quired a marked tolerance, and withstood in some of the tests as much as 10 M.L.D of the toxin.

The toxin frequently resisted boiling for 5 minutes.

*Toxic Substance B.* The organisms were grown semi-anaerobically in test tubes for 24 hours, then centrifugalized for one hour at high speed and the supernatant fluid injected intravenously. Three to five cc. of the supernatant fluid killed rabbits in from 6 to 24 hours. Passage through a Berkefeld filter removed the toxic properties. Intravenous inoculation into rabbits was followed by an incubation period of from 1 to 2 hours. The animals exhibited weakness, muscular relaxation, diarrhea, slight watering of the eyes, and died suddenly in convulsions, usually within 7 hours. This toxic substance had an aggressine-like action. It was not antigenic. Rabbits, inoculated with gradually increasing doses, lost weight; they failed to develop any degree of resistance. Autopsy findings, for the most part, showed merely engorgement of the intestinal vessels. This substance is probably identical with the toxic products in young cultures, reported by Zinsser and collaborators[1] for the streptococcus, dysentery and typhoid bacilli, and other organisms.

*Summary.* Cultures of a strain of Friedlander's bacillus were found to yield two toxic substances; one, produced in aerobic cultures, which has a selective affinity for the lungs causing small pulmonary hemorrhages and an intense edema; the other, produced under semi-anaerobic conditions of growth, is probably a non-specific toxic product possessing an aggressine-like action.

[1] Zinsser, H., Parker, J. T., and Kuttner, A., PROC. SOC. EXP. BIOL. AND MED., 1920, xviii, 49.

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## Pharmacology of Veratrum Californicum.

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*Veratrum Californicum* Durand has not been previously studied pharmacologically. Botanically, it is closely related to *Veratrum viride* and *Veratrum album,* although certain differences for identification purposes have been described by Viehover, Keenan and Clevenger, and Viehover and Clevenger.[1] The active constituents

appear to be alkaloids similar to those of the other veratrums, but these have not been isolated as yet. A study of the drug appeared desirable because of suspected activity from reported poisonings, of its easy availability and abundant supply, which is not true of the other veratrums, and of the increasing interest in the therapeutic possibilities of veratrum for the circulation. Our supply was obtained at Cisco, California, 6000 feet elevation in the Sierra Nevada Mountains. Only the underground portion of the plant was found active. This was used as a 10 per cent tincture prepared from a No. 60 powder according to the Type Process P of the U. S. P. X, using 95 per cent alcohol as menstruum, and compared with a tincture similarly prepared from *Veratrum album* (Caesar and Loretz, Germany).

Results with dogs, rabbits, pigeons and frogs indicate that the actions of *Veratrum Californicum* are qualitatively identical with those of *V. album*, but quantitatively the drug appears less toxic, and intermediate between *V. viride* and *V. album*, the lower toxicity being in its favor for therapeutic purposes. The heart is slowed and the blood pressure lowered by small or therapeutic doses through central vagus stimulation, since the slowing does not occur after section of the vagi or atropine. After the second or third dose, the heart is greatly accelerated and the blood pressure raised, continued doses eventually causing collapse and death from direct cardiac depression and paralysis. The respiration is typically slowed or inhibited with toxic doses. Provisionally, the M.F.D in frogs appears to be about 1.75 mgm. per gm. body weight, the definitely effective dose by vein in pigeons and mammals being about 5 mgm. per kilo (0.05 cc. of the 10 per cent tincture), which may slow the pulse 50 per cent and lower the blood pressure (mammals) 40 per cent, and the fatal dose, 37 to 60 mgm. per kilo (0.37 to 0.6 cc. of a 10 per cent tincture). Further work is in progress. This is a preliminary report.

[1] Viehover, A., Keenan, G. L., and Clevenger, J. F., *J. Am. Pharm. Assn.*, 1921, x, 581; Viehover, A., and Clevenger, J. F., *ibid.*, 1922, xi, 166.