

Opium.—Opium. *Opium*, Fr.; *Opium*, Ger. The concrete milky exudation obtained in Asia Minor from the unripe capsules of *Papaver somniferum*, by incision and spontaneous evaporation. (Nat. Ord. *Papaveraceæ*). (U. S. P.)

Opium should yield at least nine per cent of morphine by the process of assay.

Opii Pulvis.—Powdered opium. Opium dried at a temperature not exceeding 185° Fahr., and reduced to a moderately fine powder (No. 50). It should contain not less than twelve nor more than sixteen per cent of morphine. Dose, gr. j—gr. iij.

Opium Denarcotisatum.—Denarcotized opium. Opium freed from materials soluble in ether—odorous matters, narcotine, etc. It should contain fourteen per cent of morphine. Dose, gr. j—gr. iij.

Emplastrum Opii.—Plaster of opium. (Extract of opium, Burgundy pitch, and lead-plaster.)

Extractum Opii.—Extract of opium. Dose, gr. ss—grs. ij.

Pilulæ Opii.—Pills of opium. Dose, one to four pills. Each pill contains one grain of opium.

Pulvis Ipecacuanhæ et Opii.—Compound powder of ipecacuanha. Dover's powder. Ten grains contain one grain each of ipecac and of opium, and eight grains of sugar of milk.

Tinctura Opii.—Tincture of opium. Laudanum. Thirteen minims or twenty-five drops are equivalent to one grain of opium.

Acetum Opii.—Vinegar of opium. Ten minims or twenty drops are about equal to one grain of opium.

Tinctura Opii Camphorata.—Camphorated tincture of opium. Paregoric. Half a fluid ounce contains nearly one grain of opium. Dose, for children, from gtt. v.—gtt. xx; for adults, from ʒj—ʒj.

Trochisci Glycyrrhizæ et Opii.—Troches of licorice and opium. Dose, one to three or four.

Tinctura Opii Deodorata.—Deodorized tincture of opium. Dose, ℥v—ʒj.

Vinum Opii.—Wine of opium. (Opium, cinnamon, cloves, sherry wine.) Dose, ℥v—ʒj.

COMPOSITION.—About half of the weight of opium is made up of gum, pectin, albumen, fragments of the poppy-capsules, and calcareous salts. It contains, also, some coloring-matter, and a volatile substance in minute quantity. The proportion of water varies from twelve to thirty per cent. A large number of basic, acid, and neutral substances have been and are still being discovered in opium, hence its chemistry is very complex.

The following natural alkaloids have been found in opium. Various derivatives of these have also been described. This list, except some unimportant modifications, is taken from Flückiger and Hanbury's admirable *Pharmacographia*:

Hydrocotarnine.—Crystallizable, alkaline. Volatile at 100°. ($C_{12}H_{15}N_1O_3$.)

Morphine (morphina).—Crystallizable, alkaline. ($C_{17}H_{19}N_1O_5$.)

Pseudo-morphine.—Crystallizes with H_2O , does not unite even with acetic acid. ($C_{17}H_{19}N_1O_4$.)

Codeine (codeina).—Crystallizable, alkaline, soluble in water. ($C_{18}H_{21}N_1O_3$.)

Thebaine (thebaina).—Crystallizable, alkaline. ($C_{16}H_{21}N_1O_5$.)

Protopine.—Crystallizable, alkaline. ($C_{20}H_{25}N_1O_5$.)

Laudamine.—An alkaloid, which, as well as its salts, forms large crystals. ($C_{20}H_{25}N_1O_4$.)

Codamine.—Crystallizable, alkaline; can be sublimed. ($C_{20}H_{25}N_1O_4$.)

Papaverine (papaverina).—Crystallizable, alkaline. ($C_{21}H_{27}N_1O_4$.)

Rhœadine.—Crystallizable, not distinctly alkaline; can be sublimed. ($C_{21}H_{27}N_1O_6$.)

Meconidine.—Amorphous, alkaline; melts at 58°; not stable; the salts also easily altered. ($C_2H_{25}N_1O_4$.)

Cryptopine (cryptopina).—Crystallizable, alkaline; salts tend to gelatinize; hydrochlorate crystallizes in tufts. ($C_{21}H_{27}N_1O_5$.)

Laudanosinè.—Crystallizable, alkaline. ($C_{21}H_{27}N_1O_4$.)

Narcotine (narcotina).—Crystallizable, not alkaline; salts not stable. ($C_{22}H_{29}N_1O_7$.)

Lanthopine.—Microscopic crystals, not alkaline. ($C_{22}H_{29}N_1O_4$.)

Narceine (narceina).—Crystallizable as a hydrate; readily soluble in boiling water or in alkalies. ($C_{22}H_{29}N_1O_6$.)

The only important derivative in the therapeutic sense is *apomorphine*, obtained from morphine by the action of hydrochloric acid. This possesses active emetic property, and will be grouped with emetics.

Besides the foregoing alkaloidal and basic substances, opium contains a peculiar acid (*meconic acid*), and, according to T. and H. Smith, a peculiar form of lactic acid (*thebolactic*).

The proportion of morphine in Turkey opium should not be less than ten per cent, and in good specimens may reach fifteen per cent. Pseudo-morphine occurs in the minute quantity of 0.02 per cent. The proportion of codeine varies from one fifth to two fifths per cent. Thebaine and papaverine exist in Turkey opium in about the proportion of one per cent. Narcotine is found in considerable quantity in different varieties of opium, and ranges in amount from one and five tenths to ten per cent. Narceine varies from 0.1 to 0.71. The quantity of cryptopine and rhœadine is extremely small.

The morphine of opium exists in the drug in the form of the tri-basic meconate. The proportion of meconic acid is about three to four per cent of the crude opium.

The value of opium depends on the quantity of morphine which it contains.

Morphina.—*Morphine.* In colorless crystals, which are inflammable and wholly dissipated by red heat. It is scarcely soluble in cold water, slightly so in boiling water, and freely soluble in boiling alcohol. Nitric acid first reddens it, and then renders it yellow. With a solution of sesquichloride of iron, it assumes a deep-blue color. Its solution restores the color of litmus, previously reddened by an acid. (U. S. P.)

Morphinæ Acetas.—Acetate of morphine. A white, yellowish-white, crystalline or amorphous powder, slowly losing acetic acid when kept for some time and exposed to the air, having a faintly acetous odor, a bitter taste, and a neutral or faintly alkaline reaction. When freshly prepared, the salt is soluble in twelve parts of water and in sixty-eight parts of alcohol; if it has been kept for some time, it is incompletely soluble in water, unless a little acetic acid is added. Dose, gr. $\frac{1}{8}$ —gr. ss.

Morphinæ Hydrochloras.—Hydrochlorate of morphine. In snow-white, feathery crystals, wholly soluble in water and in alcohol. Dose, gr. $\frac{1}{8}$ —gr. ss.

Morphinæ Sulphas.—Sulphate of morphine. In snow-white, feathery crystals, which are wholly soluble in water. Dose, gr. $\frac{1}{8}$ —gr. ss.

Pulvis Morphinæ Compositus.—Compound powder of morphine (Tully's powder). (Morphine sulphate, one part; camphor, twenty parts; glycyrrhiza, twenty parts; precipitated carbonate of calcium, twenty parts; and sufficient alcohol to make a mixture.) Dose, gr. j—gr. x.

Trochisci Morphinæ et Ipecacuanhæ.—Troches of morphine and ipecacuanha. (Morphine, ipecac, sugar, oil of gaultheria, mucilage.)

Codeina.—Codeine. White, or yellowish-white, more or less translucent, rhombic prisms, somewhat efflorescent in warm air, odorless, having a slightly bitter taste and an alkaline reaction. Soluble in eighty parts of water at 60° Fahr. and in seventeen parts of boiling water; very soluble in alcohol and in chloroform; also, soluble in six parts of ether. Dose, gr. ss—gr. ij.

Various salts of codeine are now prepared, but the sulphate is the most important and desirable.

The other alkaloids of opium are not official.

Narcotinæ Hydrochloras.—Hydrochlorate of narcotine (not official). Dose, gr. ij—gr. x, as an antiperiodic.

ANTAGONISTS AND INCOMPATIBLES.—As regards chemical antagonism, the alkaline carbonates, lime-water, and the salts of iron, lead, copper, zinc, mercury, and Fowler's solution, are incompatible with the preparations of opium. Notwithstanding this chemical incom-

patibility, the metallic salts are frequently given in conjunction with opium, and the systemic effects of both are produced. Astringent vegetables (tannin) are also incompatible; they limit physiological activity by forming tannate of morphine, which is not readily soluble.

In cases of opium-poisoning, if any portion of the drug remain unabsorbed in the stomach, the most prompt and efficient emetic should be used. Apomorphine should be injected subcutaneously, if the patient is unable to swallow; if conscious, the sulphate of copper may be administered by the stomach. In a case of opium narcosis which resisted ordinary emetics, violent emesis was induced by a solution of bicarbonate of sodium, followed by a solution of tartaric acid. In the absence of other and more active emetics, powdered mustard may be administered—a tablespoonful to a teacupful of warm water. When the opium swallowed is in solution, the stomach-pump should be used if the narcosis is profound. Cold affusion, artificial respiration, when the breathing flags, and faradization of the chest-muscles, are measures of great practical utility. The author has personally witnessed in several cases the excellent effects of faradization, first, in causing such irritation of the surface as to produce reflex excitation of the respiratory center; and, second, inducing contractions of the respiratory muscles. As a peripheral irritant, faradization is more humane and seemly, and also more efficient, than flagellation.

The action of opium is antagonized, at least in a part of the sphere of its influence, by belladonna. These agents are opposed as regards their influence on the intra-cranial circulation, on the pupil, on the respiratory organs, and on the heart. Opium in lethal doses dilates the arterioles and veins; belladonna contracts them, and, by energizing the cardiac movements, substitutes an active for a passive congestion. *It can not be too strongly insisted on in this connection that belladonna in too great quantity, or too long in action, exhausts the irritability of the unstriped muscular fiber, and thus induces the very state which its administration was intended to relieve.* The state of the pupil, the action of the heart, and the condition of the reflex movements, are the guides to the administration of belladonna in cases of opium narcosis. The smallest quantity of belladonna which will dilate the pupil, raise the tension of the arterial system, deepen the respiration, and re-establish the reflex excitability, should be used. The author has a strong conviction, arising from some painful personal experience, that *it is a fatal error to attempt to restore a patient in opium narcosis to complete consciousness by repeated doses of belladonna.* The action of these agents combined is to produce profound sopor, and this is not a condition of danger so long as the pulse, respiration, and reflex movements are in good condition. To substitute belladonna narcosis for opium narcosis is only increasing the hazard under which the patient is already struggling. Impatient to afford relief, and assuming that the

tendency to sleep must be obviated, the physician too frequently, as the history of many cases plainly shows, repeats the doses of belladonna until its action greatly preponderates, and the irritability of the cardiac ganglia is completely exhausted. The author, therefore, feels himself warranted in repeating that *the utility of belladonna consists in its power to maintain the action of the heart, and the respiration, until elimination has taken place*, and that even coma is of little importance provided the respiration, circulation, and reflex movements are properly maintained.

The hypodermatic injection of atropine is the most efficient and satisfactory method of employing this physiological antagonist. Not more than $\frac{1}{10}$ of a grain of the sulphate should be administered at a dose, and this may be repeated every fifteen minutes (up to three doses) until dilatation of the pupil, increased power of the cardiac movements, deeper respiration, warmth and dryness of the skin, and flushing of the face, are produced. No more can be accomplished by the largest doses, and the results of the antagonism must be awaited. Belladonna continues longer in action than opium. In a succeeding chapter, devoted to the consideration of the combined administration of opium and belladonna, or morphine and atropine, the nature and degree of the antagonism will be more fully elaborated.

Coffee, with its active principle (*caffeine*), is also an antagonist to opium. Good results have undoubtedly been obtained by the free use of black coffee, in milder cases of opium narcosis. The unpleasant confusion of mind, and vertigo, which in so many subjects are experienced after the subsidence of the effects of a medicinal dose, may sometimes be removed by a cup of strong coffee. These cerebral effects may be prevented, or relieved when they occur, by a full dose of bromide of potassium. This discovery, if we may dignify so small a matter by so imposing a title, was briefly announced by the author in the first edition of his work on "Hypodermatic Medication," and was afterward more fully set forth in a special memoir by Da Costa, of Philadelphia.

Gubler has shown that some of the cerebral effects of opium are antagonized by quinine. Tartar emetic and digitalis also oppose to some extent the action of this remedy on the intra-cranial circulation.

SYNERGISTS.—The cerebral and hypnotic effects of opium are promoted by alcohol and its derivatives (notably chloral), and, within certain limits, by the mydriatics. The sudorific action of opium is increased by ipecacuanha.

PHYSIOLOGICAL ACTIONS.—As opium is a very complex substance, made up of numerous principles which differ remarkably among themselves, it will conduce to a better understanding of its actions to consider, first, opium as a whole, and then follow with some details regarding its individual constituents.

The physiological effects of opium are best studied as respects—1. Small medicinal doses; 2. Full medicinal doses; 3. Lethal doses.

1. The preparations of opium have a disagreeable, bitter, and rather nauseous taste. Dryness of the mouth and fauces, huskiness of voice, and diminution in the sense of taste, occur in a short time after administration of the drug has begun, and continue during the whole period of its influence. To the dryness succeeds a viscid secretion, which contains excrementitious matter having a foul odor. When opium does not produce nausea, the appetite may not be impaired, may be even increased; but the rule is that the desire for food is lessened by opium. The secretion of mucus, and of the special glandular apparatus of the gastro-intestinal mucous membrane, is lessened by opium, and hence the digestion and the peristaltic movements are less active. The excretions being thus locked up, dullness and hebetude are experienced, the skin looks muddy, the tongue is coated, and the breath is offensive. When the influence of the opium ceases, it not unfrequently happens that the constipation is succeeded by relaxation of the intestines, and rather profuse and fetid evacuations, and increased urinary discharges, take place.

The action of the heart becomes stronger, and the arterial tension rises. When opium agrees, the sense of fatigue vanishes, and muscular movements become more rapid and easy. The face flushes a little, the pupil contracts slightly, the conjunctivæ may be somewhat injected, and the expression of the eye more brilliant. At this stage the ideas flow more rapidly, but are less sustained and orderly. The appreciation of time, the sequence of events, and the sense of moral fitness, are diminished. The cerebral excitement is, after a period which varies in different individuals, succeeded by calm, by drowsiness, and sleep when it occurs is usually disturbed by visions and dreams, often of a frightful character. In most subjects, after the sopor has passed off, headache, vertigo, confusion of mind, nausea, constipation, and muscular hebetude, are experienced.

2. When full medicinal doses are administered, the symptoms above described occur in a more intense degree. The stage of cardiac stimulation and of cerebral excitement is of much shorter duration; and the stage of intoxication and sopor not only comes on more quickly, but is much more pronounced. At first the pulse is increased in frequency and the respiratory movements are more rapid; but the cardiac pulsations soon diminish in number and force, and the respirations become sighing in character and more shallow. There is also present decided dryness of the mouth, fauces, and larynx, and swallowing becomes somewhat difficult and the voice grows husky. Nausea and vomiting, or at least weight and oppression of the epigastrium, ensue. Confusion of ideas, vertigo, somnolence, are succeeded by deep sleep, contracted pupils, slow and relaxed pulse, slow and snoring

respirations, a perspiring skin, and, in many persons, an intense general pruritus, which, however, is more harassing at the nasal orifices.

Persons not habituated to the use of opium usually experience, after a full medicinal dose has expended its force, very distressing sequela, referable to the cerebro-spinal system. The most important of these after-effects are headache, confusion of mind, vertigo—which is especially severe on assuming the erect posture—nausea, retching and vomiting, complete anorexia, and constipation. A mild but defined hepatogenic jaundice not unfrequently occurs, and the urine is tinged with the coloring-matter of the bile.

3. A lethal dose of opium causes but a transient excitement; the stage of narcosis quickly supervenes, and the functions of animal life are often rather abruptly suspended. The patient soon lapses into a condition of insensibility, with a slow and feeble, or, it may be, rapid and feeble, action of the heart; slow respiration, shallow and quiet or stertorous; face at first flushed, but soon becoming shrunken, pallid, and cyanosed; skin wet; pupils minutely contracted and insensible to stimulation; unconsciousness profound, with muscular relaxation and abolition of reflex movements. This state of opium narcosis is with difficulty distinguished from alcohol narcosis, from cerebral hæmorrhage—especially in the *pons*—and from uræmic coma. An attentive consideration must be given to all available facts in the history of the case, to the surroundings of the patient, and to the odor of the breath or other excretions, for the symptoms of one of the states above mentioned may be represented in another, even to the inequality of the pupils, since a case of opium narcosis has been reported in which such inequality existed.

There are no characteristic structural alterations produced by opium. The brain presents the appearance known as the “wet brain” by pathologists; the subarachnoid spaces and the ventricles contain an abnormal quantity of serum; the intra-cranial veins are engorged, and the *puncta vasculosa* are somewhat more numerous. The right cavities of the heart and the large venous trunks are usually distended with soft coagula. These appearances are largely due to the mode of dying. In consequence of the diminishing frequency of the respiratory movements, the blood is imperfectly decarbonized, and the capillary circulation of the lungs is impeded. The action of the heart being weak and the resistance *a fronte* increased, it is obvious that venous stasis must take place.

It is necessary now to consider somewhat more minutely the nature and degree of the action of opium on the different organs and systems of the body. It will save space and avoid repetitions to study these actions in connection with the several principles contained in opium.

THE PHYSIOLOGICAL ACTION OF THE ALKALOIDS OF OPIUM.—1.

Morphine.—The peculiar powers of opium are represented chiefly in the morphine which it contains. In opium of good quality the proportion of morphine is from ten to fifteen per cent. The actions of the other principles contained in opium differ widely; and as they all possess some activity, the sum of their effects must so far influence the result that the powers of opium and morphine must vary somewhat in kind as well as in degree. One sixth of a grain of morphine is about equivalent in activity to one grain of average opium.

In general terms, it may be stated that morphine differs from opium in the following respects:

Morphine is less stimulating, less convulsant, and more decidedly hypnotic and anodyne than opium.

Morphine constipates less and affects the contractility of the bladder more than opium.

Morphine has less diaphoretic action and produces much more pruritus than opium.

The physiological action of morphine is best studied as administered subcutaneously. In a short period—from a few seconds to a few minutes—after the insertion of an ordinary dose—one sixth to one fourth of a grain—under the skin, the symptoms of morphine narcosis begin. A sense of heat and flushing of the face—after, in most subjects, a very transient pallor—fullness of the head, giddiness, *tinnitus aurium*, and frequently nausea, are experienced. Deep-seated epigastric pain is often felt, and loud borborygmi occur. The vertigo may be so considerable as to render walking uncertain and staggering, or to render the upright position impossible. Injection of the conjunctivæ and contraction of the pupils occur at the same time the cerebral effects are experienced. The lips have a bluish appearance, the mouth and tongue become dry, swallowing is painful, and the voice has a husky tone. When these physiological effects are produced, pain and spasm are relieved, and an indescribable feeling of content takes possession of the mind. A condition of somnolence in many persons, in others of extreme wakefulness, with intense mental activity, is experienced. When sleep occurs, it is usually deep but not calm, the respirations are slow, noisy, and labored. Not unfrequently the sleep is disturbed by dreams and visions, or the individual passes into a somnambulistic state, from which he is aroused with difficulty. The action of the heart is diminished in frequency, but a decided rise takes place in the arterial tension. On ophthalmoscopic examination, a marked increase in the vascularity of the retina, and blurring of the papillæ, can be discerned.

Soon after a hypodermatic injection has been practiced, itching of the nose, and often of the whole cutaneous surface, is experienced. The skin is at first dry, but, after a time, diaphoresis begins and is sometimes profuse. The relaxation of the skin is coincident with a

fall in the arterial tension. The secretions of the mucous surfaces are at first arrested, as well as those of the skin. If the morphine be administered after a full meal, digestion is suspended for a time. The intestinal movements are also arrested for a short period, and constipation is therefore produced; but, very frequently indeed, no change takes place in the time in which the alvine discharges occur, or in their number. Partly in consequence of the increased action of the skin, the quantity of urine discharged is lessened, and, at the same time, difficulty is encountered in its emission. When the desire is felt, an interval of less or greater duration elapses before the flow begins, and, as the contractile power of the bladder and of the ejaculatory muscles is diminished, the discharge is feeble and slow, and the last drops linger in the urethra.

With the decline of morphine narcosis a majority of subjects, probably, experience headache, confusion of mind, anorexia, and nausea.

When a lethal dose of morphine has been administered by any mode, profound narcotism quickly ensues; the pulse becomes slow and feeble, or rapid and feeble; the respirations also become very slow and shallow; the skin cold and sweating; the face pale, cyanosed, and ghastly; the conjunctivæ deeply injected; the pupils minutely contracted, and reflex movements entirely abolished. Respiration ceases before the action of the heart, as a rule, but in some instances very sudden death ensues from paralysis of the heart.

Half a grain is the smallest dose of morphine which has proved fatal to an adult. Five cases, according to Taylor, have been recorded in which one grain of the muriate caused death.

A consideration of the symptoms produced in man by morphine, and the results of experiments on animals, prove that it chiefly affects the cerebro-spinal functions. In the lower animals, the spinal more; in man, the cerebral more than the spinal functions. Morphine first raises and afterward lessens the action of the heart and arteries; first stimulates the pneumogastric end-organs and cardiac motor ganglia, and afterward paralyzes both. It causes death chiefly through paralysis of the muscles of respiration.

2. *Codeine*.—According to the author's observations, the codeine of commerce corresponds closely in action to morphine, but is much feebler. Four grains of codeine are about equivalent to one grain of morphine. It has anodyne and hypnotic qualities. Codeine produces sleep freer from disturbance, and the after-effects are less disagreeable, than those of morphine. The special direction to the pneumogastric nerve ascribed to it by some observers, seems to the author to exist in nature.

3. *Narcotine*.—This alkaloid is singularly inappropriately named. It has but feeble narcotic power. In children considerable doses produce a calmative effect and drowsiness, but these results are not ob-

served in adults. Experiments on animals have shown that narcotine is a convulsant. While pigeons are poisoned only by two or three grains of morphine, administered subcutaneously, the same quantity of narcotine causes fatal convulsions. The reverse is true in man. Narcotine is allied in action to berberine, and alkaloids of that group, so far as the effects on man are concerned; and to thebaine, picrotoxin, strychnine, and brucine, so far as the effects on animals are concerned.

4. *Narceine*.—The most contradictory observations have been published on the action of this principle. By Bernard, Béhier, and Eulenburg, it is held to possess remarkable hypnotic power, and to be free from stimulating and convulsant action; by Fronmüller, Harley, Da Costa, Mitchell, and others, it is considered feeble, if not inert. The physiological actions of narceine, therefore, remain *sub judice*. Until further researches are made with chemically pure narceine, and by competent observers, it will be safer to give no opinion on the subject of its actions and uses.

The other alkaloids of opium are curiosities of chemical and physiological research, and may be dismissed in a few words.

Cryptopine is in a much greater degree than narceine an hypnotic and anodyne.

Thebaine has a strong convulsant action in animals.

Various circumstances modify the action of opium. These are chiefly *age, sex, idiosyncrasy, habitual use*, and certain states of the system, as the presence of *pain, uræmia*, etc.

The extremes of life are relatively more susceptible to the action of opium, and especially is the susceptibility to its action great in early life. Fatal opium narcosis has ensued in a nursing infant whose mother had taken a medicinal dose. A single drop of laudanum has produced lethal effects in a child under six months of age. Women are more easily affected by opium than men, and they are more apt to be thrown into a condition of hysterical excitement than put to sleep. Nausea, vomiting, headache, and depression, much more frequently occur in women than in men. As a rule, therefore—but to this rule there are, of course, numerous exceptions—women are less favorable subjects for the administration of opium than men.

More than age or sex is the action of opium influenced by idiosyncrasy. There are persons so easily affected by it that the minutest quantity will cause uncontrollable vomiting, faintness, vertigo, and alarming prostration. It is never safe to administer morphine hypodermatically to such subjects, unless in an extremely small dose.

The habitual use of opium diminishes in a remarkable degree the susceptibility to its action. Numerous instances are on record in which a pint or more of laudanum has been taken daily, or several hundred