(ii) hydrolysis with alkali, distillation of the acetic acid from a sulphuric or phosphoric acid solution and collection of the acid in an excess of alkali.

Kuhn and Roth[4] developed a procedure in which hydrolysis and subsequent distillation of acetic acid were carried out in a single flask. The main objection appears to be that the design of the apparatus permits the carry-over of sulphuric acid, either in mist or droplet form if rapid distillation or bumping occurs.

Wiesenberger[5] drew attention to the slowness of Kuhn and Roth's method and to errors associated with it in a review of methods available for determination of acetyl groups. Later[6] he evolved a method with a claimed high degree of accuracy and precision. This method is now widely used and accepted for determination of acetyl groups and saponification methods are not viewed with favour. The apparatus used by Wiesenberger is described in British Standard 1428 : Part C 2 : 1954. Wiesenberger's method splits off *N*-acetyl groups with sulphuric or phosphoric acid and *O*-acetyl groups with aqueous or methanolic sodium hydroxide solution. The resulting acetic acid is then isolated by a number of successive distillations and titrated with 0·01N sodium hydroxide using phenolphthalein indicator. Reference to the British Standard quoted above will show that elaborate precautions have been taken to prevent carry-over of other acids and it is clear that unless this type of apparatus is used and the technique of distillation followed in detail unsatisfactory results will be obtained. For the initial treatment of most *O*-acetyl compounds any one of the four hydrolysing solutions mentioned above is satisfactory. Wiesenberger's original method was intended for micro (3–10 mg of sample) application, but it is also reported to be 'highly satisfactory' for semi-micro work (20–30 mg of sample). In this case double the quantities of reagents used in the original method[5] are used and the titration of the acid is carried out with 0·05N sodium hydroxide. Precise details of a suitable method are not possible since the hydrolysing reagent will vary from substance to substance, but for a fairly simple *O*-acetyl compound the following procedure might be employed:

> Introduce 20 to 30 mg of sample into the Wiesenberger flask and add an anti-bumping device (a small piece of platinum is commonly employed) followed by 4 ml of 4N sodium hydroxide (aqueous). Heat for thirty minutes at 150° to 155°, allow to cool somewhat and then immerse the flask in an ice-bath. Run 2 ml of specially-prepared sulphuric acid solution (see below) down the condenser tube, followed by 6 ml of water. Then detach the flask from the condenser using a total of 3 ml of water to rinse down the condenser and the joint surface of the flask. Connect the distillation head to the flask and clamp the condenser at an angle of 45° for distillation of the acetic acid. Place 2 ml of water in the funnel above the flask and trap. With the flame of a micro-burner under the flask continue heating until vapour has condensed in the vapour trap

making up to a definite volume. An aliquot part is brominated as given under Salicylic Acid (p. 558).

Tablets of Aspirin and Phenacetin, *B.P.C.* Contain 3½ grains of aspirin and 2½ grains of phenacetin. These tablets are assayed by dissolving in dilute sodium hydroxide solution, extracting the phenacetin with chloroform, then heating the aqueous residue to hydrolyse the aspirin and determining the salicylic acid, either by extraction with ether after acidification as given under Compound Tablets of Aspirin, or by bromination as given under Salicylic Acid. The sodium citrate hydrolysis method given above for the determination of aspirin can also be applied directly to this preparation.

Tablets of Aspirin, Phenacetin and Codeine, *B.P.* (Compound Tablets of Codeine). Contain 4 grains of aspirin, 4 grains of phenacetin and ⅛ grain of codeine phosphate.

Although selection from the modifications of assays given above for the various compound aspirin tablets can be used the usual assay is the following:

> Shake a portion of powdered tablets with excess alkali and extract with chloroform. Determine the aspirin in the aqueous residue as given under Tablets of Aspirin and Phenacetin. Wash the chloroform extracts with dilute acid, evaporate and weigh the phenacetin. Make the acid washings alkaline with ammonia, extract with chloroform, evaporate and weigh or titrate the codeine.

Since the amount of codeine present is comparatively small, use of a single weighed portion of material suitable for the ingredients in larger proportions will tend to give errors from weighing or titrating small amounts of codeine. It is preferable, although longer, to weigh out a separate 5-g portion of sample for the latter, eliminating the other ingredients as above. The *B.P.* direction to extract the codeine with standard acid and back-titrate is not recommended; it has not been repeated for **Soluble Tablets of Aspirin, Phenacetin and Codeine,** *B.P.* (the same ingredients with citric acid and calcium carbonate).

Many methods have appeared in the literature during recent years which depend upon chromatographic or ion-exchange separation of the ingredients. The following method[4] has been found to be very satisfactory for routine determination of both Compound Codeine Tablets and Soluble Compound Codeine Tablets.

> Take a sample of 20 tablets, determine the average weight and powder. Take about 4 g of the powder, accurately weighed, and boil under reflux with 60 ml of 70 per cent ethanol for five minutes. Wash down the condenser with 10 ml of 70 per cent ethanol. Shake well and strain the warm solution through a loose, cotton-wool plug into a 100-ml graduated flask. Wash the first vessel with two 10-ml portions of 70 per cent ethanol and run the washings through the plug into the flask. Cool the solution, dilute to volume, shake and filter, rejecting the first 20 ml of filtrate. Place

Toughened Silver Nitrate, *B.P.* Contains 95 parts of silver nitrate and 5 parts of potassium nitrate, fused together and poured into suitable moulds.

It is assayed by dissolving 0·5 g in 50 ml of water, adding 5 ml of concentrated nitric acid and titrating with 0·1N ammonium thiocyanate to ferric alum, shaking vigorously when nearing the end-point. 1 ml 0·1N = 0·01699 g $AgNO_3$.

Mitigated Silver Nitrate, *B.P.C.* Contains 20 parts of $AgNO_3$ and 40 parts of KNO_3, fused together and poured into suitable moulds.

Assayed as Toughened Silver Nitrate using 1·5 g.

The organic compounds **silver protein** and **mild silver protein** may be assayed for silver by the following methods. Each in its turn has been adversely criticised but they all give reasonably accurate results:

(i) To 1 g in a Kjeldahl flask add 10 ml of concentrated sulphuric acid and 5 ml of concentrated nitric acid. Heat until colourless, adding more nitric acid if necessary. Cool, add 20 ml of water and boil off the oxides of nitrogen. Finally, add 100 ml of water and 5 ml of concentrated nitric acid and titrate with 0·1N ammonium thiocyanate, adding a small crystal of iron alum as indicator. 1 ml 0·1N = 0·01079 g Ag.

(ii) Destroy organic matter by incinerating about 2 g in a porcelain crucible, add 10 ml of concentrated nitric acid, heat until no more coloured fumes are evolved, dilute with water and titrate as in (i).

A rapid method of estimation by Kogan[1] gives good results:

(iii) To 1 g in a conical flask, add 15 ml of 1 : 1 nitric acid and boil for a few minutes until a pale yellow solution is obtained. Cool and dilute with 30 to 40 ml of water. Add potassium permanganate until a pink colour persists for one minute and finally titrate the solution as above. The end-point of this method is not always quite sharp.

Eye-drops of Silver Protein, *B.P.C.* (containing 5 per cent), and **Eye-drops of Mild Silver Protein,** *B.P.C.* (containing 20 per cent), are assayed by method (ii) above after evaporating to dryness.

1. KOGAN, G., *Pharm. Zentralhalle,* 1928, **69,** 228.

SOAPS

The estimation of soaps in pharmaceutical preparations is generally made by acidifying an aqueous solution with hydrochloric acid, extracting the liberated fatty acids with ether or light petroleum, washing the solvent free from mineral acid, and evaporating the solvent. If ether is used the residual fatty acids contain moisture; the latter is eliminated by re-evaporating after adding ethanol or acetone. Slight esterification is probable by this procedure when ethanol is used. The fatty acids should be examined by the methods given under Oils and Fats.

Liniment of Soap, *B.P.* A solution of soap prepared by the interaction of 4 per cent w/v of oleic acid with potassium hydroxide and 4 per cent of camphor in diluted alcohol, containing a small proportion of rosemary oil.

The fatty acids are determined as follows:

> Add 7 ml of 10 per cent sodium hydroxide solution to 25 ml of liniment in a separator and extract twice with portions of light petroleum. Wash the light petroleum layers with water and add the washings to the main aqueous solution. Acidify with dilute sulphuric acid and extract the fatty acids with light petroleum, evaporate, add 5 ml of acetone, again evaporate, dry the residue at 80° for two hours, and weigh.

The extracted oleic acid should have an acid value of 195 to 202 and an iodine value of 85 to 92.

Spirit of Soap, *B.P.C.* Soft soap, 65 per cent w/v in 90 per cent alcohol.

Determine the fatty acids by direct extraction after diluting and acidifying (calculated 28·6 per cent w/v fatty acids).

Ethereal Solution of Soap, *B.P.C.* A potash soap made from oleic acid with alcohol and ether, perfumed with oil of lavender.

The error due to lavender oil in the extracted fatty acids is a maximum of 0·2 per cent; to eliminate this a preliminary extraction by the *B.P.* method for unsaponifiable matter in oils would be necessary, otherwise acid soap would be retained by the solvent. The customary three extractions of the fatty acids is unnecessary; by experiment a third extraction with ether, which was washed with water and evaporated, yielded no weighable residue. The *B.P.C.* assay uses light petroleum for extraction; either solvent can be used.

> To 10 ml in a separator add 20 ml of water and 20 ml of N hydrochloric acid; extract with two successive quantities of 20 ml of ether. Mix the ether solutions in a separator and wash with two 10-ml portions of water. Transfer the ether solutions to a weighed flask, remove the solvent, add 5 ml of acetone, evaporate, dry the residue at 80° and weigh to obtain the proportion of oleic acid by weight in volume. Multiply the weight found by 1·121 and calculate the proportion by volume in volume.

Minimum content of oleic acid should be 33 per cent by volume. Free alkali should be absent.

1. *Analyst*, 1937, **62**, 36.
2. *Analyst*, 1935, **60**, 537.
3. *Analyst*, 1937, **62**, 865.
4. *Analyst*, 1946, **71**, 301.

STARCH

A simple, accurate determination of starch is not possible, and it is usually determined by a 'difference' figure; but if it is present as a pure