matter soluble in Alcohol (90 p.c.) contained in the Gum Resin used; it also contains about 85 p.c. w/v of Absolute Alcohol. A few drops of the Tincture evaporated on a water-bath yield a residue giving a violet coloration when moistened with Nitric Acid.

Not Official.

GARGARISMA MYRRHÆ (*Squire*).—Tincture of Myrrh, 1; Honey, 1; Infusion of Roses, 18.

This has appeared in *Squire's Companion* since 1864 and is now incorporated in the *B.P.C.*

TINCTURE OF MYRRH AND BORAX.—*See* BORAX.

Not Official.

NAPHTHALINUM.

NAPHTHALENE.

$C_{10}H_8$, eq. 127·10.

Crude Naphthalene is a hydrocarbon, crystallising from coal-tar. When purified by sublimation it occurs in white micaceous scales, with a characteristic odour, melting at 80° C. (176° F.).

Solubility.—Insoluble in Water; soluble 1 in 25 of Alcohol (90 p.c.); 1 in 1½ of Chloroform; 1 in 3 of Ether; 1 in 7½ of Oil of Turpentine; 1 in 8 of Olive Oil; slightly soluble in Glycerin.

Medicinal Properties.—Antiseptic; the fine powder is dusted over ulcers and wounds, and is useful for disinfecting cavities. It is given as an intestinal disinfectant. A parasiticide in scabies, as 10 p.c. solution in Olive Oil, or as an Ointment.

Crude Naphthalene in balls and other shapes is used to protect furs and woollen articles from moths.

Dose.—Usual dose, 2 to 5 grains = 0·13 to 0·32 gramme, every four or six hours. Larger doses have been given, but are apt to upset digestion, and in some cases to produce toxic symptoms.

Prescribing Notes.—*It has a nauseous taste and odour; when given internally it may be enclosed in a cachet or capsule; or made into pills with* 1 *of Compound Tragacanth Powder to* 12, *and massed with 'Diluted Glucose.'*

Foreign Pharmacopœias.—Official in Austr., Dutch, Ger., Ital., Jap., Mex., Russ., Swed., Swiss and U.S. Not in the others.

Tests.—Naphthalene melts at 80° C. (176° F.) and boils at 218° C. (424·4° F.), it volatilises slowly at the ordinary temperature and completely with further heat, it burns with a luminous smoky flame. It should not possess an acid reaction to blue Litmus paper moistened with Water, indicating the absence of free acids, *e.g.*, Sulphuric Acid. It should dissolve colourless in warm concentrated Sulphuric Acid if quite pure, but a decided pinkish tint is observed if the sample contains 1 p.c. of impurity, the coloration becoming a deeper pink or even brown the larger the proportion of foreign matter present. 0·5 of a gramme when ignited with free access of air should leave no weighable residue, indicating the absence of mineral impurity.

NAPHTHALINUM PRÆCIPITATUM.—A fine powder, obtained by dissolving the crystals in hot Alcohol, and pouring into a quantity of cold Water, Recommended as less irritating than the powdered crystals.

PULVIS NAPHTHALINI (*Rossbach*).—Purified Naphthalene, 75 grains: Sugar, 75 grains; Oil of Bergamot, ½ minim; divide into 20 powders. In vesical catarrh.—*L.* '85, i., 360.

NAFTALAN.—A dark, greenish-black, unctuous substance, insoluble in Water, soluble in Ether and in Chloroform; an extraction product of a naphtha from the Caucasus containing about 96 p.c. Soap. Used in various skin diseases, and stated to be a good vehicle for the application of antiseptic preparations.—*L.* '99, i. 1234; *B.M.J.E.* '99, i. 92; *P.J.* '01, ii. 124; *B.M.J.E.* '05, i. 40. It may be applied (*B.M.J.E.* '05, ii. 64) as an ointment or in the form of suppositories.

Naphthalini Tetrachloridum.—Glistening, white crystals, insoluble in Water.

Dose.—2 to 10 grains = 0·13 to 0·65 gramme.

NAPHTHOL.

BETA-NAPHTHOL.

BETA-MONO-HYDROXY-NAPHTHALENE.

$C_{10}H_8O$, eq. 142·98.

FR., NAPHTHOL; GER., BETANAPHTHOL; ITAL., NAFTALOLO.

White, or pale yellowish, lustrous, crystalline laminæ or as a white or almost white crystalline powder, having a faint odour suggestive of Phenol, and a sharp, biting but not persistent taste.

It is described in the *U.S.P.* as a monatomic Alcohol, occurring in coal-tar, but usually prepared from Naphthalene; the *B.P.* states that it is derived from Naphthalene-sulphonic Acid.

It should be kept in well-closed bottles of a dark amber tint and protected as far as possible from the air.

There are two isomeric Naphthols, **Alpha-Naphthol** and **Beta-Naphthol,** bearing the same relation to Naphthalene as Phenol does to Benzol.

Solubility.—Nearly insoluble in Water; soluble 1 in 2 of Alcohol (90 p.c.); 3 in 4 of Ether; 1 in 24 of Chloroform; 1 in 12 of Olive Oil; 1 in 40 of Glycerin.

Aqueous solution of Boric Acid will dissolve comparatively small quantities of Naphthol.

Medicinal Properties.—Disinfectant; intestinal antiseptic. Given in summer diarrhœa of children, and in typhoid and intestinal dyspepsia; prolonged administration, especially of large doses, may lead to nephritis. Used in parasitic skin diseases and in chronic eczema in form of ointment.

Dose.—3 to 10 grains = 0·2 to 0·65 gramme.

Prescribing Notes.—*Given in* **cachets** *or* **pills**. *A good pill can be made by adding a small quantity of Compound Powder of Tragacanth and Dispensing Syrup, or 'Diluted Glucose,' q.s. Also administered dissolved in Oil, which is then emulsified. It can be made into an Ointment with Lard, Soft Paraffin or Lanolin Ointment; for Kaposi's Ointments, see below.*

When no prefix is attached to the name, Beta-Naphthol should be used. The name is also written Napthol.

Should be kept in dark amber-tinted well-stoppered bottles.

Not Official.—Lassar's Itch Remedy, Naphthol-Camphor, Pommade Naphtholée, Parogenum Naphtholis, Unguentum Naphtholi, Unguentum Naphtholi Compositum, Vasolimentum Naphtholi, Asaprol, Benzonaphthol, Betol, Epicarin, Quinaphthol.

Foreign Pharmacopœias.—Official in Austr., Belg., Dan., Dutch, Fr., Ger., Hung., Ital., Jap., Mex., Norw., Russ., Span., Swed., Swiss and U.S.

Tests.—Beta-Naphthol when pure melts at 122° C. (251·6° F.) and boils at 286° C. (546·8° F.); the *B.P.* gives the above m.p. but not the boiling point; the *U.S.P.* and *P.G.* give the above-mentioned m.p. and boiling point.

A hot saturated aqueous solution yields a blue fluorescence with one drop of Ammonia Solution; if some Chlorine Solution be added to a cold saturated aqueous solution a white turbidity is produced, and on the addition of Ammonia Solution a green or brownish coloration is produced. In performing this test the *U.S.P.* uses in the place of Chlorine Water a solution of Chlorinated Lime and requires that it should produce a yellow colour. The *B.P.* requires that 10 c.c. of a 1 p.c. boiling aqueous solution should yield a white precipitate becoming brown upon the addition of 10 drops of 3 p.c. aqueous Ferric Chloride Solution. A saturated aqueous solution yields no colour upon the addition of a few drops of Iodine T.S. followed by an excess of Sodium Hydroxide Solution. It is distinguished from its isomer Alpha-Naphthol by the m.p., Alpha-Naphthol melting at 95° C. (203° F.); by the reaction with Chlorinated Lime Solution, Alpha-Naphthol giving a dark violet colour; by the test with Ferric Chloride Solution, Alpha-Naphthol giving a violet coloration with the latter reagent; and by the test with Iodine Solution and excess of Sodium Hydroxide Solution, which produces an intense violet coloration with Alpha-Naphthol.

The more generally occurring impurities are free acid, Naphthalene, organic impurities, and impurities of a mineral or inorganic nature. It should possess a neutral reaction towards Litmus paper previously moistened with Alcohol (90 p.c.). Naphthalene and organic impurities may be detected by the Ammonia test given in small type below. 0·5 of a gramme when ignited with free access of air should leave no weighable residue.

Residue.—When heated it readily sublimes, and is volatilised from its aqueous or alcoholic solution with the vapour of Water or Alcohol, *U.S.P.* It should leave no residue on ignition, *B.P.* and *U.S.P.* 0·2 gramme should not leave a weighable residue after ignition, *P.G.*

Ammonia.—Beta-Naphthol should be soluble in 50 parts of Ammonia Water without residue, and the solution should not have a deeper colour than pale yellow, *U.S.P.* and *P.G.*

Chlorinated Lime.—A cold saturated aqueous solution should not show a violet colour with solution of Chlorinated Lime, *P.G.* and *U.S.P.*, the latter stating that the colour should be pale yellow on the addition of Chlorinated Lime to an aqueous solution.

Not Official.

UNGUENTUM NAPHTHOLI (Kaposi's Ointment).—Beta-Naphthol, 60 grains; Prepared Lard, 1 oz.

Beta-Naphthol, 10; Lard, 90.—*B.P.C.*

POMMADE NAPHTHOLÉE.—Beta-Naphthol, 10; Vaseline, 90.—*Fr.*

UNGUENTUM NAPHTHOLI COMPOSITUM (Kaposi).—Naphthol, 15; Prepared Chalk, 10; Soft Soap, 50; Lard, 100.

Official in Austr., β-Naphthol, 10; Precipitated Chalk, 5; Soft Soap, 28; Lard, 57.

LASSAR'S ITCH REMEDY.—Beta-Naphthol, 0·25; Peru Balsam, 10; Spirit Soap, 25.—*Hager.*

VASOLIMENTUM NAPHTHOLI.—Beta-Naphthol, 10; Vasoliment Liquid, 90.—*Hager.*

Parogenum Naphtholis. *Syn.* Naphthol Vasoliment.—Naphthol, 10; Parogen, *q.s.* to produce 100.—*B.P.C.*

ASAPROL. ABRASTOL (Calcium Beta-naphthol-alpha-monosulphonate).—A white powder, soluble in Water. Has been recommended as an antipyretic and analgesic, in sciatica, muscular and chronic rheumatism and in chronic nephritis.—*T.G.* '93, 182; '94, 252; *Pr.* liii. 52; *M.A.* '95, 8; *Y.B.T.* '94, 462; '95, 159.

Dose.—5 to 15 grains = 0·32 to 1 gramme.

BENZONAPHTHOL. $C_{10}H_7C_6H_5CO_2$, eq. 246·23.—It may be prepared by the action of Benzoyl Chloride on Beta-Naphthol. A white, odourless, tasteless powder, almost insoluble in Water and Ether; soluble in Chloroform.

Intestinal antiseptic, and disinfectant. Has been found useful in typhoid.—*Pr.* li. 213. In tropical dysentery.—*L.* '95, ii. 169; *P.J.* '95, ii. 238.

Dose.—5 to 15 grains = 0·32 to 1 gramme.

Official in Fr., Mex., Span. and Swiss.

Tests.—Benzonaphthol melts at 107° to 108° C. (224·6° to 226·4° F.), the *Fr. Codex* (1908) gives 110° C. (230° F.), it dissolves in Sulphuric Acid with the production of a pale yellow colour; if the Sulphuric Acid solution be diluted with Water and rendered alkaline with an excess of Ammonia Solution, a green fluorescence is produced. When warmed with Potassium Hydroxide Solution it is decomposed; if the solution be exactly neutralised with diluted Sulphuric Acid, it yields with Ferric Chloride T.S. a buff coloured precipitate. The Benzoic Acid separated from the salt should possess the m.p. and answer the tests given under Acidum Benzoicum. A small quantity warmed with Potassium Hydroxide Solution, cooled, rendered faintly acid by the addition of diluted Sulphuric Acid yields on the addition of Chlorinated Lime Solution a yellow colour but no dark violet coloration.

BETOL. NAPHTHALOL β-Naphthol Salicylic Ester. Beta-Naphthol Salicylate, β-Naphthol Salicylic Acid Ester. $C_{10}H_7 \cdot C_7H_5O_3$, eq. 262·11.—In tasteless, small white crystals, or as a white, odourless, tasteless and crystalline powder; insoluble in Water, soluble in Alcohol and in fixed Oils. Recommended in rheumatism, cystitis and intestinal fermentation.

It may be prepared by the action of Phosphorus Oxychloride on a mixture of Sodium Beta-Naphthol and Sodium Salicylate.

Dose.—2 to 8 grains = 0·13 to 0·52 gramme as a **powder,** or in **pills** with Glucose.

Official in Fr. (Salicylate de Naphtyle-β) and Ital.

In **pencils** for gonorrhœa containing 20 p.c. of Betol with Oil of Theobroma.

Tests.—Beta-Naphthol Salicylate melts at 95° C. (203° F.), which figure is also given in *Fr. Codex* (1908), when shaken with Water and filtered, the filtrate should be neutral in reaction towards Litmus paper. When treated with Sulphuric Acid it yields a yellow coloration and in the course of a few minutes a lemon-yellow coloured solution, which on the addition of a drop of Nitric Acid changes to a brownish-green. A 1 p.c. solution of the salt in Alcohol (90 p.c.) yields with 1 drop of a strongly diluted Ferric Chloride Solution a violet coloration, but the highly diluted Ferric Chloride Solution is only rendered turbid, and no coloration is produced, when 10 to 20 drops of a 1 p.c. solution of the salt in Alcohol (90 p.c.) is added to it. When heated with Potassium Hydroxide Solution it is decomposed, forming Potassium Beta-Naphthol and Potassium Salicylate. If the solution be carefully neutralised with Hydrochloric Acid it yields on the addition of Ferric Chloride T.S. a violet coloration, the salt is also decomposed by concentrated acids yielding Salicylic Acid and Beta-Naphthol; the separated Salicylic Acid should possess the m.p. and answer the tests given under Acidum Salicylicum. When heated with Potassium Hydroxide Solution, cooled and slightly acidified with diluted Sulphuric Acid it yields on the addition of Chlorinated Lime a yellow but not a dark violet coloration. 0·5 of a gramme of the salt when ignited with free access of air should leave no weighable residue.

Alphol is the Salicylate of α-Naphthol Ester.

EPICARIN (Beta-oxynaphthyl-orthoxy-meta-toluylic Acid). — Colourless needle-shaped crystals, or a pale yellow powder, insoluble in Water, soluble in Alcohol and Ether. Employed in the form of a 10 to 20 p.c. Ointment in psoriasis, eczema and other skin affections, and in the form of a 5 to 10 p.c. alcoholic solution for seborrhœa capitis and lichen planus.—*Y.B.P.* '02, 177.

The Sodium salt of the above is also known commercially.

Tests.—Epicarin melts at 199° C. (390·2° F.), it dissolves readily in Alcohol (90 p.c.), yielding a solution which gives on the addition of Ferric Chloride T.S. a deep blue colour; it yields when treated with concentrated Sulphuric Acid a reddish-brown solution possessing a strong green fluorescence; when mixed with Potassium Hydroxide Solution and shaken with Chloroform a yellowish turbidity is produced subsequently changing to a yellowish-green. When heated with free access of air it should leave no weighable residue.

NAPHTHOL-CAMPHOR.—Mix 2 of Camphor with 1 of Beta-Naphthol to a viscous consistency, insoluble in Water, soluble in Oils; it is strongly antiseptic.—*Hager.*

A difference of opinion appears to exist as to the harmlessness of this preparation for the treatment of certain localised tuberculous lesions. On the one hand, no grave sequels were shown to have followed 10,000 injections; and on the other, 12 deaths are reported after its use.—*L.* '04, ii. 1893; *P.J.* '05, i. 177.

QUINAPHTHOL (Quinine Beta-naphthol-sulphonate).—A yellow crystalline powder, sparingly soluble in Water and in Alcohol.

Intestinal antiseptic. Useful in typhoid.—*P.J.* '87, ii. 83.

Dose.—8 to 10 grains = 0·52 to 0·65 gramme, three or four times a day.

Tests.—Quinaphthol fuses at 185° C. (365° F.), when ignited with free access of air it leaves no weighable residue.

Sodium-Naphthol (Microcidin) readily soluble in Water, **Hydronaphthol, Lactonaphthol (Lactol)**, and **Naphthol-Camphor** have also been introduced as possessing properties similar to those of Naphthol; **A-Oxynaphthoic Acid** forms soluble salts with alkalis, which are antiseptics.

* * *

Not Official.

NICKEL.

A metal closely allied to Cobalt, with which it is generally associated in minerals. Commercially it is largely contaminated with Copper, Iron, and sometimes Cobalt. Alloyed with Copper and Zinc, it forms **German Silver.** Easily soluble in mineral acids, forming salts of a characteristic green colour.

NICCOLI BROMIDUM.—Green, hygroscopic crystals, soluble in Water, Alcohol, and Ether.

Sedative. Recommended in epilepsy.

Dose.—1 to 5 grains = 0·06 to 0·32 gramme.

In solution, or in **pills.**

SYRUPUS NICCOLI BROMIDI.—Granulated Nickel, 137 grains; Bromine, 377 grains; Water, 12 fl. oz.; digest them in a pint flask at a gentle heat until reaction ceases, filter, add Sugar, 24 oz., and sufficient Water to make 32 fl. oz.

Each fl. drm. contains 5 grains of Nickel Bromide, which is an average dose. —*A.J.P.* '86, 592.

NICCOLI SULPHAS.—Greenish-blue crystals, readily soluble in Water.

Dose.—$\frac{1}{2}$ to 1 grain two or three times a day in chlorosis; is best given on a full stomach, as otherwise it is apt to produce nausea. In somewhat larger doses it has also been given in locomotor ataxy.

The toxicology of **Nickel Carbonyl.**—*B.M.J.* '07, ii. 687.

Not Official.

NITROGLYCERIN.

Syn.—GLYCERYL TRINITRATE; GLONOIN; TRINITRIN; TRINITRO-GLYCERIN.

$C_3H_5(NO_3)_3$, eq. 225·47.

When pure it is a heavy, colourless, oily liquid. Explodes violently on percussion, and under some circumstances spontaneously.

A **10 p.c. solution** in Alcohol is commercial, and is used in making the Tabellæ.

Solubility.—Very slightly soluble in Water; readily in Alcohol (90 p.c.); mixes with Ether and with Chloroform.

Medicinal Properties.—Chiefly given for angina pectoris associated with aortic disease, spasmodic asthma and the dyspnœa of acute bronchitis; in hæmoptysis and in headache, neuralgia or hemicrania if associated with pallor. It reduces arterial tension in chronic Bright's disease and acts as a diuretic and diminishes the albuminuria. Chemically, it is a nitrate, but its physiological action resembles the Nitrites. It is similar to that of Amyl Nitrite, but its action is slower and more prolonged.

Of service in migraine, especially when combined with Strychnine, but not for the attack itself; its service is obtained by continuous administration between the attacks (Gowers).—*B.M.J.* '06, ii. 1622.

Preferred to Amyl Nitrite by some in hæmoptysis, because of its more lasting effect.—*L.* '08, i. 565.

For hæmoptysis give two tabellæ in the 24 hours, breaking them up into small pieces, and letting the patient take a piece every hour.—*Pr.* '07, 1. 335.

In optic atrophy, *M.A.* '95, 261; in neuralgia and sciatica, in uræmic dyspnœa, in all forms of vomiting.—*M.P.* liv. 515; *M.A.* '95, 37, 445, 497, 520; *Pr.* li. 140; in arterio-sclerosis, *T.G.* '93, 736; in warding off, and (hypodermically) during paroxysm of epilepsy, *B.M.J.E.* '93, ii. 32; in gall-stone colic, *L.* '96, i. 353.

Dose.—$\frac{1}{200}$ to $\frac{1}{50}$ grain = 0·0003 to 0·0013 gramme, the average dose being $\frac{1}{100}$ grain = 0·0006 gramme.

Prescribing Notes.—*The Solution may be given on Sugar, or in the form of Tablets, or diluted with Water.*

Official Preparations.—Liquor Trinitrini and Tabellæ Trinitrini.

Not Official.—Haustus Trinitrini, and Tabella Nitroglycerini Composita.

Antidotes.—Ergot, Atropine, Strychnine, cold applications to the head.

Foreign Pharmacopœias.—Official in Jap., Mex. and Span.

Tests.—Nitroglycerin has a sp. gr. of 1·6 and, when pure, is colourless, but the commercial product generally has a yellow colour. It solidifies at 8° C. (46·4° F.), and is then very dangerous to handle. When smartly struck or compressed, or when dropped on an iron plate heated to 257° C. (494·6° F.), it explodes with great violence. It is decomposed by Alcoholic Potassium Hydroxide Solution, yielding a mixture of Potassium Nitrate and Nitrite, Potassium Acetate and Formate. When treated with a solution of Ferrous Sulphate acidified with Hydrochloric Acid, gives the brown coloration characteristic of Nitrites and Nitrates.

Official Preparations.

LIQUOR TRINITRINI. SOLUTION OF TRINITRIN. *B.P.Syn.*—SOLUTION OF NITROGLYCERIN.

Trinitroglycerin of commerce, $17\frac{1}{2}$ grains; Alcohol (90 p.c.), *q.s.* to yield 4 fl. oz.

1 minim contains $\frac{1}{110}$ of a grain.

Dose.—$\frac{1}{2}$ to 2 minims = 0·03 to 0·12 c.c.

In severe cases of angina pectoris or asthma, the dose is sometimes increased.

Foreign Pharmacopœias.—Official in Dutch (Solutio Nitroglycerini), Dan., Jap., Mex. and Span, 1 in 100; U.S. (Spiritus Glycerylis Nitratis), 1 in 100. Not in the others.

Tests.—Solution of Nitroglycerin has a sp. gr. 0·830 to 0·836. The official gravity is 0·840. It is a clear, colourless liquid, possessing a neutral reaction towards Litmus paper. The presence of a due amount of Nitroglycerin is officially ensured by a test of which the following are the essential details:—A measured quantity of 10 c.c. of the solution when mixed with 10 c.c. of Water yields a clear solution when cooled to 15·5° C. (60° F.), but a turbidity is produced in the mixture upon the further addition of 1 c.c. of Water, the Nitroglycerin separating out as an oily liquid when the mixture is still more largely diluted. If only 1 drop of this oily liquid be placed upon bibulous paper and sharply struck with a hammer a violent explosion results.

TABELLÆ TRINITRINI. TRINITRIN TABLETS. *B.P.Syn.*—TABLETS OF NITROGLYCERIN.

These tablets, made of chocolate, now weigh 5 grains instead of the $2\frac{1}{2}$ grains in *B.P.* '85, but they contain as formerly $\frac{1}{100}$ of a grain = 0·0006 gramme of Trinitroglycerin.

Dose.—1 or 2 tablets.

Not Official.

HAUSTUS TRINITRINI.—Solution of Trinitrin, 1 minim; Spirit of Chloroform, 5 minims; Tincture of Capsicum, 2 minims; Peppermint Water, to $\frac{1}{2}$ oz.—*Westminster.*

TABELLA NITROGLYCERINI COMPOSITA.—Nitroglycerin, $\frac{1}{100}$ grain; Menthol, $\frac{1}{50}$ grain; Capsicin, $\frac{1}{100}$ grain; Theobroma Paste, *q.s.*—*Westminster.*

Not Official.

NUCLEIN. NUCLEOL.

The nucleins are compounds of simple proteids with phosphorised bodies, and occur in Yeast, Milk, Yolk of Egg, Thyroid and Thymus glands, etc. Numerous varieties are supposed to exist. Nuclein is extracted by digestion with Pepsin and dilute Hydrochloric Acid, and purification of the residue by repeated solution and precipitation in dilute alkali and dilute acid respectively.

Nuclein is the best known chemical constituent of the nucleus of the white blood corpuscles.

NUCLEIC OR NUCLEINIC ACID.—A white or greyish-white amorphous powder, slightly soluble in Water, insoluble in Alcohol (90 p.c.), and in Ether. It is readily soluble in solutions of Sodium or Potassium Hydroxides with the formation of the corresponding Nucleinates, and it is in the form of 5 p.c. aqueous solutions of these salts that it is chiefly used medicinally.

Medicinal Properties.—A powerful germicide. Stated to possess nutritive properties, and to be useful in increasing the resisting power of the system to pathogenic germs. It has been employed in the treatment of tuberculosis, in anæmia, and in neurasthenia. It has also been employed in diphtheria, and puerperal and scarlet fevers.

1 p.c. solution of nucleinate of Sodium, in physiological solution, subcutaneously injected to moderate peritoneal inflammation after perforation in typhoid, and thus to lessen the risks of subsequent surgical interference. Within 3 days, 3 doses are given.—*B.M.J.* '07, i. 1515.

Prescribing Notes.—*It may be administered hypodermically in the form of a sterilised* 5 *p.c. solution, dose* 17 *minims* = 1 *c.c., or by the mouth as a solution of similar strength, in doses of* 1 *to* 2 *fl. drm.* = 3·6 *to* 7·1 *c.c.*

ARGENTI NUCLEINAS (Nargol).—A light brownish-yellow powder, containing about 10 p.c. Silver, soluble 1 in 4 of Water. Used as an injection, ¼ to 1 p.c. solution, in gonorrhœa.—*B.M.J.* '01, ii. 1333; *L.* '01, ii. 1809; *M.A.* '02, 701.

CUPRI NUCLEINAS (Cuprol).—A green, colourless, impalpable powder, soluble in Water. Its solution is stated not to coagulate albumen. Has been found useful in powder form in cases of trachoma. Also as a 5 to 10 p.c. aqueous solution in conjunctivitis. Is stated to be less irritating than the Sulphate.—*L.* '01, ii. 729, 1809.

FERRI NUCLEINAS (Triferrin. Ferrinol).—A brown, amorphous, odourless powder, soluble in Water. Has been recommended in anæmia.—*B.M.J.E.* '02, i. 104; ii. 16, 104; *C.D.* '02, i. 580.

Dose.—5 grains = 0·32 gramme.

HYDRARGYRI NUCLEINAS (Mercurol).—A pale yellowish-brown amorphous powder, soluble 1 in 5 Water, insoluble in Alcohol (90 p.c.). Its solution does not coagulate albumen. It has been used as a 2 p.c. injection in urethritis. —*L.* '00, ii. 871. As an antiseptic in the form of a 2½ to 5 p.c. solution in the treatment of diseases of the nose and ear.—*L.* '00, ii. 1726; *T.G.* '01, 92. Given with success in the treatment of syphilis, in average doses of 2 grains three times a day.—*L.* '01, ii. 1039. In gonorrhœa as an injection in the form of a 2 p.c. solution.—*T.G.* '01, 15. Has been found useful in combination with Chloretone and Boric Acid in the treatment of various acute and chronic affections of the skin and mucous membrane.—*T.G.* '01, 636.

SODII NUCLEINAS.—A white or greyish-white amorphous powder, soluble in Water. Employed medicinally, as above described, in the form of a 5 p.c. solution.

NUX VOMICA.

NUX VOMICA.

FR., NOIX VOMIQUE; GER., BRECHNUSS; ITAL., NOCE VOMICA; SPAN., NUEZ VOMICA.

The dried ripe Seeds of *Strychnos Nux-vomica*, L.

Imported from India, Ceylon, and Cochin China.
The chief source of Strychnine and Brucine.

The total alkaloids have been found to vary between 1·25 and 3·9 p.c. (some Ceylon Seeds gave 5·3 p.c.), but the value of total alkaloids as a medicinal standard is considerably reduced by the fact that the ratio of Strychnine to Brucine may vary as much as 3 to 1 and 1 to 2. The official galenical preparations of Nux Vomica are standardised to a definite percentage of Strychnine, but the *B.P.* does not state what amount of Strychnine should be present in the Seeds. The *U.S.P.* requires that they shall yield not less than 1·25 p.c. of Strychnine; the *P.G.* not less than 2·5 p.c. of total alkaloids as calculated from the result of the official volumetric process, using a factor based on equimolecular proportions of Strychnine and Brucine. The *Brussels Conference* has agreed upon a standard of 2·5 p.c. of total alkaloids. The *Fr. Codex* (1908) has adopted the recommendation of the *Brussels Conference*, and requires that the dried powdered seeds should yield not less than 2 nor more than 3 p.c. of total alkaloids. From 1 to 1·25 p.c. of Strychnine has been suggested (*Y.B.P.* '03, 252) as a suitable standard for inclusion in the next *B.P.*; the dual standard of percentage of total alkaloids and percentage of Strychnine not being advocated. The establishment of a Strychnine standard upon a dual basis by calculating the Brucine into terms of Strychnine has been suggested, *Y.B.P.* '06, 237.

Medicinal Properties.—An excellent gastric and general tonic. Recommended in atonic dyspepsia, in general debility, and in convalescence. It stimulates peristalsis, and therefore is a frequent and valuable ingredient in medicines for chronic constipation. It is also a cardiac and respiratory stimulant. Useful in paralysis of reflex origin, in peripheral paralysis due to alcohol, lead, tobacco, or to diphtheria; in all chronic paralytic affections, except those in which there is organic lesion of nerve-centres or inflammation of brain or spinal cord. *See* also STRYCHNINA.

A report on eight cases of chronic pulmonary tuberculosis, treated with a 'simple mixture of nux vomica, gentian and acid,' compared with similar cases treated with 'Malt and Oil,' results compare most favourably.—*L.* '03, ii. 1016.

Dose.—*In powder* 1 to 4 grains = 0·06 to 0·26 gramme.

Ph. Ger. maximum single dose, 0·1 gramme; maximum daily dose, 0·2 gramme.

Prescribing Notes.—*$\frac{1}{13}$ grain Strychnine is contained in 1½ grains of Extract, 5½ minims of Fluid Extract, 33 minims of Tincture.*

Official Preparations.—Of the **seeds,** Extractum Nucis Vomicæ Liquidum and Strychnina; of the **Liquid Extract,** Extractum Nucis Vomicæ and Tinctura Nucis Vomicæ.

Not Official.—Brucine.

Antidotes.—Emetic of Zinc Sulphate, Mustard, or Ipecacuanha, or hypodermic injection of Apomorphine; Animal Charcoal; Potassium Bromide or Chloral; Amyl Nitrite inhalations; Chloroform or Ether to relax the muscles; hypodermic injection of Curare.—*Murrell.*

Foreign Pharmacopœias.—Official in Austr., Belg., Dutch, Ger., Jap., Russ. and Swiss, Semen Strychni; Dan., Fr. (Noix Vomique), Hung., Ital. (Noce Vomica), Mex. and Span. (Nuez Vomica), Norw., Port. (Noz Vomica), Swed. and U.S.

Descriptive Notes.—Nux Vomica Seeds are imported from Ceylon, Bombay, Cochin, Madras, and Calcutta. They vary in size and in alkaloidal content, the largest usually yielding most alkaloid; the Ceylon and Bombay Seeds are richer than those imported from Madras and Cochin. The Seeds vary from ¾ to 1 in. (19 to 25 mm.)

in diameter and from $\frac{1}{8}$ to $\frac{1}{4}$ in. (3 to 6 mm.) in thickness. They are circular, nearly flat or somewhat plano-convex, and occasionally irregularly bent, greyish-green in colour, with a satiny lustre from the appressed hairs, the margin rounded or in some kinds acute with a protuberance at the edge indicating the position of the radicle, internally consisting of hard, tough, and horny albumen, in the centre of which is found an embryo with thin, leafy, cordate, palmately-veined cotyledons. The taste is intensely and persistently bitter. *B.P.* gives the same measures as above for the Seeds, *U.S.P.* diameter 15 to 30 mm., thickness 3 to 5 mm. The microscopical characters of the powder are the non-porous thick-walled endosperm cells (*P.G.*), containing fixed Oil and aleurone grains (*U.S.P.*), the hair bases with linear specially formed pits and the cylindrical fragments of the upper part of the hairs, which have a striated appearance.

Tests.—Nux Vomica Seeds may be assayed for their percentage content of Strychnine by any one of several excellent processes. That of the *U.S.P.* is essentially as follows:—A weighed quantity of 20 grammes of the Seeds in No. 60 powder is introduced into an Erlenmeyer flask and is first macerated for 1 hour, with frequent intervals of shaking, with 200 c.c. of a mixture composed of 137·5 c.c. of Ether, 44 c.c. of Chloroform and 13·5 c.c. of Alcohol (94·9 p.c.) and 5 c.c. of Ammonia Solution and subsequently allowed to stand for 12 hours. A measured quantity of 100 c.c. of the clear liquid is decanted into a second separator, the measuring vessel washed out with a little Chloroform and the washings added to the main quantity. The alkaloids are then extracted from the chloroformic solution by agitation with 15 c.c. of Normal Volumetric Sulphuric Acid Solution, care being taken to avoid the formation of emulsion during the shaking; after complete separation the lower acid layer is separated, the Ether-chloroform solution is separated, washed with 2 successive quantities each of 5 and 3 c.c. of Normal Volumetric Sulphuric Acid Solution. The acid liquids in each case are separated as previously and mixed with the main acid quantity. The complete extraction of the alkaloids from the Ether-Chloroform liquid is ensured by testing a drop of the acid liquid with Mercuric Potassium Iodide (Mayer's) Solution, and if a precipitate is produced the shaking is repeated with a further quantity of 5 c.c. of Normal Volumetric Sulphuric Acid Solution; the acid solutions are mixed and sufficient Ammonia Solution added to render the solution alkaline, and the liberated alkaloids are extracted by thoroughly shaking first with 25 c.c. of Chloroform and subsequently repeating the extraction with two successive portions, each of 15 c.c. of Chloroform. The chloroformic solution is in each case separated, transferred to a tared flask, the mixed chloroformic solutions evaporated to dryness on a water-bath and the residue dissolved in 15 c.c. of 3 p.c. Sulphuric Acid by warming it on the water-bath. The solution is allowed to cool and 3 c.c. of a cooled mixture of equal volumes of Nitric Acid (sp. gr. 1·42) and Distilled Water added; the liquid, after it has been rotated a few times, is set aside for exactly 10 minutes, with 3 intervals of gentle rotation; the liquid is transferred to a separator containing 25 c.c. of a 10 p.c. w/v Sodium Hydroxide Solution, the flask being washed out with 3 successive small quantities of Water and the washings added to the main quantity of liquid, which, if not turbid, is mixed with a further measured quantity of 2 c.c. of the Sodium Hydroxide Solution. The liberated alkaloids are then extracted by well rotating the mixture for a few minutes with 20 c.c. of Chloroform, the extraction being repeated with 2 successive quantities of 20 c.c. of Chloroform; the Chloroform solution is separated in each case, filtered through a small filter paper, previously moistened with Chloroform, into a tared flask, the filter and funnel washed with 5 c.c. of Chloroform and the mixed Chloroform solutions evaporated very carefully to dryness on a water-bath. The alkaloidal residue is dissolved in 6 c.c. of Tenth-normal Volumetric Sulphuric Acid Solution, 5 drops of Iodeosin Test Solution are added, about 80 c.c. of Water and 20 c.c. of Ether, the excess of acid is titrated with Fiftieth-normal Volumetric Potassium Hydroxide Solution. The number of c.c. of Fiftieth-normal Potassium Hydroxide Solution is divided by 5, the quotient subtracted from 6, the difference multiplied first by 0·0332 and then by 10 yields the percentage of Strychnine present in the sample. The above process for the separation of Strychnine and Brucine is that originally suggested by Gordin, but, as originally introduced into the *U.S.P.*, it was modified in two essential particulars, such modifications having been vigorously protested against by the author of the process, who considered the modifications quite unwarranted. The method originally suggested by Gordin (*Proc. Amer. Pharm. Assoc.* '02, 341) states, first, that the mixed alkaloids might be dissolved in 15 c.c. of a 3 p.c. Sulphuric Acid Solution by the aid of the water-bath heat, and after the solution is cooled to the ordinary temperature 3 c.c. of a specially prepared and cooled mixture of equal parts of strong Nitric Acid (sp. gr. 1·420) are to be added. Secondly, the mixed Chloroform solutions containing the residual Strychnine are directed to be mixed with 2 or 3 c.c. of pure Amyl Alcohol [b.p. 128° to 132° C. (262·4° to 269·6° F.)], previous to evaporation to dryness. Nitric Acid of a sp. gr. of 1·40 does not affect the oxidation of the Brucine to the extent that an acid of a sp. gr. of 1·42, and requires the addition of a small quantity of Sodium Nitrite to start the reaction. The insufficiency of the original *U.S.P.* official Nitric Acid (sp. gr. 1·40) had been also pointed out (*Proc. Amer. Pharm. Assoc.* '07, 55, 781); however carefully the evaporation of the Chloroform solution is conducted, without the addition of the Amyl Alcohol there is a considerable liability to a loss due to decrepitation, but with the addition of 2 or 3 c.c. of pure Amyl Alcohol no decrepitation takes place. It will be noted that the *U.S.P.* omits the use of Amyl Alcohol. Farr and Wright (*Y.B.P.* '06, 226) have experimented with the *U.S.P.* Nitric Acid process for the determination of Strychnine; they appear to be of the opinion that, notwithstanding the condemnation of the process as contained therein, that process, with slight modifications in the working details, gives perfectly satisfactory results, and that subsequent work has thoroughly established its reliability. The exact details of the process as they have applied it are as follows:—The total alkaloids obtained in the usual way from 5 c.c. of the liquid extract or 25 c.c. of the Tincture are dissolved by the heat of a water-bath in 15 c.c of 3 p.c. Sulphuric Acid Solution, the temperature of the solution adjusted to 50° C. (122° F.); 3 c.c. of a mixture of equal volumes of Nitric Acid (sp. gr. 1·42) and Water added and the mixture set aside for 10 minutes, it is transferred to a separator and shaken with Chloroform, the Chloroform solutions run into a tared dish containing 3 c.c. of Amyl Alcohol. It will be noticed that the above modification by Farr and Wright of the *U.S.P.* process rectifies the identical objections which were urged against the strictly *U.S.P.* process, namely, the gravity of the Nitric Acid Solution used for the oxidation of the Brucine and the addition of Amyl Alcohol to prevent loss by decrepitation of the Strychnine residue. The original process of the *U.S.P.* recommended the use of Nitric Acid of specific gravity 1·40, but the list of alterations and corrections (1907) has altered the specific gravity of the acid to 1·42.

Another modification of the *U.S.P.* method of separating Brucine and Strychnine is described (*A.J.P.* '07, 6). The alkaloidal residue is dissolved in 15 c.c. of 3 p.c. Sulphuric Acid; to the solution is added 3 c.c. of a mixture of equal volumes of Nitric Acid (sp. gr. 1·4) and Distilled Water. Then add 1 c.c. of a 5 p.c. Solution of Sodium Nitrite in Water and, after rotating the liquid a few times, set it aside for exactly 30 minutes, stirring it gently 3 times during the interval; the solution is then made alkaline and shaken out with Chloroform in the usual way.

The influence of Nitrous Acid in the oxidation of Brucine by Nitric Acid has been closely studied by Reynolds and Sutcliffe (*J.S.C.I.* '06, 512), and they conclude that Stoeder's and Gordin's addition led to slightly more accurate results than Keller's original process; of the two, that of Gordin should have the preference, as it is more expeditious. The short Nitric Acid process is generally capable of accurate results if the following points are attended to:—(1) For the amount of total alkaloid up to 0·4 of a gramme, the reacting solution should contain at least 7 p.c. of Nitric Acid. (2) The reaction should be stopped after 10 minutes, when the Brucine is entirely oxidised. (3) The temperature should not exceed 25° C. (77° F.). (4) Excess of Potassium or Sodium Hydroxide should be used to liberate the Strychnine, and not Sodium Carbonate or Ammonia Solution. (5) The Nitric Acid used should be added in the form of sp. gr. 1·42 and not more diluted, otherwise it may be necessary to add a trace of Nitrite to start the reaction.

The *P.G.* process is a volumetric one: a weighed quantity of 15 grammes of the Seeds dried at 100° C. (212° F.) and reduced to a middling fine powder is shaken with 100 grammes of Ether and 50 grammes of Chloroform, and then mixed with 10 c.c. of a solution of 2 parts by weight of Sodium Hydroxide Solution (15 p.c.) and 1 part by weight of Water, and the residue is allowed to stand for 3 hours with intervals of vigorous shaking. A measured quantity of 15 c.c. or a sufficient quantity of Water to cause the powdered Nux Vomica to agglomerate and the supernatant Chloroform-Ether solution to separate completely clear, is then added. After standing for an hour 100 grammes of the clear Ether-Chloroform solution are filtered through a dry, well-covered filter into a flask, and about half of the liquid distilled; the remaining Chloroform-Ether solution is transferred to a separator, the flask being washed out with 3 successive quantities each of 5 c.c. of a mixture of 3 parts by weight of Ether, and 1 part by weight of Chloroform. The alkaloids are extracted from the mixed liquids by agitation with 10 c.c. of Tenth-normal Volumetric Hydrochloric Acid Solution. After complete separation of the liquids sufficient Ether is added to cause the Chloroform-Ether solution to float on the top of the acid liquid, the latter is filtered through a small filter previously moistened with Water into a flask of 100 c.c. capacity. The Chloroform-Ether solution is shaken with 3 successive quantities, each of 10 c.c. of Water, the aqueous liquids being filtered through the same filter, the filter is washed with Water and the mixed filtrate and washings diluted with Water to 100 c.c. A measured quantity of 50 c.c. of this solution is removed, introduced into a flask of white glass of about 200 c.c. capacity; 50 c.c. of Water and sufficient Ether to form a layer of 1 cm. added, and the mixture titrated with Hundredth-normal Volumetric Potassium Hydroxide Solution, using 5 drops of Iodeosin Solution as an indicator of neutrality; not more than 15 c.c. of Hundredth-normal Volumetric Potassium Hydroxide Solution shall be necessary to neutralise the excess of Tenth-normal Hydrochloric Acid; the number of c.c. of Hundredth-normal Volumetric Hydroxide Solution used divided by 10, the quotient multiplied first by 2, then subtracted from 10 and the difference multiplied by 0·00364 (the mean molecular equivalents of Strychnine and Brucine), then by 10 gives the percentage of total alkaloid present in the Seeds.

Preparations.

EXTRACTUM NUCIS VOMICÆ. Extract of Nux Vomica.

Prepared from Liquid Extract of Nux Vomica, and readjusted by means of Milk Sugar to contain 5 p.c. of Strychnine.

The *B.P.* extract is prepared by the evaporation of the liquid extract, which is officially required to contain 1·5 p.c. w/v of Strychnine. The solid extract is officially required to contain 5 p.c. of Strychnine.

The *U.S.P.* extract is prepared direct from the powdered Seeds, the menstruum being a mixture of Acetic Acid and Water; it is required to contain 5 p.c. of Strychnine. The *P.G.* extract is also prepared from the powdered Seeds, using the menstruum Alcohol (68 to 69 p.c.), and is required to contain not less than 17·5 p.c. w/w of mixed alkaloids. The Extract official in the *Fr. Codex* (1908) is prepared from the Nux Vomica Seeds in No. 22 powder, the menstruum being Alcohol (70 p.c.). It is required to contain exactly 16 p.c. of total alkaloids in conformity with the recommendation of the *Brussels Conference*.

Dose.—¼ to 1 grain = 0·016 to 0·065 gramme.

Ph. Ger. maximum single dose, 0·05 gramme; maximum daily dose, 0·10 gramme.

Often prescribed with Aloes and Ipecacuanha.

This Extract is intended to be about two-thirds the strength of that in *B.P.* 1885. *Ph. Ger.* Extractum Strychni is standardised to contain 17·5 p.c. of total alkaloids, and is therefore rather stronger than *B.P.* 1885.

Foreign Pharmacopœias.—Official in Austr., Belg., Dan., Dutch, Fr., Ger., Hung., Jap., Russ., Span. and Swiss, use 68 to 70 p.c. Alcohol; Ital. and Mex., 80 p.c.; Norw. and Swed., 65 p.c.; Port., 90 p.c.; U.S. extract with Acetic Acid and Water, and subsequently add Alcohol (95 p.c.). All from the Seeds. Austr., Belg., Dutch, Fr., Span. and Swiss adopt the International Standard, 16 p.c. of alkaloids; Dan. and Swed., 15 to 17 p.c.; Ital., 10 p.c.; Mex., 15 p.c.; Russ., 15 p.c.; U.S., 5 p.c. of Strychnine. Ger. and Jap., 17·5 p.c.

Tests.—No official method is given for the determination of the Strychnine in the *B.P.* extract, it being apparently assumed that the liquid extract used in its preparation contains the necessary proportion of alkaloid.

The *U.S.P.* dissolves in a beaker a weighed quantity of 2 grammes of the extract in 25 c.c. of a mixture of 16 c.c. of Ether, 5 c.c. of Chloroform, and 4 c.c. of Ammonia Solution; transferring it when dissolved to a separator and washing the beaker with a little Chloroform, transferring the washings also to the separator. The alkaloids are extracted by agitating the mixture for a few minutes, the aqueous layer is transferred to a second separator, the Ether solution and the first separator being washed with a little Water and the washings separated and added to the second separator. The alkaloids remaining in the aqueous liquid are extracted by agitation with 2 successive portions each of 15 and 10 c.c of Chloroform, the Chloroform solutions are separated and added to the Ether solution contained in the first separator. The complete extraction of the alkaloids from the aqueous liquid is ensured by removing a few drops, rendering them acid and testing with Mercuric Potassium Iodide (Mayer's) Solution, and if a reaction is obtained repeating the shaking with a fresh quantity of 10 c.c. of Chloroform. The alkaloids are extracted from the mixed Ether-Chloroform solutions contained in the first separator by agitation with 3 successive quantities each of 15, 10, and 10 c.c. of 3 p.c. Sulphuric Acid Solution, the acid layer being in each case separated, mixed and transferred to another separator; sufficient Ammonia Solution to render the mixture alkaline is added and the liberated alkaloids are extracted by agitation with 3 successive quantities of 15 c.c., 10 c.c., and 10 c.c. of Chloroform; the Chloroform solutions are separated in each case, transferred to a beaker, and evaporated on a water-bath. The alkaloidal residue is dissolved in 15 c.c. of a 3 p.c. Sulphuric Acid Solution whilst still on the water-bath, removed and allowed to cool. A measured quantity of 3 c.c. of cooled mixture of equal volumes of Nitric Acid (sp. gr. 1·42) and Water are added, the liquid rotated a few times, set aside for exactly 10 minutes, during which it is gently stirred 3 times. The red liquid is transferred to a separator containing 25 c.c. of a 10 p.c. w/v Sodium Hydroxide Solution, the beaker washed with 3 successive very small amounts of Water and the washings transferred to the separator, a further quantity of 2 c.c. of the Sodium Hydroxide Solution being added, should the liquid be not quite turbid. The liberated alkaloids are extracted by agitation with 20 c.c. of Chloroform, adopting a rotatory motion, the complete extraction of the alkaloids being ensured by shaking with 2 further successive quantities of 10 c.c. of Chloroform, the same rotatory method being adopted in the shaking; the Chloroform solutions are separated in each case, filtered through a small filter previously wetted with Chloroform into a tared flask; the filter and funnel are washed with 5 c.c. of Chloroform. The mixed Chloroform liquids evaporated very carefully to dryness on a water-bath, the alkaloidal residue is dissolved in 10 c.c. of Tenth-normal Volumetric Sulphuric Acid Solution, about 90 c.c. of Distilled Water and 20 c.c. of Ether and about 5 drops of Iodeosin Solution are added and the excess of Volumetric Acid Solution is titrated with Fiftieth-normal Volumetric Potassium Hydroxide Solution; the number of c.c. used is divided by 5, the quotient is subtracted from 10, the difference is multiplied first by 0·0332 and then by 50, which yields the percentage of Strychnine present in the extract.

The *P.G.* dissolves a weighed quantity of 1 gramme of the extract in 5 grammes of Water and 5 grammes of Absolute Alcohol, and adds to this solution 50 grammes of Ether and 20 grammes of Chloroform, and after vigorous shaking adds 10 c.c. of a 1 in 3 solution of Sodium Carbonate and allows the mixture to stand for an hour with frequent intervals of vigorous agitation. A weighed quantity of 50 grammes of the clear Chloroform solution is filtered through a dry, well-covered filter into a flask, and about half of the liquid is distilled, the remaining Chloroform solution is introduced into a separator, the flask is washed with 3 successive quantities each of 5 c.c. of a mixture of 3 parts by weight of Ether, and 1 part by weight of Chloroform, and the alkaloids are extracted from the mixed liquids by shaking with 50 c.c. of Hundredth-normal Volumetric Hydrochloric Acid Solution. When the clear liquids have completely separated, and after the addition of sufficient Ether to cause the Chloroform-Ether solution to float on the acid liquid, the latter is separated, filtered through a small filter previously moistened with Water into a stoppered flask of white glass of a capacity of about 200 c.c. The Chloroform-Ether solution is washed with 3 successive quantities each of 10 c.c. of Water, the washings filtered through the same filter, the filter washed with Water, and the mixed filtrate and washings diluted with Water to about 100 c.c. After the addition of sufficient Ether to form a layer of 1 cm., sufficient Hundredth-normal Volumetric Potassium Hydroxide Solution is added to neutralise the excess of the Volumetric Acid Solution, Iodeosin Solution being employed as an indicator of neutrality. The number of c.c. of hundredth-normal alkali solution subtracted from 50, the difference multiplied by 0·00364 (the mean molecular equivalent of Strychnine and Brucine) and the product multiplied by 100, and this product divided by 0·711 yields the percentage of total alkaloids present in the extract.

EXTRACTUM NUCIS VOMICÆ LIQUIDUM. LIQUID EXTRACT OF NUX VOMICA.

A fluid prepared by percolation with Alcohol (70 p.c.) and standardised to contain 1·5 grammes of Strychnine in 100 c.c.

The liquid extract is officially required to contain 1·5 p.c. w/v of Strychnine. The *U.S.P.* Fluid Extract is required to contain 1 p.c. w/v of Strychnine; neither the *P.G.* nor the *Fr. Codex* (1908) contains a Fluid Extract of Nux Vomica.

Dose.—1 to 3 minims = 0·06 to 0·18 gramme.

Foreign Pharmacopœias.—Official in Mex. and U.S. The *U.S.P.* extracts with a mixture of Alcohol (95 p.c.) 3, Water 1, to which Acetic Acid has been added; it is standardised so that each 100 c.c. of finished Fluid Extract shall contain 1 gramme of Strychnine.

The *Brussels Conference* agreed to prepare the Extract by means of Alcohol (70 p.c.) and to an alkaloidal strength of 16 p.c.

Tests.—Fluid Extract of Nux Vomica has a sp. gr. of 0·945 to 0·965; it contains from 9 to 12 p.c. of total solids and about 58 p.c. w/v of Absolute Alcohol. The proportion of total solids may amount to as much as 20 p.c., but will largely depend upon the Strychnine content of the Seeds used in preparing the liquid extract. It has been pointed out (*Y.B.P.* '06, 236) that it is evident, in fixing the official standard at 1·5 p.c., somebody has blundered, for it is palpably impossible to produce from a drug which rarely contains as much as 1·5 p.c. of Strychnine, a 1 in 1 preparation standardised to contain that amount.

The *B.P.* method of determination, which has been very severely and adversely criticised, is essentially as follows:—A measured quantity of 10 c.c. of the liquid extract is evaporated to the consistency of a thick syrup by heating on a water-bath, and the resulting extract is dissolved in 20 c.c. of Water, transferred to a separator and the solution mixed with a solution of 5 grammes of Sodium Carbonate in 25 c.c. of Water. The liberated alkaloids are extracted by agitation with 3 successive quantities each of 10 c.c. of Chloroform, the Chloroform solutions being in each instance separated and transferred to a second separator. Unless the fat has been previously extracted from the Seeds a considerable quantity of fatty matter is present, which gives rise to the formation of troublesome emulsions at this stage of the process, the Chloroform obstinately emulsifying and refusing to separate. The alkaloids are in turn extracted from the mixed chloroformic liquids by agitation with 3 successive quantities each of a third part of a mixture of 6 c.c. of diluted Sulphuric Acid with 25 c.c. of Water. The acid solutions are in each instance separated, mixed, diluted with Water to 175 c.c. and transferred to a stoppered bottle in which after being made up to 200 c.c. with Potassium Ferrocyanide Solution they are well and frequently shaken for thirty minutes. The separation of the mixed alkaloids is based on the insolubility of the Strychnine as compared with that of the Brucine Ferrocyanide, an observation due to Beckurts, and subsequently utilised by Dunstan and Short (*Y.B.P.* 1883, 469), for the determination of

Strychnine in the presence of Brucine. Unless strict attention be paid to the temperature at which the precipitation is carried out and that the solution be well agitated during the addition of the Ferrocyanide, Brucine will be also precipitated with Strychnine. The mixture is allowed to stand for 6 hours to allow complete precipitation, the supernatant fluid is decanted, filtered through a small filter, the precipitate transferred to the same filter, the precipitate remaining in the bottle is also transferred to the filter by washing it out with some of the clear filtrate and then with Water containing one-fortieth of its volume of diluted Sulphuric Acid, and the precipitate is washed until the washings are free from bitterness. If this stage of the process be strictly followed considerable loss of alkaloid will result, as the Strychnine Ferrocyanide is not completely insoluble in this menstruum. The precipitate is then transferred to a separator, mixed with 5 c.c. of Ammonia Solution, and well shaken, and the liberated alkaloids are extracted by agitation with 2 successive quantities each of 15 c.c. of Chloroform; the Chloroform solutions in each instance being separated, transferred to a tared flask and the mixed chloroformic liquids evaporated on a water-bath, the residue being dried for 1 hour at a water-bath temperature, or preferably till constant in weight; cooled and weighed. If the final Chloroform solutions are evaporated, as officially directed, in a counterpoised dish, there is considerable liability to loss by decrepitation, which may be avoided by the addition of a few c.c. of Amyl Alcohol to the chloroformic liquids previous to evaporation. The calculated yield of alkaloids from the 10 c.c. of liquid extract directed by the *B.P.* to be employed in the test is 0·32 of a gramme, and the process upon which the separation was founded directs the employment of any quantity of liquid yielding not more than 0·2 of a gramme of mixed alkaloids. Several useful suggestions have been made with a view of overcoming the defects of the Pharmacopœia process. Farr and Wright have suggested (*Y.B.P.* '00, 450) the following modifications: that the volume of liquid taken should not exceed 5 c.c. of the liquid extract or 30 c.c. of Tincture, that 200 c.c. of Water at a stated temperature, preferably 38° C. (100·4° F.) should be employed and a correction made for the Strychnine dissolved, and that in carrying out the process the Pharmacopœia instructions as to a simple agitation without stirring and as to the length of time allowed for precipitation of the Strychnine are to be strictly observed, as success depends altogether upon the conditions under which the process is carried out. Bird has suggested the addition of 2 c.c. of pure Amyl Alcohol to the final Chloroform solution of the alkaloid before evaporation: it prevents decrepitation of the Strychnine when the residue dries. He has also suggested the removal of the fat by a preliminary shaking out with Chloroform in acid solution before starting the assay, the traces of alkaloid dissolved by the Chloroform solution of the fat being recovered by shaking the Chloroform solution again with acid. Naylor (*Y.B.P.* '05, 364) is of opinion that the difficulties attending that part of the official process which refers to the separation of the

Brucine and Strychnine, even assuming the adoption of the minute precautions proposed by Farr and Wright, cannot confidently be affirmed to have been surmounted, and it is imperative that attention to details of an unusually exacting character be carefully observed if results claiming to be concordant are to be obtained. Later results have shown that a more expeditious, easier, and certainly a more accurate method of separating Brucine from Strychnine consists in oxidising it with Nitric Acid in the presence of Sulphuric Acid. The process was worked out by Gordin and is given *in extenso* in the *Proceedings of the American Pharmaceutical Association* 1902, vol. l., p. 336. The residue of total alkaloids obtained in the assay of Nux Vomica or its preparations is dissolved in 15 c.c. of 3 p.c. Sulphuric Acid Solution by the aid of a water-bath heat, the solution is cooled to ordinary temperature and 3 c.c. of a previously prepared and cooled mixture of equal parts of strong Nitric Acid (sp. gr. 1·42) and Water added to the alkaloidal solution; the liquid is set aside for exactly 10 minutes, shaking it gently 3 or 4 times during this time. The red liquid is transferred to a separator containing 20 to 25 c.c. of a 10 p.c. w/v Sodium Hydroxide Solution, and the vessel in which the digestion of the alkaloids has taken place is washed 3 or 4 times with very small amounts of Water, the washings being added to the contents of the separator. In the event of the liquid not being turbid a further addition of 1 or 2 c.c. of the Sodium Hydroxide Solution should be made; the liberated alkaloids are shaken out with 3 successive quantities of 20 c.c., 10 c.c. and 10 c.c. of Chloroform. The chloroformic liquids are separated, filtered through a small filter paper previously moistened with Chloroform into a tared flask, the filter washed with Chloroform. To the mixed Chloroform solutions are added 2 or 3 c.c. of pure Amyl Alcohol distilling between 128° and 132° C. (262·4° to 269·6° F.), the mixed solutions are evaporated to dryness, the residue dried for about 2 hours at a temperature of 135° to 140° C. (275° to 284° F.), and when cold weighed. If the fat be removed, as suggested above by Bird's modification, the mixed alkaloids can be separated by the above process, the combination of the two processes yielding results of a satisfactory and concordant nature.

The *U.S.P.* method of determining the Strychnine in the Fluid Extract is as follows:—A measured quantity of 10 c.c. of the Fluid Extract is transferred to a porcelain evaporating basin and evaporated on a water-bath to dryness, the residue whilst warm being dissolved in a mixture of 16 c.c. of Ether, 5 c.c. of Chloroform, and 4 c.c. of Ammonia Water, the solution being transferred to a separator, the dish rinsed with a little Chloroform and the washings added to the separator, which is carefully shaken for a few minutes. After the liquids have separated the aqueous layer is removed to another separator, the Ether-Chloroform liquid is washed with a little Water and the washings added to the second separator, and the aqueous liquid in the second separator is shaken with 2 successive quantities each of 15 and 10 c.c. of Chloroform, which are added to the Chloroform solution in the first separator. Complete extraction of the alkaloids is ensured by acidifying a few drops of the aqueous liquid remaining after Chloroform extraction and testing with Mercuric Potassium Iodide (Mayer's) Solution; if a reaction is obtained, a further shaking with 10 c.c. of Chloroform is carried out. The alkaloids are extracted from the Ether-Chloroform mixed with the Chloroform liquids in the first separator by shaking with 3 successive quantities each of 25, 10 and 10 c.c. of Normal Volumetric Sulphuric Acid Solution. The acid solutions are separated in each case, transferred to a separator, and the mixed acid solutions rendered alkaline with sufficient Ammonia Solution, and the liberated alkaloids shaken out with 3 successive quantities each of 25, 10 and 10 c.c. of Chloroform. The Chloroform solutions are separated in each case, transferred to a beaker, and the mixed chloroformic liquids evaporated to dryness on a water-bath. The alkaloidal residue is dissolved in 15 c.c. of 3 p.c. Sulphuric Acid Solution by the heat of the water-bath, allowed to cool, mixed with 3 c.c. of a cooled mixture of equal volumes of Nitric Acid (sp. gr. 1·42) and Distilled Water, and after rotating the liquid a few times, set aside for exactly 10 minutes, during which interval it is gently stirred on 3 successive occasions. The red liquid is transferred to a separator containing 25 c.c. of 10 p.c. w/v Sodium Hydroxide Solution, the beaker washed with 3 successive very small quantities of Water, and the washings transferred to the separator; a further quantity of 2 c.c. of the Sodium Hydroxide Solution is added in the event of the liquid not becoming turbid. The liberated alkaloids are extracted by shaking well (adopting a rotatory motion) with 3 successive quantities of 20, 10 and 10 c.c. of Chloroform, the Chloroform solutions in each case being separated, filtered through a small filter previously moistened with Chloroform, the filter and funnel washed with 5 c.c. of Chloroform; the mixed Chloroform solutions and washings carefully evaporated by means of the water-bath to avoid decrepitation, and the alkaloidal residue is dissolved in 10 c.c. of Tenth-normal Volumetric Sulphuric Acid Solution, about 80 c.c. of Water and 20 c.c. of Ether. The excess of acid is titrated with Fiftieth-normal Volumetric Potassium Hydroxide Solution, using 5 drops of Iodeosin T.S. as an indicator of neutrality. The number of c.c. of Fiftieth-normal Volumetric Potassium Hydroxide Solution required divided by 5, the quotient subtracted from 10, the difference multiplied first by 0·0332 and then by 10 yields the percentage of Strychnine present in the Fluid Extract.

TINCTURA NUCIS VOMICÆ. TINCTURE OF NUX VOMICA.

N.O.Syn.—TINCTURA STRYCHNI.

Liquid Extract of Nux Vomica, 2; Distilled Water, 3; Alcohol (90 p.c.), *q.s.* to yield 12.

It is about twice the strength of the *B.P.* 1885 Tincture.

The *B.P.* Tincture of Nux Vomica is required to contain not less than 0·24 p.c. w/v nor more than 0·26 p.c. w/v of Strychnine. The *U.S.P.* Tincture is required to contain 0·1 p.c. w/v of Strychnine. The *P.G.* Tincture is required to contain not less than 0·25 p.c. w/v of mixed alkaloids.

The *B.P.* Tincture is prepared from the standardised liquid extract. The *U.S.P.* Tincture is prepared from the standardised extract. The *P.G.* Tincture is prepared from the powdered Seeds. The Tincture official in the *Fr. Codex* (1908) is prepared in accordance with the recommendations of the *Brussels Conference*, namely, from the extract, using Alcohol (70 p.c.), and is required to contain 0·25 p.c. of total alkaloids.

Dose.—5 to 15 minims = 0·3 to 0·9 c.c.

Ph. Ger. maximum single dose, 1·0 gramme; maximum daily dose, 2·0 grammes.

Foreign Pharmacopœias.—Official in Austr., Belg., Dan., Dutch, Ger., Ital., Jap., Norw., Russ., Span., Swed. and Swiss, 1 in 10; Hung., Mex. and Port., 1 in 5; all prepared from the **seeds.** U.S., 1 Extract in 50. All by weight, except U.S.

Tests.—Tincture of Nux Vomica should have a sp. gr. of 0·890 to 0·915. It contains from 2 to 3 p.c. w/v of total solids and about 64 p.c. w/v of Absolute Alcohol. It is officially required to yield the percentage of Strychnine shown above. The *B.P.* method of determination is similar to that adopted for the assay of the liquid extract, 100 c.c. of the Tincture are evaporated to the consistency of a thick extract and the process continued as described under the Liquid Extract. The same comments as there appear are naturally applicable to the adaptation of the process to the Tincture.

The *U.S.P.* method is to evaporate a measured quantity of 100 c.c. of the Tincture to dryness on the water-bath, and to determine the amount of Strychnine present by the method of assay as given under Extractum Nucis Vomicæ. The final multiplication by 50 must in this instance be omitted, as the result will represent the percentage w/v of Strychnine present in the Tincture. The remarks regarding the Nitric Acid process for the separation of Brucine and Strychnine apply here. The German Pharmacopœia evaporates a weighed quantity of 50 grammes of the Tincture in a tared evaporating dish to the weight of 10 grammes and transfers the residue to a stoppered vessel with 5 grammes of Absolute Alcohol; the mixture is shaken with 50 grammes of Ether and 20 grammes of Chloroform, 10 c.c. of a 1 in 3 Sodium Carbonate Solution (which has been used to transfer the last traces of the residue left in the evaporating basin to the stoppered vessel) added, and the mixture allowed to stand for 1 hour with frequent intervals of vigorous shaking. A weighed quantity of 50 grammes of the clear Chloroform-Ether solution is filtered through a dry, well-covered filter into a flask, and about half the liquid distilled, the remaining Chloroform-Ether solution is introduced into a separator, the flask is washed with 3 successive quantities of 5 c.c. of a mixture of 3 parts by weight of Ether, and 1 part by weight of Chloroform, and the alkaloids are removed from the mixed fluids by shaking thoroughly with 40 c.c. of Hundredth-normal Volumetric Hydrochloric Acid Solution. After complete separation sufficient Ether is added to cause the Chloroform-Ether solution to float on the surface of the acid liquid. The latter is filtered through a small filter previously moistened with Water into a stoppered flask of about

200 c.c. capacity, the Chloroform-Ether solution is washed with 3 successive quantities each of 10 c.c. of Water and the washings filtered through the same filter, which is finally washed with Water, and the mixed filtrate and washings are diluted with Water to about 100 c.c. After the addition of sufficient Ether to form a layer of about 1 cm., the excess of volumetric acid is titrated with Hundredth-normal Volumetric Potassium Hydroxide Solution, using 5 drops of Iodeosin Solution as an indicator of neutrality, the mixture being well shaken after each addition. It is required that not more than 17 c.c. of the Hundredth-normal Solution shall be necessary. The number of c.c. of Hundredth-normal Volumetric Potassium Hydroxide Solution required is subtracted from 40, the difference multiplied by 0·00364 (the mean molecular equivalents of Strychnine and Brucine), the product multiplied by 100 and divided by $33\frac{1}{3}$ yields the percentage w/w of total alkaloids present in the Tincture.

STRYCHNINE.—*See* STRYCHNINA.

Not Official.

BRUCINE ($C_{23}H_{26}N_2O_4.4H_2O$, eq. 462·85).—Colourless, transparent, monoclinic crystals, containing about 15 p.c. of Water. Its salts are bitter, and most of them crystallisable.

It should be kept in well-stoppered glass bottles of a dark amber tint and protected as far as possible from contact with air, as the crystals quickly effloresce when exposed to dry air.

Solubility.—But slightly soluble in Water; 1 in 20 of Alcohol (90 p.c.), 1 in 2 of Chloroform, with separation of the combined Water.

Brucine resembles Strychnine in its physiological action, but is weaker.

Dose.—$\frac{1}{10}$ to $\frac{1}{2}$ grain = 0·006 to 0·032 gramme.

It possesses analgesic properties, in 5 p.c. solutions of the **Sulphate** or **Nitrate** applied locally.—*T.G.* '85, 376; '86, 18.

Tests.—Brucine rapidly loses its Water of crystallisation when exposed to dry air or over Sulphuric Acid at 100° C. (212° F.) it becomes anhydrous, the anhydrous product melting at 178° C. (352·4° F.) the aqueous solution is lævogyrate; the alkaloid dissolves in concentrated Sulphuric Acid without colour. Concentrated Nitric Acid, or Sulphuric Acid containing Nitric Acid, produces a blood-red coloration, passing to orange and finally to yellow. The salts produced when Brucine is neutralised with acid are neutral in reaction towards the customary indicators of neutrality, and the alkaloid may therefore be titrated direct with Normal or Tenth-normal Hydrochloric or Sulphuric Acid Solution, using Iodeosin Solution as an indicator of neutrality. 1 c.c. of Normal Sulphuric or Hydrochloric Acid Solution is equivalent to 0·39133 gramme of anhydrous Brucine or 0·46285 gramme of hydrated Brucine. Brucine should be free from Strychnine, its presence may be detected by oxidising the Brucine with Nitric Acid, shaking out the Strychnine by an immiscible solvent and applying the Sulphuric Acid and Potassium Bichromate test when no violet or purple-violet coloration should be produced.

OLEA.

In the British Pharmacopœia the term **Oleum** is applied to an Oil (whether expressed or distilled), as it is also in Austr., Dutch, Ger., Hung., Jap., Russ. and U.S. The other names for fixed and volatile Oils respectively are: Belg., **Oleum** and **Essentia**; Dan.,