with a slight excess of ammonium hydroxide, the precipitate, after washing, is dissolved in diluted sulphuric acid, and re-precipitated with ammonium hydroxide and the resulting precipitate washed until free from sulphates. This precipitate, when dried in a desiccator was a light brown powder apparently free from resinous and gummy material. This was the product mentioned in the physiological experiments in the following paper.

Since Dr. Chillingworth's experiments, we have been able to further purify gelseminine and we have separated this substance into two parts,—one more highly colored and weaker, the other very much lighter and stronger in physiological action.

During the next year, we shall continue this investigation and have strong hopes of bringing the so-called gelseminine into such a state of purity that it may be analyzed for its elementary chemical constituents.

The gelsemine used by Dr. Chillingworth was a purified product resulting from the purification of the alkaloid obtained from this year's lot of drug. It was perfectly white, and apparently free from any of the uncrystallizable coloring matters or uncrystallizable alkaloids.

PHYSIOLOGICAL STUDY OF GELSEMINE AND GELSEMININE.

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In this paper I will adhere strictly to the physiological action of the alkaloids of gelsemium. For the chemistry and preparation of these active principles consult F. A. Thompson,[1] L. E. Sayre,[2] E. D. Reed,[3] Kimberly, Robertson and Vanderkleed,[4] and L. E. Sayre.[5]

We will first take up the physiological actions of gelsemine and gelseminine in detail and later will draw our conclusions.

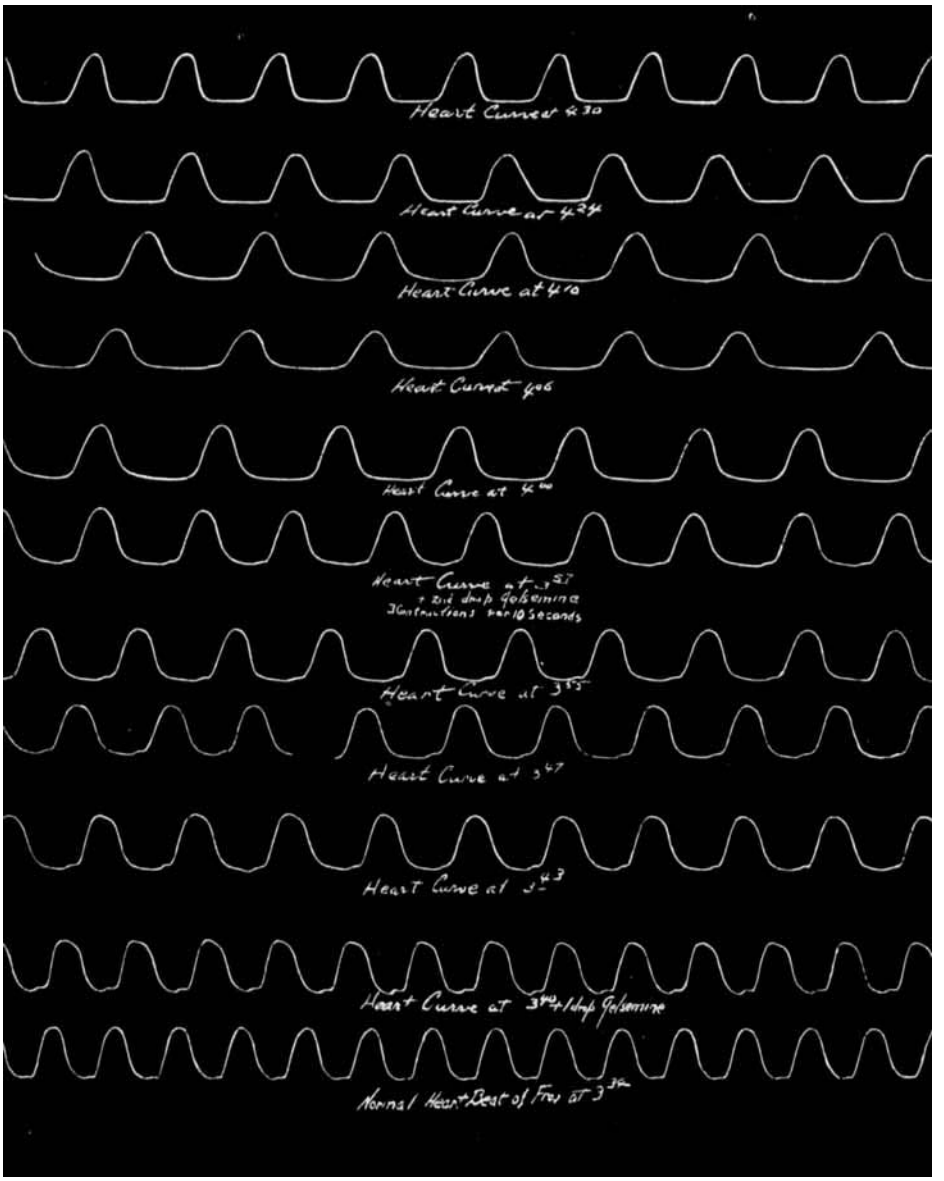
Throughout these experiments two standard solutions were used (one of the active principle gelsemine and the other of the active principle gelseminine) so made that one cubic centimeter of the solution equalled .001 gram of the alkaloid.

Our results though not extensive enough to serve as a basis for far reaching conclusions, nevertheless are of enough importance perhaps to add to the observations of others, and we hope suggest certain lines of experimentation which might be followed up to good advantage.

The two standard solutions referred to above were prepared for us by Prof. L. E. Sayre, Dean of the School of Pharmacy at the University of Kansas. This being the first time that the two alkaloids of Gelsemium have been successfully isolated in the pure state.

The literature on the action of these alkaloids is very confusing and unsatisfactory. Prof. C. Binz, of Bonn, is by far the clearest on this subject and we cannot do better than to quote in brief: "Gelsemium paralyzes the motor centers of the brain as well as the respiratory center in the medulla oblongata. Sen-

[1]Thompson, F. A.: Phar. Era, 1887, page 3.
[2]Lloyd Library: Sept., 1910.
[3]Proc. A. Ph. A., 1908, page 855.
[4]Jour. A. Ph. A., 1912, April.
[5]Jour. A. Ph. A., 1912, May.



EXPERIMENT No. 1.

sibility remains intact, and the irritability of the muscles and the motor nerves is retained. ' Death is produced by paralysis of respiration." Bartholow states that, "Gelsemium dilates the pupils owing to paralysis of the circular fibers."

Recently Prof. Sayre contends that the actions of these two alkaloids are not the same and that the action of one often masks the action of the other.

Experiment No. 1. Frog—weight 35 grams. Showing the true action of the alkaloid gelsemine upon the frog's heart.

Time	Rate	Remarks
3.34	60	Normal.
3.40	60	One drop of gelsemine applied to the heart.
3.43	52	Gradual slowing with increasing diastole, systole still complete.
3.47	50	No marked change.
3.55	46	Heart continues to slow.
3.57	44	Second drop of gelsemine applied.
4.00	36	Here is best seen the action of this alkaloid.
4.06	30	Slowing most marked at this time, systole less complete—diastole prolonged.
4.15	36	Beginning recovery of tone of heart. Rate picking up.
4.30	46	Shows continued recovery of heart from gelsemine.

This experiment shows the typical action of gelsemine, it also shows that its action is not as intense as that of gelseminine—in other words the alkaloid is not as powerful. It is to be noted that here we employed two (2) drops of the preparation to get definite results. Also the absolute recovery of the heart (in about twenty-five minutes suggests that the action is not lasting.

Experiment No. 2. Frog—weight 37 grams. Showing the true action of the alkaloid gelseminine upon the frog's heart.

Time	Rate	Remarks
2.20	65	Normal.
2.24	60	One drop of gelseminine applied to the heart, note immediate slowing.
2.27	54	Slowing more marked.
2.31	50	Systole failing, diastole more marked.
2.35	48	
2.40	40	Tendency to stay in diastole.
2.45	28	Here we find the heart dropping a beat. Rate and output much decreased.
2.47	24	
2.52	20	
2.54	18	Typical gelseminine action.
2.59	14	Characteristic pauses between systole.

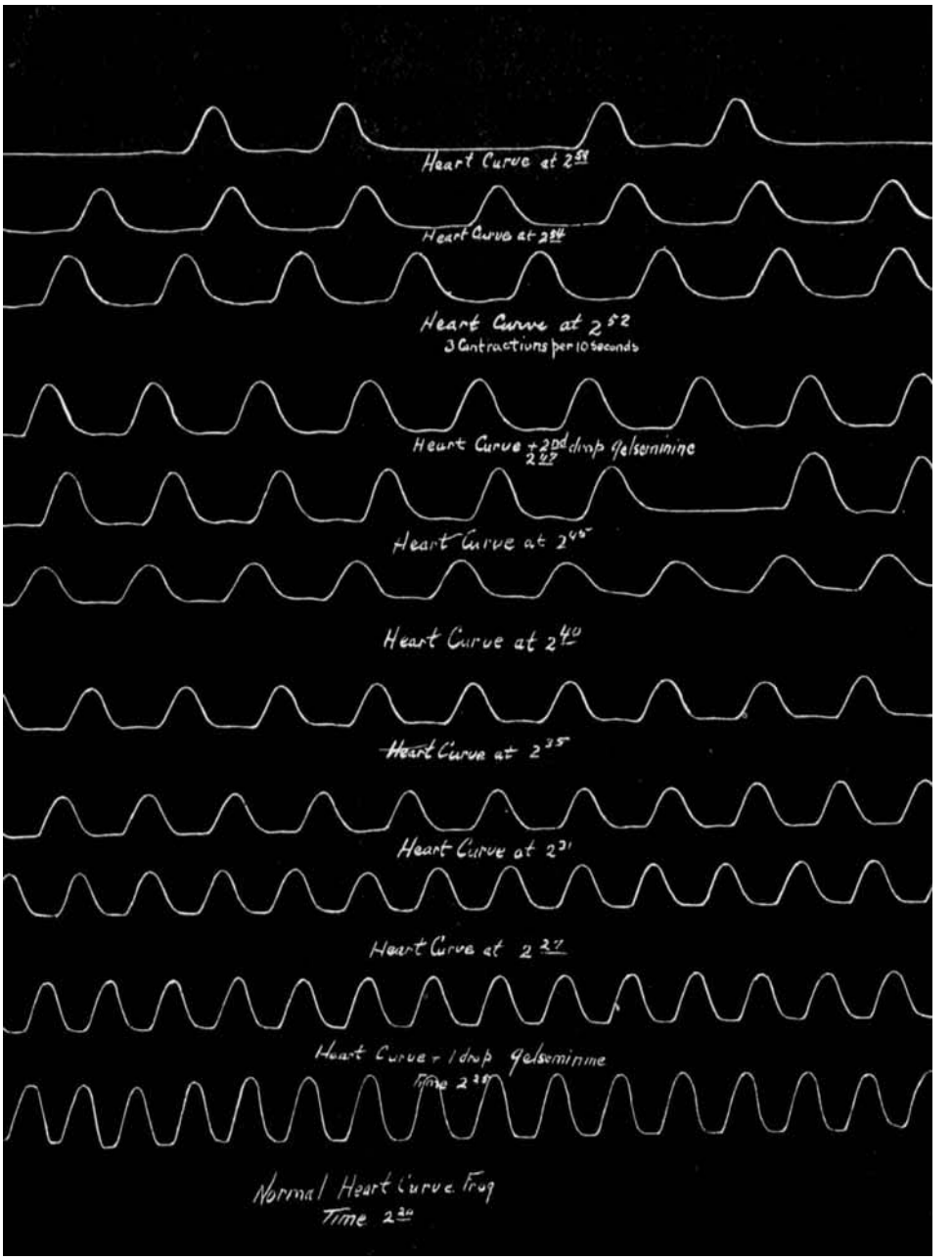
This experiment shows the intense action of the alkaloid gelseminine upon the heart. However it must be borne in mind that this action is via the central nervous system and not as might be first supposed to direct action upon the cardiac muscle.

This primary action upon the nervous tissues we will dicuss later on.

Experiment No. 3. Turtle (medium.) Showing typical gelseminine action upon the heart.

Time	Rate	Remarks
10.55	60	Normal.
10.57	..	One drop of gelseminine applied to the heart.
10.59	50	Slowing of ten beats per minute obtained in two minutes.
11.00	50	
11.04	28	Marked slowing: Systole very imperfect, diastole slightly prolonged.
11.06	25	See above.
11.10	20	Rapid failure of heart in all its phases.
11.14	20	
11.18	00	Heart stopped in diastole.

This record is of especial interest in that it is a well known fact that the



EXPERIMENT No. 2.

heart of a turtle will stand violent abuse—in fact Howell states that after complete stoppage of the heart by electrical stimulation it can be made to resume beating and will recover at the end of four hours.

One drop of gelseminine as is shown in this experiment will completely stop the heart of the turtle in exactly twenty-three minutes, thus showing the marked strength of this alkaloid.

Experiment No. 4. Frog—weight 31 grams. Showing the action of the alkaloid gelsemine on the living frog.

Time	Remarks
3.35	Injected fifteen drops of gelsemine solution into dorsal lymph sac.
3.37	Movements retarded slightly.
3.38	Stimulation required to produce movements.
3.40	Can still retract both legs.
3.42	Cannot swim.
3.43	Respiration is rapid: seems to retain air in lungs.
3.45	Foam at mouth: respirations sixty per minute.
3.46	Reflexes still O. K.
3.48	Same condition.
3.52	Respiration is slower and irregular: hard to count.
3.55	Same condition.
3.58	Abdomen opened: stomach distended with air.

Here we see for the first time the toxic action of gelsemine, caused by the large injection (15 min.) of this alkaloid. In this experiment the heart rate was sixty beats at the end of the experiment, showing that even in toxic doses, the heart of the frog is not affected by gelsemine. Furthermore the sole site of action was centered upon the respiration through the respiratory center of the medulla. This experiment suggests that this solution must be applied direct to the heart in order to produce slowing.

Experiment No. 5. Frog—weight 36 grams. Showing the action of the alkaloid gelseminine on the living frog.

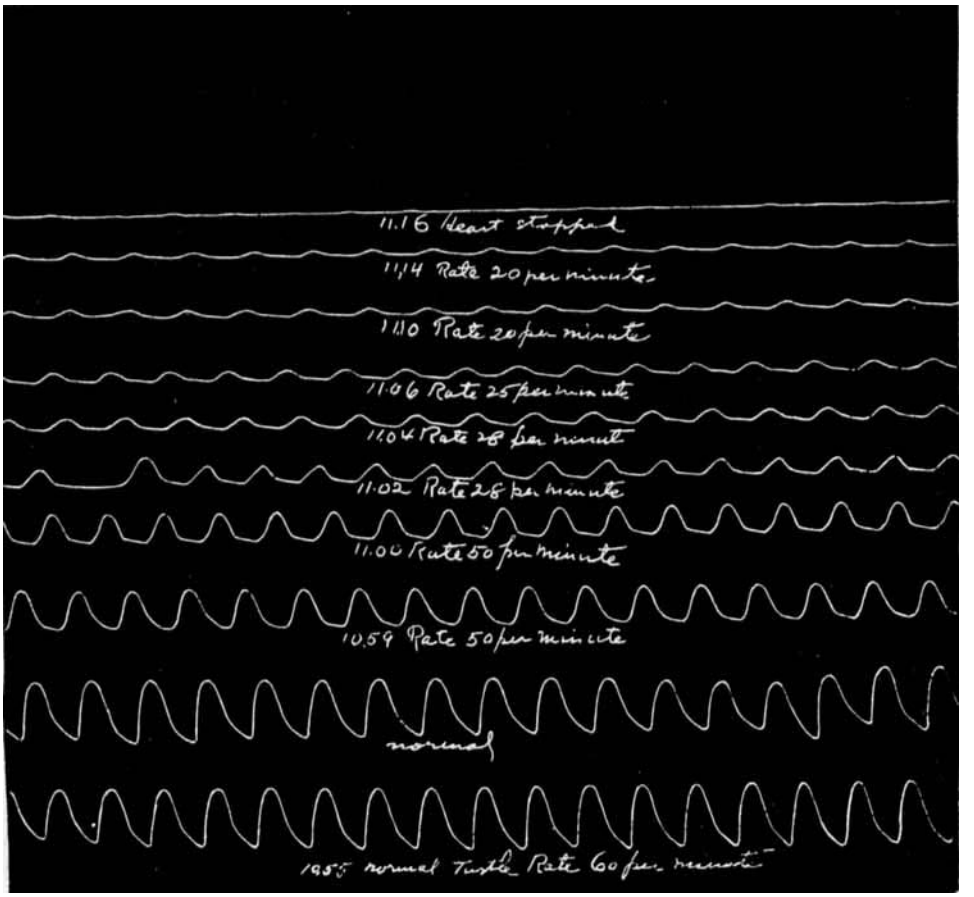
Time	Remarks
2.22	Injected seven drops of gelseminine solution into dorsal lymph sac.
2.23	Movements retarded at once.
2.24	Same.
2.25	Cannot retract the legs.
2.30	Cannot swim.
2.31	Respiration upset: rapid and very irregular: retains air in the lungs and stomach.
2.32	No attempt to recover when placed on back. All power of motion lost.
2.33	Fibillary twitchings.
2.35	Swallows often when trying to breathe.
2.37	Abdomen opened: frog died at 2:36: stomach distended with gas(due to swallowing movements).
	Abdominal organs greatly congested. Heart stopped in extreme diastole.

The full meaning of this experiment is best obtained by comparing it with Exp. No. 4. Noting that only one half as much alkaloid was used and that at the end of the experiment the frog was dead, also note the condition of the heart and the early loss of the reflexes.

It will be seen then that here we get marked depression from the start and that again the site of action is upon the respiratory center. We must also observe the muscular twitchings caused by this toxic dose of the alkaloid gelseminine.

Experiment No. 6. Dog—weight 15.5 K. Showing the effect of gelseminine upon blood pressure. A. C. E. mixture used.

The carotid artery was dissected out and connected by means of a glass cannula to an upright glass tube. This cannula had previously been filled with a saturated solution of magnesium sulphate to prevent clotting. The column of blood was next allowed to remain stationary in the tube for five minutes at the end of which time five (5) drops of the gelseminine solution was injected into the jugular vein. Three (3) minutes later we observed a direct fall in blood pressure amounting to fifty (50) mm. of Hg.



EXPERIMENT No. 3.

Ten minutes later a second injection of five (5) drops was given and we again obtained a drop in blood pressure of twenty (20) mm. of Hg. It will be noted that this dog was not given the customary dose of morphine in order that this factor should not enter into our conclusions.

In Experiment 7 a second dog was used as above but we replaced the gelseminine with gelsemine, using twice the dose used in Exp. No. 6. After the total injection of twenty (20) drops of the gelsemine solution we noted a fall in blood pressure amounting to but 12 mm. of Hg. Here again we see the difference in action.

In results of this nature this question naturally presents itself—where is the action located? Is it in the muscle itself or is it in the central nervous system.

We believe we have answered this question in the following experiment. A frog was pithed in the usual way and next the thigh muscles of one leg were ligated, care being taken to leave the great sciatic nerve free.

The alkaloid was now injected as before into the dorsal lymph sac and the results carefully noted. After a short period of quiescence, sudden fibrillations were noted in both legs. This fact, supported by the fact that in all our experiments the respiration failed long before the heart beat, confirms in a way the earlier investigators, and tends to show that the action of these two alkaloids is primarily upon the central nervous system. The action on the heart and blood pressure we likewise explain through the inhibitory influence carried by the vagi. The dilatation of the eye we attribute to the nervous relaxation of the circular fibers.

CONCLUSIONS.

1. From the evidence at hand it is evident that the action of these alkaloids is upon the central nervous system, and that the action upon the heart is secondary via the vagi.

2. Furthermore as will be seen by examining experiments No. 1 and No. 2, the strength of the alkaloid gelsemine is only about one fourth as great as that of gelseminine, also that the action in the case of gelseminine is much more lasting and profound. Again, these two alkaloids seem to have but little action in common.

3. The therapeutic value of these alkaloids has doubtless been overlooked; and now that they are to be obtained in the pure state their definite action will be utilized.

I wish to express my sincere thanks to my assistant, Mr. L. R. Hoffman, for his valuable aid.

BE AN ORIGINATOR.

Every tub should stand on its own bottom is a homely old proverb, but it is just as true now as when first spoken. Why should an intelligent druggist seek to imitate some successful preparation instead of trying to make one better? If the success of the article is due to good advertising and has merit, then the men who put their brains and money into it deserve their success and reward. If it is a fraud and is successful only because of the credulity and ignorance of the people, the druggist should shun it and not try to grab a few dollars by trailing behind the band wagon with a feeble imitation. It never pays. It is a mighty small man who is satisfied with the crumbs from the table; a real man wants to sit at the table himself, and this means that every druggist should be an originator, not an imitator. The follower always gets the leavings, the leader gets the prizes and the honors.—*American Druggist.*