent would have been noted in an initial evaluation in the mouse, but not another rodent, the rat.

REFERENCES

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