

which includes 0.009% creatinine nitrogen, so that the base fraction may be stated to contain 0.09% basic nitrogen. About 11% of this falls into the purine group from which we isolated adenine as picrate and a substance not xanthine which agreed upon analysis with the formula $C_5H_4N_4O_2$. Separation by means of silver and baryta gives a "histidine" fraction from which nothing but a very doubtful trace of histidine picrolonate could be obtained. It contains considerable material giving the diazo color test. In the arginine fraction amounting to about 24% of the basic nitrogen a considerable quantity of arginine was isolated as picrolonate. Aside from a trace of creatinine picrate also found in this fraction more than half of the material is unaccounted for. In the lysine fraction a very small part of the nitrogen is accounted for by the isolation of lysine picrate equivalent to 0.05 Gm. lysine nitrogen from a solution containing about 1.0 Gm. of nitrogen.

Isoleucine was incidentally identified.

KALAMAZOO, MICH.

STUDY ON THE ANTI-DIABETIC PROPERTIES OF *TECOMA MOLLIS*.*¹ PRELIMINARY REPORT.

BY G. G. COLIN.

For many years we have been deeply interested in the researches carried out by several investigators who have devoted much time to the scientific study of pancreatic hormones of animal origin.

More recently it has been found that active metabolizing vegetable tissue contains an insulin-like substance which lowers blood sugar.^{2,4,6,7} Dr. J. B. Collip¹ experimented with old dry leaves of *Diascia spicata* with negative results.

We have experimented with dry leaves of *Tecoma mollis*¹⁵ (commonly known as "Tronadora" in this country) and obtained a decrease of blood sugar in the diabetic patient. This herb has been and is used considerably by diabetics on account of its beneficial effect. Many of them claim to have been cured by it. This material is carried by all druggists as dry leaves and as a fluidextract, and it is hard to find a doctor who has not prescribed it or at least heard of it.

Dr. Manuel Barreiro of Dr. Gabriel Malda's Clinic has had experience with the administration of this drug and informed us that in many cases very remarkable results are obtained by the use of a simple infusion of Tronadora.

There are, of course, a hundred varieties of herbs claimed to have various curative properties, but in the majority of cases the claimed therapeutic value is mostly imaginary. Bearing this in mind we thought it would be interesting to determine as far as possible the actual therapeutic value of this drug.

Upon questioning some diabetics who have used this drug we found that in some of them sugar in the urine had decreased and finally disappeared in from

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EDITOR'S NOTE: The author will welcome cooperation of an institution, equipped for the investigation of the physiological action of this material.

2 to 3 months. Two cases in particular were interesting, one diagnosed as hepatic diabetes and the other as pancreatic diabetes. The urine in both patients became sugar-free in about 3 months. These patients state that they are eating a free diet and even indulge in eating candy in moderate amounts without sugar appearing in the urine.

Diabetics take this drug in the form of an infusion or as fluidextract. The first step in this investigation was to ascertain the composition of the drug. According to the Mexican Pharmacopœia the composition is as follows:

Fatty matter.....	1.24- 2.10%
Resins.....	12.00-14.00%
Alkaloid soluble in chloroform.....	0.28- 0.30%
Alkaloid soluble in ether.....	0.03- 0.05%

From the method of preparation of extracts commonly used, whether hot water extraction or using 80% alcohol as menstruum, the alkaloidal content of the drug does not appear in the extract. Our examination of the solutions prepared by either method failed to show the presence of alkaloids.

The fluidextract contained a fairly large amount of gums and resins which were easily precipitated by dilution with 2 to 3 volumes of water and allowing to stand several hours and filtering. This precipitate contains a large amount of gums and resins easily soluble in 10 per cent NaOH and a very small amount of insoluble residue. Examination of the solution free from gums and resins when treated with several reagents gave the following reactions:

Reagent.	Solution acidified with HCl.	Solution without HCl.
Millon		×××
Picric acid	—	—
Mayer	—	—
Hydrochloric acid	××	
Nitric acid	××	
Acetic acid		—
Absolute alcohol		—
Phosphotungstic acid	×××	×
Wagner		××
Potassium ferrocyanide and acetic acid		—
Lead acetate		×××
Saturated ammonium sulphate		×××
Magnesium sulphate		××
Biuret		× faint
K ₂ Ce ₂ O ₇		×
Bromine		×

With hydrochloric and nitric acids the precipitate redissolved on warming and reappeared on cooling. With phosphotungstic acid the amount of precipitate increased upon acidifying with hydrochloric acid. The greatest amount of precipitate was obtained with Millon, lead acetate, and ammonium sulphate reagents. From these results, the proteins present appear to be proteoses. The abundant precipitate obtained with Millon's reagent suggests the presence of a protein, such as tyrosin, since it precipitates phenol derivatives in which one hydrogen atom has been substituted by a hydroxyl group. In order to confirm this assumption, proteins were precipitated by saturation with ammonium sulphate,

filtered, washed, redissolved and treated with the same reagent. Since gallic acid is present and this substance is precipitated by this reagent, there is a possibility that the proteins were not or could not be thoroughly freed from contamination with gallic acid by the process used.

The solution was also treated with gelatin and with hide powder, but the coloration produced upon adding FeCl_3 persisted after the process of detannization.

The fact that a simple infusion of the drug has anti-diabetic properties led us to prepare an aqueous extract by a method similar to that employed by Dr. Nixon of Texas in the preparation of an injectable solution of *Castella Nicholsoni*.¹⁴

This extract for hypodermic use was tested for toxicity in guinea-pigs and rabbits; 2 cc. per Kg. wt. in the guinea-pig and 3.5 cc. per Kg. wt. in the rabbit proved to be harmless. There was no formation of abscess nor any other apparent undesirable effect.

Chopra and Bose¹³ experimented in India with an herb called *Cephalandra Indica*, but when they injected it they found it had no effect.

In order to determine whether the Tronadora extract would have any effect on blood sugar when applied subcutaneously to the diabetic, we tested it in small doses at the Hospital de Jesús Nazareno, under the supervision of Dr. Alvaro Sosa.

The results were positive as far as blood sugar is concerned. Blood sugar determinations were made with a Kuttner's microcolorimeter. Patient E-9, a woman 48 years old, married, weighing 43 kilos—the results were as follows: Average blood sugar before treatment 0.560 per cent.

	Date.	Blood sugar before injection.	Blood sugar 2 hours later.	Per cent.
1	2/ 8/26	0.472%	(1 cc.) 0.452 (fasting)	4.2
2	2/18/26	0.436%	(1 cc.) 0.372 (fasting)	14.5
3	2/19/26	0.388%	(1 cc.) 0.316 (fasting)	18.6
4	2/23/26	0.412%	(2 cc.) 0.360 (not fasting)	12.1

Experiments 1, 2 and 3 were made in the morning, about 2½ hours after breakfast and before lunch. Experiment 4 was carried out to determine the effect of food upon blood sugar when under action of the extract injected. Two hours after the injection of 2 cc. and allowing the patient to have her lunch, there was an increase in blood sugar to 0.420 per cent, but five hours later blood sugar had fallen to 0.360 per cent.

PATIENT E-12, A WOMAN, MARRIED, 62 YEARS OLD, WEIGHING 43 KILOS.

1	1/12/25	0.560%	(1 cc.) 0.340%	39.3
2	2/10/26	0.436%	(1 cc.) 0.360%	17.4
3	2/10/26	0.376%	(1 cc.) 0.368%	2.1
4	2/15/26	(1 cc.) 0.256%	..
5	2/18/26	(1 cc.) 0.300%	..
6	2/19/26	0.324%	(1 cc.) 0.208%	35.8
7	2/23/26	0.372%	(1 cc.) 0.350%	5.9

It will be noticed from the foregoing that blood sugar did not rise to its original glucose content. These results confirm Dr. J. B. Collip's¹ statement that vegetable extracts do not have as quick an action as insulin, but their effect is more lasting. The extract used was called 2 N (twice normal) or each cc. representing the active substance of 2 Gms. of material.

In some instances a decrease of 36 to 39 per cent of the original blood sugar value was obtained. The patients stood the injections without any discomfort. The injections were always applied subcutaneously, in the buttocks.

Due to lack of facilities we have not been able to determine the effect of the extract on the respiratory quotient, nor have we been able to define whether our results could have been improved had we met with good coöperation from the patients regarding diet. Considerable difficulties were experienced in trying to control the diet of the patients.

We were unable to establish any relation between blood sugar and sugar excretion in the urine. Much to our surprise, even at the lowest blood sugar levels obtained, sugar in the urine was relatively high. Before the treatment both patients had from 6 to 7 per cent glucose in the urine (by Benedict's method) and the lowest content recorded during the experiments was 4 per cent. The sugar in the 24-hour specimens never fell below 250-300 Gms., even when blood sugar was as low as 0.200 per cent. Later, we discovered that the patients were not strictly following our orders regarding diet, since they were given large amounts of white bread and beans.

Patient E-9 felt much better. There never were even traces of acetone and diacetic acid in her urine. However, Patient E-12 had a severe case of acidosis. Diacetic acid and acetone were present invariably except in three analyses, but since the diet control was not efficient we could not determine the cause of the disappearance of these two substances. Patient E-12 had been previously treated with insulin without any results.

This investigation is far from complete. We have found ourselves highly handicapped from lack of facilities, coöperation and apparatus, but we think it is worth while to determine more definitely the physiological action of this extract when administered subcutaneously. We have no specific data regarding the effects of its oral administration although it is commonly taken that way. Our knowledge of its effect orally administered comes from the patients themselves. The two patients treated did not show any signs of improvement when the extract was given to them for a period of 60 days—30 drops before meals, three times daily.

CONCLUSIONS.

1. A vegetable extract possessing hypoglycemia properties has been prepared.
2. Its effect is apparent when injected subcutaneously. A fall in blood sugar is observed two hours after injection of 1 cc.
3. The solution can be sterilized by boiling without affecting its properties.
4. The clinical data obtained furnish no evidence of its beneficial effects when administered orally.
5. Sugar in the urine could not be controlled, presumably due to a faulty diet.
6. Further investigation is needed to determine more definitely the physiological action of the extract studied.

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- April 14, 1926.

THE RELAXING ACTION OF SOME AROMATIC ESTERS.

BY E. V. LYNN AND DOROTHY GASTON.

Theoretically the relaxation of spasmodic conditions of muscle or nerve may be described by the term antispasmodic but by custom this word is usually restricted to any substance which will relieve strong contractions of unstriated muscular tissue. This effect may be gained by depressing the cerebral, spinal or medullary centers which control, by action upon the peripheral nerve ends, ganglionic or post-ganglionic, or by direct effect upon the muscles. The first two methods are very effective and often utilized, but the accompanying secondary and side actions are generally undesirable or even dangerous. The opiates and atropine are good illustrations.

Of all the drugs which act directly upon the muscle structure, the nitrites are preëminent, but papaverine is the most important compound of the group from our standpoint. The antispasmodic action of papaverine was first reported¹ in 1902 and has since been extensively investigated. Macht, during a long series of experiments, noted that those opium alkaloids of the papaverine class which contained the benzyl group were relaxing, while the morphine alkaloids, which did not have this group, were not possessed of the property.² He, therefore, examined the action of several benzyl derivatives of a simpler nature and found that benzyl alcohol and a number of its esters are capable of relieving spasmodic contractions of excised muscular tissue of the blood vessels, intestines, ureter, uterus, etc. Benzyl benzoate was then introduced to the trade for therapeutic purposes and the succinate has since followed it. The acetate, acetylsalicylate and others have also been used occasionally. Administered by mouth they seem practically harmless in fairly large amounts, and the apparent lack of clinical success has, therefore, been rather surprising, for there seems no question at all about the paralyzing

¹ Pal, *Zeit. f. Physiol.*, p. 68 (1902).

² Macht, *J. Pharmacol.*, 8, 155, 261 (1916); 9, 197 (1916); 9, 287 (1917); 10, 96 (1917); 11, 419 (1918).