DIFFERENCES IN THE EFFECT OF EPHEDRINE ISOMERS
ON BLOOD PRESSURE IN RATS

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It is well known that ephedrine has long been used as an antitussive drug and that the
natural ephedrine is a levorotatory isomer. Among there isomers of ephedrine, 1-, dl-, and
d-, the former two are used as medicinal therapy and the pharmacological effects have been
reported by many investigators.

Fujii (1), Pak and Read (2) and Chen et al. (3) stated that ephedrine isomers have simi-
lar effects with different potencies. Patil et al. (4) examined the relative pressor potencies
of ephedrine isomers in anesthetized dogs and found that d-pseudoephedrine in doses of 0.33
to 3.3 mg/kg caused a slight rise in blood pressure, followed by a transitory fall; doses higher
than 9.9 mg/kg produced only a depressor effect. In the present study, the effects of ephe-
drine isomers on blood pressure in rats were compared, and differences in the actions of
three ephedrine isomers, 1-, dl-, and d-forms were observed.

For the blood pressure experiments, male and female Wistar strain rats weighing 150
to 250 g were used in groups of 3-5. The animals were anesthetized with urethane (1.75 g/
kg s.c.) and were heparinized (1 U/g i.v.).

Solution of each isomer was injected into the femoral vein. Right carotid arterial blood
pressure was led through a polyethylene cannula to a pressure transducer (Nihon Kohden

Fig. 1. Pressor effect of ephedrine isomers and depressor effect of d-ephedrine
after dl- or 1-ephedrine intravenous injection in anesthetized rats.

EPH: ephedrine M.B.P: mean blood pressure tracings are from different rats.
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Fig. 2. Influence of reserpine, propranolol and dibenamine on the depressor effect of d-ephedrine and inversion of adrenaline after injection of 1-ephedrine
A: reserpinized rat (5 mg/kg i.p. before 24 hr)  EPH: ephedrine
B: inversion of blood pressure by adrenaline  M.B.P: mean blood pressure
C: injection of propranolol (1 mg/kg i.v.)
D: injection of dibenamine (5 mg/kg i.v.)

MPU-0.5) and recordings were made using a Nihon Kohden RM-150 polygraph.

In anesthetized rats, blood pressure increased after the first injection of any one of the isomers (1 and 10 mg/kg i.v.) (Fig. 1-A). The second injection of 10 mg/kg of d, dl- or 1-isomer increased blood pressure but to a lesser extent while the second injection of d-isomer decreased blood pressure after the first injection of dl- or 1-isomer in the same rat (Fig. 1-B). Neither dl- nor 1-isomer produced such a decrease after injection of d- or 1-isomer (Fig. 1).

In reserpinized (5 mg/kg i.p. before 24 hr) rats, the depressor effect of d-isomer was not produced and conversely d-isomer caused a slight rise in blood pressure (Fig. 2-A). After the injection of 1-isomer, 9-action of adrenaline disappeared and 9-action of adrenaline appeared (Fig. 2-B). The depressor effect of d-isomer was not blocked by propranolol but was blocked by dibenamine (Fig. 2-C and D). The fall in blood pressure produced by the d-isomer is considered to be an indirect action of the d-isomer in liberating substances such as catecholamines or serotonin since the fall disappeared in rats treated with reserpine. The indirect action of d-isomer is produced as a result of being masked 9-action of d-isomer by 1-isomer (Fig. 2). The fall in blood pressure is produced by the depressor effect of a substance other than by 9-action of catecholamine as the depressor effect of d-isomer was not blocked by propranolol, an adrenergic 9-blocker. A correlation with the action of serotonin is thus suggested since the fall in blood pressure disappeared by administration of dibenamine and phenoxybenzamine.

The indirect action of d-isomer is now being examined in addition to its action on blood vessels and the action of liberating such substances as catecholamine, serotonin and others.

REFERENCES
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EFFECTS OF FASTING ON THE HENLE’S LOOP FUNCTION OF RAT KIDNEY

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It is generally known that sodium excretion into the urine increases for several days when a normal person fasts completely. While this phenomenon has been the subject of numerous investigations (1-5), the mechanism of urinary losses of sodium and the location in the nephron where it occurs are obscure. Some authors (2, 5), however, have suggested a localization of the phenomenon to be Henle’s loop and distal tubules by clearance experiments. Therefore, the present experiments were performed to clarify the changing of the function of the Henle’s loop of the fasted rat kidney using the single nephron perfusion technique.

Male Wistar rats weighing 150-260 g were used in the experiments. Rats of the control non-fasted group were given free access to a dry pellet diet (Na 84 mEq/kg, K 110 mEq/kg) just prior to experiment and those of the fasted group were deprived of food 18 to 24 hr prior to experimental procedures. All rats were given tap water.

The animals were anesthetized with Nembutal (50 mg/kg, Abbott) i.p. and placed on a heated table. After tracheotomy, the femoral vein and the left ureter were catheterized, and the left kidney was exposed. During these surgical procedures, 1 ml of Ringer’s solution was infused intravenously to replace surgical losses.

The loop of Henle was perfused according to the method of Cortney et al. (6) as previously described (7, 8). The proximal tubular segment was filled with colored oil to stop the flowing of glomerular filtrate, and the perfusion pipette was inserted into the late proximal tubule in order to perfuse the single nephron. One percent NaCl solution colored with 0.05% lissamine green was used as perfusate and the perfusion rate was 19 nl/min. A collection was made from the early segment of the distal tubule of the same nephron.

Left ureteral urine was collected at appropriate intervals for 2 to 4 hr. Blood samples were collected by heart puncture after the experiment.

The osmolarities of the tubular samples and ureteral urine were estimated with a microosmometer. The sodium concentration of the tubular fluid was determined with an ultramicro-flamephotometer (Erma, Model 677), the sodium and potassium concentrations in

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