ash, structural elements of the plant, selective solvent extractives and volatile oil. The alcoholic extractive was examined and several isolations were made.

REFERENCES.

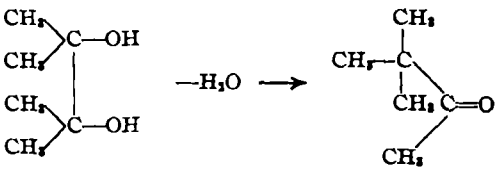
(1) *U. S. Forest Service Circular* No. 134.
(2) *Guide for Chemistry 40*, for Pharmacy Students, *University of Wisconsin Bull.*, page 13.
(3) Treadwell and Hall, *Analytical Chemistry*, 2, page 86 (1928).
(4) *Ibid.*, page 78.
(5) *Ibid.*, page 603.
(6) *A. O. A. C. Methods*, page 41 (1920).
(7) *Ibid.*, page 43.
(8) *Ibid.*, page 180.
(9) *Ibid.*, page 39.
(10) *Ibid.*, page 45.
(11) *Ibid.*, page 96.
(12) *Ibid.*, page 259.
(13) Wallis and Goldberg, *Quart. J. Pharm. Pharmacol.*, 4, 28 (1931).
(14) Clevenger, *Am. Perf. Ess. Oil. Rev.*, 25, 467 (1928).

---

## A CONTRIBUTION TO THE PHARMACOLOGY OF PINACOLONE.*

BY JOHN C. KRANTZ,[1] JR., C. JELLEFF CARR, RUTH MUSSER AND FRANCES F. BECK.

The replacement of the hydrogen atoms in the glycols by alkyl groups confer upon them hypnotic activity. This activity in general increases with the molecular weight of substituent groups. These compounds, known as pinacones, have been investigated pharmacologically. By dehydration of tetramethylethylene glycol, pinacolone is obtained as shown by the following equation:



Thus pinacolone is unsymmetrical trimethyl acetone. No record of a study of the pharmacology of pinacolone was found in the literature (1).

Owing to the structural relationship of pinacolone to the useful hypnotics, the pinacones, the authors decided to investigate its pharmacology.

### PREPARATION AND PROPERTIES.

Pinacolone was prepared for us by Dr. Wilton C. Harden of the firm of Hynson, Wescott and Dunning. The method (2) consists of dehydrating pinacol hydrate by means of concentrated sulfuric acid. Pinacolone is a colorless, oily liquid with a strong camphoraceous odor. It boils at 106° C. and is very soluble in alcohol and ethereal solvents, but is sparingly soluble in water.

---

* Scientific Section, A. PH. A., Dallas meeting, 1936.

[1] Department of Pharmacology, School of Medicine, University of Maryland.

### BACTERIOLOGICAL TESTS.

The similarity of pinacolone to the characteristic mint oils prompted a bacteriological investigation. Frank Hachtel of the Department of Bacteriology of this institution observed that pinacolone, 1:100 aqueous solution, failed to kill the typhoid bacillus and staphylococcus aureus in 15 minutes.

### PERFUSED LEG VESSELS OF THE FROG.

The experimental procedure developed by Läwen (3) and Trendelenberg (4) for perfusing the leg vessels of the frog was employed. All observations were made during the first 30 minutes of the perfusion. One and five-tenths-cc. volumes of various strengths of pinacolone in Ringer's solution were injected into the perfusion fluid. In concentrations of from 0.1 to 0.5 per cent, pinacolone produced no effect (7 experiments). In 1.0 per cent concentration, marked vasoconstriction was observed (3 experiments) reducing the number of drops per minute to approximately $^1/_3$ the normal value.

### HYPNOTIC ACTIVITY.

In the white rat, by stomach tube, small doses of pinacolone failed to exhibit hypnotic activity. In the rabbit, by inhalation, anesthesia was not induced; by rectal administration, doses eliciting any apparent effect, produced no hypnosis but convulsions and death.

In the rat 0.2 to 0.3 cc. per 100 Gm. of rat, by stomach tube (8 experiments) was fatal. Death was not preceded by hypnosis.

The drug produced marked muscular activity, incoördination of the extremities and exophthalmus. Respiration was labored and greatly diminished in rate. At death respiration ceased prior to cardiac stoppage. Upon autopsy, the stomach and intestines were distended with fluid and gas. The liver showed small hemorrhagic areas. Macroscopically the kidneys were normal. The tracheal mucosa was somewhat hyperemic without hemorrhage. Macroscopically the lungs appeared normal.

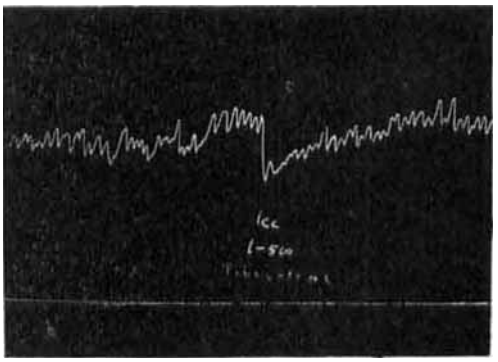


Chart 1.—Effect of pinacolone on isolated guinea pig uterus.

### SMOOTH MUSCLE.

On the isolated uterus of the virgin guinea pig (5 experiments) in concentrations varying from 1:5,000,000 to 1:50,000, pinacolone produced a slight but significant relaxant action. In 1:500 solution, its relaxant action is shown in Chart 1.

### PERFUSED AMPHIBIAN HEART.

On the perfused heart of the frog *in situ* (2 experiments) pinacolone exhibited in 1:50,000 dilution an increased ventricular contraction accompanied by an incom-

plete relaxation of the myocardium. Long perfusion of this solution produced slowing and death. In 1:500 dilution, complete stoppage occurred within 30

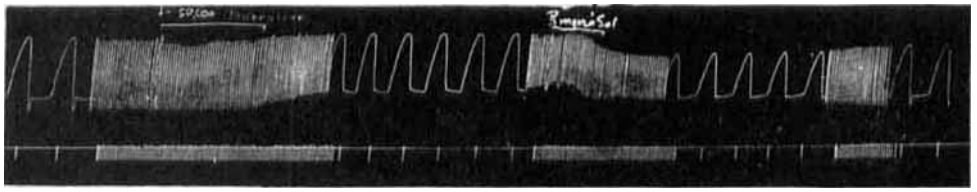


Chart 2.—Effect of pinacolone on the perfused heart of the frog.

seconds with recovery upon perfusion with Ringer's solution. The ventricle stops in diastole prior to auricular stoppage. A typical experiment is shown in Chart 2.

BLOOD PRESSURE IN DOGS.

Under ether anesthesia, pinacolone was administered in doses of 2 cc. by a small tracheal aspirating bottle. A slight depressor response was elicited without significant effect on the respiration. A 2 per cent pinacolone solution in normal salt solution was injected intravenously in doses of 3 to 5 cc. A prompt depressor

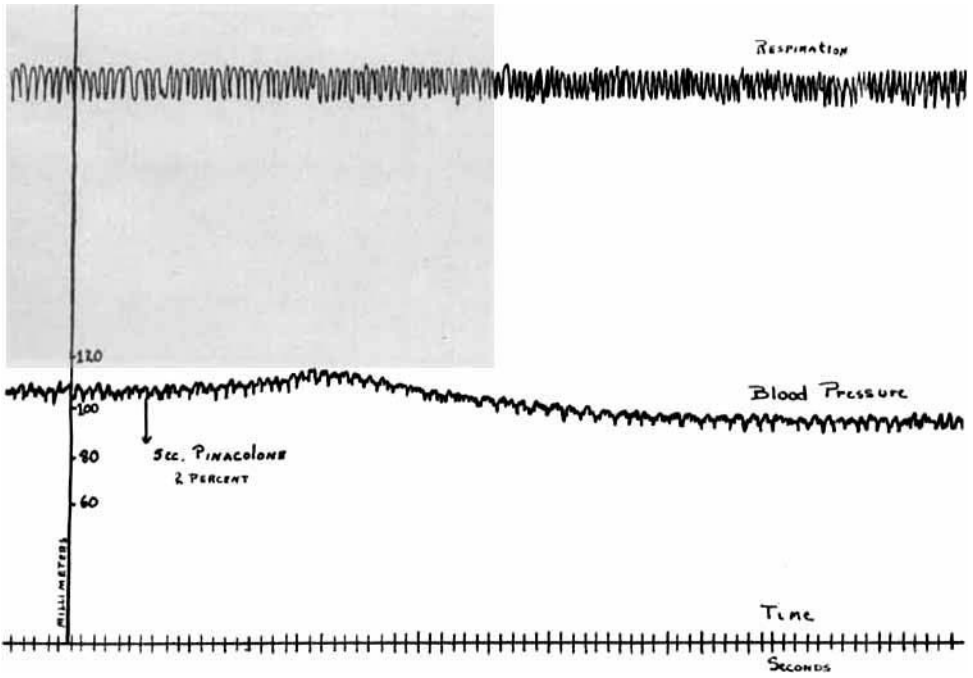



Chart 3.—Effect of pinacolone on blood pressure in the dog.

response (3 animals) was elicited occasionally preceded by a slight rise in blood pressure. The depressor response was not obliterated by massive intravenous doses of ergotamine tartrate, 20 mg. per Kg., or after destruction of the brain. A typical blood pressure response is shown in Chart 3.

NERVE CONDUCTIVITY.

The blood pressure and respiratory effects produced by faradization of the sciatic nerve of the dog (2 experiments) under ether anesthesia were obliterated by a sling of pinacolone. After washing with normal salt solution, nerve conductivity was restored to normal. In a rabbit's cornea (1:500) pinacolone produced hyperemia of the conjunctiva and chemosis. No perceptible local anesthetic action was observed.

DISCUSSION.

The removal of a molecule of water from tetramethylene ethylene glycol with the formation of pinacolone destroys the hypnotic properties of the former and increases its toxicity. The major pharmacologic response elicited by pinacolone is that of reducing the blood pressure, which persists after massive doses of ergotamine and decerebration. The authors attribute the depressor response to vasodilation and cardiac depression.

SUMMARY.

The pharmacology of pinacolone has been studied; as a dehydration product of pinacone it is of interest that hypnotic properties are absent.

REFERENCES.

(1) Oswald, Adolf, "Chemische Konstitution und Pharmakologische Wirkung," Berlin (1924), page 85.

(2) Marvel, C. S., Ed., "Organic Synthesis," Vol. V, John Wiley and Sons, Inc., New York City (1925) page 91.

(3) Löwen, A., *Arch. exptl. Path. Pharmakol.*, 51, 416 (1904); through Sollmann and Hanzlik.

(4) Trendelenburg, P., *Ibid.*, 63, 165 (1910); through Sollmann and Hanzlik.

---

## THE STABILITY OF DIGITALIS POTENCY AS DRUG.*,[1]

BY L. W. ROWE AND H. W. PFEIFLE.

Many contributions can be found in the literature which deal with the stability of the active principles of liquid preparations of digitalis and the majority agree that even the highly alcoholic tincture and fluidextract at times may deteriorate rapidly. On the other hand, very little can be found about the stability of the crude drug and while some seem to take it for granted that the drug is very stable, others infer that much depends upon the conditions of storage, and that the drug can lose activity quite appreciably.

Van Wijngaarden (1) in an article on the storage of powdered digitalis leaves used the cat method exclusively for assay purposes and reported, (1) a severe loss of activity in fresh, undried digitalis leaves even in 4 or 5 days, (2) that 55° to 65° C. is the best drying temperature for the fresh leaves, (3) that the dried powder will keep at least two years without loss of activity in an ordinary stoppered flask.

Chapman and Morrell: The Potency and Standardization of Digitalis in Canada (2) make the following statement:

---

* Scientific Section, A. PH. A., Dallas meeting, 1936.

[1] Research Laboratories of Parke, Davis & Company, Detroit, Michigan.