Oesterle, (1911), states, regarding the oxymethylanthroquinones, that *aloe emodin* reduced, forms chrysophanic acid, but oxidized, forms *rhein,* while chrysophanic acid oxidized, likewise forms *rhein.*

Tutin and Clewer, (1911), state that the anthroquinone derivatives from rhubarb,—*rhein, emodin, aloe-emodin, frangula-emodin, emodin-monomethyl-ether* and chrysophanic acid, are derived from medicinally inert glucosides; that only *aloe-emodin* and chrysophanic acid possess purgative properties, and that most of the purgative value of the drug, lies in a non-glucosidic resin which they isolated.

Rosenthaler, (1911), presents a list of anthroquinone drugs distinguished from one another by the physical characters of their micro-sublimates and the color-reaction of these sublimates in alcoholic solution with ferric chloride solution.

Schmidt, (1912), describes *frangulin, (rhamnoxanthin),* ($C_{21}H_{20}O_9$), as occurring in lemon-yellow, glistening, fine needle-crystals, odorless and tasteless, melting at 228° to 230° C. It is almost insoluble in water and in cold ether, but soluble in 180 parts of 80% hot alcohol. Concentrated sulphuric acid dissolves it with a dark-red color and with caustic alkalies it forms solutions of a purple-red color. By boiling with an alcoholic solution of hydrochloric acid, it becomes converted into *rhamnose* and *frangula-emodin,* ($C_{15}H_{10}O_5$), which forms bright-red, glistening needles melting at 255° C. It is insoluble in water, slightly soluble in alcohol and easily in chloroform and benzol In ammonia it dissolves with a red, slightly bluish color.

(To be continued.)

A NEW METHOD FOR THE ESTIMATION OF GLYCERIN IN PHARMACEUTICAL PREPARATIONS.

C. H. BRIGGS, M. S.

Glycerin is one of the most common and generally used substances in pharmacy and yet its quantitative determination in pharmaceutical preparations presents many difficulties. On several occasions in our laboratory it has been necessary to attempt to assay for glycerin such preparations as elixirs, tooth-pastes, shaving soaps, liquid face creams, and essences of pepsin, and the results have been far from satisfactory. Several methods with necessary modifications to adapt them to the particular preparations were tried, but in some cases the duplicate results showed marked variations, thus making doubtful the reliability of the process.

The official methods for the determination of glycerin in wines are not applicable to all pharmaceutical preparations because of interfering substances and, to say the least, they are long and tedious. (See Allen's Organic Analysis, Vol. 1, page 167.)

It would seem therefore that a simple and reliable method for the estimation

of glycerin, applicable to all pharmaceutical preparations, is much to be desired. For pharmaceutical purposes it is not necessary that the method shall be extremely accurate, for if the results do not vary more than 2% from the actual glycerin content, this will meet all practical requirements.

Pharmaceutical preparations contain such a wide range of substances such as sugars, salts, organic acids, soaps, proteids, resins, colors, etc., that it is almost impossible to separate the glycerin in a pure condition by means of solvents and precipitants. It occurred to the writer that perhaps the glycerin could be separated from many of these substances by distillation in a vacuum, provided some liquid could be added with which the glycerin is not miscible and which would also distil and help carry over all of the glycerin. Glycerin boils at 162° C. at 10 m. m. pressure, but by the law of partial pressures, it will vaporize at a lower temperature if distilled with some substance with which it is not miscible. After the trial of several substances it was found that santal oil was best adapted for this purpose, and that, if a small amount of glycerin was distilled with a relatively large amount of santal oil, the glycerin was completely carried over. It was also found that the glycerin could be readily separated from the santal oil in the distillate by dissolving the oil in purified petroleum benzine and washing out the glycerin with small quantities of water in a separatory funnel. The glycerin in the combined aqueous solutions could then be estimated by various methods, but the writer prefers evaporating off most of the water at a low temperature and completely de-hydrating the glycerin in a vacuum over sulphuric acid. This procedure has not been noted elsewhere in the literature.

The glycerin used in these tests was of the ordinary U. S. P. grade and when about two grams were dried in a vacuum over sulphuric acid for 24 hours, it lost about 3% of moisture. Water was then added and the solution evaporated to a thin syrup at about 50° C. After drying for 24 hours in a vacuum as above the same weight of anhydrous glycerin was recovered, showing that none had been lost by the de-hydration.

Two determinations by the above distillation method of a 20% solution of glycerin in water gave 99.3% and 100.8% of the glycerin, showing that where there are no interfering substances the method works satisfactorily.

The method was next tried on a mixture containing 10% of sugar and 10% of glycerin. Three determinations gave 110, 109 and 108% of the glycerin taken. A test with Fehling's solution showed that some of the sugar was decomposed and carried over with the distillate. The addition of a small quantity of slaked lime to the distillation flask prevented the sugar from going over but it also held back part of the glycerin. Calcium carbonate did not prevent the sugar from being carried over but calcined magnesium oxide worked better and three determinations of the glycerin in a solution containing 20% of sugar and 20% of glycerin, using one-half gram calcined magnesia, gave 100.1%, 101.5% and 99.9% of the glycerin content. The use of more magnesia did not work as well.

In order to test the method on products containing various ingredients, samples

were prepared of six preparations of widely different character. The amount of glycerin found was as follows:—

	Glycerin used	Glycerin found
Elixir Gentian Glycerinated N. F.	50%	49.4% 48.9%
Tooth Paste	50%	48.1% 48.6%
Shaving Soap	25%	27.6% 26.7%
Essence of Pepsin	20%	18.8% 19.7%
Elixir Lactated Pepsin	10%	10.5% 11.4%
Stearic Acid Cold Cream	8%	7.2% 8.1%

While these results are not as accurate as the writer at first hoped for, still considering the wide range of the preparations, the results are fairly satisfactory as they give a good indication of the amount of glycerin present and probably accurate enough for all pharmaceutical purposes.

The method is not applicable without some modification to preparations where there is a large amount of sugar and a small amount of glycerin, as some of the sugar decomposes and is carried over. One test was made on such a preparation by repeating the distillation and the result was slightly low.

The length of time required to complete a test by this method is about two days, but four or five tests can be made per day, so that the actual time consumed is about two hours per assay.

The apparatus found most convenient for this assay consisted of a 500 cc. distillation flask with the side neck bent so that the flask would be inclined to an angle of 45° when in use. The top of the flask was cut off to within 1½ inches of the side neck, and the flask was closed with a rubber stopper fitted with a glass tube drawn to a very fine capillary. The flask was connected to an ordinary straight tube condenser, the side neck being inserted well into the condenser. For a receiver an 8 oz. Squibb separatory funnel was used and the end of the condenser was bent slightly and inserted into the large end of the separatory funnel so that the funnel rested horizontally. This enabled the vacuum to be connected to the small end of the separatory funnel and at the same time allowed the funnel to act as a receiver for the distillate.

The method in detail is as follows:—

Take sufficient of the sample to obtain about two grams of glycerin and place in the 500 cc. side neck distillation flask with one-half gram of calcined magnesium oxide. Warm on a steam bath for five minutes. Now add 75 cc. of santal oil and distil in vacuo until about two-thirds of the oil has been distilled. Rinse the

condenser with about 100 cc. of purified petroleum benzine and add to the distillate. Now rinse the condenser well with 5 cc. of water and add to the distillate. Stopper the separatory funnel, shake well, and draw off the aqueous layer into a second separatory funnel. Extract the benzine oil solution three times with 5 cc. of water to completely remove the glycerin and add to the first extract. Shake the combined aqueous extracts with 30 cc. of petroleum benzine to remove traces of oil. Allow to stand one-half hour and draw off the aqueous layer into a tared four inch petrie dish. Rinse the separator with 5 cc. of water and add to the glycerin extract. Evaporate off most of the water at a low temperature (not over 50° C.) and de-hydrate in a vacuum dessicator over sulphuric acid for 24 hours or to constant weight. This anhydrous glycerin is very hydroscopic and must be weighed quickly. To convert to ordinary commercial glycerin divide the weight obtained by .97.

The distillation must be carried out cautiously at first to prevent bumping. After the water has passed over, the distillation proceeds quietly and can be carried out rapidly. A free flame should be used and this should be held in the hand and kept in constant rotation around the bottom of the flask.

In conclusion the writer wishes to express his thanks and indebtedness to Mr. W. B. Parker, who carried out the assays and did most of the experimental work in connection with this paper.

Scientific Department Parke, Davis & Co., August 26, 1914.

A SIMPLIFIED GLYCERIN ASSAY.

F. T. BRADT.

The object of this investigation has been to work out a simple, rapid, and accurate method of estimating the quantity of glycerin in a sample reasonably free from impurities.

The wide variation in results of assays in recent years was deemed of sufficient importance to warrant the appointment of committees in this country and Europe to study methods of analysis and recommend the ones that gave most satisfaction. As a result it was agreed that the acetin method should be the basis on which glycerin should be bought and sold, but that the dichromate method might continue to be used for technical purposes in a properly standardized form. The exact procedure to be followed in purification was described very minutely and also the actual process of assay. The dichromate method was substantially the same as that proposed by Hehner, using solid dichromate for oxidation, an excess of ferrous ammonium sulphate, and dilute dichromate solution to titrate the excess.

Many other methods, besides these two well-known ones, have been suggested for the assay of glycerin, and some of them are well worth a brief review.

In 1891 [1]Benedikt and Zsigmondy proposed to oxidize glycerin with potassium permanganate in alkaline sol. precipitate the manganese by treatment with H_2O_2,

[1] Zeit. Angew. Chem., 1891, 400–401.