PHARMACOLOGICAL ACTION OF EPHEDINE

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Since the isolation of ephedrine from the Chinese drug Ma Huang [Nagai, 1887, 1892, Chen and Schmidt, 1924], several additional bases have been obtained from the same plant. They have been identified as *d*-pseudoephedrine, *nor-d*-pseudoephedrine, *l*-methylephedrine, *d*-methylpseudoephedrine, 'nor-l-ephedrine, and methylbenzylamine by Chou [1926], Smith [1927, 1928], Nagai and Kanao [1928, 1930], and Chen, Stuart, and Chen [1931], respectively. Recently one of us [Chou and Mei, 1934] described the isolation of a new base, to which the name ephedine was gievn. The substance is optically inactive, melts at 87°C, and forms soluble salts with mineral acids. Its empirical formula was determined to be $C_8 H_{18}N_2O_3$.

For pharmacological studies, the hydrochloride of ephedine, m.p 90°C, was used The most unexpected reaction is the effect upon blood pressure. Unlike other bases of Ma Huang, ephedine lowers blood pressure. As shown in fig. 1, a dose of approximately 4 mg/kg in a cat caused a fall of 21 mm Hg. The pressure returned to the original level in 20 seconds. In another animal, one half of this dose also produced a depression of blood pressure. During the fall of pressure, the amplitude of respiration commenced to be augmented slightly (fig. 1)

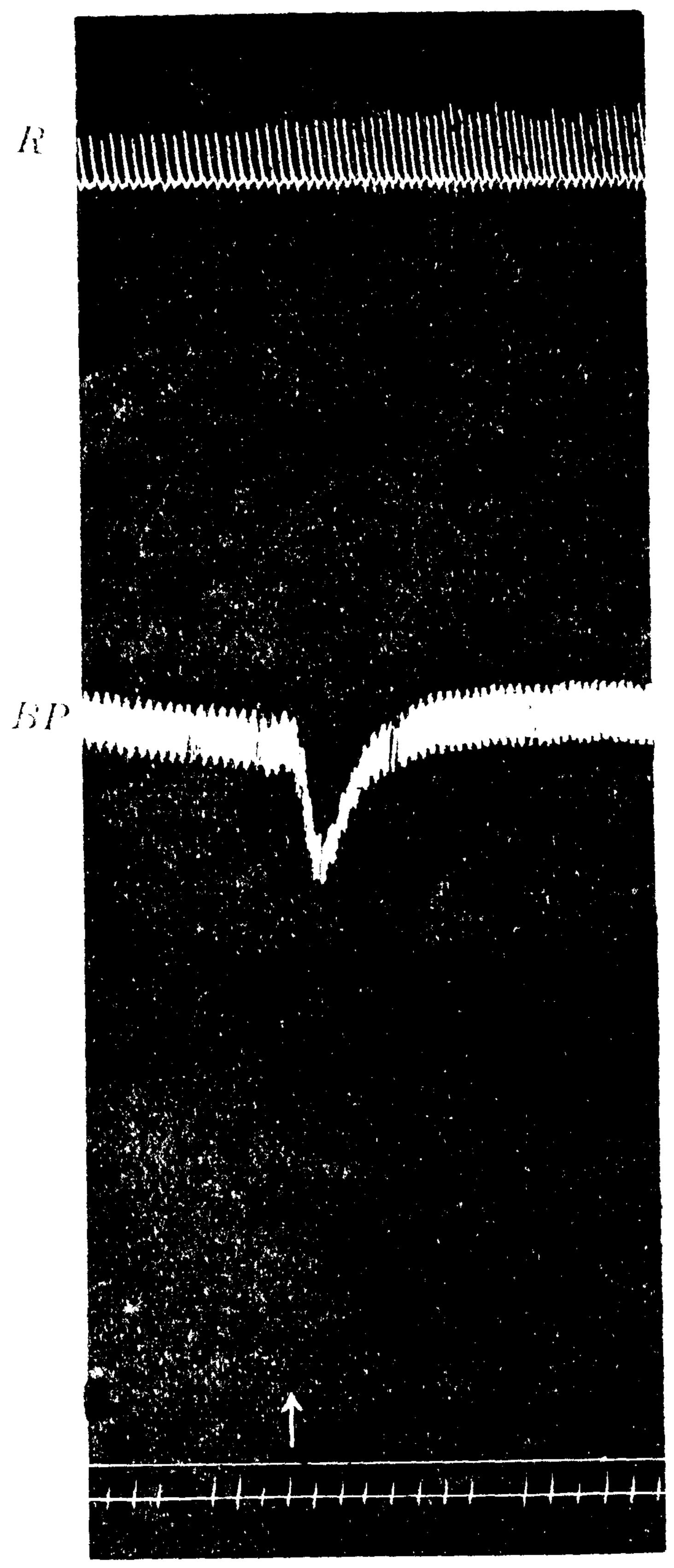


Fig. 1. Action of ephedine on blood pressure (BP) and respiration (R).

Cat, female, 2.491 kg, was injected intravenously, at arrow, with 10 mg of ephedine hydrochloride.

Of the isolated organs, four strips of rabbits' small intestines were tested with ephedine hydrochloride. It was found that concentrations varying from 1:25,000 to 1:10,000 promptly induce a slight inhibition followed by a pro-longed increase of amplitude of contraction. An example is illustrated in fig. 2. In two instances, there was a simple stimulation without the initial inhibition.

Contraction occurs when the guinea pig's isolated uterus is treated with ephedine hydrochloride. Definite responses can be observed with concentrations of 1:12,500 to 1:10,000. The tone which is primarily increased returns to the initial level in 6 to 7 minutes (see fig. 3).

Ephedrine hydrochloride in 1 per cent aqueous solution neither dilates nor constricts the rabbit's pupil.

Owing to the limited supply of material on hand, we did not attempt to determine definitely the mode of action of ephedine. It is probable,

however, that the substance stimulates smooth muscles, and depresses the heart which accounts for the fall of blood pressure. Previously, one of us (K.K.C.) with Wu and Henriksen [1929] reported similar results with several amines which have relatively long side chains. The slight augmentation of respiration may be secondary to circulatory changes.

SUMMARY

Ephedine, a new base isolated from Ma Huang, lowers blood pressure, contracts isolated guinea pigs' uteri, and augments peristalic move-

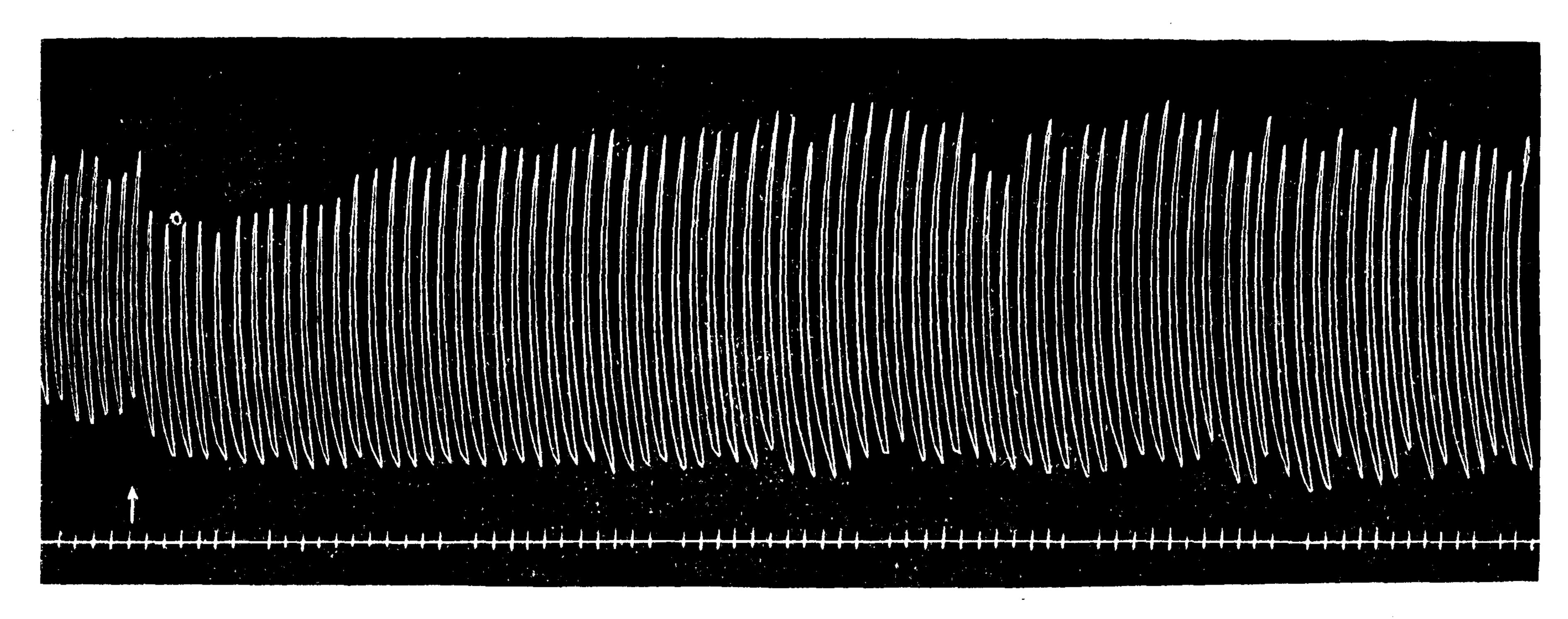


Fig. 2. Action of ephedine on isolated rabbit's small intestines.

A strip was immersed in Locke-Ringer's solution, maintained at 38°C. At arrow, ephedine hydrochloride was added to make a concentration of 1:10,000. Notice the primary inhibition followed by stimulation.

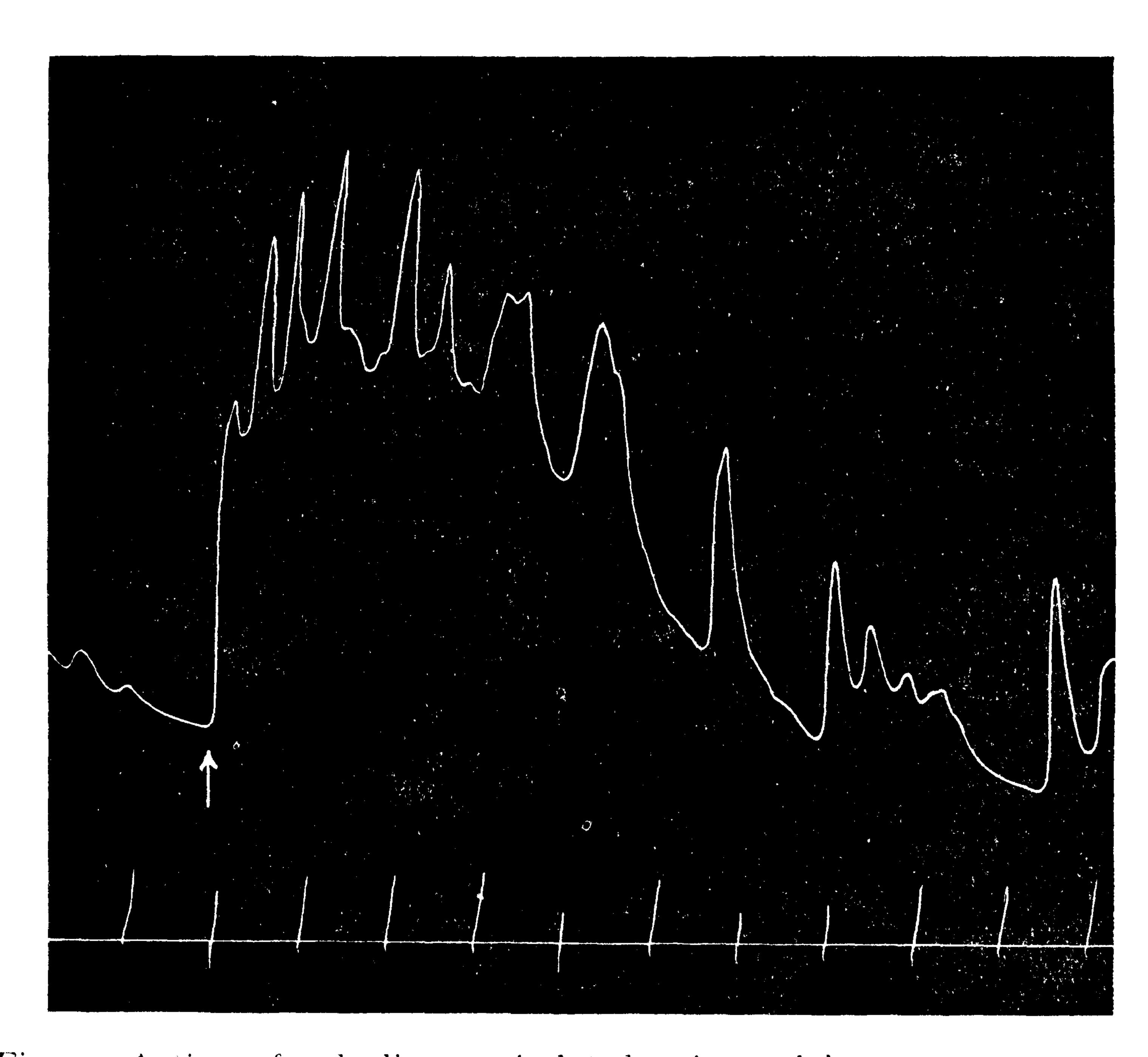


Fig 3. Action of ephedine on isolated guinea pig's uterus.

A strip of the right horn was immersed in Locke-Ringer's solution, maintained at 38°C. At arrow, ephedine hydrochloride was added to make a solution of 1:12, 500.

ments of isolated rabbits' small intestines sometimes preceded by a slight inhibition. It increases respiratory excursions as the blood pressure falls.

LITERATURE

	(1924)	Proc. Soc. exp. Biol., N. Y., 21 , 351. J. Pharmacol., Baltimore, 24 , 339. J. Amer. pharm. Ass., 14 , 189.
CHEN, K. K., Wu, C. K. AND HENRIKSEN, E.	(1929)	J. Pharmacol., Baltimore, 36, 363.
CHEN, A. L., STUART, E. H. AND CHEN, K. K.	(1931)	J. Amer. pharm. Ass., 20, 339.
Chou, T. Q.	(1926)	J. biol. Chem., 70, 109.
CHOU, T. Q. AND MEI, P. F.	(1934)	Chinese J. Physiol., 8, 161.
Kanao, S.	(1930)	Ber. dtsch. chem. Ges., 63B, 95.
NAGAI, N.	(1887)	Pharm. Z., 32, 700.
NAGAI, N.	(1892)	Yakugaku Zassi, 120, 109.
NAGAI, N. AND KANAO, S.	(1928)	Ibid, 559 , 845. (Abstract in German) 101.
SMITH, S. SMITH, S.		J. chem. Soc., London, 2056. Ibid, 51.
Wallin, U.	(1940)	$\mathbf{J}_{\mathbf{I}}$

廊 黃 副 素 之 藥 理 作 用

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超承掇與梅斌夫從麻黃中提出一新有機蘇物名 Ephedine · 已載 於本雜誌,第八卷第二期。此物能降低血壓,增加離體的荷蘭猪子宮 之收縮與離體的兎腸之蠕動,並微助呼吸。