

may therefore be occasionally placed instead of brucia in the two foregoing formulæ.

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### MORPHIA, AND ITS SALTS.

It appears from the chemical researches of MM. Seguin, Sertuerner, Robiquet, Robinet, Pelletier, and Couerbe, that opium is composed of, 1, a fixed oil; 2, caoutchouc; 3, gum; 4, fecula; 5, resin; 6, ligneous matter; 7, morphia; 8, narcotine; 9, narceine; 10, meconine; 11, codeine; 12, meconic acid; 13, another brownish acid. Among these mention will only be made of such as refer to therapeutical employment.

M. Robiquet's late researches go to show that neither codeic acid nor codeate of morphia exist in opium: that which has been taken for them being in fact an acid salt, or the hydrochlorate of morphia. This salt will even vary with the nature of the saline solution to which the opium is submitted. Thus it may be a sulphate or a nitrate of morphia, according as the sulphate of soda or nitrate of potass be used to obtain the supposed codeate.

M. Robinet has, however, ascertained the fact that morphia has the property of producing a blue colour by the action of the per-salts of iron—a property by which morphia, when used for poisoning purposes, might possibly be detected.

#### *Preparation of Morphia.*

M. Robiquet employs the following method. A concentrated solution of opium is boiled with a small quantity of magnesia—10 grammes, or a little more than 2 drachms and a half, to a pound of opium—for a quarter of an hour. A greyish deposit forms, which is filtered and washed with cold water. Being well dried, the precipitate is then treated with weak alcohol, and

allowed to macerate for some time with a heat under ebullition, by which a very little morphia and a great quantity of colouring matter are withdrawn. The mass is again filtered and washed with cold alcohol. Subsequently, it is taken up by a greater quantity of rectified alcohol, which is kept boiling; and while in that state, is filtered once more; on cooling, the liquor yields morphia, which is discolored by repeated crystallizations and animal charcoal.

Dr. Thomson (*Annals of Philosophy*, June, 1820) has given the elementary composition of, and the following mode of obtaining, morphia. He precipitates a strong infusion of opium by caustic ammonia, separates the whity-brown precipitate by filtering, evaporates the infusion to a sixth of its bulk, and again adds ammonia, by which a fresh precipitate of pure morphia is procured. This he receives on a filter and washes with cold water. When it is completely drained he dashes it with a small quantity of alcohol and passes it through a filter, the alcohol taking up a large portion of the colouring matter and some little morphia. He then dissolves the morphia in acetic acid and treats the solution with ivory-black, in order to withdraw all colour from it. This mixture is frequently shaken for twenty-four hours and is then thrown on a filter; the liquor passes into the recipient totally colourless, and being then treated with ammonia, morphia is precipitated in the form of a white powder. By solution in alcohol and spontaneous evaporation it is then procured in regular crystals, which are perfectly white and of an opaline transparency, without smell but intensely bitter, and representing four-sided rectangular prisms.

The manner most usually followed at present is that of M. Hottot: it is a modification of that of Serturner.

MM. Henry and Plisson have a method of obtaining morphia without using alcohol: it furnishes a very pure article, but the quantity procured is less than by Robiquet's method. Opium is infused in water acidulated

with hydrochloric acid and concentrated to two-thirds. When the fluid is cold a slight excess of liquid ammonia or diluted caustic soda is added. The deposit is then treated with water very slightly acidulated with hydrochloric acid until the acid ceases to be saturated. The united solutions are then carefully evaporated in a sand-bath. The crystals formed are impure and brown. They are separated from the mother-water, which is again evaporated and decomposed by ammonia and the crystals are purified by repeated crystallization. This hydrochlorate of morphia dissolved in water is then decomposed by a slight excess of ammonia, and the precipitate is pure morphia: if required to crystallize, it must be dissolved in hot alcohol, which is evaporated.

M. Blondeau says he obtains pure morphia by aiding the fermentation of the aqueous solution of opium, by which a viscid colouring matter is destroyed, and morphia in greater quantity and of purer quality than by any other process is obtained.

*Elementary composition of Morphia.*

M. Bussy and MM. Dumas and Pelletier have made various analyses of morphia, the results of which are given in the following table:—

M. Bussy.	MM. Dumas and Pelletier.
Carbon.....69.0	Carbon.....72.02
Hydrogen..... 6.5	Hydrogen..... 7.61
Azote..... 4.5	Azote..... 5.53
Oxygen.....20.0	Oxygen.....14.84

According to Brande (*Annals of Philosophy*, 1824) the chemical constitution of morphia is,

Carbon .....	72.0
Azote .....	5.5
Hydrogen .....	5.5
Oxygen .....	17.0

M. Liebig's analysis is,

		Atoms.
Carbon .....	72.340 =	C. 34.
Azote.....	4.995 =	A. 1.
Hydrogen .....	6.366 =	H. 36.
Oxygen .....	16.299 =	O. 6.

He also ascertained that morphia is a hydrate; anhydrous morphia is opaque and has a thick, resinous, and yellowish appearance.

The representative of the atom of morphia as deduced from its combination with hydrochloric acid is 3613, which gives the composition of the hydrate.

Water .....	112.48
Morphia .....	7226.00

#### *Action of Morphia on Man and the lower Animals.*

Pure morphia, though sparingly soluble, and therefore presenting difficulties in its detection as the narcotic principle of opium, has nevertheless been proved to be so beyond the possibility of doubt. My own clinical experience is in confirmation of the fact; for I have seen decidedly narcotic effects proceed from so small a dose as a quarter or half a grain, which effects are still more palpable when the salts of morphia are employed, probably on account of their greater solubility.

It is now more than fifteen years since I first used the acetate, the sulphate, and the muriate of morphia medicinally; and I have ascertained that all the advantages of opium may be derived from them without its unpleasant effects. (See *Nouv. Journ. de Med.* 1818.) I found the muriate less beneficial than the acetate and sulphate, and discontinued its employment: perhaps further trials of it are worthy to be made.

#### *Preparation of the Acetate of Morphia.*

This salt may be made by a direct combination of acetic acid and morphia in a capsule and slow eva-

poration to dryness in a stove at  $25^{\circ}$ ; this mode has been had recourse to on account of the extreme deliquescence and difficult crystallization of the salt.

It may be also obtained by dissolving morphia in alcohol, filtering the solution, saturating the liquor with acetic acid, and evaporating to dryness. This product is an acetate with excess of base, as may be proved by dissolving it in water, when the excess of morphia remains undissolved. This however may occur to the perfectly neutral acetate, for that salt has the property when placed in water of separating into two others, one with an excess of acid and soluble, the other with excess of base and insoluble: this, joined with the difficulty of procuring an accurately neutral acetate, renders the sulphate a preferable salt for medicinal purposes.

A crystallized acetate may however be obtained by dissolving morphia in alcohol, saturating with acetic acid, filtering and leaving the liquid to evaporate slowly in a capsule covered with gauze; the acetate then crystallizes on the sides of the capsule in ramified figures.

#### *Preparation of Sulphate of Morphia.*

Morphia is dissolved in diluted sulphuric acid. The warm solution being evaporated gives silky crystals on cooling. This salt closely resembles the sulphate of quinia, with which it might be confounded, but that its crystallization is much more compact, and that it becomes red when nitric acid is added, which is not the case with sulphate of quinia.

It may be likewise obtained by dissolving morphia in alcohol, saturating with sulphuric acid and evaporating.

M. Pelletier is of opinion that this salt is preferable to the acetate, because it may always be obtained the same, whereas the acetate is frequently mixed with narcotine, which is more soluble in alcohol than morphia is. The acetate is moreover in part decomposed by the drying process that is requisite to preserve it. Besides which, as the sulphate readily crystallizes, a

subsalt is never formed, as is the case in preparing the acetate obtained by evaporation.

Sulphate of morphia is soluble in twice its weight of distilled water; it is composed of

		Atoms.
Acid .....	10.35	= 2
Morphia .....	75.35	= 1
Combined water .....	4.66	= 2
Water of crystallization.....	9.64	= 4

*Mode of administering pure Morphia.*

Though morphia is considerably less soluble than its salts, I have often used it in pills containing a quarter or half of a grain, in chronic and painful diseases. Its effect appears to me to be more permanent than that of the salts; much however will depend on the type of the diseases treated with it.

*Employment of the Salts of Morphia.*

In the preparations of these salts I have endeavoured to imitate as nearly as possible the most commonly used preparations of opium.

*Syrup of Morphia.\**

Clarified simple syrup .....	1 livre.
Acetate of morphia .....	4 grains.

This may be used instead of the syrup of poppies and is even preferable, the degree of potency being arbitrary. The dose is a coffee spoonful (80 minims) every three hours until sleep is procured, though a single spoonful taken at bed-time is frequently sufficient for the purpose.

*Syrup of Sulphate of Morphia.*

Clarified syrup.....	1 livre.
Sulphate of morphia.....	4 grains.

\* So in the French text; the acetate is plainly meant.—Tr.

The dose is the same as of the preceding syrup.

I employ this syrup when patients are accustomed to the syrup of the acetate. In general these salts of the medicinal alkalis may be maintained in their action on the system by simply varying them, no increase in the dose being then necessary.

*Solution of Acetate of Morphia.*

Acetate of morphia ..... 16 grains.  
Distilled water. .... 1 ounce.

Three or four drops of acetic acid and a gros (65 minims) of alcohol should be added to keep the salt in solution.

This solution may be used as a substitute for laudanum, Rousseau's drops, tincture of opium, &c. The dose is from six to twenty-four drops.

*Solution of Sulphate of Morphia.*

Some patients cannot bear the acetate of morphia, in which cases the sulphate may replace it in the preceding formula, sulphuric acid being substituted for acetic. The dose will be the same.

The acetate and sulphate may be used in pills, electuaries, and mixtures, in the dose of a quarter of a grain to two or three grains in twenty-four hours. I have given as much as four grains of them, both in hospital and in private practice, without inconvenience.

The activity of this remedy has been much exaggerated: it is by no means the violent poison it has been imagined to be. A large dose, and its retention of it on the stomach, are necessary to induce poisonous effects; and as in such dose it seldom fails to cause vomiting, these effects are likely to be of rare occurrence.

*Solution of the Citrate of Morphia.*

Black drop has long been employed in Great Britain,

and is now in extensive use in America. Various means are employed in making it, all however implying the combination of an impure vegetable acid with opium. The acids most commonly used are the citric and acetic, and some aromatic and saccharine substances are added.

The physicians who employ this preparation assert that it does not irritate the stomach, causes no headache, vertigo, nausea, &c., and that it has none of the exciting properties of opium.

Dr. Porter, of Bristol, has introduced a preparation which seems to exhibit all the above advantages: he calls it *liquor of citrate of morphia*. It is thus prepared.

Take of opium four ounces, citric acid two ounces, to which add a pint of water, and macerate for twenty-four hours; then filter.

Dr. Porter calls this a citrate of morphia: but it evidently contains morphia, narcotine, and all the other crystallizable products latterly found in opium. In preparing it, pure morphia or the extract of opium deprived of narcotine, should be used, by which a compound more nearly approaching to a pure citrate would be procured. It would then be less exciting and more exclusively narcotic than Porter's preparation.

*The applications of the Citrate of Morphia* have been treated of by the American physicians. They say that its effects are quicker than, but not so permanent as those of opium in substance or tincture; and that it is more active than opium, one part being equivalent to about three parts of the latter when a small dose suffices, but where large doses are required only a double power is to be expected.

Lime water, the liquor ammoniæ, and other alkaline fluids, decompose this solution of the citrate of morphia, and should therefore never be prescribed with it.

The tartrate of morphia has the same properties as the citrate. The latter generally shows its narcotic effects in ten minutes. Some practitioners are of opi-



nion that the citrate is less effectual in dysenteric purging than the other preparations of opium.

I frequently substitute the following formula for that of Porter:

*Solution of Citrate of Morphia.*

Pure morphia.....16 grains.  
Citric acid ..... 8 grains.

Dissolve in one ounce of distilled water, and colour it with two gros of the tincture of cochineal. The dose is from 6 to 30 drops during the day.

The salts of morphia may be used in the endermic mode, in the same manner as was stated of strychnia. Larger doses of it may be administered in this way. The neuralgiæ are the principal diseases in which it has been so used.

The relative quantities of morphia in Turkey and English opium have been examined by M. Hennel, who found that 700 grains of Turkey opium contained 48 grains, and the English opium 35 grains.

[According to Dr. Copland, the best salts of morphia for medicinal use are the muriate and the acetate. It is perhaps difficult to assign a reason for the fact, but he says that, in a case of extreme watchfulness, he found the acetate to fail, and the muriate to succeed in procuring sleep, though the dose of each was the same. He makes a practical remark which deserves attention: in two cases of nervous affections, in which he was induced to prescribe morphia in small doses, an alarming degree of sinking and faintness succeeded. The possibility of this occurrence has been verified in my own person only a few weeks ago. Having been rendered sleepless by drinking green tea, I was induced to take black drop, in which citrate of morphia predominates; the consequences were most alarming to myself and those around me, and it required large and frequently repeated doses of brandy to prevent

the utter annihilation of the pulse, and the sinking of the powers of life. Hence it might be judicious to combine morphia and its salts with some aromatic or stimulant spirit, particularly where general debility is present. Dr. C. tells me of two cases, in which opium in every shape, even in black drop and Batley's solution, produced the distressing sensations of sinking and impending dissolution; but in which morphia, with the addition of an aromatic spirit, (*spiritus caryophyllæ* or *myristicæ*,) was tolerated without any unpleasant sensations.

Dr. Charles Lee (*New York Medical and Physical Journal*, 1829) strongly recommends a tepid wash, composed of two grains of sulphate of morphia to one ounce of water, in acute conjunctivitis. It renders the intolerance of light much less urgent, and gives ease from the hot and throbbing sensations in and about the diseased organ.

Bellingeri, in a *Memoir on Neuralgia*, which may be found in the *Annali Universali di Medicina*, for April, 1833, states that acetate of morphia is of little use taken internally, but is more efficient when used in friction, with oil, on the neuralgic part, or sprinkled on the denuded dermoid surface.

He also quotes a case of violent and obstinate hiccup, wherein acetate of morphia was used by the endermic method over the epigastrium. A curious effect ensued; it produced a sensation of compression of the back part of the head: the patient could neither move nor speak; both epididymes swelled. In the course of an hour these symptoms disappeared, and were replaced by a general and intolerable itching, particularly of the forehead, nose, chin, and scrotum; at length, after two hours, the itching ceased, and the hiccup was found to be cured.

Black drop is a most uncertain preparation: I daily hear the most discordant opinions given as to its power, as compared with tincture of opium, some esteeming it as only equivalent to the latter, others as of double, treble, or quadruple strength. It might be well if

each surgeon-apothecary at least prepared a solution of acetate of morphia of determinate strength, and regulated his doses by it, rather than by the liquor opii sedativus, of which he can have no knowledge, until perhaps it has done mischief.—*Tr.*]

*Extract of Opium deprived of Morphia.*

A certain quantity of morphia always remains with the opium after the process for the extraction of that alkaline base. Taking M. Robiquet's hint on the subject, I made some experiments with the residue in question, and found that it still has a narcotic power, though much inferior to the common aqueous extract. Four grains are scarcely equivalent to a grain of the latter, and to a quarter of a grain of morphia.

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NARCOTINE.

Though I have no reason to consider this substance in the light of a medicine, yet it may not be out of place shortly to give its physiological history.

*Action of Narcotine on the Animal System.*

One grain dissolved in oil induces in dogs a state of stupor, which might be mistaken for sleep, though from that it materially differs; for the eyes are open, the respiration by no means so deep as in sleep, and it is impossible to rouse the animal from his dull and stupid condition. Death generally supervenes within twenty-four hours.

Combined with an active acid, the effects are altogether different: animals bear as much as 24 grains without perishing; and while under its influence they are agitated by convulsive movements resembling those caused by camphor, together with the similar signs of fear, backward movements, the same incapability of pro-