

work, it was 151; in 1902, 77; in 1903, about 50, and it has remained since that date at about 40. I consider that for a city the size of Havana this means the practical extermination of the disease, as that number of cases in the ordinary course of events would be brought in from the outside, or be due to mistakes in diagnosis.

Panama, I suppose, is as favorable a place for the development of malaria as could be found. The towns of Colon and Panama, at the termini of the canal, are not large enough to do away with the breeding of anopheles; that is, anopheles breeding in the suburbs can very well travel to the centers of these towns, and the population living along the canal in little villages a mile or two apart, between Colon and Panama, are ideally situated for the development of malaria. About one-third of the canal runs through a low alluvial and marshy plain, and the other two-thirds pass through a hilly and mountainous country. Along the banks of the little rivulets, which run in every direction, the anopheles breed just about as well as in the marshy level country, and the very general infection of the population by malaria causes most of the anopheles near human habitations to become infected.

We knew from the experience of our predecessors on the Isthmus that malaria would be our greatest trouble, and we did what we could toward correcting the conditions. Our greatest endeavor has been toward draining the localities near all towns and dwellings, so as to make the ground as dry as possible, and in order to leave as few breeding places as possible for the mosquitoes. In places that could not be drained, oil was used very freely.

With a large body of laborers such as we have here, I think an equally important measure is the giving of prophylactic doses of quinin. We also screened as many of the houses as possible and influenced all inhabitants to use mosquito-bars. These measures followed up persistently have had a great effect in reducing the malaria.

With a force of 22,000 men on the pay rolls during February, we had only twenty-two per thousand incapacitated every day on account of sickness. As I said before, fully three-fourths of this sickness was due to malaria, but the total would not be a large sick rate in a healthy locality in the United States. In my wards at Ancon I have personally treated 1,055 cases of malaria in the last six months. In each of these cases a blood examination was made and the character of parasite recorded. The estivo-autumnal variety largely predominated, but the attacks in general were mild and yielded easily to treatment. Among these 1,055 cases we have had only five deaths. So far as personal care for malarial fever is concerned, I believe that the most important thing the individual can do is to take a small dose of quinin daily. While this will not always prevent attacks, in a given body of men it will enormously reduce the number, and I think will prevent a severe type of the disease when it comes. The good results we have had in hemoglobinuric fever have surprised me most. In these wards we have had twenty cases of hemoglobinuric fever in the past eight months, and of these we have lost three.

The treatment has been the persistent use of quinin as soon as we could get hold of the patient. For the first three or four days the quinin is given hypodermically, but as soon as the patient ceases to vomit it is given by mouth; twenty grains in the twenty-four hours hypodermically and thirty by mouth has been the or-

inary course. I have seen no evil results that could fairly be attributed to the administration of quinin, and I have often wondered if it could be the same disease which the English have on the west coast of Africa and in which so many of their leading practitioners think that quinin does harm.

The malaria we have here at present among the whites seems to me about as grave, and no graver, than the malaria which I treated in the garrisons along the gulf coast in the United States.

I look forward very hopefully to a diminution in the prevalence of malaria down here. It seems to me that by the continuance of our present measures we ought still further to decrease malaria. Year by year the ditching will decrease the number of anopheles near the habitations along the Canal Zone, and the treatment of the patients in hospital and the constant giving of prophylactic quinin will decrease the number of people who are liable to spread the infection, and I believe that these two forces will act and react as time goes on. Our conditions have been as trying in the past year as they are likely to be. We have had a larger force of men than the French had. The population was very generally infected with malaria, and the ditching and draining had just been completed. All these conditions ought to improve steadily as time goes on, and it seems to me a perfectly rational hope that malaria will decrease in the same ratio. Even if we can not decrease malaria below what it is at present, we will have succeeded in building the canal with no greater number of days lost from disease than if we were building it at home. I hope to do better than this.

A COMPARISON OF THE PHARMACOLOGIC ACTIVITY OF THE FLUID EXTRACT OF SQUILL PREPARED ACCORDING TO THE UNITED STATES PHARMACOPEIA 1890 AND 1900.

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Quite a number of more or less important changes in the method of making some of our important standard pharmaceutical preparations have been introduced in the new eighth edition of the United States Pharmacopeia. One of the most radical of these changes is the substitution of acetic acid (10 per cent. absolute acid) in place of alcohol (95 per cent.) as the menstruum for making fluid extract of squill. During the past eight years it has been my privilege to examine personally, or to check the results obtained by an assistant, many samples representing thousands of pounds of fluid extract of squill and other heart tonics for physiologic activity. The method of assay has been substantially that given in an article published in *THE JOURNAL*¹ for making quantitative pharmacological assays of the heart tonics.² For the sake of clearness it may be explained that the strength of the given preparation is determined by a comparison of the minimum fatal dose per gram body weight of frog of the unknown and the known standard, the minimum fatal dose of each being determined at the same time by injecting the properly diluted preparations into the abdominal lymph sacs of frogs of the same size and species and kept under the same conditions. The standard adopted for squill

1. *THE JOURNAL*, A. M. A., Oct. 22, 1898.

2. Further details of this method of assay will be found in the 1905 edition of the National Dispensatory, page 1728.

has been a fluid extract prepared according to the seventh edition of the United States Pharmacopeia from first-class drug, and possesses the average physiologic activity of several fluid extracts produced from different lots of drug, made by the same formula.

Records for the past two years show that the strength of fluid extract of squill (U. S. P., 1890), as it is obtained from the manufacturer, fluctuates between 30 and 140 per cent. of the standard. Usually the activity of the percolate has been found to approximate the strength of the standard within 10 per cent., in this respect being much more uniform in activity than similar preparations of digitalis, which have been found to fluctuate between 50 and 300 per cent. standard.

Immediately after the issuance of the eighth edition of the United States Pharmacopeia, a commercial lot of fluid extract of squill was made according to the new formula which differs so radically from that previously employed. Some difficulty was experienced in making the percolate, and the final product when physiologically assayed was found to possess about 30 per cent. of the activity of the standard. At first it was thought that the drug was not completely exhausted and repercolation was resorted to, but subsequent tests showed that the physiologic action of the second percolate was not materially more active than the first (Table 1).

TABLE 1.—FLUID EXTRACTUM SCILLÆ, UNITED STATES PHARMACOPEIA, 1900. PERCOLATED AND TESTED OCTOBER, 1905.
STRENGTH OF UNKNOWN.

Cage.	No.	Weight.	Dose per gm.	Result.
6	1	29 gms.	.0016	Lived.
6	2	27 gms.	.0018	Lived.
6	3	32 gms.	.0020	Lived.
6	4	22 gms.	.0024	Lived.
6	5	24 gms.	.0028	Lived.
7	1	28 gms.	.0035	Lived.
7	2	30 gms.	.0040	Lived.
7	3	25 gms.	.0045	Lived.
7	3	25 gms.	.0045	Lived.
7	4	26 gms.	.0050	Died.
7	5	31 gms.	.0055	Lived.
8	1	31 gms.	.0045	Lived.
8	2	25 gms.	.0050	Lived.
8	3	35 gms.	.0055	Died.
8	4	31 gms.	.0060	Died.
8	5	32 gms.	.0065	Died.

STRENGTH OF STANDARD.				
4	1	23 gms.	.0010	Lived.
4	2	25 gms.	.0012	Lived.
4	3	26 gms.	.0014	Lived.
4	4	23 gms.	.0016	Lived.
4	5	28 gms.	.0018	Died.
5	1	23 gms.	.0012	Lived.
5	2	25 gms.	.0012	Lived.
5	3	28 gms.	.0014	Died.
5	4	22 gms.	.0015	Died.
5	5	27 gms.	.0016	Died.

Table 1.—Minimum fatal dose of standard .0015; minimum fatal dose of fluid extract being assayed between .005 and .0055. The dose was not closely determined as the product was much below strength, and it was deemed advisable to fortify it by continuing percolation.

It seemed desirable as a check to examine the product of several reputable firms. Accordingly there was obtained on the open market the fluid extract of squill from three different houses made according to the new and the old formulæ. These were assayed as above, except that the end results were checked more closely (Table 2).

The names of these manufacturers are not given for obvious reasons, being designated simply by the letters A, B and C.

TABLE 2.—COMPARATIVE STRENGTH OF FLUID EXTRACT OF SQUILL BOUGHT ON THE OPEN MARKET.

U. S. P., 1890.	U. S. P., 1900.
Menstruum 95 per cent. alcohol.	Menstruum about 10 per cent. acetic acid by weight.
A 26 p. c. as active as standard.	44 p. c. as active as standard.
B 100 p. c. as active as standard.	33 p. c. as active as standard.
C 135 p. c. as active as standard.	50 p. c. as active as standard.

Sample A, United States Pharmacopeia, 1890, for some reason, probably owing to poor drug or imperfect

extraction, is the least active alcoholic fluid extract of squill that has ever come to my attention. It is of therapeutic interest likewise to note the great variation in the activity of both the 1890 and 1900 preparations.

In order to be more certain of the results obtained from the use of the menstrua, four experimental lots of fluid extract of squill were made, two according to the United States Pharmacopeia, 1890, and two according to the United States Pharmacopeia, 1900, all from the same drug, extreme care being taken that the directions given be followed exactly so far as possible. No special difficulty was experienced in employing the alcoholic menstruum, but in the case of the acetic acid, after repeated trials, it was found absolutely impossible to percolate the drug according to the directions given, suction being finally resorted to in order completely to exhaust the drug (Table 3).

TABLE 3.—COMPARATIVE STRENGTH OF FLUID EXTRACT OF SQUILL PREPARED FROM THE SAME LOT OF DRUG ACCORDING TO THE UNITED STATES PHARMACOPEIA OF 1890 AND 1900.

1. U. S. P. 1890, 140 per cent. as active as standard fluid extract.
2. U. S. P. 1890, 140 per cent. as active as standard fluid extract.
3. U. S. P. 1900, 60 per cent. as active as standard fluid extract.
4. U. S. P. 1900, 60 per cent. as active as standard fluid extract.

It may be observed that activity of both products is high as compared with the results given in Table 2. This probably is due to the great care exercised completely to exhaust the drug and to the high quality of the drug.

In order to meet any objections that might be offered against the results as shown by the special method of assay employed, the work was checked by experiments on dogs showing the comparative activity of the two products in producing changes in the blood pressure, which is perhaps the most characteristic physiologic action of the members of the digitalis series (Tables 4 and 5 and Figs. 1 and 2).

Experiment No. 8, Nov. 22, 1905 (Charts 1 and 2).

Dog, weighing 14 kilos, was anesthetized with chlorotone and morphin. A manometer tube was connected with the right carotid; the time-marker recorded seconds.

At 10:45 a. m. the pulse rate was 100, blood pressure 46 mm., mercury, respiration 8.5 a minute. At 10:45.5 a. m., 0.3 c.c. of fluid extract of squill (U. S. P., 1890), diluted to 5 c.c. with physiologic salt solution, was slowly injected into the femoral vein.

At 10:46.5 a. m. pulse rate was 102 blood pressure 54 mm., mercury, respiration 8.

At 10:51.5 a. m. pulse rate was 96, blood pressure 55mm., mercury, respiration 7. The dog was kept quietly in place on the table until 2:40 p. m., when the experiment was repeated.

At 2:40 p. m. pulse rate was 116, blood pressure 48 mm., mercury, respiration 5.5 a minute.

At 2:41 p. m. 0.3 c.c. of fluid extract of squill (U. S. P., 1900), diluted to 5 c.c. with physiologic salt solution, were injected into the femoral vein.

At 2:41.5 p. m. pulse rate was 124, blood pressure 50 mm., mercury, respiration 8.

At 2:46.5 p. m. pulse rate was 138, blood pressure 45 mm., mercury, and respiration 11.

In this experiment particular notice should be given to the tracing (Fig. 1), which shows more strongly than words that the 1900 preparation produces very slight digitalis action. It may be objected that this animal was kept on the table until it was exhausted before the second part of the experiment was continued. Table 5 gives similar results, but is not open to this objection, as the animal received an injection of the 1900 product when first put on the table.

Experiment No. 10, Nov. 23, 1905 (Charts 3 and 4).

Dog, weighing 12 kilos, was anesthetized with chlorotone and

morphin; a canula was inserted in the right carotid; no attention was paid to respiration.

At 8:46 a. m. pulse rate was 102, blood pressure 47 mm., mercury.

At 8:46.5 a. m. 0.3 c.c. of the fluid extract of squill (U. S. P., 1900), diluted to 5 c.c. with normal salt solution, were injected into the femoral vein. It at once produced a transient fluctuating rise in blood pressure, which subsided very quickly to normal.

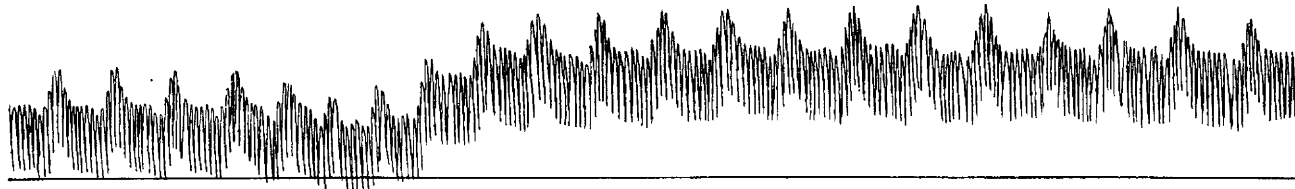
At 8:48 a. m. pulse rate was 104, blood pressure 46 mm., mercury.

At 9:15 a. m. pulse rate was 98, blood pressure still 46 mm.

At 9:20 a. m. pulse rate and blood pressure were the same as at 9:15. Fluid extract of squill (U. S. P., 1900), 0.3 c.c., was injected as before.

At 9:22 a. m. pulse rate was 100, blood pressure 52 mm., mercury.

At 9:27 a. m. pulse was 94, blood pressure 50 mm., mercury.



Pulse rate 100
Blood pressure 46 mm.
Respiration 8.5 a minute.
10:45 a. m.

Seconds

↑ Finished injection into femoral vein
3 c.c. Fluidextractum Scillæ (U. S. P., 1890)
diluted to 5 c.c. with physiologic Saline
solution. Injected very slowly. 10:45½ a. m.

Pulse rate 102
Blood pressure 54 mm.
Respiration 8 a minute.
10:46.5 a. m.

Pulse rate 96.
Blood pressure 55 mm.
Respiration 7 a minute.
10:5:15 a. m.

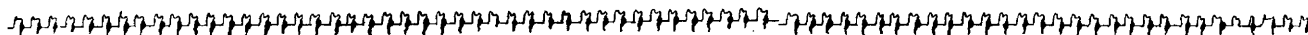
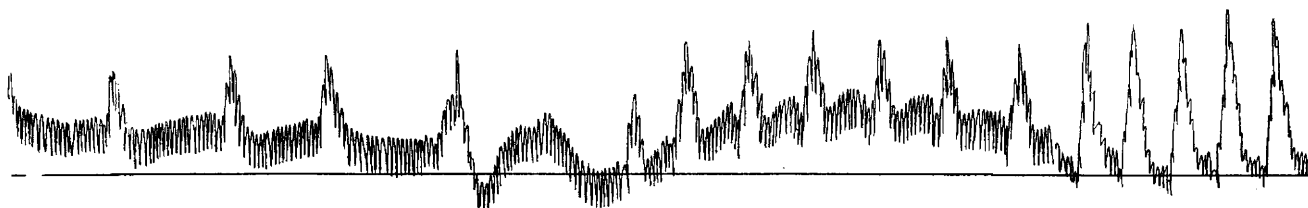


CHART 1. Experiment No. 8. Nov. 22, 1905. Dog—wt., 14 kilos. Anesthetic chlorotone and morphin.



Pulse rate 116
Blood pressure 48 m.m.
Respiration 5.5 a minute.
2:40 p. m.

Seconds.

< 0.3 c.c. Fluidextractum Scillæ (U. S. P.,
1900) diluted as in Chart 1. 2:40 p. m.

Pulse rate 124
Blood pressure 50 mm.
Respiration 8+ a minute.
2:41 p. m.

Pulse rate 138
Blood pressure 45 mm.
Respiration 11 a minute.
2:46.5 p. m.

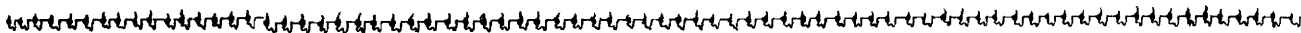
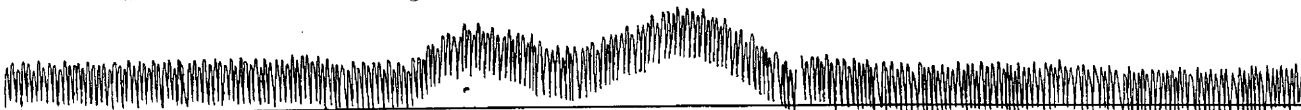


CHART 2.—Same dog as in Chart 1.

Normal tracing carotid

Canula in right carotid.



Pulse rate 102.
Blood pressure 47 m.m.
8:46 a. m.

Seconds.

↑ Finished injecting 0.3 c.c. Fluid ex-
tractum Scillæ (U. S. P., 1890) diluted to
5 c.c. with physiologic saline solution in
femoral vein. 8:46.5 a. m.

Pulse rate 104.
Blood pressure 46 mm.
8:48 a. m.

Pulse rate 98.
Blood pressure 46 mm.
9:15 a. m.

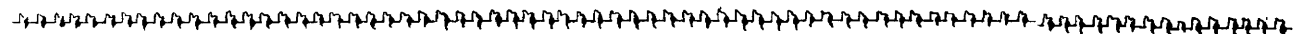


CHART 3.—Experiment No. 10. Nov. 23, 1905. Dog—wt. 12 kilos. Anesthetic, chlorotone and morphin.



Pulse rate 98.
Blood pressure 46 m.m.
9:20 a. m.

Seconds.

↑ Finished injecting 0.3 c.c. Fluidex-
tractum Scillæ (U. S. P., 1890) diluted to
5 c.c. with physiologic saline solution.

Pulse rate 100.
Blood pressure 52 m.m.
9:22 a. m.

Pulse rate 94.
Blood pressure 50 m.m.
9:27 a. m.

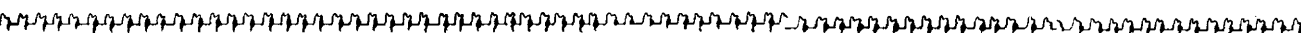


CHART 4.—Same dog as in Chart 3.

CONCLUSIONS

From these results we may conclude that acetic acid is not so satisfactory a menstruum as alcohol for making a fluid extract of squill. The therapeutic results obtained from the use of fluid extract of squill (United States Pharmacopeia, 1900.) will be variable and considerably less than would be expected from the use of the 1890 preparation. It would seem desirable that physicians in prescribing squill should indicate that they desire the preparation of the United States Pharmacopeia, 1890, when they wish to obtain the usual therapeutic action of squill.

130 Longfellow Avenue.

A CASE OF HEMORRHAGE FROM THE STOMACH, DUE TO CIRRHOSIS OF THE LIVER, IN WHICH GASTROENTEROSTOMY WAS DONE ON THE SUPPOSITION THAT THERE WAS GASTRIC OR DUODENAL ULCER.*

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PHILADELPHIA.

NARRATIVE OF CASE.

Patient.—A man of 40 years of age, of rather medium height and weight, family history negative.

Previous History.—There was no tendency to tuberculous or other constitutional disease, and he had never had syphilis. He had always enjoyed good health, was a steady, hard worker in an office where he had large business responsibilities, and he took unusually good care of his health. He lived in the country, where he walked, and rode a bicycle. He ate plain food and never touched liquor or tobacco. About thirteen years previously he had had a severe attack of typhoid fever with very high temperature, but from this he made a complete recovery. His wife said that he had never been ill, and had never taken any medicine beyond an occasional dose of calomel for his liver, which at times had been torpid. He was a dark brunette with rather sallow skin, but his three children have about the same color and appearance.

History of Present Illness.—During the past summer he had great anxieties and business cares involving much additional care and responsibility, and for this reason, he told me, he had been particularly careful of his own health, lived on the simplest kind of food, had special bottled milk brought to his office which he drank between meals, as a precaution against letting his health run down. He could not recollect having had the slightest indigestion or any symptoms referable to his stomach.

Hemorrhage.—On Sept. 21 he reached his home in the country at 10:30 p. m., having been hard at work in his office in the city until late, and went out to the toilet in the yard. He strained quite hard at stool and then came in through the kitchen, which had been closed up and was very hot. He felt nauseated, picked up a basin, and vomited a large amount of blood, which, by actual measurement, was a quart and a pint.

Treatment.—His wife, hearing him come into the house but not in from the kitchen, went to look for him, and got to him just at the end of the vomiting attack. He was so weak that she put him down flat on the kitchen floor, and his pulse disappeared entirely from the wrist. His wife, who is a physician, gave him strychnin and ergot hypodermically. His little daughter had been ill with typhoid fever and there was in the house and ready a sterile salt solution with apparatus for

intracellular infusion. This his wife got at once and pumped into him one quart of the solution, aided by a trained nurse who was in the house, and then she summoned other assistance. Undoubtedly the man would have died from the loss of blood if this plan of treatment had not been instituted so promptly. Some of the saline solution was also injected into the bowel, and after its use brownish-red blood came away.

Subsequent History.—Conditions improved, and in about two hours he was lifted by two men and carried into the next room and laid flat on his back on a mattress on the floor. In less than half an hour he had another severe hemorrhage from the stomach, vomiting without effort one quart and half a pint of blood. His collapse was most profound, and Dr. T. Branson, who had been hastily summoned, and Dr. McCollin gave him strychnin and ergot hypodermically, and thirty drops of adrenalin (repeated in an hour) was given by the mouth. Morphine was also administered. His condition was so bad and his weakness so profound that they could not remove his outer clothing, and he was kept flat on the floor for five days. He was seen at this time also by Dr. Musser, who agreed in the diagnosis of ulcer and advised that a gastroenterostomy be done. This was also urged by Dr. Branson, but Dr. John H. Gibbons, who saw him at the same time, was opposed to immediate operation.

At the end of five days the man was taken to the Bryn Mawr Hospital and kept under observation for two weeks. Nothing whatever was given him by the mouth and he was nourished entirely by the rectum. The bowel was irrigated daily with normal salt solution, and tarry evacuations persisted until about the twelfth day. Peptonized broth and other peptonized preparations were given every six hours. Malted milk enemata were tried, but were always expelled. For two weeks the man had no food by the stomach, and, while the rectum retained the nourishment introduced into it, he became cross, irritable and slightly delirious as the result of extreme hunger. He was taken back to his home on October 7, where I saw him for the first time on October 9.

On this date an enema was given, and after some straining he complained of distress and gas in the stomach and bowel. On inserting a rectal tube to carry off the gas the end became covered with tarry material and on irrigation more was found. No food was given by the mouth for twenty-four hours. The irrigations were dark-colored for five days.

The patient reacted well from this setback, but the anemia was much more marked. With cautious use of food by the mouth and rectal feeding his general condition improved very much and his color showed he was making blood fast.

On the morning of October 15 he awakened his wife, who was lying asleep on the foot of his bed, to tell her that he felt very uncomfortable in his stomach—he had a feeling of distension and nausea. Almost immediately he vomited a considerable quantity of blood, and during the day he passed tarry material from the bowel. This day he was brought in an ambulance to the city, where, after his arrival, he again vomited a little blood and had black, tarry stools.

Consultation.—Dr. M. J. Lewis saw him with Dr. McCollin and me in consultation. He was extremely pale, showing evidences of internal hemorrhage, although his pulse was fairly good. He had edema of the feet and fluid in the abdomen; but this we thought to be confined to the large bowel and was probably a collection of fluid blood. The heart's action, considering the profound anemia, was good. The kidneys were acting well and the spleen and liver did not seem to be altered in size from the normal. His temperature was slightly above normal. He had vomited some little blood the day before, and had passed, and was passing, dark, tarry material from the bowel. His condition was so extremely grave that we deemed it best to wait, if possible, for a few days before deciding on operation, to enable him to regain the ground lost from this additional hemorrhage. He was given adrenalin chlorid, strychnin and nourishment by the bowel.

Examination of Blood and Urine.—On this date the following examinations were made of the urine and blood:

Urine: Light amber, clear, no sediment, acid reaction; sp.

* Read before the College of Physicians of Philadelphia, Feb. 7, 1906.