

A CHEMICAL COMBINATION BETWEEN MORPHINE AND ASPIRIN.*

BY C. B. JORDAN AND MARGARET S. KLEMME.¹

Our attention was called to the unusual narcotic effects produced by capsules supposed to be prepared in accordance with the directions in the following prescription:

Dover's Powder
Phenacetin
Acetylsalicylic Acid of each 2 grains
Send 15 such capsules

Sig.: One every 3 or 4 hours with plenty of water.

The capsules caused the patient to go into a stupor somewhat resembling sleeping sickness. The dose was repeated before the attending physician surmised that there was something wrong in the compounding of the prescription. The physician said:

"I took one of these capsules myself, and it produced signs and symptoms in me which I am sure were more marked than would have been produced by one fourth grain of morphine. The signs and symptoms produced in another individual were also much more marked than would have been produced by the same quantity of morphine, so that I am convinced from this standpoint that these capsules contain more than one fourth grain of morphine."

Our first report made on the capsules to the physician, is as follows:

First. When the capsules reached us, the material was massed in a solid condition and separated from the walls of the capsule. When the capsule was opened the material easily dropped out, but was very hard, and it was necessary to cut it with a knife or break it with a pestle. We have no explanation for the hardness of this material, since capsules made according to the directions of this prescription did not contain hard material, unless the ingredients were massed with honey or glycerin or something of that sort. We were informed that the material was not massed. We can offer no explanation for this material setting as it did, unless some chemical action unknown to us took place.

Second. We prepared capsules according to the directions of this prescription, using our own Dover's powder. The Drug Company sent us a sample of their Dover's powder, and we made capsules according to the prescription, using their Dover's powder. The following experiments were performed on these three kinds of capsules: (a) The solubility of the material in water and alcohol was determined. The capsule submitted to us dissolved completely, leaving no residue that could be detected by our highest power microscope. Our capsules did not dissolve but left considerable residue in which it was easy to detect histological features of ipecac and of opium. The capsule made from the Drug Company's Dover's powder did not dissolve completely, but left a residue in which it was easy to identify the histological features of opium and ipecac. From this experiment we are sure that the capsules sent us did not contain any Dover's powder.

Third. The capsules were tested for the presence of phenacetin, aspirin and morphine, and all these were found to be present.

Fourth. Five guinea-pigs were given capsules made according to the prescription from our Dover's powder. No appreciable results were indicated. A day later, these same five guinea-pigs were given capsules as follows: Three were given capsules made according to the prescription from the Dover's powder submitted by the Drug Company and one was given one of the capsules prepared from our Dover's powders and one was given one of the capsules sent us. The first four pigs showed no appreciable reaction. The last pig (the one that received the capsule sent us) showed no reaction for about three and one-half hours and then began to show stupor. This increased until the pig did not respond to outside stimuli, but sat in the corner

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of his cage showing considerable stupor, which did not pass away until about six hours after its appearance. This proves conclusively that the capsule contains a narcotic much stronger than could possibly be secured from a capsule filled according to the directions on the prescription.

"From the above experiments we are sure that these capsules did not contain Dover's powder, but did contain aspirin, phenacetin and morphine."

The Drug Company involved believed that, if an error was made, the material used instead of Dover's powder was heroine or dionin. With this in mind we made further tests and the second report is as follows:

"*First.* All the material of the capsule readily dissolves in chloroform. Morphine hydrochloride does not dissolve in chloroform, but heroine does.

"*Second.* *Very careful tests* compared with known material convince us that the material present gives all color reactions of morphine and does not give the color reaction of heroine.

"*Third.* A quantitative analysis of the contents of the capsule shows only $\frac{1}{10}$ grain of morphine.

"*Fourth.* We are fully convinced that we are working with a chemical compound that has been formed within the capsule, and since it is an unknown compound, it is impossible for us to make a quantitative determination that we can fully rely on. We are preparing mixtures of phenacetin, aspirin and morphine, and moistening them and allowing them to stand, in hopes that we can secure a substance similar to the contents of the capsule."

The third report reads as follows:

"Acting on your suggestion, we have carefully tested dionin by all the tests we know, which are color reactions, and I am inclosing a copy of our chart of tests. Study these tests and I believe you will come to the conclusion that the mixture in your capsule resembles morphine hydrochloride much more than it does dionin.

"We have made a mixture of two grains each of morphine hydrochloride, aspirin and phenacetin, and have heated the mixture occasionally on the radiator. We find that the reaction is taking place similar to the reaction in your capsule. We also find that the solubility of the mixture in chloroform is increasing. You will remember that the solubility of mixture in chloroform was the one surprising thing to us, as fresh mixtures of morphine hydrochloride, aspirin and phenacetin do not dissolve in chloroform. We have also tested this mixture that we heated and find that our tests give results similar to that given by your capsule. This is reported in column six of the color chart.

"We still believe that your capsule contained morphine, phenacetin and aspirin, and that a chemical action had taken place in the capsule."

The report of the color tests is as follows:

Reagent.	REPORT OF TESTS.				
	I. Morphine hydrochloride.	II. Dionin.	III. Dry Substances. Morph. HCl + aspirin + phenacetin.	IV. Dionin + aspirin + phenacetin.	V. Your capsule.
Sulphuric acid + 0.005 Gm. selenious acid	Blue to green to brown	Bright green to brown to yellow	Green to brown to yellow	Green to brown to yellow	Blue to green to brown to yellow
Sulphuric acid + 0.005 Gm. molybdic acid	Purple to pink	Brown to bluish	Purple	Brown	Purple
Sol. of formaldehyde + 1 drop sulphuric acid	Purple to wine	Brown to brownish purple	Purple to wine purple	Brown to purple	Purple to wine
Nitric acid	Reddish orange to yellow	Yellow	Orange red to yellow	Yellowish green	Reddish yellow

REPORT OF TESTS—(Concluded).

	Aqueous Solutions of:					
	I. Morph. HCl.	II. Dionin.	III. Morph. HCl + aspirin + phenacetin.	IV. Dionin + aspirin + phenacetin.	V. Your capsule.	VI. Our heated mixture of No. III.
Pot. ferricyan. T.S. + 1 drop FeCl ₃ T.S.	Blue	Blue, after long time	Blue, slowly	Blue, slowly	Blue, slowly	
FeCl ₃ T.S.	Greenish blue	Yellow	Greenish blue	Yellow	Purple	Purple
FeCl ₃ T.S. + heat	Brown	Brown	Brown	Wine	Purple	Purple

REPORT OF THE PHYSIOLOGICAL TEST ON GUINEA-PIGS.

Date.	Time.	Pig.	Dose.	Effect on:			
				Respi- ration.	Heart action.	Eye.	Reflex.
Dec. 10	10:00 A.M.	1	Aspirin	None	None	None	None
			Phenacetin				
			Our Dover's P. each 2 grs. 15 capsules				
Dec. 10	10:00 A.M.	2	Same	None	None	None	None
Dec. 10	10:00 A.M.	3	Same	None	None	None	None
Dec. 10	10:00 A.M.	4	Same	None	None	None	None
Dec. 12	8:30 A.M.	1	Drug Co.'s Dover's P.	None	None	None	None
			Aspirin Phenacetin each 2 grs. 15 capsules				
Dec. 12	8:30 A.M.	3	Same	None	None	None	None
Dec. 12	8:30 A.M.	4	Same	None	None	None	None
Dec. 12	8:30 A.M.	2	Suspected capsule	None	None	None	None
	10:30 A.M.	2		Slower	Slower	None	None
	12:30 P.M.	2		Slower	Stupid and inactive	None	None
	8:30 P.M.	2			Stupid and inactive	None	None
Becomes practically normal after 24 hours.							
Dec. 16	9:05 A.M.	1	1/16 gr. morph. sulph.	None	None	None	None
Dec. 17	10:40 A.M.	3	1/8 gr. morph. sulph.	None	None	None	None
Dec. 18	12:20 P.M.	2	1/4 gr. morph. sulph.	None	None	None	None
Dec. 21	9:10 A.M.	2	Morph. hydrochl. 1 grain				
			Phenacetin				
	10:10 A.M.	2	Aspirin each 2 grains	Slow	Stupid	None	None
	12:30 P.M.	2		Slow	Stupid	None	None
	1:30 P.M.	2		Slow	More active	None	None
2:00 P.M.	2		Faster	More active	None	None	

Test for Cl in the capsule from Drug Company *positive*.

CONCLUSIONS.

1. The suspected capsules contained morphine hydrochloride, aspirin and phenacetin.

2. A chemical combination probably took place between the morphine hydrochloride and the aspirin, giving the product a narcotic effect resembling heroine. We believe this to be true because the physical conditions of the contents of the capsule and the pronounced narcotic effect produced indicated it. The contents of the capsule prepared from morphine hydrochloride, aspirin and phenacetin, slightly moistened and heated occasionally on the radiator, underwent the same physical change and produced a similar pronounced narcotic effect.

3. We believe that when prescriptions containing aspirin and morphine are called for, the pharmacist should be very careful that the material be dry and *the patient should be cautioned*.

4. The suspected chemical combination of morphine and aspirin should be further investigated.

THE PRESCRIPTION DEPARTMENT.*

BY ROBERT J. RUTH.

Some time ago a friend of mine, whom I had not seen for a couple of years, dropped into my office. He is a pharmacist located in a town of goodish size about 150 miles from New York. He is no Babbitt and whenever I have the opportunity for a visit with him, I carry away a good thought or two to ponder over.

He has been in business for perhaps a quarter of a century, has owned several drug stores in various locations in the same town, but to my knowledge has never owned more than one store at a time.

Possessing an excellent education, academic as well as scientific, and being a prominent member of this ASSOCIATION, he has—as one would suspect—always felt a strong leaning toward the professional side of pharmacy. Although some of his stores have been large establishments, with much miscellaneous merchandising and fountain business in evidence, they have always presented a highly dignified appearance and exuded an atmosphere strongly smacking of professionalism. The man's appearance and personality enhanced the reputation for accurate and trustworthy prescription compounding which his stores always enjoyed in the community.

Last week he told me that he has moved to a new location and that his store is now a strictly professional pharmacy, with no fountain or side lines, and that he is doing splendidly. He has at last found it possible to open the flood gates to a suppressed desire and practice professional pharmacy exclusively.

Included among the interesting contents of the narrative which he related was the statement that under present conditions only one drug store in fifty can operate successfully as an exclusive prescription store.

After he left, I reflected upon that statement. It means that in this broad land of ours with its more than one hundred million inhabitants, there is only enough prescription and other professional work available to support about 1000 strictly professional stores. I believe my friend is correct in his estimate.

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