NEW TESTS FOR SOME PURGATIVE DRUGS.*

BY E. H. GRANT.

This paper describes some new tests for the identification of the following purgative drugs listed in the United States Pharmacopoeia IX and National Formulary IV: Scammony Root, Jalap, Gamboge, Podophyllum, Senna, Rhubarb, Cassia Fistula, Chionanthus. The arrangement of these drugs in this paper is for convenience in describing the various tests, bringing similar ones together, rather than by a botanical or other systematic scheme. The reader is referred to the above mentioned authorities for a full description of the drugs.

Scammony.—The sample, after being dealcoholized by evaporation if it contains alcohol, is extracted with chloroform. The chloroform extract is evaporated in a small beaker, and after cooling, the residue is treated with 2 mils of a cold alcoholic solution of potassium hydroxide (40 grammes per liter). In the presence of scammony a pleasant, fruity odor slowly develops. On heating, the odor is intensified slightly and often changes to one resembling that of peppermint. In the cold, leptandra gives a faint, scarcely noticeable odor which can be easily distinguished from that given by scammony if samples of each are run for comparison. On heating, the odor given by leptandra is very rapidly intensified. For this reason, care must be taken not to add the potassium hydroxide solution until the beaker is cold. Jalap is slightly soluble in chloroform in the presence of alcohol and will give a slight odor in this test if alcohol is not excluded. Mexican scammony (*Ipomoea orizabensis* Ledanois) acts similarly to scammony, but the two odors may be distinguished if compared with those given by authentic samples of each of the drugs.

Jalap.—The sample, freed from alcohol, is extracted with chloroform, as noted above, until all of the scammony is removed. It is then extracted with ethyl acetate, the solvent is drawn off and evaporated. The residue on evaporation is allowed to cool and is then treated with 2 mils of the potassium hydroxide solution. In the cold, very little odor develops, but on heating slightly there is a strong, ethereal odor, very similar to that given by leptandra.

Leptandra.—The sample is extracted with a mixture of alcohol (1 part) and chloroform (3 parts). A portion of this extract is evaporated and the residue treated with alcoholic potassium hydroxide. In the cold, only a very faint odor develops. On heating slightly a strong, fruity odor develops. The solution is heated a few minutes on the water bath to saponify the resins, then diluted with water, acidified with dilute hydrochloric acid and extracted with chloroform. This extract is evaporated, and the residue when cold is treated with saturated potassium permanganate solution. An odor of benzaldehyde develops. This test depends on the cinnamic acid derivatives 3 : 4 dimethoxycinnamic acid and *p*-methoxycinnamic acid.[1] It cannot be used to identify leptandra when present as the eclectic concentration "leptandrin" or similar preparations, since these acids are washed away during the process of manufacturing the concentration.

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[1] Powers and Rogerson, *Trans. Chem. Soc.*, 97, 1944–56, 1910.

As jalap is only very slightly soluble in chloroform-alcohol mixture and leptandra only slightly so in chloroform, the three drugs above mentioned can be differentiated with care.

Gamboge.—This drug is characterized by its intense yellow color, soluble in most of the organic solvents.

Four mils of an ether extract of the sample are shaken with 12 mils of water and 0.5 mils of a 0.5% copper acetate solution. If gamboge is present, a brownish orange to blood red color is produced in the ether.

By the use of the above tests and the usual tests for aloes and calomel, it is possible to identify aloes, scammony, jalap, gamboge and calomel all in the same three compound cathartic pills U. S. P.

Podophyllum.—The sample is extracted with chloroform, a portion of this extract is evaporated and the residue taken up in 2 mils of glacial acetic acid. A small crystal of mercuric nitrate is added. A red orange to blood red color is produced in the presence of podophyllum. Sometimes aloes or wild cherry bark may give a scarcely perceptible change in color under these circumstances. If a drop of nitric acid or a small crystal of sodium nitrite is substituted for mercuric nitrate, podophyllum gives the same color as it does with mercuric nitrate, while sometimes aloes and wild cherry bark give strong colors, resembling that given by podophyllum. This test will detect 0.01 gramme of podophyllum in the presence of 0.2 gramme of aloes, and in the proven absence of aloes will give indications of the presence of smaller amounts of podophyllum.

After I had discovered this test, I came across a reference in the literature which I have since been unable to locate again, to the coloration given by podophyllotoxin with nitrous acid in glacial acetic acid, but no mention was made of aloes or wild cherry bark.

Senna and Rhubarb.—Considerable work by numerous chemists has been done on the identification of drugs containing oxyanthraquinone derivatives. Senna is the most troublesome of these drugs to identify, on account of the slow chemical changes in these oxyanthraquinone derivatives which take place in its extracts on keeping, but all of these drugs show more or less change. The method of preparation, the menstruum used and the age of the extract all have profound influences on the depth and shade of color obtained in the various color reactions. A fresh, aqueous infusion of senna gives the Bornträger reaction only faintly or not at all. In attempting to identify senna when present as the whole or ground leaf, it is best to extract with dilute alcohol and apply the tests to this extract rather than to extract the sample with chloroform or ether direct, or to make an aqueous infusion.

The following test is given by senna, rhubarb, or rhapontic rhubarb (*Rheum raponticum* L.), but not by any of the other drugs. If the sample is in liquid form, it is acidified with dilute hydrochloric acid and enough alcohol or water is added to adjust the alcoholic content to about 20%, and then the mixture is extracted with chloroform. If the sample is in solid form, it is acidified and extracted with a mixture of chloroform, 3 parts, and alcohol, 1 part. This extract is shaken in a glass stoppered cylinder with an equal volume of saturated bromine water. A few drops of ammonia water, slightly more than enough to combine with all of the bromine, are added and the mixture is again shaken. After effervescence from

escaping nitrogen has ceased, the aqueous layer should separate out fairly colorless. If it has a strong pink tint, an insufficient amount of bromine was used and the test must be repeated. The cylinder is then allowed to stand undisturbed for an hour. In the presence of senna rhubarb, or rhapontic rhubarb, a pink zone slowly forms in the liquid immediately over the chloroform and finally spreads through the aqueous layer. In the presence of frangula a slight, pink coating forms over the chloroform, but this color is insoluble in the aqueous solution. In the presence of the other drugs of this group, or of phenolphthalein, no pink coloration is formed, and even large amounts of these drugs or of frangula do not interfere with the detection of senna and rhubarb.

Since all of the color in this test is concentrated at first in a very narrow zone, thus showing off in contrast with the rest of the aqueous layer, foreign coloring matters do not interfere as much as they do with some of the other color tests for this group of drugs. The limit of sensitiveness of this reaction is about 20 milligrammes of either rhubarb or senna, which is not quite as delicate as the Bornträger reaction. The presence of considerable alcohol is absolutely essential in the test.

Butternut Bark of Root and Cassia Fistula.—Both of these drugs contain compounds which give red or pink colors in the Bornträger test. The coloring matter in butternut bark is too easily destroyed to be of very appreciable value as an aid in identifying this drug. It is destroyed or rendered insoluble in the process of making a pilular extract of the drug, but it may sometimes be identified in liquid preparations which contain the fluid extract of butternut bark.

The sample is acidified and extracted with chloroform. This extract is shaken with a small amount of 10% sodium acetate solution. The aqueous layer is brownish yellow in the presence of cassia fistula or the above mentioned coloring matter from butternut bark. The sodium acetate solution removes the coloring matter of these two drugs very completely from the chloroform and does not extract any of the oxyanthraquinone derivatives (emodin, etc.), which may be present at the same time. The purified chloroform extract can be used for the identification of drugs containing such derivatives (cascara sagrada, senna, etc.). A small amount of the brown coloring matters in cascara is removed in this process, so that the color reactions given by this drug after purification of the extract will be a clearer pink, with less of a brown tint, than in the ordinary way of making these tests.

Sodium acetate solution will remove not only the coloring matters from cassia fistula and butternut bark, but also a host of other natural coloring matters which would otherwise interfere with the Bornträger and other reactions. Whenever, in testing for emodin, the analyst gets a yellow color on shaking the chloroform extract with dilute ammonia, it would be well for him to purify the extract by shaking it with sodium acetate solution.

The sodium acetate solution containing the coloring matters from cassia fistula or butternut bark is removed, acidified and extracted with chloroform. Separate portions of this chloroform extract are removed and shaken with various alkaline solutions. Butternut bark gives a pink color with ammonia and brown with solutions of borax or sodium phosphate. Cassia fistula gives a more or less pink color according to the alkalinity of the solution. It gives a pink color in the aqueous layer if the chloroform is shaken with dilute solutions of ammonia, bleach-

ing powder or borax, pink with a brownish tinge with sodium phosphate solution, very light pink with sodium benzoate solution and yellow with sodium acetate solution. The chloroform in each case becomes colorless. Sodium chloride solution or distilled water alone do not extract any of the color from chloroform.

Chionanthus.—The sample is extracted with chloroform. Separate portions of this extract are evaporated and treated with concentrated sulphuric acid containing the various chemicals noted.

Concentrated H_2SO_4 alone—red, developing only after a few minutes. On the addition of formaldehyde (40% solution) to the above, the color is intensified and takes on more of a violet hue. The color with sulphuric acid and formaldehyde develops immediately and not after a short time, as with the acid alone.

H_2SO_4 + $K_2Cr_2O_7$—violet, changing to brown.
H_2SO_4 + Ammonium Vanadate—purple with red streaks, finally all purple.
H_2SO_4 + $FeCl_3$—reddish brown changing to purple.
H_2SO_4 + Phenol—orange.
H_2SO_4 + Alphanaphthol—cherry.
Fröhde's reagent—brown.

SUMMARY.

New tests are described for the identification of scammony root, jalap, leptandra, gamboge, podophyllum, senna, rhubarb, cassia fistula and chionanthus when present in galenical preparations. The tests for gamboge, podophyllum, senna, rhubarb and chionanthus are quite characteristic. The other tests while being far from conclusive are of value in assisting to identify the drugs.

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ABSTRACT OF DISCUSSION.

E. L. PATCH: In the carrying out of color tests on mixtures we should bear in mind that there are many substances, the nature of which are unknown, that may give the color tests which we would limit to a specific substance. I recall in working upon color tests for cod liver oil that nearly all fish liver oils, regardless of the species of fish, gave similar color reactions. I would, therefore, advise extreme care in applying color tests to organic mixtures.

ARNO VIEHOEVER: We must admit that these tests are only make-shifts. However, that fact should not condemn them, as they are of great service to the average druggist who has neither the time nor facilities for isolating the active principles of the drugs and mixtures which he is compelled to test and who is forced to depend on the help which he has in his store to carry out these tests.

ALEXANDER G. MURRAY: It is true that color reactions which are not performed upon the isolated principle but upon mixtures are open to objection as the possibility of error is very great. But those of you who have had experience in the analysis of medicinal preparations of unknown composition, particularly patent medicines, will appreciate the usefulness of these tests; even though they cannot be depended upon entirely, they at least may give some indication of what is present and thereby point out to the analyst what he may expect to find, thus permitting him to select more accurate methods for confirming these findings. I happen to know that Mr. Grant has done careful work on the methods which he has reported and that they are not merely make-shifts.

E. H. GRANT: I realize as well as any of you that these methods do not yield dependable results in all cases, but some indication of what is present in a mixture is better than nothing at all.