ciated with demonstrable pneumococcus-destroying powers in the blood. The technique employed was the same as that used by the above mentioned workers. This consists, briefly, in seeding varying quantities of pneumococci into mixtures of rabbit serum and leucocytes contained in small tubes, which are then sealed with paraffined corks and attached to an apparatus inside the incubator whereby constant agitation is carried on during incubation.

It was found that the rabbit serum-leucocyte mixtures possessed the power to kill avirulent pneumococci in relatively large numbers but failed to inhibit the growth of virulent organisms even in minute quantities. The results of numerous experiments in which all three types of pneumococci were employed indicated that the ability of a strain of penumococcus to grow in rabbit's blood is dependent on its virulence for the rabbit. The extreme susceptibility of the very young rabbit to certain strains of pneumococcus of low virulence for full-grown animals was found to be associated with an absence of pneumococcidal properties in the blood of the young rabbit. These findings suggest that the relatively susceptible animals possess the same type of defense mechanism against pneumococcus infection as do the highly pneumococcus-resistant species.

3085

Isolation and comparative action of ephedrine pseudo-ephedrine from ma-huang. (Ephedra vulgaris, var. helvetica).

TSAN-QUO CHOU and B. E. READ.

[*From the Department of Pharmacology, Peking Union Medical College, Peking, China.*]

The alkaloids ephedrine and pseudo-ephedrine were isolated by Nagai[1] and Merck,[2] respectively, from *Ephedra vulgaris*. The Chinese drug Ma-huang, variously identified as *Ephedra vulgaris, Rich. var. helvetica, Hk. et Thoms.*,[3] *Ephedra equisetina, Bge.*,[4]

[1] Nagai, *Pharm. Ztg.*, 1887, xxxii, 700.

[2] Merck's Berichte, 1893, 13.

[3] Botanical Nomenclature, Commercial Press, Shanghai, 1917, 1004.

[4] Cowdry, N. H., *J. N. China Royal As. Soc.*, 1922, liii, 158.

has been recently studied by K. K. Chen and Carl F. Schmidt.[5, 6] From this they isolated the alkaloid ephedrine and conducted various physiological experiments. They gave the following physical constants for ephedrine and its salts:

Ephedrine m. p.	210° C.
Ephedrine HCl m. p.	214° C. [α] 25/D −35°.
Ephedrine H_2SO_4 m. p.	242° C.

It has been found that the basic substance isolated from Ma-huang, contains about 20 per cent of pseudo-ephedrine as well as ephedrine, the former being identical in all respects with that obtained by the action of HCl upon ephedrine. The ephedrine, having a melting point of 43°, and being considered to be laevo-rotatory up to now, is found to be dextro-rotatory in water and laevo-rotatory in alcohol. Its specific rotation suffers no change towards the action of dilute HCl, Na_2CO_3 and pepsin in acid solution. Some difference in optical activity has, however, been observed by the introduction of trypsin into its alkaline solution.

Salts of both ephedrine and pseudo-ephedrine were prepared and studied. Generally speaking the salts of ephedrine are better crystallized and less soluble in water and alcohol than those of pseudo-ephedrine. The remarkable *difference in solubility of their oxalates* in cold water affords a good means of separating ephedrine from pseudo-ephedrine, whenever a mixture of these two isomers has to be dealt with.

SALTS OF EPHEDRINE.

Hydrochloride. $C_{10}H_{15}ON.HCl$. prismatic needles, m.p. 216° C. [α] 22/D −32.5°. Easily soluble in alcohol and water. Its aqueous solution is stable at boiling temperature.

Sulphate. $C_{10}H_{15}ON$ ½ H_2SO_4. (Analysis = 7.48 per cent S) hexagonal plates, m.p. 257° [α] 22/D −30° difficulty soluble in alcohol, easily soluble in water, neutral to litmus.

Oxalate. 2 $C_{10}H_{15}ON$, $C_2H_2O_4$. prismatic needles from water m.p. 245°C. with decomposition, neutral to litmus, *only very slightly soluble in cold water.*

Phosphate. $C_{10}H_{15}ON$. H_3PO_4. (Analysis = 11.7 per cent P) crystallized from alcohol in long silky needles m.p. 178°C. acid to litmus.

---

[5] Chen, K. K., and Schmidt, Carl F., *J. Pharm. Exp. Therap.*, 1924, xxiv, 339.

[6] Chen, K. K., *Am. Pharm. Assn.*, 1925, xiv, 189.

SALTS OF PSEUDO-EPHEDRINE.

Hydrochloride. $C_{10}H_{15}ON.HCl$. crystallized from alcohol in stout needles. m.p. 179-181° C. $[\alpha]$ 22/D + 58.75°, very soluble in water and in alcohol.

Sulphate. $C_{10}H_{15}ON$ ½ H_2SO_4 prismatic needles, no sharp m.p. $[\alpha]$ 22/D + 52.5°, easily soluble in water and in alcohol.

Oxalate. 2 $C_{10}H_{15}ON.C_2H_2O_4$. needles. m.p. 218° with decomposition difficulty soluble in alcohol. *Very soluble in cold H_2O,* neutral to litmus.

As far as is known pseudo-ephedrine is very similar to ephedrine in its physiological action. Previous workers have laid particular emphasis on its mydriatic effect. (See Ladenburg und Oelschlägel,[7] Lewin et Guillery,[8] and Günsberg.[9]) The latter states that, "Pseudoephedrine is a powerful mydriatic. Ten per cent solution excites the sympathetic nerve and dilates the pupil after fifteen minutes."

Reference books[10] make the general statement that like ephedrine, "pseudoephedrine is also poisonous." This statement appears to be based on scant information. A set of preliminary experiments conducted in these laboratories show that pseudoephedrine is less toxic than ephedrine for rabbits.[11] When introduced subcutaneously and intravenously the M.L.D. is about 500 milligrams and 100 milligrams respectively, which makes its toxicity relative to ephedrine about 0.645. If pseudoephedrine exhibits the same excellent clinical results obtained with ephedrine, it would be preferable for use on account of its lower toxicity.

---

[7] Ladenburg und Oelschägel, *Bericht. Chem. Gesell.*, 1889, xxii, 1823.

[8] Lewin et Guillery, *Wirkungen von Arzneimitteln und Giften auf das Augen*, 1913, Berlin.

[9] Günsberg, *Virchow's Arch.*, 1891, cxxiv, 75.

[10] Henry, T. A., Plant alkaloids, 2nd edition, Philadelphia, 1924.

[11] Chen, K. K., PROC. SOC. EXP. BIOL. AND MED., 1925, xxii, 404.