

or more of the tests of the Association of Official Agricultural Chemists, as the present test gives an unfair reaction.

- Samples A Dickinson's first run without alcohol
- B Dickinson's first run with 15% alcohol
- C Dickinson's middle run
- D Dickinson's middle run with 15% alcohol
- E Dickinson's last run
- F Dickinson's last run with 15% alcohol

Other samples, open market: No. 1, Dickinson's; 2, Humphrey's; 3, Ponds. No other samples were available on the market in Washington.

A STUDY OF THE EMODIN-BEARING GROUP OF CATHARTICS. PART I.

BY PETER VALAER, JR.

For the past twenty years the writer has been interested and fascinated by what is regarded by many to be the most baffling group of crude drugs. The principal members of this group are cascara, rhubarb, frangula, aloes and senna. They are known to many as emodin-bearing drugs, whose cathartic action depends perhaps upon certain oxymethyl-anthraquinones for their activity. The word "perhaps" is projected into this paragraph for reason that there are eminent members of the pharmaceutical chemical profession who do not share this opinion. Their reasons will be discussed later along with certain chemical data.

The writer has planned to divide the "Study of the Emodin-Bearing Group" into five parts discussing each group member separately. Cascara is the best known and most widely used of this group.

There has been developed in the chemical laboratory of the Bureau of Prohibition a method by which the presence of emodin-bearing drugs are detected and estimated. It is based on the Bornträger reaction (*Z. anal. Chem.*, 19 (1880), 165). When the group of drugs whose virtues depend principally upon the resinous hydroxyanthraquinone bodies and other anthraquinone compounds in the solution are made acid and are extracted with ether and the ether extract made strongly alkaline with ammonia, a red color of a certain shade is caused to develop. Application is made of this test as a basis for the quantitative estimation of, for instance, cascara in medicinal preparations under examination. Under certain carefully observed conditions the depth of color extracted by the ether and the color developed on the treatment with ammonia varies almost directly in proportion to the amount of cascara or other emodin-bearing drugs present.

Twenty-five cc. of the medicine is measured with a pipette into a 250-cc. separatory funnel, 2 cc. *N/10* acid introduced to make the material acid, 50 cc. of sulphuric ether is then added and the funnel shaken for exactly five minutes. The material is allowed to settle, the acid liquid is then drawn off; the funnel shaken and allowed to stand and the process of shaking and drawing off repeated until all the aqueous liquid remaining in the funnel is completely stripped out. If any emodin-bearing drugs are present, the upper layer is yellow; rhubarb causing the deepest shade, and aloes the smallest amount of color from a given amount of material. (See a future paper concerning emodin drugs other than cascara.)

The Lovibond's tintometer is depended upon to standardize the colors developed for these comparisons. A brief description of the apparatus is as follows:

The Lovibond tintometer used in these experiments is sold by Eimer and Amend, and is an instrument by which the depth of color of liquids can be accurately measured in degrees, placed in their position in a permanent color scale and registered for reproduction at any time. It consists of a graded series of standards made of colored glasses, numbered according to their depth of color and an instrument for holding the glasses and the object to be measured.

The yellow ether extract is poured into the $\frac{1}{16}$ -inch cell and the color matched against the yellow slides. 10 cc. of the above extract is introduced into a 100-cc. Nessler tube and 10 cc. of strong ammonia (sp. gr. 0.90) added. The mixture is shaken and allowed to stand ten minutes. It is then diluted to 50 cc. volume and mixed. As soon as the ether portion rises to the top it is flicked off and some of the red liquid poured into the $\frac{1}{8}$ -inch cell of the tintometer and carefully matched against the red tinted slides as in the manner before described.

The yellow extract and the emodin red produced vary almost directly with amount of cascara present and bear a simple ratio to each other. If the yellow ether extract reads 2 in $\frac{1}{16}$ -inch cell, the red developed reads 1.0 in $\frac{1}{8}$ -inch cell.

Twenty U. S. P. fluidextracts were obtained from the open market and from some of the leading drug houses of the United States, and two U. S. P. fluidextracts were made in this laboratory from standard ground cascara. These fluidextracts were used in the manufacture of preparations containing 15 minims of the extract to each fluidounce, using in some instances wine and in others diluted alcohol as the base. This being the average cascara content of laxative tonics. 25 cc. of this material was treated as before described.

| | Color (yellow) $\frac{1}{16}$ " cell. | Color (red) $\frac{1}{8}$ " cell. |
|-----------------|---------------------------------------|-----------------------------------|
| Highest reading | 3.2 | 1.6 |
| Lowest reading | 2.0 | 1.0 |

Preparations containing 30 minims to the ounce read approximately twice as much of both yellow and red, and preparations containing $7\frac{1}{2}$ minims to the ounce, one-half as much.

The yellow color extracted by the ether and the red color developed by the addition of ammonia is reasonably permanent if kept stoppered. Portions of these colored extracts have been used as exhibits in revocation and other hearings, holding their character apparently without change for several days. The yellow color extracted from cascara can be faithfully reproduced with potassium chromate in aqueous solution. The red alkaline solution is more difficult to imitate.

The readings made on the 22 U. S. P. fluidextracts of cascara referred to were made several years ago, and the color readings of each extract will not be gone into, except mentioning the highest and lowest readings, all the extracts falling between these.

Since January 1929 there have accumulated in the laboratory other samples made by some large manufacturing drug houses, and some made by smaller concerns, some of these extracts were furnished directly by manufacturers and some samples were purchased in the open market. All samples were unbroken packages. Besides the method already outlined there was used another method called for convenience the "hydrolysis method." Both methods are now employed in judging the amount of cascara or other emodin-bearing drugs that are present, the only difference between the two methods is that a 25-cc. portion of the preparation under examination being digested with 2 cc. concentrated sulphuric acid.

EXAMINATION OF FLUIDEXTRACTS OF CASCARA U. S. P.

Solids, ash and alcohol were determined on undiluted fluidextracts—the color readings were made in accordance with the method below, using preparations consisting of 25% alcohol and containing in each fluidounce 15 minims of fluidextract.

Method for Color Reading.—Extract 25 cc. of the preparation, made acid with 2 cc. *N/10* H₂SO₄, extract with 50 cc. of ordinary sulphuric ether in separatory funnel—draw off aqueous liquor several times as it settles and take 10 cc. of the yellow ether extract and 10 cc. of strong ammonia and place in a colorimetric tube (Nessler), mix; allow to stand until some of the remainder of the yellow ether extract is read in 1/16-inch cell, then make the mixture in the Nessler tube up to 50 cc. volume with water. Flick off the ether which rises to the top and read the red color in a 1/8-inch cell.

TABLE I.

READINGS OF FLUIDEXTRACTS OF VARIOUS MANUFACTURERS.

| Fluidextract of Cascara Sagrada. | Solids. | Ash. | Alcohol. | Color readings. See method below. | Date. |
|----------------------------------|---------|-------|----------|---|--------|
| No. 1 | 23.82 | 1.510 | 24.8 | Yellow 1/16" cell 1.0 Red 1/8" cell 0.6 | 5-1-29 |
| No. 2 | 31.102 | 1.328 | 23.2 | Yellow 1/16" cell 2.5 Red 1/8" cell 1.3 | 5-1-29 |
| No. 3 | 28.022 | 1.022 | 23.8 | Yellow 1/16" cell 1.6 Red 1/8" cell 0.86 | 5-1-29 |
| No. 4 | 24.546 | 0.974 | 21.9 | Yellow 1/16" cell 1.4 Red 1/8" cell 0.7 | 5-1-29 |
| No. 5 | 25.242 | 0.958 | 23.1 | Yellow 1/16" cell 1.5 Red 1/8" cell 0.8 | 5-1-29 |
| No. 6 | 19.122 | 0.970 | 22.2 | Yellow 1/16" cell 1.0 Red 1/8" cell 0.52 | 5-1-29 |
| No. 7 | 28.16 | 0.920 | 22.4 | Yellow 1/16" cell 1.2 Red 1/8" cell 0.68 | 5-4-29 |
| No. 8 | 26.070 | 1.226 | 18.8 | Yellow 1/16" cell 1.9 Red 1/8" cell 1.0 | 5-1-29 |
| No. 9 | 25.674 | 1.098 | 25.3 | Yellow 1/16" cell 1.6 Red 1/8" cell 0.88 | 5-1-29 |

THE EXAMINATION OF U. S. P. FLUIDEXTRACTS OF CASCARA (BY THE HYDROLYSIS METHOD) I. E., DIGESTING WITH SULPHURIC ACID.

Preparations were made with U. S. P. Fluidextracts of Cascara. Each preparation contained in each fluidounce 15 minims of fluidextract; 25 cc. of each preparation was treated in an Erlenmeyer flask with 2 cc. of concentrated sulphuric acid, shaken thoroughly and allowed to stand over night; refluxed over a steam-bath for 30 minutes using a tube condenser. The material was transferred to a separatory funnel, shaken with 50 cc. of ordinary ether for exactly 5 minutes, allowed to settle; the aqueous layer was drawn off, shaken and again allowed to settle. The remaining aqueous material was again drawn off. This process was repeated until all the aqueous liquor was stripped out as completely as possible.

Unlike the method for the color readings for free emodin, there is a tendency for material to stick on the inside of the separatory funnel. The yellow extract can be separated from this last material by transferring into another separatory funnel. Keep all ether extracts stoppered up as completely as possible as the yellow color becomes concentrated on evaporation.

Take 10 cc. of the yellow ether extract and 10 cc. of strong ammonia and place in a colorimetric tube (Nessler); mix, allow to stand until some of the remainder of the yellow color is read in

$\frac{1}{16}$ -inch cell, then make the mixture in the Nessler tube up to 50 cc. volume with water, allow to settle, flick off the ether which rises to the top and read the red color in $\frac{1}{8}$ -inch cell.

Readings Made May 27 to 29, 1929, Inclusive—All Materials Are New Fluidextracts.—After 1-hour standing very little change in color took place. The examination of the readings for cascara show that usually when the free emodin is low it is balanced by a corresponding larger combined emodin reading. The readings for the total emodin are several times that of the free emodin. Apparently, some of the fluidextracts are of an inferior character giving poor combined and free emodin readings.

The red readings in the $\frac{1}{8}$ -inch cell are not pure red but a rose shade making it necessary to use a weak yellow slide with the red slide to get the exact comparison.

TABLE II.

SHOWING COLOR READINGS DUE TO FREE AND COMBINED EMODIN AFTER DIGESTION WITH SULPHURIC ACID—(SEE METHOD ABOVE).

| Fluidextract Cascara. | Yellow in $\frac{1}{16}$ " cell. | Red in $\frac{1}{8}$ " cell. |
|-----------------------|----------------------------------|------------------------------|
| No. 1 | 8.6 | 5.5 red, 0.5 yellow |
| No. 2 | 6.8 | 4.4 red, 0.6 yellow |
| No. 3 | 5.6 | 4.0 red, 0.9 yellow |
| No. 4 | 6.4 | 5.0 red, 0.8 yellow |
| No. 5 | 6.0 | 4.5 red, 0.7 yellow |
| No. 6 | 3.6 | 2.0 red, 0.5 yellow |
| No. 7 | 2.0 | 2.0 red, 1.3 yellow |
| No. 8 | 4.6 | 3.5 red, 1.5 yellow |
| No. 9 | 2.1 | 1.9 red, 1.2 yellow |

EXAMINATION OF SAMPLES OF U. S. P. FLUIDEXTRACT CASCARA AND AROMATIC FLUIDEXTRACT OF CASCARA.

Solids, alcohol and ash were determined on the undiluted fluidextracts using A. O. A. C. methods. The color readings were made on preparations containing 15 minims per fluidounce of fluidextract cascara and 30 minims per fluidounce of aromatic cascara in diluted alcohol (25%) alcohol approximately.

Method for Color Readings—before Hydrolysis (Free Emodin).—Extract 25 cc. of the preparation, made acid with 2 cc. $N/10$ H_2SO_4 ; extract 5 minutes with 50 cc. of ordinary sulphuric ether in separatory funnel; draw off the aqueous liquor several times as it settles and take 10 cc. of the yellow ether extract and 10 cc. of strong ammonia and place in a colorimetric tube (Nessler); mix, allow to stand until some of the remainder of the yellow ether extract is read in $\frac{1}{16}$ -inch cell, then make the mixture in the Nessler tube up to 50 cc. volume with water. Flick off the ether which rises to the top and read the red color in a $\frac{1}{8}$ -inch cell.

Method for Color Readings—after Hydrolysis (Total Emodin).—The cascara preparation contained in each fluidounce 15 minims of fluidextract and 30 minims per fluidounce of aromatic cascara. Twenty-five cc. of each preparation was treated in an Erlenmeyer flask with 2 cc. of concentrated sulphuric acid, shaken thoroughly and allowed to stand over night; refluxed over a steam-bath for 30 minutes, using a tube condenser. The material was transferred into a separatory funnel, shaken with 50 cc. of ordinary ether for exactly 5 minutes, allowed to settle; the aqueous layer shaken and again allowed to settle. The remaining aqueous material was again drawn off. This process is to be repeated until all the aqueous liquor is stripped out as completely as possible.

Take 10 cc. of the yellow ether extract and 10 cc. of strong ammonia and place in a colorimetric tube (Nessler) mix, allow to stand until some of the remainder of the yellow color is read in $\frac{1}{16}$ -inch cell, then make the mixture in the Nessler tube up to 50 cc. volume with water, allow to settle, flick off the ether which rises to the top and read the red color in $\frac{1}{8}$ -inch cell.

TABLE III.

| Lab. no. | Substance and manufacture. | Alcohol. | Solids. | Ash. | Free emodin. | | Total emodin. | |
|----------|---|----------|---------|------|-------------------|------------------|---------------------------------------|-------------------|
| | | | | | $\frac{1}{16}$ ". | $\frac{1}{8}$ ". | Digested with 2 cc. conc. H_2SO_4 . | $\frac{1}{16}$ ". |
| 73225 | Aromatic Cascara 30 minims to ounce. Control 9E1006 | 9.7% | 56.6 | 3.7 | 1.8 Y | 1.0 R 0.4 Y | 3.0 Y | 1.7 R 1.9 Y |
| 73226 | Cascara 15 minims to ounce. Control 8L2484 | 21.36% | 27.1 | 1.3 | 2.1 Y | 1.9 R 1.0 Y | 3.2 Y | 2.4 R 1.8 Y |
| 72052 | Cascara 30093 \times 832634 | 20.0 | 25 | 1.2 | 1.1 Y | 0.6 R | 4.9 Y | 3.0 R 2.0 Y |
| 72053 | Cascara 7065 \times 833034 | 22.8 | 26 | 1.3 | 1.1 Y | 0.6 R | 4.6 Y | 3.0 R 2.1 Y |

After 24 hours and 48 hours standing there seemed to be no change in color; the aromatic cascara and the bitter cascara gave the same yellow and red readings as before. This is very convenient in busy laboratories subject to frequent interruptions. The Nessler tubes left standing are always stoppered securely.

Examination of preparations containing Fluidextract of Cascara U. S. P. 15 minims per fluid-ounce (alcoholic content approximately 25%).

To determine whether it is necessary to evaporate the alcohol from the preparation in making the color readings indicating the presence of emodin-bearing drugs.

Columns 1 and 2 of the following table indicate the readings obtained by the following method:

Method for Color Readings.—Extract 25 cc. of the preparation, made acid with 2 cc. $N/10 H_2SO_4$, extract with 50 cc. of ordinary sulphuric ether in a separatory funnel; draw off the aqueous liquor several times as it settles and take 10 cc. of the yellow ether extract and 10 cc. of strong ammonia and place in a colorimetric tube (Nessler); mix, allow to stand until some of the remainder of the yellow ether extract is read in $\frac{1}{16}$ -inch cell, then make the mixture in the Nessler tube up to 50 cc. volume with water. Flick off the ether which rises to the top and read the red color in a $\frac{1}{8}$ -inch cell.

Columns 3 and 4 of the table, are results of the same method except that 25 cc. of the preparation is evaporated almost to dryness, taken up with approximately 25 cc. of water and the process carried on as described above.

TABLE IV.

| Material. | No. 1 yellow. | No. 2 red. | No. 3 yellow. | No. 4 red. |
|-----------------------|------------------------|-----------------------|------------------------|-----------------------|
| Fluidextract Cascara. | $\frac{1}{16}$ " cell. | $\frac{1}{8}$ " cell. | $\frac{1}{16}$ " cell. | $\frac{1}{8}$ " cell. |
| No. 1 | 0.8 | 0.3 | 0.8 | 0.4 |
| No. 2 | 2.5 | 1.4 red 0.8 yellow | 2.2 | 1.4 red 0.5 yellow |
| No. 3 | 2.4 | 1.2 red 0.4 yellow | 2.2 | 1.2 red 0.3 yellow |
| No. 4 | 1.9 | 0.8 red 0.3 yellow | 1.7 | 1.0 red 0.3 yellow |
| No. 5 | 1.9 | 0.9 red 0.3 yellow | 1.7 | 1.0 red 0.3 yellow |
| No. 6 | 1.1 | 0.5 red 0.2 yellow | 1.1 | 0.6 red 0.2 yellow |

From the results shown there is little to choose from the two methods. Not having to evaporate off the alcohol makes the process more simple and quicker.

The following method was suggested by H. C. Fuller (1) for the assay of cascara and submitted by him to the A. O. A. C. This method is used in the author's

laboratory, it is applied on the ground bark (5 Gm.), the fluidextract (5 cc.) and on medicinal preparations (50 cc.), containing cascara as an ingredient.

Introduce 5 Gm. of the powdered drug into an Erlenmeyer of 500 cc. capacity; add 200 cc. of chloroform and 50 cc. of 25% sulphuric acid; attach to a reflux container (water cooled) using cork stopper covered with tin foil. Apply low heat of Bunsen flame and allow the chloroform to boil for two and one-half hours. At the end of that time allow to cool and then transfer to separatory funnel, washing out flask with a little fresh chloroform.

Draw off the chloroform solution into another separatory funnel. Add 50 cc. chloroform to the acid mixture, agitate and after separation has taken place, run chloroform into that previously collected. Repeat procedure three times. Discard the acid mixture.

Collect the chloroform shake-outs in an Erlenmeyer or distilling flask, recover about $\frac{2}{3}$ of the solvent by distillation and pour the balance into a separatory funnel washing thoroughly to remove final traces of anthraquinones; agitate the chloroform with 25 cc. of 10% sodium hydroxide; draw off chloroform and subject to another treatment with 10% sodium hydroxide. Repeat again; draw off chloroform and wash with 25 cc. of water three times.

Unite the alkaline solutions and washings, add the excess of hydrochloric acid and shake out five times with chloroform. Discard the acid and wash the chloroform solution by shaking with 50 cc. of water; let settle completely, filter chloroform through cotton in stem of funnel into a distilling flask or Erlenmeyer and recover a portion of the solvent. Then pour the balance into a tared dish, washing out distilling flask with chloroform; evaporate the solvent; dry at not over 100° for thirty minutes, cool in desiccator and weigh. The weight represents the total anthraquinone bodies in the drug. Preserve the residue for the method described below.

COLORIMETRIC DETERMINATION.

Treat the residue of anthraquinone derivative obtained by the gravimetric assay described above with 10 cc. of 10% potassium hydroxide, wash into a 100-cc. graduated flask with distilled water and make up to volume. Ten cc. of this solution is then diluted with water to 50 cc., a portion introduced into a one-eighth-inch cell of a Lovibond tintometer and matched against the red slides. Note depth of color and report degrees observed.

Transfer 20 cc. of the alkaline liquid by means of pipette to a separatory funnel, add an excess of hydrochloric acid and extract with 25- and 15-cc. portions of ether. Collect the ether solution in a 50-cc. graduated flask and make up to volume with ether. Introduce a portion of this ether solution into a $\frac{1}{16}$ -inch cell of a Lovibond tintometer; match against the yellow slides, note depth of color and report degrees observed.

The table below shows four independent analyses using the above method on the same samples of standard ground cascara bark.

| Observer. | Grams of residue in 5 Gm. material. | Ether extract $\frac{1}{16}$ " cell. | Emodin reaction red $\frac{1}{8}$ " cell. |
|---|--|---|--|
| J. D. McIntyre | 0.2288 | Yellow 9.8 | Red 4.25 |
| | | Red 0.4 | Yellow 0.54 |
| G. Edmonds | 0.2478 | Yellow 10.0 | Red 4.52 |
| | | Red 0.5 | Yellow 1.0 |
| Peter Valaer, Jr. | 0.2735 | Yellow 11.5 | Red 4.5 |
| | | Red 0.5 | Yellow 0.54 |
| Bradshaw (heated $\frac{1}{2}$ hr.—30 min.) | 0.221 | Yellow 9.8 | Red 4.52 |
| | | Red 0.9 | Yellow 1.00 |

In reading the red in the $\frac{1}{8}$ -inch cell often there is a slight "off shade" which is usually connected by a low tint yellow slide—rarely more than $\frac{1}{10}$ that of the red. The Cascara Evacuant was not averaged in the list of fluidextracts.

A qualitative analysis was made to determine the inorganic constituents in the ash obtained from several fluidextracts.

TABLES SHOWING FLUIDEXTRACT ANALYZED BY ABOVE METHOD—USING 5 CC. FOR THE DETERMINATION.

| Manufacturer. | % residue. | Color (red) 1/16" cell. | Yellow 1/16" cell. |
|---------------|------------|----------------------------|-----------------------|
| 1 | 1.019 | 2.4 | 1.9 |
| | 0.936 | 2.3 | 2.2 |
| 2 | 1.382 | 5.24 | 3.8 |
| | 1.407 | 6.00 | 4.8 |
| 3 | 1.016 | 3.0 | 2.5 |
| 4 | 1.694 | 5.0 | 4.0 |
| 5 | 2.030 | 4.0 | 3.0 |
| 6 | 1.81 | 5.87 | 5.2 |
| 7 | 1.69 | 3.6 | 2.7 |
| 8 | 0.38 | Trace red | 0.4 yellow |
| 9 | 0.942 | 2.8 | 2.4 |
| 10 | 1.314 | 5.8 | 5.6 |
| 11 | 1.11 | 2.9 | 2.2 |
| | 1.11 | 2.9 | 2.2 |
| 12 | 1.54 | 2.5 | 2.5 |
| 13 | 1.81 | 2.9 | 2.7 |
| 14 | 2.09 | 4.0 | 3.7 |
| Average | 1.43 | 3.8 | 3.2 |

The analysis disclosed no unusual heavy metals in the ash with the exception perhaps of the presence of manganese. This metal was found in all our specimens of cascara. The other metals found in the ash or cascara were magnesium, iron, calcium, sodium and potassium. The per cent of iron was very small and the ash of cascara was not nearly so rich in iron oxide as was the case with the ash of aloes; reading in the latter case was as high as 40% of Fe_2O_3 in the ash.

Advantage is taken in this method of the ever-present manganese in cascara as a basis for its isolation and ultimate determination.

Determination of manganese in preparation and the per cent in the ash.

Fifty cc. of the solution is evaporated to dryness and ashed; (use ash for above solids and ash determination) dissolve in 15 cc. of 25% nitric acid, transfer into a Nessler tube; wash the dish with 10 cc. water; add washings; add 10 cc. approximately $N/10$ AgNO_3 and 0.5 Gm. of ammonium persulphate; warm in a live steam-bath 30 seconds; cool, make up to 100 cc. volume.—Compare with standards made by diluting 1 cc., 0.5 cc., 0.25 cc. and 0.125 cc. of one-hundredth normal potassium permanganate, treating the $N/100$ KMnO_4 , with all the reagents above and oxidized in the manner above described. The manganese in preparations containing 15 minims the fluidextract of Cascara in each ounce of diluted alcohol will range in per cent of manganese from 0.00025 to 0.00070 Gm. in 100 cc. of the preparation and from 1% to 2.4% in the ash. Allowing the Nessler tubes to stand stoppered over night insures a clear reading.

In order to judge the quantity of cascara present in a tonic preparation, the following determinations are made:

Solids.—Measure 10 to 50 cc. of the preparation into a tared platinum dish, evaporate to dryness on a steam-bath; heat the residue for 30 minutes in a constant temperature oven at 100°C ., report grams in 100 cc. (solids due to 15 minims fluidextract of cascara in alcohol range from about 0.6 to 0.9 Gm. in 100 cc.).

Ash.—Ignite the above solids at dull redness in a muffle furnace to a white ash. (Ash of cascara, 15 minims to ounce, in dilute alcohol, will range from about 0.020 to 0.035 Gm. in 100 cc.)

Color of Preparation.—Pour some of the finished preparation into the 1/16-inch cell of the Lovibond tintometer and match against the yellow slides, matching the shade as nearly as pos-

sible by the addition of red slides. The color of a preparation of fluidextract of Cascara in alcohol, 15 minims to ounce, will read from about 12.6 yellow, 1.2 red to about 16.0 yellow, 1.6 red.

The colorimetric emodin methods, before and after hydrolysis, described in the beginning should be used. Preparations containing 15 minims to the ounce of cascara usually read from 2 to 3 yellow, and 1 to 1.5 red before hydrolysis and, after hydrolysis, yellow $\frac{1}{16}$ -inch cell 6 to 11, and 3 to 5.5 red in $\frac{1}{8}$ -inch cell of the Loviband tintometer.

The proposed A. O. A. C. Cascara Assay (see method). The total extract in preparations containing in each fluidounce 15 minims of fluidextract will range from about 0.05 to about 0.09 Gm. in each 100 cc. The residue taken up as outlined in the method reads 1.3 to 2.6 yellow in the $\frac{1}{16}$ -inch cell, and 1.4 to 2.4 red in the $\frac{1}{8}$ -inch cell.

Taste, Odor and Physiological Test.—With even a small amount of experience one can form a fairly good opinion as to whether the cascara that is claimed in a preparation is present.

It has been the invariable experience in our laboratory with hundreds of tonic preparations claiming this drug, that the presence of the "emodin reactions" is followed by corresponding physiological reaction, and when the preparations show weak emodin reactions, the physiological action is also weak.

When a sample of a medicinal preparation, suspected of being short of cascara, is subjected to the various determinations suggested in this article, there is no difficulty in showing its sub-standard character. The most useful determination being in our experience, the colorimetric emodin readings, before and after hydrolysis.

The following table gives the analysis of eight preparations made with cascara from as many leading manufacturing drug houses. The proposed A. O. A. C. method with its colorimetric reading of residues was also determined on these

TWENTY PER CENT ALCOHOL CONTAINING IN EACH FLUIDOUNCE 15 MINIMS FLUIDEXTRACT OF CASCARA.

| Manu- fac- turers no. | Solids Gm., 100 cc. | Ash Gm., 100 cc. | Color of prepara- tion read in $\frac{1}{16}$ " cell, color brown. | % Mn in the prepara- tion. | % Mn in ash. | Colorimetric Emodin. | | | |
|--------------------------------|---------------------------|---------------------|--|-------------------------------------|-----------------|--|---|--|---|
| | | | | | | Before hydrolysis. $\frac{1}{16}$ " cell Y. | Before hydrolysis. $\frac{1}{8}$ " cell R. | After hydrolysis. $\frac{1}{16}$ " cell Y. | After hydrolysis. $\frac{1}{8}$ " cell R. |
| 1 | 0.789 | 0.029 | 15 yellow 1.6 red | 0.00066 | 2.3 | 2.4 | 1.1 | 7.4 | 3.4 |
| 2 | 0.869 | 0.029 | 14 yellow 1.6 red | 0.00028 | 1.0 | 2.6 | 1.2 | 6.4 | 3.5 R 0.4 Y |
| 3 | 0.630 | 0.028 | 14.6 yellow 1.7 red | 0.00028 | 1.0 | 2.4 | 1.1 | 9.0 | 4.8 |
| 4 | 0.664 | 0.022 | 12.6 yellow 1.2 red | 0.00028 | 1.3 | 2.2 | 1.0 | 5.6 | 3.2 |
| 5 | 0.491 | 0.029 | 13.9 yellow 1.7 red | 0.00044 | 1.5 | 2.0 | 1.0 | 9.4 | 4.0 |
| 6 | 0.855 | 0.034 | 14.1 yellow 1.5 red | 0.00056 | 2.0 | 2.4 | 1.2 | 11.5 | 5.2 |
| 7 | 0.792 | 0.027 | 14.5 yellow 1.5 red | 0.00066 | 2.4 | 2.1 | 1.0 | 6.8 | 3.0 |
| 8 | 0.838 | 0.030 | 15.6 yellow 1.6 red | 0.00066 | 2.2 | 2.1 | 1.0 | 7.0 | 3.8 R 0.4 Y |

preparations but is not shown in the table. The determination of glucosides by a method proposed by Dr. Dohme was also made on the eight cascara preparations; the result was unsatisfactory, and hence omitted.

Bastedo (2), in his "Materia Medica, Pharmacology and Therapeutics," claims that the activity of the vegetable drugs, aloes, frangula, cascara, rhubarb and senna depend upon resinous bodies known as emodins, tri-oxymethylanthraquinone, or a close relative of these.

Sollman (3), in "Manual of Pharmacology" claims that anthraquinone or emodin cathartics—the active constituents of senna, rhubarb and cascara—depend on the glucosidal compounds which accompany these drugs. The pure substances are in themselves too irritant, but the action is graded by their slow liberation and the presence of colloid extractives. The most common of these substances is emodin.

From the *Bulletin* of the Royal Academy of Medicine (Belgian) (4) we obtain the following expression. "Not only do the hydroxymethylanthraquinone produce the purgative effect but other substances must be taken into account with which these form complexes whose structures have not been defined. The anthraquinone being undoubtedly an integral part of the puragine complex and the determination of the anthraquinones afford a useful indication of the value of the particular drug. It is stated by Beal and Okey (5) that emodin is characteristic of frangula, rhubarb and cascara and these drugs owe their cathartic properties to the anthraquinone derivatives.

In certain experiments conducted in 1924 using a large corps of nurses as subjects, Dr. Henry C. Fuller (6) reached the following conclusions concerning the significance of the anthraquinone constituents of cascara in relation to the physiological effect of the drug. It is therefore apparent, that the anthraquinone derivatives are of significance in the physiological action of cascara. It is also apparent that the physiological activities depend on the stimulus of some substance, probably enzyme in character.

REFERENCES.

- (1) Fuller, *J. Assoc. Official Agr. Chem.*, 5 (1922), 577; 7 (1920).
- (2) Bastedo, "Materia Med. Pharmacology and Therapeutics."
- (3) Sollman, "Manual of Pharmacology."
- (4) *Bull. Royal Acad. Med. Belg.* (4) (1913).
- (5) Beal and Okey, *J. Am. Chem. Soc.*, 39 (1917), 716.
- (6) Unpublished report.

NARCOTIC IMPORT QUOTAS.

The Federal Narcotics Control Board has announced its decisions regarding permits for the importation of crude opium and coca leaves for the calendar year 1930, involving a considerable reduction from the importations of last year. The quotas are set at 128,000 pounds of opium and 201,500 pounds of coca leaves, of which 151,500 will be Peruvian and 50,000 Java leaves. This is the first year that permits have been based on calendar years, the change being made to place the statistics in harmony with those of the League of Nations. In the fiscal year ended June 30, 1929, actual imports were 144,925½ pounds of opium and 242,834 pounds of coca leaves, of which 150,727 pounds were Peruvian and 92,107 were Java leaves. No explanation was made for the decrease, except that it was felt that 1929 imports were above normal, in order to replenish stocks depleted by an influenza epidemic.

INTERNATIONAL CONGRESSES.

The International Hygiene Congresses will be held in Dresden, Germany, May 15th to September 30th, conducted under the joint governmental auspices of the German Reich, the Free State of Saxony and the City of Dresden; its world significance is indicated by the participation of more than 200 scientific associations, the League of Nations and the individual governments of 20 countries. An itinerary has been arranged for those who will attend as delegates; *en route* a postgraduate course of round table discussions will be participated in by the members of the party. Conditions in the larger cities will be studied by arrangement of government officials and associations; among the cities named in the invitation to the A. Ph. A. are Liverpool, London, Brussels, Cologne, Dusseldorf, Berlin, Potsdam, Prague, Vienna, Salzburg, Munich, Oberammergau, Lucerne, Montreux, Geneva and Paris.